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HOUSE OF COMMONS

Special Committee on
FOOD AND DRUGS

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HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

PROCEEDINGS

No. 1

THURSDAY, APRIL 23, 1964
TUESDAY, MAY 12, 1964

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

20796—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Gauthier	Orlikow
Asselin (*Richmond-Wolfe*)	Horner (*Jasper-Edson*)	Prud'homme
Basford	Howe (*Hamilton South*)	Roxburgh
Casselman (Mrs.)	Jorgenson	Rynard
Côté (*Longueuil*)	Macaluso	Slogan
Enns	Mackasey	Whelan
Francis	Marcoux	Willoughby—24
	Nesbitt	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

ORDERS OF REFERENCE

MONDAY, March 9, 1964.

Resolved,—That a Special Committee be appointed to continue the enquiry into and to report upon (*a*) the hazards of food contamination from insecticides, pesticides, and other noxious substances; and (*b*) the safety and cost of drugs, begun by a Special Committee at the past Session;

That the Committee consist of 24 Members to be designated later by the House;

That the Committee be empowered to send for persons, papers, records, and to report from time to time, and to print such papers and evidence from day to day as may be deemed advisable;

That the minutes of proceedings and evidence of the Special Committee at the past Session be referred to the said Committee and be made a part of the records thereof;

That the provisions of Standing Orders 66 and 67(1) be suspended in relation thereto.

Attest.

FRIDAY, April 17, 1964.

Ordered,—That the Special Committee on Food and Drugs appointed March 9, 1964, be composed of Messrs. Armstrong, Asselin (*Richmond-Wolfe*), Basford, Casselman (Mrs.), Côté (*Longueuil*), Enns, Francis, Gauthier, Harley, Horner (*Jasper-Edson*), Howe (*Hamilton South*), Jorgenson, Macaluso, Mackasey, Marcoux, Mitchell, Nesbitt, Orlikow, Prud'homme, Roxburgh, Rynard, Slogan, Whelan, and Willoughby.

Attest.

FRIDAY, April 24, 1964.

Ordered,—That the quorum of the Special Committee on Food and Drugs be reduced from 13 to 8 Members; and that the said Committee be empowered to sit while the House is sitting.

Attest.

TUESDAY, May 19, 1964.

Ordered,—That the Special Committee on Food and Drugs be empowered to meet in Montreal on Thursday and Friday, May 28th and 29th, 1964.

Attest.

LEON J. RAYMOND,
The Clerk of the House.

20796—1½

REPORTS TO THE HOUSE

The Special Committee on Food and Drugs has the honour to present its

First Report

Your Committee recommends:

1. That its quorum be reduced from 13 to 8 members;
2. That it be empowered to sit while the House is sitting.

Respectfully submitted,

HARRY C. HARLEY,
Chairman.

(This Report was concurred in Friday, April 24, 1964)

The Special Committee on Food and Drugs has the honour to present its

Second Report

Your Committee recommends that it be empowered to meet in Montreal on Thursday and Friday, May 28th and 29th, 1964.

Respectfully submitted,

HARRY C. HARLEY,
Chairman.

Note: This report was concurred in Tuesday, May 19, 1964.

MINUTES OF PROCEEDINGS

THURSDAY, April 23, 1964
(1)

The Special Committee on Food and Drugs met at 11.00 o'clock a.m. for organization purposes.

Members present: Messrs. Asselin (*Richmond-Wolfe*), Basford, Enns, Francis, Harley, Howe (*Hamilton South*), Macaluso, Mackasey, Marcoux, Mitchell, Prud'homme, Roxburgh, Rynard, Slogan, Whelan (15).

The Clerk of the Committee attending and having called for nominations, Mr. Asselin moved, seconded by Mr. Howe, that Mr. Harry C. Harley be elected Chairman of the Committee.

There being no other nominations, Mr. Francis moved that nominations close.

Mr. Harley was declared duly elected Chairman and took the Chair. He thanked the members of the Committee for his election.

On motion of Mr. Mackasey, seconded by Mr. Rynard, Mr. Mitchell was unanimously elected Vice-Chairman.

The Chairman read the Order of Reference.

On motion of Mr. Francis, seconded by Mr. Enns,

Resolved (unanimously)— That a subcommittee on Agenda and Procedure comprising the Chairman, the Vice-Chairman, and one representative of each of the groups of the House be appointed.

Mr. Enns moved, seconded by Mr. Roxburgh, that the quorum of the Committee, set at 13 pursuant to Standing Order 67(2), be reduced to 8 members.

Whereupon Mr. Mitchell, seconded by Mr. Macaluso, moved in amendment thereto "That the quorum be reduced to 10". The amendment was negatived on the following division: YEAS, 6; NAYS, 7.

The motion of Mr. Enns having been put was resolved in the affirmative on the following division: YEAS, 9; NAYS, 2.

It was therefore *resolved* to recommend to the House that the quorum of the Committee be reduced from 13 to 8.

On motion of Mr. Asselin, seconded by Mr. Howe,

Resolved (unanimously),—That pursuant to its order of reference, 750 copies in English and 500 copies in French of the Committee's Minutes of Proceedings and Evidence be printed.

On motion of Mr. Macaluso, seconded by Mr. Francis,

Resolved (unanimously),—That the Committee seek permission to sit while the House is sitting.

The Committee agreed that the order of business be left to the subcommittee on Agenda and Procedure and submitted to the Committee for its approval.

At 11.20 a.m. on motion of Mr. Basford, the Committee adjourned to the call of the Chair.

Gabrielle Savard,
Clerk of the Committee.

TUESDAY, May 12, 1964
(2)

The Special Committee on Food and Drugs met at 9.40 a.m. today. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Asselin (*Richmond-Wolfe*), Basford, Francis, Harley, Jorgenson, Macaluso, Mackasey, Marcoux, Orlikow, Roxburgh, Rynard, Whelan (12).

The Chairman announced the names of the Members who will act with him on the steering subcommittee on agenda and procedure, namely, Messrs. Mitchell, Francis, Rynard, Marcoux, Howe (*Hamilton South*), and Gauthier; he presented the First Report of the said subcommittee as follows:

"The Subcommittee recommends:

1. That the Committee hold its meetings on Tuesdays and Fridays at 9.30 a.m.;
2. That the Committee first consider the safety of drugs;
3. That the Committee invite the Honourable Minister of National Health and Welfare and the Director of Food and Drug Directorate and his officials before calling other witnesses;
4. That in view of the absence of Dr. Morrell until the 11th of May, the Committee do not hold meetings before his return;
5. That the Committee seek permission of the House to sit in Montreal on May 28th and 29th, that the Clerk of the Committee accompany the Committee, and that the payment of any reasonable travelling and living expenses incurred therefor be authorized."

After discussion, on motion of Mr. Macaluso, seconded by Mr. Marcoux,

Resolved,—That the First Report of the Subcommittee on Agenda and Procedure presented this day be adopted.

The Chairman submitted a schedule of meetings and a list of proposed witnesses. After discussion, it was agreed to invite associations or persons wishing to present briefs to send a sufficient number of copies for the use of the members one week in advance of the formal presentation of their submission.

At 10.30 a.m., on motion of Mr. Macaluso, the Committee adjourned to 9.30 a.m. Thursday, May 21st, to hear the Director of the Food and Drug Directorate.

Gabrielle Savard,
Clerk of the Committee.

DELIBERATIONS

TUESDAY, May 12, 1964.

The CHAIRMAN: Gentlemen, there now is a quorum. If I may call the meeting to order, I first would like to announce the names of the members of the steering committee: Messrs. Mitchell, Francis, Dr. Rynard, Dr. Marcoux, Dr. Howe, Mr. Gauthier and the Chairman.

The steering committee met on Thursday, April 30, 1964.

Members present: Messrs. Harley, Mitchell, Rynard, Howe and Francis.

I would like to read its first report:

The steering committee agreed to recommend that the order of business be as follows:

1. That the committee hold its meetings on Tuesdays and Fridays at 9:30 a.m.
2. That the committee first consider the safety of drugs;
3. That the committee invite the Hon. Minister of National Health and Welfare and the director of the food and drug directorate and his officials before calling other witnesses;
4. That in view of the absence of Dr. Morrell until the 11th day of May, the committee do not hold meetings before his return;
5. That the committee seek permission of the house to sit in Montreal on May 28 and May 29, that the Clerk of the committee accompany the committee, and that the payment of any reasonable travelling and living expenses incurred therefor be authorized.

Would the committee like to take up these items one by one? The first is:

That the committee hold its meetings on Tuesdays and Fridays at 9.30 a.m.

Mr. MACALUSO: I so move.

The CHAIRMAN: Perhaps we might go over the whole report and adopt it as a whole.

The second item is:

That the committee first consider the safety of drugs.

The feeling here was that the whole thing be developed along with the medical services which have not yet reported. I think Dr. Rynard asked a question in the house the other day and the answer was that the committee would not be reporting at the earliest before the end of May.

Mr. MACALUSO: They also are going into the question of safety.

The CHAIRMAN: This is one of the matters and perhaps the most controversial.

Mr. MACALUSO: Is it not the intention of this committee to deal with the question of the cost of drugs; that is, that we will deal with it anyway, either by dealing with the royal commission report or the calling of our witnesses.

The CHAIRMAN: Oh yes, eventually we will get into that subject.

Mr. MACALUSO: Why not include both subjects now; we could deal with the cost after we have dealt with the safety of drugs, and by that time the report should be available.

The CHAIRMAN: You mean to try and cover both references at the same time?

Mr. MACALUSO: No, no. I, for one, do not know how you are going to divide these subjects when we have witnesses appear before this committee.

Is it the intention of the steering committee that we deal with the safety of drugs first and then when the report comes in, if there was a suggestion to deal with costs, the same witnesses would have to be brought back again?

The CHAIRMAN: That is possible. However, I am assuming the subject of the safety of drugs will take some time and probably we would not get into the matter of the cost of drugs until the fall. But, if the committee wishes, there is no reason, when these witnesses are here, why they cannot be examined on both subjects at the same time, if they are prepared to answer questions on both topics.

Mr. ORLIKOW: Mr. Chairman, why do we not commence as you suggest. It will only be a couple of weeks until we get the report of the commission, at which time we can peruse it. I think we have to bear in mind how little has been done up until now despite the fact the restrictive trade practices commission has looked into this subject, and we are going to have to spend some time on that. I believe we should leave the question when we shall commence it until we see what is in that report.

Mr. JORGENSON: Mr. Chairman, it is going to be difficult, as has been suggested, to divide the two subjects as the witnesses called for one will be the same witnesses called for the other. It might be that after we receive the report we may want to accentuate the cost factor.

The CHAIRMAN: May we follow Mr. Orlikow's suggestion, that we proceed with the witnesses which I will suggest and, if anyone wishes to ask these witnesses questions in respect of costs at that time they will be free to do so.

Mr. BASFORD: Mr. Chairman, I think the steering committee should consider how quickly we are going into the question on the cost of drugs. I do not want to see this subject put over until sometime in the fall. I must say this is one of my interests in the committee, and I think the bulk of the members would agree with me in this respect. I certainly would disapprove of the steering committee putting examination in respect of the cost of drugs over until next fall.

The CHAIRMAN: I made that statement because there is only a certain limited number of meetings to be held before the summer recess, if we have one. If we did start now it would be fall before we completed the discussion.

Mr. BASFORD: But, if we started in the fall it would be possible that we may not complete it at all.

The CHAIRMAN: Perhaps we would the day before Christmas.

Mr. MACALUSO: Mr. Chairman, why not deal then with the safety feature first. I do not know how we can divide the two topics unless we call witnesses who do research work in respect of the safety of drugs and then the cost accountant witnesses so far as the cost is concerned. That would seem logical to me. Why not leave our topic of discussion safety and cost; we then could deal with the safety feature first and then the cost after the report comes out, as Mr. Orlikow suggested.

Mr. RYNARD: Mr. Chairman, I think that is a reasonable suggestion. In my opinion the prime consideration must be the safety and then the cost comes later. Anyone who has had any experience in prescribing drugs, as you yourself have had, always does his best to make sure he is prescribing a safe drug. We could deal with the cost later.

Mr. MACALUSO: I would agree that the safety feature is the most important one at the present time.

The CHAIRMAN: If that is satisfactory to the committee we will continue.

The third recommendation is that the committee invite the Minister of National Health and Welfare and the director of the food and drug directorate and his officials before calling other witnesses.

I am sure most members are aware that the minister has just been discharged as a patient from hospital. You will remember that at the beginning of our committee meetings last year the Minister of National Health and Welfare gave a full statement covering all of the terms of reference. It is my feeling there will be very little purpose in inviting her to attend at this time. However, if it is the wish of this committee to call her in respect of specific aspects, then the committee may do so at a later date. She will be available at any time. She has not returned to her work as yet. Is this satisfactory to the committee?

Some hon. MEMBERS: Agreed.

The CHAIRMAN: Dealing with the fourth item on this report, that in the absence of Dr. Morrell the committee do not hold meetings until his return, today is May 12 and I think Dr. Morrell has returned. In view of that fact, and in view of the fact that on Friday a great many members of this committee will have to be elsewhere it is my feeling that we should start our meetings one week from today at which time we shall hear the head of the drug directorate, Dr. Morrell.

Some hon. MEMBERS: Agreed.

The CHAIRMAN: The fifth point is that the committee seek permission from the House of Commons to sit in Montreal on May 28 and 29.

An hon. MEMBER: What is the purpose of this, Mr. Chairman?

The CHAIRMAN: The purpose of this recommendation is seek permission to visit some drug companies in Montreal. Your steering committee felt that other than the doctors and druggists who are members of this committee a great many of the members are not aware of the methods drug companies use in manufacturing drugs, and the precautions and safety measures which are employed. We felt that a visit to two drug firms and a research laboratory would be very worth while to members of this committee. We have actually lined up, for the consideration of this committee, a trip to Montreal during which we will visit these two drug companies and a clinical laboratory. There are very few companies which manufacture drugs in Ottawa. The two drug manufacturing centres are Toronto and Montreal, and in view of the fact that Toronto is much further away than Montreal we felt that it would be to our interests to visit these companies in Montreal. I might point out that we have received invitations from these companies in Montreal. We have chosen a Thursday and Friday for our visit. We will visit the Ayerst, McKenna & Harrison firm in Montreal. Dr. Rynard, is that firm a British controlled firm. or a United States company

Mr. JORGENSON: I believe it is a United States company, Mr. Chairman.

Mr. RYNARD: All the drug companies which operate in Canada are controlled by the United States, with the exception of the Frosst Company.

The CHAIRMAN: Ayerst, McKenna & Harrison Company is a United States controlled firm. We also intend to visit the Frosst company which is a completely Canadian company. We would then visit the Hotel Dieu Hospital clinical investigation unit under the direction of Dr. Jacques Genest who will give us some idea of how these drugs are applied in clinical investigations. Our trip is scheduled to last two days, which I suggest is a short period of time, considering what we intend to cover. We are scheduled to leave early on the morning of Thursday and depart from Montreal at eight o'clock daylight saving time Friday evening. Any members who wish to stay in Montreal will, of course be able to do so, and that is their own concern.

Mr. ROXBURGH: Why would a member wish to stay in Montreal?

The CHAIRMAN: I have never seen it myself.

Mr. RYNARD: You are not too old to dream.

Mr. ROXBURGH: One is never too old to dream, but that is a poor place to dream.

Mr. MACALUSO: Mr. Chairman, I think the recommendations of the steering committee are excellent. I certainly feel, as perhaps do many lay members of this committee, that such a trip would be of great interest. Can we expect to attend briefing sessions during this trip?

The CHAIRMAN: It is very obvious from our schedule that this will be a very packed and concentrated visit. Once the members of this committee arrive in Montreal they will be more or less in the hands of the officials of these firms who intend to present their manufacturing procedures to us as quickly as possible.

Mr. MACALUSO: I take it during our tour through the facilities we will be briefed? I am very interested in this aspect of drug production.

The CHAIRMAN: At the Ayerst, McKenna & Harrison company we will receive some introductory remarks and then be taken on a tour through the chemical laboratory and a pilot plant. We will then go to luncheon, following which we will receive some explanatory remarks in respect of the biology aspect by the medical director and the director of quality control. We will then be taken on a tour through the biological quality control facilities.

Speaking personally, I have been through a drug firm before and I found it a very rewarding experience. What is the feeling of the committee on this? Are the dates suitable? These dates are quite suitable to the firms concerned.

Mr. ROXBURGH: Let us not worry about the dates. If some of us cannot be there, that is it.

Mr. MACALUSO: I think it will help us in our deliberations here, Mr. Chairman.

The CHAIRMAN: As is mentioned, we will have to ask the permission of the house for this because we do not have authority to move from place to place. We can present this report on Wednesday and then make our arrangements. We will obviously go down by train, and as I said we will be completely in their hands when we get there as far as what we do is concerned. There will be more than adequate time for you to ask questions.

Mr. WHELAN: Would it be necessary to ask permission for every trip we plan, for every visit to one of these plants?

The CHAIRMAN: We would have to ask permission each time unless we ask for authority to move from place to place, but as I remember it, this was in the original terms of reference and it was deleted. If what we have said meets the approval of the committee, would someone move that the steering committee report be adopted?

Mr. MACALUSO: I move that the report be adopted.

Mr. MARCOUX: I second the motion.

The CHAIRMAN: Gentlemen, I would like to discuss the proposed agenda with you. I will mention to you whom we have invited and from whom we have received letters of acceptance. I will then throw the meeting open for any suggestions on who the members think should appear before the committee. On May 19, 22 and 26 we have invited Dr. Morrell of the food and drug directorate. We have given that department three full days. It was my feeling that during this time we should probably only have meetings from about 9:30 a.m. to 11 a.m. In this way the committee would not be rushed and would not have to get all the information at one sitting. We have therefore given Dr. Morrell's department three different days of sitting.

Mr. MACALUSO: If things go right, we will be off on Monday?

The CHAIRMAN: There has been no word from the house.

Mr. MACALUSO: I think it will be a little difficult to get a quorum here on Tuesday, May 19 at 9:30 a.m.

The CHAIRMAN: Is it definite we are not sitting on Monday.

Mr. MACALUSO: It is pretty definite, as I understand it.

The CHAIRMAN: Would it be suitable to make that Wednesday from 9:30 a.m. to 11 a.m.?

Mr. RYNARD: Why not Thursday?

Mr. MACALUSO: Thursday would be best because Wednesday is a full caucus day.

The CHAIRMAN: Thursday and Friday. Is it suitable to the committee that we meet on Thursday, May 21 and Friday, May 22, the two consecutive dates, and have Dr. Morrell and his department appear before us?

It is agreed.

The CHAIRMAN: I did not realize that we would be having a holiday.

Dr. Morrell and his department will be here on May 21, 22 and 26. On May 28 and 29 we will go to Montreal if the House of Commons so approves. On June 2, representatives of the Canadian Medical Association will be present; Dr. Kelly has accepted. At that time, Dr. Kelly will be appearing with two other doctors; he will have with him Dr. Wightman, who is a very well known professor at the University of Toronto, an expert in therapeutics and medicine. I was expecting to call him as a second witness, but this may save the committee some time.

On Friday, June 5, the Canadian Pharmaceutical Association will be here; Mr. Turnbull has accepted for that date. Mr. Turnbull is the president of the Canadian Pharmaceutical Association.

For Friday, June 19, the Canadian Pharmaceutical Manufacturers' Association will be presenting a brief.

All these people have been asked to present their briefs a week ahead of time so the committee members can read them before the witnesses appear.

Mr. BASFORD: Have they been asked to present a brief only on the safety of drugs?

The CHAIRMAN: We could write a letter and ask if they would be prepared to discuss safety and cost.

Mr. BASFORD: That would help to eliminate any misunderstanding.

The CHAIRMAN: The original letter asked only for a submission on safety.

Mr. BASFORD: The steering committee wrote letters before the committee had an opportunity to discuss it.

The CHAIRMAN: I did that; I take full responsibility for it.

Mr. RYNARD: I would support that. We want to make sure of the safety before we go into cost. Cost should be of secondary importance for consideration. I support you on that point.

The CHAIRMAN: I am prepared to write letters asking them to consider cost at the same time.

Mr. ORLIKOW: There is not much point in that because when they come down there will be very lengthy and extensive questioning with regard to cost. I think, therefore, it would be better to space them—about one every two weeks.

Mr. MACALUSO: You could write to them advising them to prepare a separate brief on cost.

The CHAIRMAN: I will write to them and ask them if they would be prepared to discuss cost at a later date.

Mr. MACKASEY: I would imagine experts on cost and experts on safety are not necessarily the same people.

The CHAIRMAN: The people to whom I have been writing are not necessarily individuals, but organizations.

Mr. ROXBURGH: There is only one way in which a witness can consider cost and safety at one and the same time; that is by stipulating that, for example, safety be considered on Thursday and cost on Friday. It will be impossible to discuss safety and cost in one meeting.

Mr. MACALUSO: I agree that safety should be considered thoroughly, but I think prospective witnesses should be notified that we will be considering the cost of drugs and they will probably be called at a later date for that purpose. I suggest they be asked to prepare a separate brief on costs or an attachment to their safety brief.

The CHAIRMAN: I will do that.

Mr. MACALUSO: Then, when they come forward, we will have a chance to look at them.

The CHAIRMAN: During the last session, the committee always tried to obtain briefs a week ahead of time from associations or persons wishing to appear in order that the committee could read them before the meeting, and save time by so doing.

Mr. BASFORD: Does the list of names you have given to us comprise all the people or associations who have been invited?

The CHAIRMAN: Yes.

Mr. BASFORD: I suggest a letter be written to the Canadian Labour Congress asking them if they would like to present a brief on the safety of drugs. This is an organization which is representative of a great many people; they concern themselves with issues of this nature. They might well have some valuable information.

The CHAIRMAN: A few other people have been invited but they have not as yet answered our letters. We are ready to accept suggestions from members. Would someone like to move that associations or persons wishing to present briefs be required to send a sufficient number of copies for the use of members, the reporters and the press one week in advance of the formal presentation of their submission?

Mr. BASFORD: I would like it suggested to people who wish to appear that it would be a wise thing to do, but I would not like it to be made a requirement that they have facilities for preparing 50 copies.

Mr. MACKASEY: I imagine they can get 50 copies; they need only to have them mimeographed. If we do not make it obligatory, as we know from past experience, we will not receive any copies.

The CHAIRMAN: I think Mr. Basford was thinking of individuals who might want to appear before the committee and who would not have any facilities.

Mr. MACALUSO: That is a different case. There is no problem with associations.

The CHAIRMAN: Will you leave it to my discretion? I will ask these people to send briefs.

Mr. MACALUSO: Has there been any invitation to druggist associations or pharmaceutical associations

The CHAIRMAN: Yes. The Canadian Pharmaceutical Association will be here on June 5; the Canadian Pharmaceutical Manufacturers Association will

be here on Friday, June 13. We have invited, but as yet have had no response, from the College of General Practice of Canada and the Canadian Association of Consumers, Mrs. Plumptre.

We would like to have as witnesses some experts in clinical medicine. Dr. Wightman, who is coming here with the Canadian Medical Association, is an expert in this field. I think we should try to call as witnesses members of the special committee on drugs which looked into parnate, for example, and the World Health Organization.

Mr. RYNARD: I think that would be very useful.

May I interject something here which may not be in order at the moment? As I remember, at the last meeting of this committee we decided to set up a standing committee of people with whom we could get in touch immediately in Ottawa who could give us information on the safety of drugs. As far as I know, that committee was not set up. Dr. Brien was head of that. I wonder if we should call Dr. Brien back and re-emphasize that we do need a standing committee We should not just copy what another nation does holus bolus: the United States cuts them off; England does not. We just follow the United States. I think we are big enough—and surely smart enough—to have our own policy. I wonder why this standing committee was not carried through.

The CHAIRMAN: You are referring to Dr. Brien from London?

Mr. RYNARD: From Western.

The CHAIRMAN: May we wait until Dr. Morrell comes and then ask him what is the status of this committee?

Mr. RYNARD: I would be glad to wait. We did something last year, as I understand it, and then we never carried it through. We did not achieve the very thing we were trying to accomplish. This is all I know. This is what I want taken up: Why did we not do it? Why did we not have that committee? Why do we follow the United States and not have our own people in Canada making some decision?

Mr. ORLIKOW: I have no objection to the list of organizations you have suggested we should call. I am sure they all have a contribution to make. However, it does seem to me that so far we are very heavily weighted with organizations which are directly involved in the business. We can hardly expect the drug companies to tell us that they have not been doing everything they should. I am not saying they have not been doing so, but they have a stake in the status quo and, as I say, we cannot expect them to tell us the whole story. We can hardly expect our own department to tell us they have not been doing everything they should have done. It does seem to me that we ought to be calling people, for example, who are doing research in the universities.

The year before last I gave the chairman of that time a list of a half dozen people who should be called, and I think I could dig it out of my files. I can think of Dr. Nickerson at the University of Manitoba, who was called to Washington to testify several times by the United States committee. At the University of British Columbia there is Dr. Fowkes, the pharmacologist, and there is Dr. Selye, who spoke last week to the health committee. Dr. Lehman at Verdun, who is world famous in this field, should also be called. There are at least half a dozen people of that type who could give very pertinent information to this committee. I think their testimony is at least as important as that of anyone else because they are doing the actual work of testing drugs and they are not involved with what has been done. They can tell us if what we have done up to this stage has been sufficient or not.

Mr. RYNARD: I think Dr. Harley has Dr. Wightman on his list, and he knows the whole score on the very point you are bringing up, Mr. Orlikow.

Mr. ORLIKOW: I do not think anyone knows the whole story.

Mr. RYNARD: I certainly think he does. He knows it from the university standpoint.

The CHAIRMAN: I do not want to give the impression that this list is final; it is merely a beginning. We approached these people because they were available and we knew of them. We will probably end up with more individuals than associations, and we will be pleased to listen to suggestions. If you can find your list, Mr. Orlikow, we will be pleased to consider it. Mr. Basford has suggested that we ask the Canadian Labour Congress, and we will do that.

Mr. ROXBURGH: I suggest, Mr. Chairman, that you would not want to have all the drug organizations following immediately upon each other and then all the individuals at the end. I suggest it be set up with individuals and organizations interspersed. In my opinion that would give us an opportunity to study the whole matter efficiently.

The CHAIRMAN: You will have noticed that we will be visiting some of the drug companies as well as calling the pharmaceutical manufacturers' associations. Probably the committee would like to hear some of the evidence from some of the individual drug companies. I think we should extend our invitation to the Canadian Pharmaceutical Manufacturers' Association, and perhaps ask one wholly owned Canadian company such as Horner.

Mr. ROXBURGH: We have a few, have we?

The CHAIRMAN: Oh, yes, a few—two!

Mr. MACALUSO: What about the drug association?

The CHAIRMAN: They will be coming in June. Then I think we should ask a company with headquarters in Europe and another with headquarters in the United States. In that way we will obtain different opinions and learn how it is done elsewhere.

There is one other gentleman we might like to call—and this goes back to some extent to insecticides and pesticides. Dr. Robert Imrie of the Sick Children's Hospital is the gentleman who looks after the poison control centre at that hospital. He would give us a different approach to the safety of drugs—safety as far as children are concerned—and at the same time he would be able to discuss the poisoning aspect of drugs.

Mr. MACALUSO: There is either a Senate or a congressional report of the United States from their committee which discussed the safety and cost of drugs very thoroughly. I think they studied it for a year to two years. Would you write to the United States state department and ask if some of these reports are available?

The CHAIRMAN: You mean the Kefauver committee?

Mr. MACALUSO: There was another one after the Kefauver report.

Mr. RYNARD: It is very voluminous.

The CHAIRMAN: If you can give me the exact name of the report I will make inquiries and try to obtain several copies.

Mr. MACALUSO: I think it would be most helpful.

The CHAIRMAN: If anyone would care to give me a list of names of people they think we should call, I would be most pleased to write to them and invite them to appear before the committee.

Mr. BASFORD: Will the steering committee consider lining up the discussion of the cost of drugs?

The CHAIRMAN: As I have mentioned, I will write to the people to whom I have already written and I will tell them that in the near future we will be discussing cost and that we would like them to appear at that time also.

In connection with lining up the discussions on cost, I think it was Mr. Orlikow's suggestion that we should wait until the royal commission on health

services report is handed down and then see what they have obtained. That will give us some basis upon which to decide how much further we should go.

Mr. BASFORD: Yes, but I do not want to see the consideration of the cost of drugs side-tracked until heaven knows when. I think the steering committee should give some thought now to lining up those hearings and deciding who would be suitable witnesses. I would like to see them give some thought to having representatives of the Department of Finance here so that we can consider the ramifications of the 11 per cent sales tax on the cost of drugs, and also a matter which is of importance to me coming from British Columbia, namely, the recent action of the province of British Columbia in passing orders in council pursuant to the pharmacy act, which is now a subject before the combines investigation branch, prohibiting any effective competition in the price of drugs in British Columbia. A great many people in British Columbia, particularly those in low income groups, have been deprived of the possibility of finding cheap drugs by the action of the Pharmaceutical Association of British Columbia in prohibiting its members advertising the price of drugs. This has seriously affected people in British Columbia. I would like to see the steering committee give some thought to this.

I am sure some people will raise the objection that this is not a fit subject for the committee, and for this reason I want to give warning that I think it is a fit subject for the committee to discuss.

I also request the steering committee to call the attorney general of British Columbia before the committee, as well as those people who have made the complaint before the director of the combines investigation act, and the Pharmaceutical Association of British Columbia whose action, as I say, has materially deprived people in low income groups from buying drugs.

Mr. RYNARD: Would this be a provincial matter?

Mr. BASFORD: It is because I know some people will say it is a provincial matter that I raise it now and give some warning that I intend to pursue it. It is now before the combines investigation director and it comes under that act; therefore it could properly be investigated by this committee. Even if it were a provincial matter, our terms of reference are to consider the cost of drugs and therefore we are entitled, when we come to the subject, to examine all aspects of the ingredients of cost.

It can be said that we have not the legislative power to do anything about some of those ingredients, but I think the committee is entitled to examine those ingredients of cost and thereby shine the light of publicity upon them.

The CHAIRMAN: The steering committee will consider what you have said.

Mr. MACALUSO: From listening to Mr. Basford it has just occurred to me that we should ask the Ontario department of health and welfare to give evidence before this committee. Their officials can tell us what actions they take with regard to research and investigation as far as the safety of drugs is concerned. They do a great deal of work in this field and their brief would be most interesting and informative. That department is doing a great deal of work not only in regard to the safety of drugs but also in regard to the cost factor, although they are most involved in safety.

Mr. ROXBURGH: There is to be a report. When will that be handed down?

The CHAIRMAN: Do you mean the report of the health services?

Mr. ROXBURGH: Yes.

The CHAIRMAN: Not before the end of May.

Mr. RYNARD: I believe it will be approximately the middle of June; it was delayed a little.

Mr. ORLIKOW: I would be very surprised if they undertook the kind of detailed investigation which is going to be required. Anyone who is interested

only needs to look at the work done by the United States committee to see how much is involved. If we are going to do a good job I think it is necessary to go to the government and ask for assistance in the form of accounting services and so on, because drug companies will not be overly enthusiastic about letting this committee, or anybody else, know what is the complete situation.

Mention has been made of the provincial departments. On the question of cost, I think we should consult with some of them because they have been able to buy drugs in quantity for a fraction of the price that is paid by most people.

Mr. RYNARD: I think they are able to buy them without sales tax.

Mr. ORLIKOW: It is not just an exemption of sales tax that is concerned. In Manitoba—and I am sure Manitoba is no different from any other province—the government has been able to go to the big companies and buy the drugs more cheaply by telling them that if the price is not reduced they will buy from small companies using the generic names. They have been able to buy these drugs for a few cents as compared to dollars, and they have saved hundreds of thousands of dollars in this way. We could learn from their experience.

Mr. MACALUSO: This committee could be one of the most important special committees that has been set up in this house. The matter we are to study is a field in which everyone is interested. The public, of course, will be most interested in the work we do.

The royal commission report will be informative for us as a committee, but I do believe that this committee can perform a greater function than could the royal commission in certain fields. Although the royal commission is enabled to call any witnesses it wishes, I think perhaps the power of the house will enable this committee to obtain more information than the commission was able to obtain. Of course, I do not know what is contained in the report of the commission, and therefore I cannot say this with any degree of certainty, but I do think that, as far as the public is concerned, we form one of the most important committees in this field of drugs, and our discussions will be extensively publicized. It is therefore imperative that the steering committee and the general committee carefully discuss the course we should follow and then make as thorough and complete an investigation as possible.

Mr. FRANCIS: There has been a tremendous amount of work carried out on the cost of drugs by different departments. The research and statistics branch of the department of health and welfare has done a great deal of work. The restrictive trade practices commission has done a great deal of work, but I do not know whether they have published reports. Then the Department of Agriculture has studied the cost of drugs at length. For example, they have studied the use of drugs for veterinary purposes, and I remember their striking conclusion that it was much cheaper to buy penicillin for use with animals than for use with humans.

At the time we lay down our procedure with regard to costs we should lay down our whole agenda carefully. Our agenda concerning costs should encompass different witnessese and a different type of investigation from our agenda on safety. At that time, I think the committee should review its procedure and the witnesses it wishes to call.

Mr. MACKASEY: The way in which the conversation has veered in this particular meeting is indicative of the problems we will encounter if we try to discuss cost and safety at one and the same meeting. To be against the high cost of drugs is like being against sin. We are all against the high cost of drugs.

Mr. BASFORD: What about sin?

Mr. MACKASEY: I am afraid that because of the impact of the high cost of drugs we will find ourselves losing track of the necessity of ensuring the safety

of drugs. What has happened in this 20 minutes has been an indication that it is impossible to consider both at the same time.

If this committee considers that our main function is to worry about the safety of drugs, then it is to that end that we should gear our efforts. If we have a witness who is prepared to talk first about safety and then about the cost of drugs, quite obviously his time and our time will be taken up with cost because we are all so familiar with that aspect.

I had an open mind when I came into this meeting, but after listening I am convinced that we should consider safety as much as possible.

The CHAIRMAN: I think that is the general feeling of the committee.

Mr. MACALUSO: Yes.

The CHAIRMAN: Dr. Rynard made the point earlier that when one is dealing with cost one is dealing with someone's pocketbook and when one is dealing with safety one is dealing with lives; and this is a point that we must remember.

Mr. ROXBURGH: Yes. I do not see how they could be brought together. The only way in which one could do it would be for a witness to deal with one aspect on one day and the other aspect on another day; we certainly cannot work them together.

Mr. MACALUSO: I move that we adjourn, Mr. Chairman.

The CHAIRMAN: The meeting will adjourn until Thursday, May 21.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 2

THURSDAY, MAY 21, 1964

FRIDAY, MAY 22, 1964

WITNESSES:

Dr. C. A. Morrell, Director; Dr. L. I. Pugsley, Associate Director, Medical Section; Dr. Frank Lu, Head of the Pharmacology and Toxicology Division; and Mr. M. G. Allmark, Assistant Director of Drugs, all of the Food and Drug Directorate, Department of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

20798—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Casselman (Mrs.)
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jorgenson
Macaluso
Mackasey
Marcoux
Nesbitt
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

THURSDAY, May 21, 1964
(3)

The Special Committee on Food and Drugs met at 9:40 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Enns, Harley, Howe (*Hamilton South*), Jorgenson, Macaluso, Mackasey, Marcoux, Orilkow, Prud'homme, Roxburgh, Slogan, Whelan, Willoughby—(13).

In attendance: From the Food and Drug Directorate, Department of National Health and Welfare: Dr. C. A. Morrell, Director; Dr. L. I. Pugsley, Associate Director; Dr. Frank Lu, Head of the Pharmacology and Toxicology Division; Dr. Richard Graham, Dr. D. C. Jessup, Mr. M. G. Allmark, and Miss E. M. Ordway.

The Chairman introduced Dr. Morrell and invited him to address the Committee.

Dr. Morrell read a statement of action taken by the Department of National Health and Welfare since the appointment of the Special Committee of the Royal College of Physicians and Surgeons to study the procedures used by the Food and Drug Directorate for dealing with new drugs.

Dr. Morrell, assisted by Dr. Lu and Dr. Pugsley, answered questions thereon.

The Chairman announced that the Director of the Food and Drug Directorate will be available for further questioning Friday, May 22, and also Tuesday, May 26.

At 11 o'clock a.m. the Committee adjourned to 9:30 a.m. Friday, May 22.

FRIDAY, May 22, 1964
(4)

The Special Committee on Food and Drugs met at 10 o'clock a.m. today. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Côté (*Longueuil*), Enns, Harley, Howe (*Hamilton South*), Mackasey, Marcoux, Rynard, Slogan, Willoughby —(10).

In attendance: From the Food and Drug Directorate, Department of National Health and Welfare: Dr. C. A. Morrell, Director; Dr. L. I. Pugsley, Associate Director; and Mr. M. G. Allmark, Assistant Director of Drugs.

The Chairman briefly outlined the proposed itinerary for the Montreal visit of the Committee on May 28 and 29.

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Dr. Morrell made a further statement on the question asked by Mr. Slogan yesterday with regard to the bureau of standards. He was further examined about marketing of new drugs, introduction of new drugs for clinical trial in Canada, testing, and related matters.

Questioning concluded, the Chairman announced that the Secretary of the United Nations, Mr. U Thant will address the House of Commons next Tuesday, May 26, at 10 a.m., and the Committee agreed to cancel its meeting for that day.

At 11 o'clock a.m. the Committee adjourned to meet in Montreal Thursday next, May 28.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

THURSDAY, May 21, 1964.

The CHAIRMAN: Gentlemen, there is a quorum present and we will start our meeting.

First of all, I would like to ask the members if they received last year issue number 16 of the proceedings, which included the final report of the committee on insecticides and pesticides. I know I did not receive that report and I was wondering if everyone else was in the same position as I?

Some hon. MEMBERS: No.

The CHAIRMAN: Then, we will have them sent out to you from the distribution office.

Gentlemen, we have with us this morning Dr. Morrell, the director of the food and drug directorate along with a good number of his staff; I will not attempt at this time to introduce them.

Dr. Morrell will be with us for three days. We have set this time aside because we thought there would be a lot of evidence and a great number of questions which the committee would wish to put to Dr. Morrell.

It was the feeling of the steering committee that we probably should meet until approximately 11 o'clock this morning and then break off at a convenient time. Dr. Morrell will be back tomorrow and again on Tuesday.

Dr. Morrell has furnished copies of the Food and Drug Act and regulations for those who did not receive them during our last hearings. There probably will be some new members who have not received copies of these to date.

I think the best thing to do at this time would be to introduce Dr. Morrell to the committee. I think most of you already know Dr. Morrell. I would ask him to give a statement which he has prepared in respect of changes which have taken place since the last time he appeared before this committee.

Mr. MACKASEY: Are there copies available of Dr. Morrell's statement?

Dr. C. A. MORRELL (*Director, Food and Drug Directorate, Department of National Health and Welfare*): I gave a copy of my statement to the reporters and I have just the one copy left.

Mr. Chairman, do you wish me to read my statement or have you any other wishes in this respect?

The CHAIRMAN: I think it would be better to have Dr. Morrell read his statement to the members of the committee. Is that agreed?

Some hon. MEMBERS: Agreed.

Dr. MORRELL: The statement which I am going to read is a statement of the action that has been taken by the Department of National Health and Welfare since the appointment of the special committee of the Royal College of Physicians and Surgeons. A number of things have been done and I will enumerate them in this report which I am going to read to you.

Since the appointment of the special committee of the Royal College of Physicians and Surgeons of Canada to study the procedures used by the food and drug directorate for dealing with new drugs and especially since the report of that committee was received by the minister, a number of actions have been taken to increase the protection of the public in respect of the sale and use of drugs by the Food and Drugs Act and its enforcement.

These actions include (1) an amendment to the Food and Drugs Act itself, (2) additional regulations or amended regulations under this act, (3) an increase in staff of the food and drug directorate, (4) the planning of a drug adverse reaction reporting program and first steps to implement such program, (5) the use of special ad hoc committees of experts to advise on a number of matters related to enforcement of the law in the interests of public safety.

Now, in more detail I will enumerate these.

1. Amendments to the Food and Drugs Act.

The Food and Drugs Act was amended by parliament in respect of several sections on December 21, 1962:

(*a*) Section 14 of the act was amended to provide authority for closer and more effective control over the distribution of drug samples. The present section 14 the one which now exists, prohibits anyone from distributing or causing to be distributed any drug as a sample but makes an exception of the distribution of samples of drugs to physicians, dentists, veterinary surgeons or pharmacists under prescribed conditions. The effect of the new section 14 is to prohibit the distribution of drugs as samples to the general public and to provide authority by regulation to prescribe conditions for distributing drugs to the professional groups named. Regulations in respect of the latter are already in force.

(*b*) A new section (14A) was added to the act which forbids the sale of any drug described in Schedule H to the act. Only two drugs are described in schedule H to the act, namely, thalidomide and lysergic acid diethylamide.

Following the request from a number of research centers to be allowed to buy thalidomide for purely experimental purposes, either chemical or biological, possibly involving the use of animals or organisms other than humans, an exemption was made by regulation from the total prohibition of sale for those purposes only.

Such exemption was made by the authority of section 24(1)(j) of the act which permits exemptions from the requirements of the act if the conditions of exemption are prescribed by regulation.

Certain exemptions have also been made by the same means permitting a limited controlled use of LSD to determine its value and hazards in the treatment of humans.

(*c*) Although there has been undoubted authority under the Food and Drugs Act for many years to promulgate regulations concerning the introduction of new drugs to the market, it was felt to be desirable to spell out this authority in The Act.

For that reason a new section (o) was added to 24 (1) of the act providing authority to make regulations respecting method of preparation, manufacture, preserving, packaging, labelling, storing and testing of any new drug and defining the sale and conditions of sale of any new drug as well as defining, for the purposes of the act, the expression "new drug".

These are the amendments to the act itself which were passed by parliament in December, 1962.

2. Additional Regulations or Amendments to Regulations.

(*a*) For several years discussions between the officers of the food and drug directorate were held with a view to setting forth by regulation certain requirements for the facilities and controls to be used by anyone manufacturing drugs in their final pharmaceutical form. Regulations in this area were passed by Order in Council in March, 1963. They consist of sections C.01.051 to C.01.056 inclusive, and set forth requirements for the quality control in all its aspects

including standards for premises in which drugs are manufactured, qualifications of supervisory staff; requirements for testing raw and finished products, systems for recall of drug, records of tests and information on adverse reactions that may be reported. There requirements cover imported drugs as well as those produced in Canada.

(b) Regulations setting forth the limitations on the distribution of drug samples to the professions named in the act were passed in July, 1963. They are given in sections C.01.048 and C.01.049 and require that a manufacturer distribute samples of drugs only to physicians, dentists, veterinary surgeons and pharmacists. Furthermore, the manufacturer must first receive a written order signed by the physician, dentist, veterinary surgeon or pharmacist specifying the name and amount of the sample requested if the drug is a prescription drug, or a maximum single and daily dose of it is prescribed by regulation or if it is a preparation that must be labelled "for therapeutic use only" or if it is a new drug (see Schedule I to the regulations).

I call your attention to Schedule I of the regulations. This is a new schedule which has been added.

Regulations permitting a very restricted sale of Schedule H drugs were passed in July, 1963, and are contained in sections C.07.001 to C.07.006 inclusive. Lysergic acid (diethylamide), commonly known as LSD may only be sold to an institution approved by the minister for clinical use by qualified investigators in those institutions.

The use of the drug is limited to the determination of its hazards and efficacy or for laboratory research in such institutions. The minister must be informed of every sale before it is made and must approve the sale in respect to quantity and dosage form. An adequate accounting of the use of the drug by each institution must be made at the request of the minister.

The control of the sale of thalidomide is the same except that it may be sold only as the bulk chemical in powdered form for animal or chemical experiments.

The new drug regulations were completely rewritten and were passed in October, 1963. They are now included in sections C.08.001 to C.08.009. Although rewritten, they maintain many of the requirements previously in force to which are now added a number of additional sections. The revised regulations include the recommendations made by the special committee of the Royal College of Physicians and Surgeons. The new sections include a revised definition of a new drug which definitely covers significant changes in excipients as ones that will result in a drug being considered as a new drug. It also states that a new drug is one that is "new" in Canada.

A new feature of the new drug regulations is the requirement of a "preclinical submission" from the manufacturer before he may distribute a new drug for clinical trial (section C.08.005). In that respect I call your attention to section C.08.005 of the food and drug regulations in the blue pages. In such a submission the manufacturer must include prescribed information about its chemistry, the manufacturing procedures and controls used in producing and testing its purity and safety and information to justify its clinical trial. In effect, this is information to support its clinical use. The manufacturer must also provide the names and qualifications of all clinical investigators who are to use the new drug and he must ensure that such investigators have the facilities necessary and that the investigator has information about the new drug that will enable him to use it on humans with the minimum of hazard to the patient.

Following the filing of a satisfactory preclinical submission, the manufacturer may distribute his new drug for clinical trial in order to gather data and information to file a new drug submission, much as he has done in the past.

There are two new pieces of authority given the minister; the minister may stop the sale of a new drug for clinical trial or may suspend a notice of compliance of a new drug, for reasons of public health and in the latter case, for other specified serious reasons as well (C.08.006). I refer you there to section C.08.006 which spells out the reasons which may cause the minister to suspend the sale or distribution of a new drug; that is in the case of the suspension of a new drug undergoing clinical trial, or in the case that the minister insists on the recall of the new drug which is on the market.

If the "notice of compliance" is suspended, the manufacturer must recall the drug in question from the market and it returns to the status of a new drug undergoing clinical trial.

The manufacturer may appeal the decision of the minister in either case and a mechanism for such appeals is described in the regulations (see section C.08.009).

Records must now be kept by the manufacturer after he introduces a new drug on the market. These requirements are in the interests of safety and to keep the directorate informed of unexpected adverse reactions.

The third area in which changes have been made is in the increase of staff in the food and drug directorate.

The staff of the food and drug directorate has been increased by 200 positions since the formation of the special committee of the Royal College. Somewhat more than half of these positions have been assigned to the field staff, the remainder to headquarters. As anticipated, it is difficult to recruit people with certain scientific qualifications, particularly pharmacologists, physiologists, pharmacologsts, physiologists, pharmaceutical chemists and medical graduates. In some of these classes there are only a few qualified persons available and the salaries we can offer are insufficient to attract or hold them.

One of the problems in the past has been to learn at an early date of unexpected adverse reactions to drugs. An adverse reaction reporting system is now being organized to advise the directorate of such reactions noted in Canada. Teaching hospitals of the medical schools in this country are considered as suitable sources for the kind of information needed and the plan has been discussed with the deans of the medical schools and the professors of medicine. It is hoped that some definite arrangement and organization will be in effect before the end of this fiscal year.

The report of the special committee of the Royal College of Physicians and Surgeons recommended that a standing working committee be established to advise on matters pertaining to drugs. This recommendation is still under review in the department. The terms of reference and membership of the Canadian drug advisory committee are being studied with a view to ascertaining what part it can play in the light of this recommendation. Meanwhile the directorate has instituted the use of ad hoc committees of specialists in certain fields to advise on special problems requiring a knowledge and experience in considerable depth, of the subjects presented to them. The most recent of these ad hoc committees was asked to advise whether the sale of tranylcypromine should be more specifically controlled and if so, what should be done in this connection.

These ad hoc committees are in respect of special subjects in which we require advice. I have here a list of the committees which we have consulted since last fall. There is a special committee on vitamin B-12 and the intrinsic factor concentrate. This committee was called together on October 7. Then there were the representatives of the Canadian Veterinary-Medical Association to discuss the brief they had presented to the Brien committee. The Canadian Pediatric Society sent a committee to discuss their brief which they had presented to the same committee. Also, we had representatives of the Canadian Society of Clinical Investigators, because we wanted to find out

from them what information they needed before they investigated or administered a brand new drug to a patient. Finally, as you know, we have had the special committee on parnate. No report has yet been received from them. These are the special ad hoc committees to which I refer.

It seems to us that these ad hoc committees consisting of specialists in the particular areas concerned should be more helpful than a standing committee whose members cannot be expected to have the depth of knowledge or experience needed to cover all areas of the broad fields in which our responsibility lies. We have talked this over with Dr. F. S. Brien and his associates and have their concurrence in our trials of the ad hoc committee method of getting advice. This is not to say, however, that a revision of our ideas as to the functions of the Canadian drug advisory committee is not needed. Indeed more study is necessary to explore possible ways of deriving greater benefit from this committee.

Thank you, Mr. Chairman.

The CHAIRMAN: Dr. Morrell's statement will be printed in our first issue. I am not sure what the printing facilities are at the present time. However, I think the printing is fairly rapid, and we should not have any difficulty in getting the statement.

Gentlemen, the meeting is open. Are there any questions of Dr. Morrell?

Mr. ENNS: I was very much interested in that part of the report which dealt with the tightening up of controls in respect of the Food and Drug Act. It now would appear very unlikely the thalidomide tragedy would be repeated. But, I am wondering if this action has sealed forever the benefits of those new drugs which form a part of a new development. Thalidomide itself has many benefits but there is this terrible limitation. Does the Food and Drug Act, in the way it is now set out, still allow the use of certain drugs if or when the safety of such use can be proven?

Mr. MORRELL: Mr. Chairman, although thalidomide is mentioned in schedule H, which is a total prohibition in itself of the sale of thalidomide as a drug there is an exemption allowed where thalidomide is being used by research institutions in respect of animals and for chemical experiments, and if something should result from the experimental work which would be of value in thereapeutics we would have to give very careful consideration to allowing its use for any particular purpose which would be valuable. But, at the present time, we have had no such information; in other words it is possible that thalidomide could again be used as a therapeutic agent if the necessity or value of it was distinctly proven.

Mr. ENNS: But, to date the apparent dangers in respect of it seem to be limited to the pregnant mother.

Mr. MORRELL: Yes.

Mr. ENNS: Are there any reported ill effects of other uses, for example in the case of male users, or even to persons beyond the child bearing age? In that respect is consideration being given to the use of this drug?

Mr. MORRELL: Well, there were other side effects that were reported and known, but not side effects that would have led to its recall from the market. However, as you know, almost every drug which has any therapeutic value as an effective drug will have some side effects. Thalidomide was known to have had some side effects before the realization that it did cause or was certainly associated with the production of malformed children. It was for the latter reason it was recalled from the market.

Mr. ENNS: This alarms me very much. I do know that it has been reported for the treatment of migraine headaches and, in this respect, it has proven very beneficial.

Mr. MORRELL: Yes.

Mr. ENNS: I am wondering if the benefits of a drug such as this are being denied to those persons who could be helped by it because of the serious alarm which has been expressed in respect of malformed children. Is it possible to conceive that even without new development of the drug or new application of it that perhaps circumstances will change so that a limited application of the drug as it is known now can be used?

Mr. MORRELL: Yes, I have heard of the value of it in the treatment of migraine headaches. I think it was acknowledged as being a good sedative and having certain features. In fact, at one time in the early days when it was on the market, it was thought to be a very safe drug because no one could commit suicide by using it. Apparently, you could take an enormous quantity of it, have a good sleep all night and have no ill effects afterward. But, I think the hazard is the inability to control the user of thalidimode after it is on the market. I am referring now to the medicine cabinet at home; you do not know who will take a pill today. Everyone wants to take pills and if they know it is a sedative or headache pill they are more likely to take it than perhaps any other type of pill. I think it is the fear of it getting into the wrong hands that has led to the very heavy restrictions which are placed on the use of it. It is not allowed at all for the use of humans at the present time. Now, whether or not this fear ever will dissipate I do not know. But, I think it is a real problem to control the use of a drug. Even when prescriptions are given to some member of the household we believe that other people will take it. They do not know quite what it is, and they even might hand it to a neighbour and say: "This is what the doctor gave me; try it." This is the danger in respect of thalidomide.

Mr. SLOGAN: Dr. Morrell, would you mind giving us some of the other side effects of thalidomide?

Mr. MORRELL: Yes. Some had a peripheral neuritis in the arms and legs following long daily use over several months. This condition could have been stopped in the early stages if the drug was stopped but, I have heard it would persist if it was continued. Perhaps some of my own staff could give you more information than I have. Dr. Lu, could you add anything to what I have said.

Dr. FRANK LU (*Food and Drug Directorate, Department of National Health and Welfare*): There has been some indication of its effect on the thyroid gland although this did not prove as serious as peripheral neuritis.

The CHAIRMAN: Have you a question, Dr. Orlikow?

Mr. ORLIKOW: Mr. Chairman, I would like to ask Dr. Morrell a question in respect of the increase in staff which you have mentioned. I believe you said there were 200 extra people. In view of this, how much more ability has this given the department to check on the quality of these items. I hesitate to use the words "quality control" because this expression is being misused by certain drug companies for their own purposes. But, how much more ability has the department at the present time to ensure the public that prescription drugs which are distributed meet the standards set by the department?

Mr. MORRELL: Well, it certainly has added to our ability. The positions that we have and the people who subsequently have filled some of these have been of great assistance. However, all these positions are not filled to date. But, these positions are or will be filled by inspectors, laboratory chemists and some office workers, which are necessary; it also includes scientists at headquarters.

Now, I pointed out to you that we have new regulations which permit us to inspect the factory of a manufacturer who is making drugs in order to determine whether or not he has quality control features in his organization which satisfy at least the minimum requirements of the regulations. The number of plants

inspected has increased a great deal since we have obtained our new inspectors; but, I must point out to you that hiring an inspector this year, expecting him to go to work during this year and to be particularly useful, is not the way it happens. They require a training period of a couple of years. I would say that next year and the year after we will begin to feel much more the benefits of the people that have been added to our staff. It does take a good deal of time to train them. But, assuming they are trained adequately, I think it will add a great deal in that respect.

Now, methods of analyses for pharmaceuticals are always under observation and development, and we have some people on our Ottawa staff who are developing these methods. Additional people have been hired there as well as in our regional laboratory, which permits us to do more samples of drugs taken from the market. The benefits of all these will be much more marked, of course, in a year or two.

However, I want to emphasize that we are not yet, and I think it is unlikely we ever will be, able to analyse every batch of every drug put on the Canadian market. I would estimate there would be 100,000 batches of drugs of one kind or another and in one form or another each year put on the Canadian market. Of course, some of these are compound and complex drugs and the standard analytical procedures used are not altogether satisfactory because of the presence of other materials. So, we have to develop methods. But, even if this were done, 100,000 batches a year would require many many more times the number of people we have. Therefore, I want to point out again that we have to continue to do a policing action; that is, take samples from the market, analyse them and take action wherever we find there is fault. Of course, we have increased the number of samples taken of drugs from the market and as we get more people there will be more samples taken. There is that much more assurance that we are catching those that are not correct. But, there never can be a guarantee that we get everything.

Mr. ORLIKOW: Dr. Morrell, what provisions have you for testing drugs which are not manufactured in Canada. I am referring to those drugs which are imported.

Mr. MORRELL: We have the same authority over imported drugs and the same provisions. We get some of them in customs and we obtain some when they get to the Canadian distributor. We take samples there. But, the same authority is provided for imports and domestic.

Mr. ORLIKOW: The reason I asked this question is that in respect of the hearings in the United States—and I am sure we will have the same thing here—from discussions I have had with other people one of the reasons given for not using more often the generic names of drugs, which would give an opportunity certainly in the field of antibiotics or tranquilizers for very substantial savings is that they cannot be certain that the smaller company or the company which imports from Europe imports a drug which is up to standard and, therefore, it would be better if better known companies and so forth were specified. If this is a legitimate doubt, of course, then there is nothing we can do; but, if it is not it seems to me that the medical profession and the public should ensure that we are doing adequate testing and obtaining drugs of proper standard, even when they use generic names. I think plenty of evidence can be brought forward that there have been very substantial savings. An example of this is in respect of provincial hospitals. Because they have confidence in their own ability to test they are able to buy not only in quantity but to buy generic labelled items.

Mr. MORRELL: Well, I certainly understand the situation and I think they have a legitimate basis for doubt in respect of buying any drug on the market. I think as time goes on and as our staff becomes greater and better able to

cope with the vast number of products on the market things will be better. There are 25,000 or more products on the market and, therefore, the reason for doubt will be less and less as we analyse more and more samples. We know from our own analyses that there are some so-called generic drugs on the market that are satisfactory; on the other hand, we know there have been some that have not been satisfactory because we have had to take action to get them off the market. One, I think, often buys and is wise to buy on the reputation of a company. You do that in respect of purchases of other items, and I think one is wise to do it in respect of drugs. If I were a doctor prescribing drugs I am sure I would tend to prescribe from companies whom I knew. This is only natural.

Mr. ORLIKOW: That is so, Mr. Chairman; no one questions that. But, at the same time, we are not dealing in pennies; we are dealing with very substantial amounts of money which the ordinary person in a low or medium income job who has an illness and has to call a doctor for an antibiotic prescription can ill afford. I am not laying the blame on anyone but this person obtains his prescription and he is charged $10 or $12, which is a pretty big burden on him. It is not surprising if he wonders whether or not he could get the prescription cheaper. As I say, there is plenty of evidence and I hope we are going to go into this question in great detail. As you know, drug companies are the most profitable type of business that there is in existence on the North American continent. Their profit on investment capital is twice as large as the profit of automobile companies, and this is an important factor. I think the faster we can get to this question of making sure that any drug which is sold is reliable so that the doctor can be sure the drug he prescribes is reliable, the better. It would be of a great value. For example, has the department considered this question. Suppose a company wants to bring in a product and goes to the department and says: "Look, we are going to bring this product in; will you inspect it and, if it is suitable, give us some kind of letter of approval so we can tell the medical profession it is reliable and that they can use it without worry?" Have you given consideration to that kind of program?

Mr. MORRELL: Certainly, it is not within our authority. We administer laws. As you know, we have three laws for which we are responsible in respect of administering and enforcing and we have no authority for approving anything. We always take a negative attitude; we take objection to things that are not right and we say nothing about things that are right. They are supposed to be right so we have not given any consideration to approving certain plants in preference to others. But, if we have any objection to them, and we often do, we take action. As I said, we do not approve the ones who are living up to the law.

Mr. ORLIKOW: Well, this is bound to help. I am not blaming the department because certainly its job is to administer the laws and regulations that parliament and the government pass. But, this certainly tends to maintain the status quo.

I am wondering if the department has given any consideration to regulations along the lines proposed in the United States which would require the use of the generic name as well as the trade name and so on on label when drug prescription items are prepared for sale in the United States.

Mr. MORRELL: Well, Mr. Chairman, for a good many years it has been a requirement of the food and drug regulations that what you call the generic name and what is referred to in the regulations as the proper name, must be on the label in conjunction with the brand name and immediately adjacent to it. Usually it is below it, I think, and in type not less than half the size of the brand name. Now, you can only give a proper name to a single sub-

stance; when you get mixtures of substances, in my mind, it is no longer possible to give it a generic name. You have a mixture or a compound of a great many products. As you know, a great many products are compounds or mixtures of two or more things. When you list the ingredients of these drugs we want the generic name in the list. But, the name of the drug itself will be a coined name which is used by the manufacturer.

Mr. MACKASEY: Dr. Morrell, in reading between the lines I would come to the conclusion that basically your department at the present time is more concerned in the safety of the population than you are in the price of drugs.

Mr. MORRELL: We have no authority whatever over the price of drugs. I cannot alter the price of drugs through any action I take except to increase it if I demand more and more from the manufacturer by way of safety, records and so on.

Mr. MACKASEY: Am I right in assuming by an answer that you gave to Mr. Orlikow that at least under the present circumstances if a drug is labelled by the name of a reputable manufacturer it does provide some margin of safety which would not be there under the present circumstances in the case of a drug which is not labelled?

Mr. MORRELL: But, all drugs have to be labelled.

Mr. MACKASEY: Well, let us call it lobbying, if you like, or the conception that we are paying extremely high prices simply because a drug is labelled by the manufacturer for someone else. There is the conception that if an aspirin container was blank, with no symbol on it, it would be much cheaper. Although I inferred that from what Mr. Orlikow said I do not necessarily agree with it. So far as you are concerned, what is your opinion in that respect. Would you prefer to see the drugs, pills and so on, labelled by the manufacturer, as is the case now?

Mr. MORRELL: It is required by the regulations that they have the name of the drug, the dosage, adequate directions for use, the name and address of the manufacturer and so on, on the label.

Mr. MACKASEY: And I suppose this is done for the purpose of safety?

Mr. MORRELL: Yes, I suppose ultimately it is intended for that.

Mr. MACKASEY: Regardless of what it may or may not do in respect of the price the prime reason or objective is the safety factor.

Mr. MORRELL: Yes. We would not want a drug on the market and not know who was responsible for it. I think that would be a dangerous situation, if allowed to exist.

Mr. MACKASEY: I have one other question which I will put for my own personal information. You mentioned in your very fine opening remarks this morning that research information must be supplied along with a request for the sale of a new drug. Does this research information result entirely from tests conducted in Canada or do you have other recognized sources outside the country from which you accept drugs, assuming they are of the proper standard?

Mr. MORRELL: There are several ways. I presume you are speaking of adverse reactions?

Mr. MACKASEY: Yes, the clinical research that must go into it.

Mr. MORRELL: Are you inquiring about any new drug submission?

Mr. MACKASEY: Yes.

Mr. MORRELL: Oh, no; this information certainly is not entirely gathered in Canada. I would suppose the majority of our new drugs originate in the United States and the majority of the clinical material will have been gathered there. There has been no special requirement that it must be gathered in

Canada. I think if we said all our information on clinical testing or laboratory work must be done in Canada before we would consider it there would be such a bottleneck we would not get very many new drugs released because we do not have sufficient facilities.

Mr. MACKASEY: That is the point I am getting at.

Mr. MORRELL: We have not sufficient facilities for this.

Mr. MACKASEY: I have one last question, which may seem to you to be ridiculous. I would like to draw a parallel to court cases. When a drug is temporarily banned or barred by the department and, as you mentioned, the company has a right of appeal, am I right that in the time intervening during an appeal the drug is banned and, in this respect, the procedure is not similar to an appeal case in court.

Mr. MORRELL: No, the regulation makes it clear that during the time in which the information is being submitted to the committee of appeal and is dealt with the drug is banned.

The CHAIRMAN: Did you have a question, Mr. Howe?

Mr. HOWE (*Hamilton South*): No, Mr. Chairman. My question related to the generic part of it, which has been discussed.

The CHAIRMAN: Would you proceed, Dr. Slogan.

Mr. SLOGAN: Do all the drugs which go on the United States market go through the American bureau of standards?

Mr. MORRELL: No, they do not; they go to the American food and drug administration, which is the counterpart of the Canadian food and drug directorate.

Mr. SLOGAN: And, am I right in assuming we do not have a body similar to the American bureau of standards in Canada?

Mr. MORRELL: No. I suppose we do have functions which are similar, but these functions are distributed among various departments and we have no comparable body to the American bureau of standards.

Mr. SLOGAN: What I had in mind is that in the dental profession the American Dental Association has certain standards for certain of these products. For example, in the case of dental cement, it has to meet the ADA specification number 8. It is my understanding that any of the products which are on the United States market can be referred to the bureau of standards for testing to see whether or not they meet these standards. For instance, when I am using a product which meets the specification and I am quite acquainted with it and a salesman comes in with another product with which I am not acquainted, and he tells me it meets these specifications set by the United States authorities I am prepared to accept it. In view of this, I was wondering if there is not room for something like this in Canada and, perhaps, a little more co-operation between the two countries. If they have certain sets of standards for licensing their drugs in the United States and if our food and drug directorate was acquainted with these standards and a drug is accepted in the United States is it necessary to do any further testing in Canada, or can you accept their decision in respect of the drug? What I had in mind was this: I think perhaps if we could restrict ourselves to the testing of Canadian drugs, then this could be a reciprocal action so that any Canadian drugs going to the United States, with a common set of standards, would be automatically acceptable there and vice versa. If this was possible it would take some strain off the testing program in Canada.

Mr. MORRELL: Well, Mr. Chairman, I will answer the last part of Dr. Slogan's question first. I doubt very much whether the food and drug administration would accept our say so or the say so of any other country in respect

of a new drug that was offered in the United States. They would demand it go through the procedures that they require for the introduction of a new drug into the United States and, likewise, although we would accept clinical evaluation if it was adequate according to our requirements—that is, pharmacological and toxicological testing done in the United States—nevertheless, we want to see what was done and we would want to see the complete details of the manufacturers' knowledge of that drug, just as they do. I think it would be unwise to accept blindly any drug without taking a look at the requirements of any particular country, even the United States.

Mr. SLOGAN: I do not mean to say we should blindly accept it, but are the standards that much different, or are they very similar; is there room for a meeting of minds in respect of setting a common standard?

Mr. MORRELL: We do work rather closely with the food and drug administration in the United States. We do examine their regulations as they examine ours when they set up standards. There may be some local or national peculiarity which requires some differences here and there, but by and large our regulations cover the same ground in almost the same detail as the United States regulations. However, we are responsible for enforcing the Canadian regulations, and the United States food and drug administration is responsible for enforcing the regulations of their country.

In other words, we have not gone so far as to delegate to the United States authorities the authority to approve or permit a drug to be sold in Canada. We have to do that ourselves; that is a responsibility we take. Therefore, in order to make sure we are doing the right thing, we must see all of this information wherever it is gathered and judge for ourselves whether or not it meets the requirements of our law. This is what we do. I do not know whether or not the day will come when we will accept somebody else's judgment on that. That time has not yet arrived in any event.

Mr. SLOGAN: I brought this up following on what Mr. Orlikow said that even though we can order drugs by their generic names from the different companies, we have no way of knowing what is the standard behind that company, if it is a company which is unknown to us. Therefore, the tendency is to prescribe drugs from known companies. However, if there was a standard set, say by the Canadian Medical Association, which sets out the quality this drug must meet, and if this appears on the label, then, of course, it would have to be tested and approved by the government.

If the drug meets the Canadian medical specifications and is certified by the government, then when someone came up with a drug by a generic name from a new company, we would know whether or not we should accept it.

Mr. MORRELL: If the government certified it, you could have more confidence in it. However, this is not in existence at the present.

Mr. SLOGAN: I think the government is at fault to a certain extent in not doing this, because they could save the people of Canada a good deal of money by instituting such a service. The medical profession or the pharmacists are in no position to assess whether or not that drug is up to par.

Mr. MORRELL: In those instances do you think we should allow the sale of any uncertified drug at all?

Mr. SLOGAN: I think we should have a type of bureau of standards which could do a good deal for the profession and the people as a whole.

Mr. ENNS: This comes back again to the matter of the possibility of exploring further the setting up of some authority similar to the United States bureau of standards.

Mr. MORRELL: I think we had better look into that. So far as I know, the bureau of standards' work does not cover the drugs covered by the food and

drug administration in the United States; I am not aware that it does. The final authority in the United States with regard to whether or not a drug should be permitted on the market is the food and drug administration in Washington.

Mr. SLOGAN: I would suggest that perhaps this might be a part of your directorate. I believe that if this service were offered it certainly could do a great deal to encourage the use of drugs from any country.

Mr. ENNS: It also could take the form of the College of Physicians and Surgeons taking a part in dealing with approval. I wonder whether it has to be a government agency. Each professional association has some research facilities, and if they made a recommendation at least, this perhaps could be an answer.

Mr. SLOGAN: I think the profession should set a standard in co-operation with the government, but the actual testing would be by the government.

Mr. MORRELL: If the government is going to guarantee all goods sold in the country, the public must be prepared to dig down in their pocket, because it will cost a great deal more.

Mr. ORLIKOW: To expect the government to check on every product which is permitted to be prescribed in Canada, of course, would require a bigger staff and more money, but I suggest this is something which would be well worth looking at, because when one looks at the report of the director of the combines investigation branch, having to do with drugs, you will see very quickly that the Canadian consumer is paying the highest prices in the world for prescription drugs.

I certainly agree with Dr. Slogan that one cannot expect a doctor or a dentist on his own to prescribe a drug by its generic name even though it will save the patient, not only cents, but rather many dollars. I do not believe it would be difficult to present evidence on that at the appropriate time. However, you cannot even expect the doctor to do that, unless he can be certain of the product he is prescribing, and he cannot do that unless there is some agency which is prepared to test it. I suggest there could be a great saving to the consumer. I think we very easily can demonstrate that.

I am going to suggest that while this committee is sitting we call in the administrators of the hospitals and ask them what they are doing, because I know for a fact the hospital dispensaries are giving prescriptions to the patients, not only cheaper than they can buy them retail in the drugstores, but cheaper than the druggist can buy them when he buys from the manufacturer. I know this for a fact, and it can be proven very easily.

This is something which I believe we might look into. I do not think we can just brush off this question of price by saying you pay a higher price in order to get quality. If that was so, no one would question the higher price. In many cases the higher prices are being paid by people who cannot afford them without any real reason.

Mr. SLOGAN: I think it is well known that many manufacturers manufacture under different brand names at different prices, but the people at the purchasing end are in no position to know this.

Mr. MACKASEY: This is true in any field. I am a manufacturer in other commodities. I think what is said basically is true, but there is a difference. The difference in going out and buying a washing machine with a brand name and one which does not have a brand name is a difference of safety. I agree with Mr. Orlikow that it is to Canada's advantage that our drugs and medicines be made available at the lowest possible price. The only objection I have is that so long as there is a conflict between price and safety, I am on the side of safety. Our prime objective is to make sure we are not jeopardiz-

ing the safety of our people under the guise that we are going to get something more economical. I think it is a foregone conclusion that you get what you pay for.

I do not wish to become involved in a discussion concerning the high profits to the companies. I, like everybody else, watch the profits of people in all fields, and I have not seen a drug company skyrocket these days. There is competition between these companies and they endeavour to sell the product at the lowest possible price. If we encourage the bootleggers to get into the field, we are jeopardizing the safety of the people of Canada.

I believe if we investigated the distribution of drugs in Russia, where it is done through the government, we would find that despite the government monopoly they pay much more for drugs than we do because of the absence of competition. If your people provide the standards that will ensure the safety of Canadians, competition will keep the prices down.

Mr. ORLIKOW: There is no competition.

Mr. MACKASEY: This is a matter of opinion. I say there is competition. I am interested in the procedure which was outlined at the last meeting of the steering committee to the effect that the emphasis in our discussions be based on safety rather than on price. I predict that otherwise 90 per cent of our time will be taken up with questions on price, because is it a good platform. I am interested in safety and nothing else.

Mr. ENNS: We were speaking about the food and drug directorate not being in a position to approve drugs of any kind. I am wondering whether this is without precedent in terms of the government approving items. Where safety factors are involved, and so on, we have the stamp Canada approved. Perhaps it would be an idea for our food and drug directorate to evolve some body that could issue a similar stamp of approval. I have no fixed idea of how this should be done. I am thinking about it from the standpoint of the public being safeguarded by the government. That would be a further step, but I imagine staff is involved. You mentioned the addition of personnel, and you were careful to say these positions are not filled because of the limited availability of trained personnel.

These are fields which probably the committee could advantageously pursue further, rather than the matter of price at the moment, but I do agree that price is something we should look at at the proper time; however, that time is not now.

Mr. ROXBURGH: Mr. Chairman, it definitely was the understanding that we were going into the matter of safety. How does this involve price? We want to stay with one subject or the other. What is the procedure; what are we going to do? Are we going to jump from one to another? If so, we will not get anywhere.

Mr. SLOGAN: I think the two matters are very much associated. When an individual is buying a drug he is going to buy the cheaper drug and we are concerned whether or not that cheaper drug is as safe as the more expensive one. How can you divorce the two?

Mr. ROXBURGH: Do you not think we should consider only the safety factor and then take up the other question afterwards? Otherwise, we will be a long time arriving at a conclusion. If we stick to the safety factor first, we could return to the other. If a witness happens to be brought in, who otherwise would have to come back again, then we might be able to divide the meeting into the safety item first and then the other, rather than have him return. I believe we should take a stand and really stick to one thing.

Mr. SLOGAN: If you have the safety factor, the price factor would take care of itself.

Mr. ORLIKOW: At an earlier meeting I agreed there was merit in attempting to keep the two separate. I still agree with that. However, I do not suggest that Dr. Morrell, or the officials of the department, should play a very important part at the moment in the question of price, but at the same time, surely we are entitled to ask Dr. Morrell and the members of the department their opinions in respect of the further extension of testing by the department, and whether the purpose of the testing is to extend the provisions for safety, or whether the purpose of the testing could be, possibly, to reduce the price of the drugs. That is all I did. I can assure the members that if they think I dwelt a long time on the question of price, they have not seen anything. I am sure we will spend many days, weeks and months on this whole question of the cost of drugs. I do not know whether or not we are in the same category as the United States, but there the estimate is that the cost of drugs is more than the cost of medical services; so, it is not an insignificant question. I think we rapidly are approaching that situation, if we are not yet in it.

Mr. ROXBURGH: I think we should stick to the matter of safety no matter what the cost is. If we paid $10 an ounce and it was not safe, the cost would not mean anything. I think we should go along with the question of safety first, clear it up, and then get into cost.

Mr. ENNS: Rather than continue this discussion while we have witnesses here, I think we should return to the questioning. I would like to go back to the matter of schedule H. As I understand it there are just two drugs on schedule H at the present time, thalidomide and LSD. There seems to be a good deal of interest in LSD in terms of treatment of alcoholics and other uses in respect of mental hospital care. I gather that when you referred to the drug being available for clinical use, you were referring largely to these institutions?

Mr. MORRELL: Yes; there is a regulation. I have referred to it in my statement and you can look into the accurate wording of the regulation. This regulation permits the sale of LSD to institutions approved by the Minister of National Health and Welfare for use in those institutions by qualified investigators, people who are cognizant of the danger of the drug and who are psychiatrists. These institutions must be approved and they must be prepared to account for its use, if we ask them to do so. Every sale to these institutions must be recorded and approved by the department. It is being used, I believe, in 12 or 14 institutions.

If a lot of LSD is ordered, we authorize the manufacturer to release it on the basis of an application from the person in the institution who intends to use it.

Mr. ENNS: This is a question which may not be properly addressed to Dr. Morrell, but I am wondering whether the patient needs to give his consent to the use of such a drug for treatment, or is this something that the doctor does without the knowledge of the patient.

Dr. L. I. PUGSLEY (*Associate Director, Medical Section, Food and Drug Directorate, Department of National Health and Welfare*): The doctor prescribes the drug.

Mr. ENNS: I felt that possibly this was not a legitimate question to ask here.

Mr. ORLIKOW: Could Dr. Morrell tell us in what years thalidomide was used? When I say used, I do not mean in the initial testing stages, but rather the year in which it was available for general use by doctors in Canada?

Mr. MORRELL: In April, 1961, it was available in Canada.

Mr. PUGSLEY: I think about March.

Mr. MORRELL: The drug submission was accepted by us in November, 1960, and it was put on the market in April, 1961.

Mr. ORLIKOW: When was it finally withdrawn to the best ability of the company and the government?

Mr. MORRELL: Well, we notified them in March of 1962. We asked them if they would consider withdrawing it because of the reports from Europe of malformations. On March 2 they agreed to do so, and sent out the requests to their detail men and their salesmen at once.

Mr. ORLIKOW: In March?

Mr. MORRELL: In March, 1962.

Mr. ORLIKOW: When were the reports of the difficulties published in Europe, and I believe particularly in Germany?

Mr. MORRELL: The first thing we heard of it in Canada was at a meeting with the manufacturers on December 1, 1961, when they came in to report they had heard of a few cases of malformations of one kind or another that had been received in Germany, in particular, although there were some indications there were some as well in the United Kingdom. This was the first indication we had there were side effects that could be called serious in terms of malformation of children born by mothers who had taken it during the early part of pregnancy.

At that time the manufacturers told us they were sending a team to Europe to confirm or to clarify at least these reports they had heard at that time. At that meeting it was agreed that they should send at once a warning to all physicians in Canada that this was a possible side effect of the use of the drug in pregnancy. Their letters, I think, were sent out on December 5 or December 7. There were two companies involved. The letter went out at that time.

Subsequently we received reports that were rather conflicting from the manufacturers and which certainly were not clear with regard to what they had found in Germany. It was only when we saw a published article which was documented and quite clear in the *Lancet*—which I saw on February 28, because it took that long to get to me—that I became quite concerned and telephoned them on March 2 to point this out to them. I suggested they should recall the drug from the market. These are the steps in the recall of thalidomide from the market.

Mr. ORLIKOW: It seems to me there is a possibility of the same kind of difficulties occurring again if the first report you received about this difficulty came from the manufacturers. I am not being critical of a manufacturer, but he has some conflict of interest; he cannot help but have.

Mr. MORRELL: Of course.

Mr. ORLIKOW: It seems to me that perhaps the department should explore the possibility of closer co-operation between similar departments in other governments. I would think that this kind of a report should have come from a source other than the manufacturer. It may be that had there been closer co-operation, it may have come earlier than it did.

Mr. MORRELL: A great many steps have been taken since that time to do just what you are suggesting.

Mr. MACKASEY: You are suggesting there is a beneficial effect today.

Mr. MORRELL: I think everybody in the world would hear about it much, much more quickly.

Mr. MACKASEY: At least the tragedy has had that beneficial effect.

Mr. MORRELL: Yes. It has had many effects, and that is one beneficial effect.

Mr. MACKASEY: I presume the thalidomide prices sparked complaints in respect of other drugs. I have in mind one particular one, pertussin.

Mr. MORRELL: I believe that is the cough syrup.

We have had many complaints, but it is very difficult to determine cause and effect. We have looked into a number of these reports, and when you get down to it you find that the patient took several drugs at the same time and it was the last one she took which is blamed; but one does not know. This is only association; it is not proven that the drug caused the malformation. It happened to be taken at that time, but it was a long way from being proven that it was responsible for the apparent effect. This is not easy.

Recently I have been speaking to people in Europe at the World Health Organization. They are very concerned about putting out information prematurely without careful thought and investigation about drugs. You alarm a great many people and do a lot of damage when perhaps it is a very useful drug. This has been given very careful study and consideration. This is true in the United Kingdom and in the United States. One of the actions that was taken, in line with what Dr. Orlikow said, was the setting up of a position for an officer in the World Health Organization who is responsible for distributing information promptly to various countries on adverse reactions to drugs. Our own drug adverse reaction program which we are setting up is to help us pick up information in Canada which we not only can use ourselves but also provide to other countries.

The CHAIRMAN: Gentlemen, if there are no other questions at the present time Dr. Morrell will be back tomorrow morning to continue at 9.30 a.m.

In conclusion, I would like to say I think it was pretty well decided at our last meeting that to the greatest degree possible we should stick to the topic of safety of drugs. But, as you realize, the two topics are greatly interrelated; when you come to safety and cost control I think we are going to get some cross references, which are unavoidable.

Our next meeting will be held in this room at 9.30 a.m. tomorrow morning.

FRIDAY, May 22, 1964

The CHAIRMAN: Gentlemen, we now have a quorum.

Before calling upon Dr. Morrell of the food and drug directorate I have here a proposed itinerary for our trip to Montreal which I briefly will outline to you. All times are daylight saving time.

We are leaving here at 7.40 a.m. on Thursday morning and will arrive in Dorval at 9.22 a.m. We will meet there and then proceed to the Mount Royal Chemicals Limited, which is a manufacturing unit for CIBA and Sandoz. From there we will proceed in the afternoon to the Frosst Company.

We stay at the Queen Elizabeth hotel overnight and the following morning go to the Jacques Genest clinical laboratory. In the afternoon we go to Ayerst McKenna & Harrison Company. I think this will give us two fairly full days. We will be through at approximately 5.30 or 6 o'clock on Friday evening. As I say, this will be a fairly compact two days and there are luncheons in between. On Thursday night there is a dinner for those who wish to attend. However, if you have other plans for that night it is all right.

Mr. MACKASEY: Mr. Chairman, I should report that the Fawzia has been closed up. The city police walked in last week and closed the place.

The CHAIRMAN: Well, I have never been to Montreal so I do not know what you are talking about.

If anyone has not told the clerk of the committee their intentions in respect of making this trip I would ask you to do so by tonight. I would like to know how many will be making the trip.

Now, if we can take up from where we left off yesterday, Dr. Morrell has a few further statements he would like to make in respect of some of Dr. Slogan's questions.

Dr. C. A. MORRELL (*Director of the Food and Drug Directorate, Department of National Health and Welfare*): Mr. Chairman, Dr. Slogan was asking about the bureau of standards, and I believe he was interested in the American Bureau of Standards. I believe I said there was no Canadian equivalent, and I think that is true.

You also referred to standards that were set up by the bureau of standards possibly for drugs, dental fillings and so forth.

Mr. SLOGAN: I was not sure it was the bureau of standards but I was under the impression it was.

Mr. MORRELL: We have in Canada under the National Research Council a Canadian standards group which sets up Canadian specifications. This is called the Canadian Specifications Board, I believe. This board will set up specifications for any particular thing, but it seems they must agree that it is important enough to do so. Actually, they have set up standards for quality control in pharmaceutical manufacturing. These can be obtained from the Canadian Government Specifications Board, if you wish to see it. But, of course, they do not police their standards, nor does the American Bureau of Standards.

Now, of course, standards for drugs are included in the appendix to the Act itself. For example, there are four pharmacopoeias, the International Pharmacopoeia, the British Pharmacopoeia, the French Pharmacopoeia and the United States Pharmacopoeia. These are standard works which are accepted and recognized in Canada by law, and the standards for drugs, of course, are laid down in these pharmacopoeias, with which I am sure you are familiar. Then, in addition, there are three formularies, the British Pharamaceutical Codex, the National Formulary and the Canadian Formulary. These contain standards for drugs not included in the pharmacopoeias. So, there are all these standards available and, in the case of the ones I have mentioned, these are official in this country.

Dr. Slogan, I do not know whether or not I have helped you in this respect.

Mr. SLOGAN: Could, perhaps, a not so well known manufacturer go to this branch of the national research council and obtain approval by having his product inspected on request?

Mr. MORRELL: I doubt it. Dr. Pugsley has sat on the Canadian Government Specifications Board on a number of occasions and I would ask him to be more specific in that respect.

Dr. L. I. PUGSLEY (*Food and Drug Directorate, Department of National Health and Welfare*): The Canadian Government Specifications Board primarily is an organization made up of the deputy ministers of the government departments, which would have specifications for the purchase of materials for the government. The Department of National Defence has used it quite extensively in the setting up of purchase specifications for the materials they purchase. It is used also in respect of public works purchases, soaps, cleaning materials and so on. They check these purchases against the specifications and laboratory analysis. Samples of the products are submitted and are analysed. This is somewhat similar in respect of the purchase of a drug. If you put U.S.P. on a drug that signifies the drug conforms to U.S.P. specifications. They set up criteria

for the drug and our laboratories would analyse the drug against the specification set up in the U.S.P., the British Pharmacopoeia, the National Formulary, B.P. Codex and those other compendia which Dr. Morrell indicated.

Mr. SLOGAN: There is a difficulty encountered by the average professional man in judging a product that does not come from a well known source. If a product was tested in this laboratory would they then be allowed to put on their label that this was approved by the government branch.

Mr. MORRELL: Do you mean by the Canadian Government Specifications Board?

Mr. SLOGAN: Yes.

Mr. MORRELL: I do not know whether or not that is permitted. Could you give us some information on that, Dr. Pugsley? For instance could a soap for which specifications had been written by the board say this meets the Canadian Government Specifications Board specifications?

Mr. PUGSLEY: It seems to me this is more of a contract. The purchaser signifies he wants the material to comply with the Canadian Government Specifications Board standards.

Mr. MORRELL: And, he issues the standards and says they must meet that standard, and they will test it themselves to see that it does.

Mr. PUGSLEY: Yes; it is your own responsibility to see that that product complies.

Mr. SLOGAN: But the government does in a way utilize this concept?

Mr. MORRELL: Yes, for their own purposes. When the government is buying materials for its own use it can have a specification set up by this board, and then when they want to buy that product and are asking for tenders it says the product must meet these specifications. But, the Department of Public Works, and so on, have laboratories in which they check to see whether the material they are getting from the manufacturer does meet these standards.

Mr. MACKASEY: If I might interject, the municipality of Verdun specify in their tenders any government specifications but, once the goods are delivered I suppose the prime responsibility is theirs.

Mr. MORRELL: Yes.

Mr. MACKASEY: As you know, there is a great competition between the different sources in meeting these government specifications, and then it comes down to price, which is a subject in which we are interested. But, the onus is on the purchaser, the city of Verdun, to make sure that the paint supplied meets the particular standard. The city uses the services of Wernock Hersey or other independent companies in this respect.

Mr. MORRELL: Yes, that is true.

Mr. MACKASEY: And, the government simply sets up the standard.

Mr. MORRELL: Yes.

Mr. MACKASEY: Specifications are put forward in the tenders which are sent out to those interested in meeting these standards. But, as I said, it is up to the city to decide whether or not the paint they bought lives up to those standards.

Mr. MORRELL: My impression is that the same applies in respect of the American Bureau of Standards. If they set up a standard they do not enforce it; it is there for those who want to use it and, therefore, the purchaser is responsible for seeing the material he gets does meet the specifications that are laid down.

Mr. SLOGAN: I think a good deal of this comes down to the practice of labelling. But, they probably figure they are giving away trade secrets if they

set forth the formula and say this meets certain specifications or certain pharmacopoeia. But, if this were the case, I think the professions would be in a better position, at least the pharmacists, to judge these products.

Mr. MORRELL: If it is a pharmacopoeial drug in any of these pharmacopoeia it should have on there U.S.P., B.P., French Codex, British Pharmaceutical Codex, and so on. It should have on there, as I said, such and such a drug, U.S.P., or whatever it is.

Mr. SLOGAN: It should have its generic name?

Mr. MORRELL: Yes, on the label. As you know, a great many drugs are not official drugs. We call those drugs that are in the pharmacopoeia official drugs. But, so many new drugs which are being developed have not yet been placed in the pharmacopoeia and a great many do not get in there. Therefore, the only standard really that is available is the standard of the manufacturer, and he has to put the composition on the label. We check it to see that it meets that standard which he claims for it. We check it to see that it meets the composition claimed for it; that is, the manufacturer's own standard. I know it sounds very confusing, but this is the situation which exists.

Mr. SLOGAN: I think I am getting the clear picture, but I believe it still points out the necessity for a certain amount of policing, because if the form and composition are the same, the quality not necessarily is the same.

Mr. MORRELL: In the art or the science of this, we can learn a great deal more about the constituents which go into the drugs; they are not altogether inert. As you say, policing is very good. That is the job we try to do.

Mr. MACKASEY: In respect of drugs being brought into the country which are packaged for sale to consumers, are there any policing methods through the customs branch to make sure that not only is the country of origin specified, but also the ingredients?

Mr. MORRELL: If a drug is brought in, packaged and ready for sale, we have an opoprtunity to see it at the customs, and we do take samples there and hold it for testing; or we can let it go through customs and go to the distributor. There will be a distributor in this country. We can take samples for testing there and, of course, the label is examined at the time the drug is tested. This is part of our program. I cannot say we get every drug which comes in, but I think we get a fair sampling of them. We are trying very hard to increase the number of samples we take, particularly of the imported drugs.

Mr. MACKASEY: You are talking about a sampling of the quality of the drug.

Mr. MORRELL: Yes; the composition, the physiological availability, the disintegration time of the tablet—if it is a tablet—and the labelling of it. These are things we do examine against certain methods we have in our own laboratory.

Mr. MACKASEY: Quite often products in other fields are stopped at the border because the producer forgot to label it with the country of origin.

Mr. MORRELL: We want the country of origin; that is part of the law. It must be on the label.

Mr. MACKASEY: Do the normal customs officers realize the importance of this to the point that they will stop drugs as well as anything else?

Mr. MORRELL: Yes; I think so. We do not have a food and drug inspector at every customs port. I am not sure how many there are, but there are hundreds of ports, I believe. We do have an arrangement with the customs officers that when a shipment of drugs comes in they notify our nearest

inspector who goes out and looks at them. We do have our own inspectors at the largest ports who go right down and look at the manifests, and so on, and take samples at the port of entry.

Mr. HOWE (*Hamilton South*): Dr. Morrell, earlier you said that some drugs never get into the pharmacopoeia at all?

Mr. MORRELL: Yes.

Mr. HOWE (*Hamilton South*): What is the criterion which determines what drug gets in and why some never are entered? Is this not sort of a running inventory of drugs?

Mr. MORRELL: The pharmacopoeias are books published usually every five years; they may have interim revision. That is one difficulty. A drug may appear just after, let us say, the United States Pharmacopoeia latest edition has appeared and, of course, it is not in there. The choice of drugs for the pharmacopoeias, whether U.S.P. or B.P., depends on the opinion of the Pharmacopoeia Commission—and there is one in all countries which have pharmacopoeias. They decide whether the drug has been in use sufficient time to establish its value before they will consider it for the pharmacopoeia. It may be that in some countries a drug is patented, and therefore is manufactured only by one company. I think this would have an influence on the decision with regard to whether or not they would put that drug in the pharmacopoeia. Where there are a number of manufacturers making the same drug, it is rather important, I think, that they have a common standard. That is when they consider them for the pharmacopoeias.

However, a drug actually may appear on the market, be in use for two or three years, and disappear again, or become of much less importance because of some new drug that comes along. We all read about this and it is a fact. Therefore, a good many drugs do not get into the pharmacopoeia at all.

Mr. MACKASEY: Is it possible that a drug which is in common usage could never get into the pharmacopoeia for some standard reason although it is being used; or do you mean drugs which would go out of usage in the five year period?

Mr. MORRELL: They might go out of usage in the five year period, or become less important because of another compound which has been introduced which is better and more acceptable.

Mr. MACKASEY: Thank you.

Mr. RYNARD: I believe some of the older and reliable drug firms have research staffs which are exceedingly adequate in developing new drugs. Their research laboratories probably are as good as any of the government laboratories. I am wondering whether perhaps there could be a reference to their research facilities, rather than a check on the drug coming across the border. I am thinking of some of the older firms such as Pfizer or Ciba, and some others who do develop new drugs and who have very splendid research facilities. Would it not, therefore, be reasonable to assume that their research work could be accepted in the passing of a drug, and that it would only be the newer ones that would have to be researched? I am wondering why we should not be setting up research facilities in our universities that would check these and also in the departments of the pharmacopoeias.

Mr. MORRELL: I am not quite sure that I have your question. Is it your suggestion that in respect of a new drug— and I take it you mean from Pfizer, or some company of that calibre—we should accept their say so with regard to the safety and efficacy of that new drug.

Mr. RYNARD: I would think that if you looked over the material used and the work done by their competent chemists, that this could be your criteria for acceptance.

Mr. MORRELL: Let us take a hypothetical drug from Pfizer. They will collect all of the information which they have gathered in respect of that new drug, such as the manufacturing procedures, the control procedures, the pharmacology, the toxicology in animals, the pharmacology in animals, the clinical testing, and the composition of the drug right down to the last detail, and they will send this to us as a New Drug Submission. Contained in this is the work of a great many persons; not only those employed directly by Pfizer's plant, wherever it might be, but also persons they have hired, or persons who may have become interested, and who may not even have been paid. The clinical testers or investigators—and there may be dozens or 100 of them—have tried the drug on patients and have made their reports to Pfizer in detail.

We do not want just a testimonial, such as "I tried this drug on six patients and it was excellent". That is of no value to us at all. We want to know what the condition of the patient was, and we want to know his case history. This is what comes to us in the form of a New Drug Submission, and this is what we demand of every new drug, no matter by whom it is manufactured, whether it be Pfizer or a small company. Small companies are sometimes hard put to get the information because it does cost some money.

Nevertheless, in the interests of safety we have to see that they do the same things that the large companies do. But we do know, or our people in the laboratory and in administration do know a great many of these research people from Pfizer and other companies, personally. They know their value, qualifications, and so on. But we do not feel that we can just take a letter from, for example, Pfizer, saying "We have tested this new drug and have found it satisfactory. Therefore, will you agree that it should be sold in Canada?"

We cannot accept that kind of thing. The law demands certain information and we have to say this to Pfizer or to whomever it may be. With the New Drug Submission in one hand and with the law in the other hand, we have to see that all the information demanded by the law is furnished in adequate amount and in adequate quality. And then when we see something missing, or doubtful, or if there is a question in our minds as to what it means, a letter goes back asking for an explanation or for further material or data.

Mr. RYNARD: Once you have passed a drug, it ceases to be a new drug any more.

Mr. MORRELL: It is still a new drug. Again, this is a little difficult to follow. But when we receive a New Drug Submission we write a form letter to the manufacturer saying that we have examined the New Drug Submission. Let us say it is drug "A" manufactured by you, and we find that it complies with the section 308, and so and so. This is notice to the manufacturer that he is at liberty to market that new drug. It is still a new drug because, as you well know,—I am thinking of a certain drug that we talked about yesterday—there is a great deal of evidence which comes out about a new drug even after it has been on the market and used by dozens of doctors upon millions of patients. This is evidence which you cannot have with a New Drug Submission. So it is still a new drug for years after it goes on the market. New things will turn up that never appeared before in connection with the 2,000 to 5,000 patients it was used upon for test purposes. You will get other circumstances.

Mr. RYNARD: Therefore the real test is the clinical trial when it gets out to the doctors and into the hands of the public.

Mr. MORRELL: Finally, I think that is the ultimate test.

Mr. RYNARD: Why should we not have a reference of these drugs to a committee that is in charge, let us say, of university facilities across Canada,

and why not have the research done there where you can have it right at the clinical laboratory?

Mr. MORRELL: You mean that they should do the research and clinical investigation with the drug?

Mr. RYNARD: Yes, why should they not carry the drug through at the clinical level?

Mr. MORRELL: This is done in a measure, but as you know, the people and the facilities willing and available to do these clinical trials are not too numerous in Canada.

Mr. RYNARD: I was thinking of this point, that we lose a great many scientists every year across the border.

Mr. MORRELL: That is right.

Mr. RYNARD: I think we should put those people to work on the things we are talking about this morning; that is, to do research on these drugs in our universities and hospitals.

Mr. MORRELL: Yes, if they want to do it. But you cannot make them do it if they are not interested.

Mr. RYNARD: I know, but you are training young doctors and you have your research facilities and you have them right at the cross-road where they have to be tried, and moreover you have the patients right there and you can evaluate the effects of these drugs.

Mr. MORRELL: I think this is going on in Canada. We have done our best to encourage clinical trials in Canada. We cannot insist on it, or we would never have new drugs, because there are not enough people to do the clinical trials.

Mr. RYNARD: The answer would seem to be to get more research.

Mr. MORRELL: Yes, more and more and more. I think that in 10 to 20 years you will have a lot, but not yet.

Mr. CÔTÉ (*Longueuil*): Mr. Chairman, I wish to apologize for not having been able to attend the former meetings. I have just returned from hospital and I still suffer from dizzy spells from the anaesthesia. I do not know if it is normal, but I shall ask a few doctors here after the meeting. I want to know if an application was brought up concerning anablast, the serum to be used by Mr. Naessens? Was that brought up in this committee?

Mr. MORRELL: No.

Mr. CÔTÉ (*Longueuil*): There was somewhat of a problem. I wonder whose responsibility it is to see that permission is given? I am thinking of the case brought up by Mr. Naessens, who came to Canada to inject anablast upon a young fellow who was suffering from leukemia. The College of Physicians and Surgeons of the province of Quebec gave permission, but did he not come here first to the department, and did the department not say it was not their responsibility? Was this not in the same line that we have been talking about.

Mr. MORRELL: I was not in the country at the time, but I did hear of a meeting. I think Dr. Pugsley was there. He can check me if I am not giving the correct interpretation. They met in the office of our deputy minister and two questions were asked of the deputy minister. The first question, I think, was asked by the father of the child: "Will you permit this drug to be given to my son?" I think that was it, and Dr. Cameron said: "I have no comment, because I have no authority either to forbid or to interfere in any way with medical practices, or with what the doctor gives to your son. That is his business, and also the business perhaps of the College of Physicians and Surgeons of the province of Quebec". Then Mr. Naessens asked: "Will you

permit me to sell the drug?" And Dr. Cameron, I believe, said: "You can sell the drug only under the terms of the new drugs regulations and the Food and Drugs Act and Regulations. That is where this department takes a stand and an interest. It is a new drug in this country and it must meet the requirements of all new drugs, including clinical trials."

That is my understanding. Is it correct, Dr. Pugsley?

Mr. PUGSLEY: That is right.

Mr. MORRELL: That is, in essence, what was said.

Mr. CÔTÉ (*Longueuil*): Mr. Naessens went there with the father of the boy?

Mr. MORRELL: I think so, yes.

Mr. CÔTÉ (*Longueuil*): They asked the deputy minister if they could use anablast?

Mr. MORRELL: Yes.

Mr. CÔTÉ (*Longueuil*): The deputy minister said that he could use it if he had permission.

Mr. MORRELL: I do not think he put it that way. I think he said that the federal government could not interfere with what a doctor gives to a patient, because it was a matter of his own business, his knowledge, competence, conscience, and was perhaps also a matter for the Quebec College of Physicians and Surgeons, but that it was not a matter for the federal Department of National Health.

The second question related to the sale of this drug and whether it was a matter for the federal Department of National Health under the Food and Drugs Act. I must say we have very specific regulations about the introduction of new drugs into Canada. There were these two aspects involved.

Mr. CÔTÉ (*Longueuil*): You only have legislation covering the sale of drugs but not the introduction of them?

Mr. MORRELL: The act refers to sales.

Mr. CÔTÉ (*Longueuil*): Then a doctor could use a drug if he brought it into the country from another country?

Mr. MORRELL: Yes. If he could make it up in his own laboratory he could use it on his own patients only; that would be permissible because that is his business.

Mr. CÔTÉ (*Longueuil*): He could do that if he made the drug himself?

Mr. MORRELL: Yes. Doctors at one time compounded drugs, and I suppose they still can if they wish, for use on any of their patients, when they think it is going to be of benefit.

Mr. CÔTÉ (*Longueuil*): Do you consider that the doctor himself is selling that drug to his patient under those circumstances?

Mr. MORRELL: I do not think so. I think that is part of the treatment.

Mr. HOWE (*Hamilton South*): Dr. Morrell, at what stage is a new drug allowed to be introduced into a hospital for clinical trial purposes? That drug is not being sold. You have established no regulation in this regard and a manufacturer could put a new drug into a hospital free, allowing it to be used; is that right?

Mr. MORRELL: No. First of all the word "sell" is defined in the act to include distribute. "Sell" means "to have in possession for sale, to offer for sale, to expose for sale, to sell and to distribute", and that covers the situation of giving it away. A manufacturer cannot get the drug through under this regulation by giving it to a hospital free.

Secondly, before the manufacturer can put a drug out for clinical trial there must be a submission, which we call a Preclinical Submission. The manufacturer must send us all the information he has about the pharmacology, toxicology and manufacturing process as well as the trial procedure that the manufacturer is going to use. We must also know the composition of the drug. We look at that information and decide whether it is adequate or not.

There is one other aspect involved. The manufacturer must supply the clinical investigator with a good deal of this information because the clinical investigator is after all going to take the risk of putting that for the first time into a human being and he must know certain things and whether certain things have been done or not. That individual must know something about the pharmacology. He wants to know what kind of reaction to expect, as far as that can be known and predicted from the results of animal tests. All this information must be given to the clinical investigator when he is asked to try out a new drug. The manufacturer must also assure himself that the clinical investigator has the facilities for properly carrying out such a trial. This is necessary when a manufacturer is introducing a new drug for the first time into clinical trials in this country. This is also true of the United States and some other countries including the United Kingdom.

Mr. HOWE (*Hamilton South*): Then there is sort of a two stage sale process involved?

Mr. MORRELL: There is a two stage process involved, yes.

Mr. HOWE (*Hamilton South*): The definition of the word "sale" does cover the use of new drugs in clinical trial tests, and a new drug can be used in this way provided it meets your requirements; is that right?

Mr. MORRELL: Yes. We consider that marketing, as it were.

Mr. WILLOUGHBY: Mr. Chairman, I should like to ask Dr. Morrell whether investigations that have been carried out in reliable countries such as Great Britain and the United States in respect of certain drugs are acceptable to our department when the new drugs are introduced into Canada? As an example I have in mind penicillin which came from Great Britain? De we insist on trial investigations in Canada to verify the value of such a drug?

Mr. MORRELL: I think penicillin was introduced in 1942, before we had the new drugs regulations.

Mr. WILLOUGHBY: If that situation developed today would we have to wait indefinitely until our Canadian trials were carried out?

Mr. MORRELL: We would not have to wait for our Canadian trials in that event. We would have to wait, however, until the person who promoted the drug or the manufacturer of the drug had submitted to us whatever information he had available and we examined it. This would be a New Drug Submission which we examine as we do all other New Drug Submissions in order to find out whether it is satisfactory or unsatisfactory. If we found that the tests were not adequate we would have to inform the promoter, and it is our duty to do so, that it is lacking in this regard or in that regard.

Mr. WILLOUGHBY: If these drugs were recognized as being efficient by, for example, the United States government inspection system and the United States medical association investigators, would we still have to wait until the drug is tested before it is allowed into Canada?

Mr. MORRELL: I think the answer is yes, with the following explanation. The drug does not have to go through clinical trials in Canada. These trials have been carried out in the United States, but we do want to see the results of those clinical trials ourselves and examine them.

I was in the United Kingdom recently. If a drug is accepted in Canada do not think for one minute that it will be accepted in the United Kingdom holus-bolus. It would not be accepted on that basis in the United States either. The same situation exists in every country which was a law of this kind. These countries are all enforcing such laws. The drugs are scrutinized very thoroughly in the United States by the authorities and in every other country in which the new drug is introduced. There is that delay involved but the clinical trials, chemical tests and animal tests do not have to be repeated as long as the records of those tests with the results are available.

Mr. RYNARD: Perhaps I could ask a supplementary question to those asked by Dr. Willoughby. I think I understand what Dr. Willoughby had in mind. Following clinical trials, would it not be feasible from the standpoint of a standing committee of doctors to allow them to pass that drug rather than have it examined and authorized by the pharmacology department?

Mr. MORRELL: Are you referring to the Food and Drug people?

Mr. RYNARD: Yes.

Mr. MORRELL: The law does not say that, Dr. Rynard.

Mr. RYNARD: I think the suggestion was that a standing committee be set up for that purpose, I think Dr. Willoughby is suggesting that we waste a lot of time before being able to use a beneficial drug. I have in mind particular drugs in respect of which we lost a good deal of time before being able to use them. The drugs which I had in mind are thyracil, propyl-thyracil as well as penicillin. These were held up for months and months after trials had been held. This delay could well be indefinite.

Mr. MORRELL: Are you sure, Dr. Rynard, that they asked for the sale of it in this country at the same time as they asked for sale in the United States? I doubt it very much.

Mr. RYNARD: I got it from your department. I got it from New York. That is thyracil, the anti-thyroid drug. Then they developed propyl-thyracil, and so on. Mr. Willoughby has a very good point here. If it has been tried, then the group of clinicians should pass on it.

Mr. MORRELL: I think the group of clinicians would do the same as we do.

Mr. WILLOUGHBY: Would there be any restrictions on a drug in a case in which a specific medical man in this country had information and thought that drug was something he needed for a patient? Would there be any restriction on his importing that drug and using it?

Mr. MORRELL: We have often given permission for a doctor to import a new drug for use on a particular patient that is not otherwise distributed in this country.

Mr. SLOGAN: Does he have to get permission?

Mr. MORRELL: If he writes to us—and he often does—we do give permission. Sometimes they do not write to us and we do not know.

Mr. ENNS: The question I was going to ask was a follow up of Mr. Willoughby's in the area of a new drug, but this has now been dealt with in supplementary questions.

I have another question arising out of your reply to Mr. Côté about the use by an individual practitioner of drugs strictly for his own patients without any sale involved. This could, in a clinical situation, also involve drugs on schedule H, whether now or in the future? Am I right?

Mr. MORRELL: I presume it could. Again, I go back to our law which says that no person shall sell any of the drugs mentioned in schedule H. So a sale is the point at which we intervene. If a doctor has a drug in his desk that he has bought a long time ago or of which he has somehow obtained possession

and he wants to use it on a patient, we do not interfere. But if there is a sale made, we do not prosecute the doctor, we prosecute the person who makes the sale because "no person shall sell" is the wording of the act and the regulation.

Mr. ENNS: You are still always saying, "We are not interfering with medical practice as such"?

Mr. MORRELL: Yes.

Mr. CÔTÉ (*Longueuil*): There are many doctors who sell drugs.

Mr. MORRELL: They are acting as pharmacists then and we treat them as pharmacists.

Mr. CÔTÉ (*Longueuil*): They should be treated as pharmacists, I think.

Mr. MORRELL: When they sell drugs to people other than patients, people who come in and ask for the drug—

Mr. CÔTÉ (*Longueuil*): No, I mean to patients.

Mr. MORRELL: I am sure they charge for the drug but the charge is included in the fee, and I think it has always been a doctor's privilege to administer drugs to patients. I am sure he always includes that in his fee.

Mr. CÔTÉ (*Longueuil*): There is a bill which the pharmacists are trying to put through in Quebec right now. They want all drugs in Quebec to be sold through pharmacies. In Quebec some doctors sell drugs, and they are also sold in groceries and so on. The pharmacists are saying that most of the drugs are sold outside of pharmacies.

Mr. MORRELL: More than half the drugs are sold in places other than pharmacies?

Mr. CÔTÉ (*Longueuil*): Yes. So there is quite a fight going on in Quebec about that. The pharmacists say a lot of doctors sell drugs in their offices.

Mr. MORRELL: I know a number of doctors who operate pharmacies in connection with their practice, but those are operated as pharmacies, I think.

Mr. SLOGAN: You are thinking of patent medicines, are you, when you say drugs?

Mr. CÔTÉ (*Longueuil*): Yes. They do this a great deal in the country because there are no pharmacies in some of the rural districts.

The CHAIRMAN: Have you something to say, Dr. Pugsley? Mr. Allmark?

Mr. PUGSLEY: Maybe Mr. Allmark has something to add.

Mr. ALLMARK: I have a copy of bill 96 in my hand. This is a bill of which, I believe, certain sections were not acceptable to the Quebec legislature. The section dealing with the sale of drugs by doctors is one in particular to which I believe they did not agree.

Mr. CÔTÉ (*Longueuil*): And in grocery stores.

Mr. ALLMARK: The sale of drugs in certain department stores; they did not go along with that.

Mr. ENNS: And patent medicines?

Mr. ALLMARK: Yes. The pharmacists wanted exclusive sale by drug stores for this type of medicine, but this was not acceptable to the legislature.

Mr. CÔTÉ (*Lougueuil*): It is not accepted. It did not go through.

Mr. ALLMARK: No.

Mr. CÔTÉ (*Longueuil*): So they will still be selling drugs everywhere.

The CHAIRMAN: Are there any other questions, gentlemen?

If, as Chairman, I may ask a question or two there are some matters upon which I would like clarification. These questions refer to the questioning at the last committee.

At the present time in the department we talk about control and the tests the department is making. It is my understanding that the tests you are making are quantitative rather than qualitative. I am just wondering what is the percentage of the different kinds of tests. I am thinking, for example, of a certain drug reputed to contain 400 milligrams of an active substance. Do you test this drug to measure the quantity it contains? Do you actually also find out whether it is soluble in the human body so that it is actually for use by humans? Is there any way in which you can test this?

Mr. MORRELL: The answer to the first question is that the majority of our tests are quantitative, and in the case you cited it certainly would be quantitative. We would be looking to determine whether there are actually 400 milligrams of that substance in that dosage form, either tablet or capsule; so it would be quantitative.

There are some qualitative tests that we undertake, particularly under the Opium and Narcotic Drug Act. A mounted policeman, for example, may bring in to us a sample and ask whether it is or is not a narcotic drug; or a mounted policeman, or some other person, may bring in a controlled drug—that is, a barbiturate or an amphetamine—and want to know whether it is a barbiturate or whether it is an amphetamine because this information will be used in the charge against the seller. However, the majority of our tests are quantitative, because this is the important thing in the general pharmaceutical area.

In regard to whether the product will be available, I would say that we have some tests that are put down in the regulations covering this area. For example, a product that is put out in tablet form must disintegrate in the laboratory test. The laboratory test consists of agitating the tablets in simulated gastric juice for a certain time and in simulated intestinal juice for a certain time. The tablets must disintegrate or, in other words, break up into very small particles. We have found tablets—and this is a fact—that, when taken by mouth, pass entirely through the intestinal tract with very little change. In other words, if one analyses that tablet one might find that it contained 400 milligrams but that it went in at one end and came out at the other without being of any particular value to the patient. So the answer is that we do have these tests which are set up to determine the disintegration time of tablets, and the disintegration time that we have in our regulations has been correlated with physiological availability. We have done this by feeding people certain tablets and examining the excreta of the product in comparison with a standard intake to make sure they excrete the same amount as they would if the tablet were totally available.

So that in the laboratories the disintegration time has been correlated with the actual physiological human experiments and we know that they are of some value. There are many other factors that are still being investigated such as the size and crystalline structure of the active ingredient. We believe that they may have an effect on the availability to the patient. It is not only the disintegration of the tablet that is important although that also is of first importance, but we are looking further into the crystalline structure and other physical characteristics of the product and of the dosage form. So that in the future we will perhaps have additional tests to demonstrate the physiological availability.

The CHAIRMAN: Thank you, Dr. Morrell. I have one other question which I should like to put to you. I suppose anyone here would not be classed as a manufacturer according to your regulations. For instance, if I made a drug in my basement and only gave it to my patients and did not actually sell it, what would happen?

Mr. MORRELL: As you are a doctor you would not be considered a manufacturer if you compounded your own drugs and administered them only to your own patients.

The CHAIRMAN: To come back to the point someone else brought up, if I was a clever enough chemist so that I was able to manufacture thalidomide in my own basement and give it to my own patients despite schedule H, what would the situation then be?

Mr. MORRELL: You could do that as far as the law is concerned.

Mr. CÔTÉ (*Longueuil*): I have a supplementary question. Suppose a doctor was making his own drugs and made his own alcohol. Could he sell it?

Mr. MORRELL: Again, is this not a question for the College of Physicians?

The CHAIRMAN: Gentlemen, it is a few minutes to eleven. There are a few other questions I would like to ask Dr. Morrell and I am sure other members of the committee will have questions for him also. This would probably be a convenient time to adjourn the meeting.

I would like to bring to the committee's attention that it has been officially announced that U Thant will address the House of Commons on Tuesday morning at 10 o'clock. We have a meeting slated for 9:30 on that morning. It has been suggested that committee meetings be cancelled for that morning. As we are going to be in Montreal next Thursday and Friday I think it might be reasonable to cancel next Tuesday's meeting completely. We will have our trip to Montreal. On June 2, and on June 5 we will be having as our witnesses the Canadian Medical Association and the Canadian Pharmaceutical Association. Perhaps the day after that Dr. Morrell could come back and he might answer any questions that might have been brought to our attention by our trip to the manufacturing companies, by the C.M.A. and by the Pharmaceutical Association.

Mr. ENNS: I feel that next week is going to be a full enough week.

The CHAIRMAN: Would it be convenient to you, Dr. Morrell, to come back on Tuesday, June 9? This would give you a bit of a rest.

Mr. MORRELL: Yes, certainly.

Mr. RYNARD: This is off the record, Dr. Morrell, but I understand LSD got away from you in Vancouver.

Mr. MORRELL: That happened before our regulation was passed. These legal cases take a long time. I happen to know about that case. I went down to the United States Food and Drug offices in San Francisco last year about this time and they were just beginning to gather their information about this individual. They visited our Vancouver laboratory, and the mounted police in the Vancouver area gathered some information. This was well over a year ago.

The CHAIRMAN: The meeting is adjourned.

HOUSE OF COMMONS

Second Session—Twenty-Sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 3

THURSDAY, MAY 28, 1964
and
FRIDAY, MAY 29, 1964
(Sittings in Montreal)

TUESDAY, JUNE 2, 1964

WITNESSES:

Representing The Canadian Medical Association: Dr. Donald L. McNeil, M.D., of Calgary, Chairman of the Committee on Pharmacy of the C.M.A., Member of the Drug Advisory Committee, Department of National Health and Welfare, and President-Elect of the Alberta Division of the C.M.A.; Dr. K. J. R. Wightman, Professor of Medicine, University of Toronto; and Dr. A. D. Kelly, General Secretary of the C.M.A., Toronto.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

20800—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Casselman (Mrs.)
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jorgenson
Macaluso
Mackasey
Marcoux
Nesbitt
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

THURSDAY, May 28, 1964
(5)

The following members of the Special Committee on Food and Drugs proceeded by train to Montreal at 7.40 a.m. EDT: Messrs. Harley, Asselin (*Richmond-Wolfe*), Côté (*Longueuil*), Enns, Howe (*Hamilton South*), Mackasey, Marcoux, Mitchell, Prud'homme, Rynard, Whelan, and Willoughby (12).

They were met at Dorval Station by Mr. E. Glyde Gregory, President of Ayerst, McKenna & Harrison Limited, and departed for Mount Royal Chemicals Limited, the manufacturing unit for CIBA and Sandoz (Swiss-Canadian pharmaceutical companies).

Mr. Roger Larose, President of Mount Royal Chemicals Limited, welcomed the group and made introductory remarks relating to the said company. (*See Appendix "A"*)

The Committee then toured the manufacturing laboratory facilities under the guidance of pharmacists employed by the Company.

On behalf of the Committee, the Chairman thanked the President and the officer of Mount Royal Chemicals Limited for the assistance they had given to the Committee.

At 1.45 p.m. the Committee proceeded to the laboratories of Charles E. Frosst & Company where they were welcomed by Mr. John B. Frosst, President. (*See Appendix "B"*)

Mr. Earl Dechêne, the Company's chief control chemist, using charts, explained the verification procedure in relation to Food and Drug Schedule 33. He, Mr. John B. Frosst and Mr. James B. Frosst answered questions about integrity in relation to safety factor, and related matters.

A tour of the laboratories to study production methods and "in plant" quality control was provided for Members, including a visit of the radioactive laboratory, the only one of its kind in Canada.

Dr. John F. Millar, Chief Research Pharmacist, briefed the Members on Pharmacy Research; the text of his remarks is printed as *Appendix "C"*.

At the conclusion of the tour, questions were asked about production cost, money spent on research, price of drugs, and on the pharmaceutical industry in general. Mr. John B. Frosst, Mr. James B. Frosst, Mr. James M. Blanch, Dr. Millar and Dr. Lozinski supplied information.

A suggestion was made by Mr. A. Coffin, General Sales Manager, that licensing should be standard across the country.

On behalf of the committee, the Chairman thanked the officers and the scientists of the Company for their courtesy and assistance, and at 5.15 p.m. the Committee adjourned to 9.30 a.m. Friday, May 29.

20800—1½

FRIDAY, May 29, 1964
(6)

The following members of the Special Committee on Food and Drugs left the Queen Elizabeth Hotel at 9.30 a.m. for the Clinical Investigation Unit at the Hôtel-Dieu Hospital: Messrs. Côté (*Longueuil*), Enns, Harley, Howe (*Hamilton South*), Mackasey, Marcoux, Mitchell, Prud'homme, Whelan, Willoughby (10).

Dr. Jacques Laramée, Medical Director of the Hospital, welcomed the Members and expressed his appreciation of their decision to see for themselves the research being done on new drugs for the promotion of health and research.

Dr. Jacques Genest, Director of the Clinical Research Laboratory, addressed the Committee and stressed the need for more research in Canada; he explained the set up of the clinical research department which has known tremendous growth, specially in the field of radioactive isotopes, electronics, instrumentation, micro-methods of measurement, biopsies, and molecular and cellular biology.

Dr. Genest also explained the research being made in his laboratory in the field of hypertension, and discussed the need of more money for the prograss of medicine in Canada. More money is needed for research better facilities; better clinical investigation wards are also required, he stated. He made available to the members two papers, in English and French, "Symposium on Clinical Research in Canada", January 17, 1962, and "L'importance de la recherche clinique pour la santé".

A complete tour of the various laboratories and sections was provided for Members, and they were given the opportunity of questioning Dr. Genest, more particularly about the need for better facilities and grants for research.

At noon the Committee recessed for luncheon.

At 1.45 p.m. the Members departed for the laboratories of Ayerst, McKenna & Harrison Limited. They were briefed by Mr. E. Glyde Gregory, President, Dr. Roger Gaudry, Director of Research, and Dr. Arthur Dr. Grieve, Director of Quality Control, and taken on a tour of the chemical, biological and quality control laboratories and pilot plant.

The Chairman thanked Mr. Gregory and the personnel of the Company for their assistance and for the courtesy extended to the Members of the Committee during their visit to Montreal.

At 5.00 p.m. the Committee adjourned to 9.30 a.m. Tuesday, June 2, in Ottawa.

Gabrielle Savard,
Clerk of the Committee.

TUESDAY, June 2, 1964.
(7)

The Special Committee on Food and Drugs met at 9.40 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Côté (*Longueuil*), Harley, Howe (*Hamilton South*), Mackasey, Marcoux, Mitchell, Orlikow, Slogan, Whelan, and Willoughby. (11)

In attendance: Representing the Canadian Medical Association: Dr. Donald L. McNeil of Calgary, Chairman of the Committee on Pharmacy of the C.M.A., member of the Drug Advisory Committee, Department of National Health and Welfare, and President-Elect of the Alberta Division of the C.M.A.; Dr. K. J. R. Wightman, Professor of Medicine, University of Toronto; and Dr. A. D. Kelly, General Secretary, Toronto.

The Chairman read a letter from Cyanamid of Canada Limited, dated May 22, 1964 and presented the second report of the Steering Subcommittee.

After discussion, on motion of Mr. Mackasey, seconded by Mr. Willoughby, the Second Report of the Steering Subcommittee (*see evidence on page 53*) was adopted on the following division: Yeas, 9; Nays, 1.

The Chairman introduced the representatives of the Canadian Medical Association.

It was agreed that the brief which had been distributed to the Members in advance, be taken as read up to the Summary at the conclusion of the submission.

Dr. McNeil read the Summary and was questioned thereon. He was assisted by Dr. Wightman and Dr. Kelly.

Questioning concluded, on behalf of the Committee the Chairman thanked the members of the C.M.A. for their expert information on behalf of their Association.

It was *agreed*, at the suggestion of the Chairman, that instead of having Dr. Morrell and his officials appear before the Committee on June 9th as scheduled, the Committee go to visit the Food and Drug Directorate at Tunney's Pasture on that date.

On motion of Mr. Orlikow, seconded by Mr. Marcoux,

Resolved—That this Committee pay reasonable living and travelling expenses incurred by Dr. Donald L. McNeil, Dr. K. J. R. Wightman and Dr. Kelly by reason of their appearance before this Committee; and that a per diem allowance be made to them.

At 11.50 a.m. the Committee adjourned to 9.30 a.m. Friday, June 5.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

TUESDAY, June 2, 1964.

The CHAIRMAN: Gentlemen I see a quorum and we will start the meeting now, please.

I should first of all like to read a letter to the committee which I have received from the Cyanamid of Canada Limited. The letter reads as follows:

> On behalf of our Company, I have a proposal to make that I suggest should be helpful to your committee's study on the safety of drugs. The proposal is in two parts, each having direct bearing on the other.
>
> 1. That the members of your committee accept the invitation of Cyanamid of Canada Limited to spend one day at the Lederle Research Laboratories at Pearl River, N.Y. Cyanamid will provide private planes owned by our parent Company to fly your group from Ottawa to Pearl River on Tuesday, July 7, and return them to Ottawa that same evening. The facilities of our parent Company for medical research are among the largest in the world and your members would, without doubt, derive great benefit as well as good information from extremely competent personnel who would be made available.
>
> 2. Cyanamid of Canada is willing to assist your Committee by way of the preparation of a brief dealing with the safety of drugs and to submit it in both English and French. We would be prepared to appear before your Committee on July 10 to answer questions relative to the brief. We believe that our appearance before your Committee would have more meaning if it were on a date immediately following the visit to Pearl River. In addition to representatives of Cyanamid of Canada Limited, we are prepared to invite senior personnel from American Cyanamid Company to appear with us and suggest such people as Dr. Kitchfield, Director of Medical Research, and one or two others of equal stature in their specified fields as they apply to the subject under discussion.

We are most anxious to assist your Committee to reach reasonable conclusions on this important subject, and are prepared to make every effort to help you.

The CHAIRMAN: That is the correspondence I have received, gentlemen.

In keeping with that correspondence, we had a meeting of the steering committee on Wednesday, May 27, in my office which was attended by Dr. Rynard Dr. Howe, Dr. Marcoux, Mr. Mitchell and myself. We discussed the agenda and your steering committee agreed to present the following as its second report.

Your steering subcommittee recommends that the committee accept the invitation of Cyanamid of Canada Limited to visit the Lederle Research Laboratories at Pearl River, New York, provided that the House of Commons is in session at that date.

Mr. MACKASEY: What day of the week is that, Mr. Chairman?

The CHAIRMAN: July 7 is a Tuesday and the company would present a brief here on the following Friday, July 10. This arrangement is, of course,

subject to the House of Commons being in session. If the House of Commons is not in session at that time we will not make the visit. Is there any discussion in this regard? This is a one day trip. We would go down in the morning and come back in the evening.

Mr. MACKASEY: Do you wish a motion to accept the steering committee's report?

The CHAIRMAN: Yes.

Mr. MACKASEY: I so move.

Mr. WILLOUGHBY: I second the motion.

Mr. ORLIKOW: I must admit that this is the first I have heard about this suggestion and I do not want to be too critical of the offer made by this company or the steering committee's recommendation to accept, but speaking personally I am not too happy with the suggestion that the committee members make a trip at the expense of that company. One of the biggest problems which faces us in this respect is the possible conflict of interest between what is good for a company and what is good for us. As far as I am personally concerned, I am not happy about the suggestion that we make a trip at the expense of any company. If it is worth while our making a trip at all, then let us make the trip and let us request the committee itself to find the funds to pay for the trip. I am not in favour of accepting this offer.

Mr. MACKASEY: I agree in principle with Mr. Orlikow. If the funds are available I would agree with his suggestion. My remarks, of course, are not intended as any reflection upon Mr. Orlikow. I think we should try to get some objective information. We travelled to Montreal last week and I was quite impressed with the impartiality with which the tour was conducted by the sponsors. On this committee I am labouring under a certain difficulty in that I am neither a pharmacist nor a doctor, and I must seek information as I go along. I found the tour of great benefit to me.

I have enough confidence in my own integrity to go down at the expense of Cyanamid and to come back and take a completely objective view in any deliberations.

Mr. WILLOUGHBY: I feel, Mr. Chairman, much the same way, since this is purely a trip for observing the work of this company. I do not think we are under any obligation to them to commit ourselves because the expenses of our trip happen to be paid by this company. I feel we are certainly free to express our own opinions when we get back, and I concur in the comment that in the trip we had to Montreal there was no pressure brought to bear upon us; we were perfectly free to come to our own conclusions. The same thing can happen here. If we do not take advantage of these things when they are offered to us, I do not see how we can sit here and listen to briefs in regard to the method by which these products are produced and understand them thoroughly. I feel we should take up this offer and thereby improve our understanding of the problem.

The CHAIRMAN: I think Mr. Orlikow's point is that the two trips are a little different in their circumstances in that we did pay our own transportation and looked after our own accommodation on our previous trip; this time we would not be doing so.

Mr. ORLIKOW: I would not want to suggest that taking a trip as proposed would obligate the members. I am certain the members would not feel obligated. At the same time, this committee will probably be making a report at some future date which will deal with some rather controversial proposals. We have a brief today, for example, from the Canadian Medical Association in which they reject one of the key recommendations made by the Restrictive Trade Practices Commission with regard to patenting of drugs. It may be

that this committee will make some comment on that, and it seems to me that the less obligated we are to any outside organization the more the public is likely to accept our report as being completely objective. That is precisely what I had in mind in making the observations.

The CHAIRMAN: Gentlemen, may I make the suggestion that now we have brought up this matter this morning it might be a good idea to table it until Friday and make our decision at that time after the members have had an opportunity to think it over. In that way we will be enabled to proceed with our evidence this morning while giving everyone three or four days to think it over. We can decide upon the matter on Friday.

Mr. WHELAN: You have a motion, have you not?

The CHAIRMAN: We have, but it has not been voted upon.

Mr. WHELAN: Let us vote it; let us make a decision.

The CHAIRMAN: Is it the feeling of the committee that we should vote on it today? All those in favour of the motion that the second report of the steering committee be adopted as read, which says that we accept the invitation of Cyanamid to visit their parent company? Nine. Those against? One.

Motion agreed to.

Gentlemen, we will get on with our business for today. I would like to introduce the members who are representing the Canadian Medical Association today. We would like to thank them for coming, and one of them in particular who has come a lot further than the other two members. I refer to Dr. McNeil from Calgary, the chairman of the committee on pharmacy of the Canadian Medical Association, and a member of the drug advisory committee of the Department of National Health and Welfare. Beside Dr. McNeil we have Dr. Kelly, executive director of the Canadian Medical Association, and Professor Wightman from the University of Toronto. I hope you have all received a copy of the brief which has been prepared by these gentlemen, and if everyone has read it we might just go into the consideration of the brief itself. Is that acceptable? Is there anyone who has not read it?

Mr. WILLOUGHBY: I am sorry, I overlooked this brief. I did not realize I received it. It must have been somewhere in the pile on my desk. I would very much like to have a chance to study it or else to have the witness summarize it for us.

The CHAIRMAN: Is it the feeling of the committee that they would at least like the brief summarized?

Mr. ORLIKOW: Why not have it read? It is not long, and if we are going to do justice to the brief and to the importance of the organization, we should have it read.

Mr. MACKASEY: There is a very comprehensive summary at the back of the brief. It may or may not satisfy those who have not read the brief in detail. Otherwise, I would go along with Mr. Orlikow's suggestion, but there is a very good summary at the back of the brief right now.

The CHAIRMAN: Is there any other comment? What is the feeling of the committee? Do you wish the brief read, gentlemen, or is the summary satisfactory?

Mr. MITCHELL: I would suggest that the summary would be satisfactory. It is the first view I have of it but the summary certainly epitomizes very well the statements made in the first part of this submission.

Mr. SLOGAN: The brief could be taken as read and included in the minutes.

The CHAIRMAN: Very well. I would suggest then that we read the summary and then go back through the brief item by item. This would bring out the points on which the members would like to question you, Dr. McNeil.

Dr. Donald L. McNeil (*Chairman of the Committee on Pharmacy of the Canadian Medical Association; member of the Drug Advisory Committee, Department of National Health and Welfare; President-elect of the Alberta Division of the C.M.A.*): Mr. Chairman, members of the committee on drugs and food contamination. The following is the brief and summary:

The Canadian Medical Association appreciates the opportunity of presenting views which we believe to be broadly representative of the opinions of Canadian doctors. My name is Donald L. McNeil and I practise in Calgary as senior physician in the department of internal medicine, Calgary associate clinic. I am chairman of the committee on pharmacy of the Canadian Medical Association, a member of the drug advisory committee, Department of National Health and Welfare and I was recently elected to the office of president-elect of the Alberta division of the C.M.A. I am accompanied by Dr. K. J. R. Wightman, professor of medicine, University of Toronto and former chairman of our committee on pharmacy and by Dr. A. D. Kelly, general secretary of The Canadian Medical Association.

We have studied your terms of reference and in this submission we will undertake to comment on those items which lie within our competence.

You are in the first instance asked to consider and report on the hazards of food contamination from insecticides, pesticides and other noxious substances. We know that potential hazards exist but we are not aware that the contamination of foodstuffs actually occurs to the degree that it constitutes a hazard to the health of the people. It is our understanding that at the meeting of this committee held during the last session of parliament you have studied and reported upon this portion of your remit and our remarks will consequently be brief and general. In the normal course of food preparation, processing and cooking it would appear that any residue of noxious substance is removed or inactivated and we are unable to identify the occurrence of disease or disability with potential contamination. It is a fact, however, that poisoning may occur by gross overdose of the chemicals which constitute the insecticides and pesticides used in agriculture and in domestic life. The ingestion or inhalation of such substances in substantial amount may produce poisoning in the operators who apply the chemicals and accidental poisoning in children may occur in the household. The experience of Poison Control Centres in Canada is that poisoning with insecticides and pesticides occurs many times less frequently than accidental poisoning with household remedies, cleaning fluids and detergents.

We do not minimize the potential dangers of residues of pesticides contaminating agricultural products and we are generally favourable to the regulations as they exist in this country. It is observable, however, that in certain instances provincial agricultural authorities enforce very stringent residual tolerances on the basis of evidence which does not appear to be related to any health hazard. The banning of the use of dieldrin and aldrin in certain jurisdictions is a case in point. The introduction of new chemical pesticides of unknown toxicity probably justifies an attitude of extreme caution but if the investigation of all possible toxic effects of D.D.T. had preceded its use, the control and eradication of malaria in many parts of the world would not have been possible.

The second portion of your terms of reference relates to the safety and cost of drugs and here your interest and ours are closely akin. The administration of drugs is an important element in medical practice and the medical profession desires to have available in the interests of patients the most efficacious, the safest and least costly remedies. The elaboration of specific remedies directed towards the alleviation of a recognizable pathological process or to the destruction or inactivation of a known micro-organism is a development of recent years. Safety in medication is a relative term and it should be recognized that the introduction of material into the human body is never without inherent risk, and our efforts should be directed towards minimizing the hazard.

Cost should also be recognized as a relative term and true economy may follow the exhibition of efficacious remedies of high quality even though the price be high.

The education of a physician in pharmacology, materia medica and pharmacy commences with his undergraduate instruction and is directly related to instruction in physiology and biochemistry. He is taught to demand a knowledge of the chemical and physical characteristics of drugs and to reject preparations with a secret formula. The possible benefits of the use of a drug are studied and, equally important, its toxic properties and undesirable side effects are considered. The doctor's graduate instruction, his contact with colleagues, his refresher training and his reading of the scientific literature throughout his professional life, his attendance at meetings of local, provincial and national medical societies, all contribute to his growing knowledge of medicinal preparations which are such important elements in his care of patients. He is aided in his appraisal of the complexities of pharmacy by such official publications as the British Pharmacopoeia, the Pharmacopoeia of the United States, the Canadian Formulary, the British Pharmaceutical Codex and for specific product information by publications such as the Vademecum International and the Compendium of Pharmaceutical Specialties (Canada).

Drug nomenclature is complicated by the fact that the majority of pharmaceuticals have a chemical name, a proper (generic) name, and a trade name. Chemical names are uncommonly used in prescribing while proper names and trade designations represent the usual methods of identifying drugs for the use of patients. It oversimplifies the problems of terminology and economics to say that generic designations are invariably preferable to trade names and the latter commands wide acceptance among physicians because they identify the product with the manufacturer. The claims of a multiplicity of new pharmaceutical agents induce in the conscientious physician the scepsis scientifica which may be stated to be an attitude of mind which is reluctant to discard the tried and true for the sensation of the moment and to require new approaches to prove themselves safe and efficacious before he adopts them.

Canadian doctors have and must have confidence that his patient will receive the selected drug exactly as he prescribes it. Our reaction to substitution at the discretion of the pharmacist is unfavourable. Pharmacological equivalents are not necessarily identical in action with known preparations and dosage forms are often important in the way patients react to the administration of a given pharmaceutical product. A drug must not only be chemically correct, it must be presented in a state which makes it available to the body at the appropriate rate of absorption, noting the changes and alterations which take place in its assimilation and the rate of its metabolism and excretion.

The necessary confidence that the drugs available are as he presumes them to be is provided primarily by the supervision exerted by the Food and Drug Division of the Department of National Health and Welfare, by the work of well-trained pharmacists and by the products of pharmaceutical manufacturers who have attained a reputation for quality.

The work of the F.D.D. is fundamental to the provision of safe and efficacious drugs for the Canadian people. This directorate has performed its functions very well despite the handicap of a small staff and a limited budget. In its submission to the Royal Commission on Health Services the Canadian Medical Association presented its appraisal as follows:

> Food and Drugs and Narcotic Control
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> The Food and Drug Directorate is performing a most useful function in the administration of the Food and Drugs Act and the Proprietary or Patent Medicine Act. A new drug may not be sold until certain

information about it, the method of manufacture, proposed dosage and claims as to its effects, tests as to its safety and other particulars have been submitted to the minister. When one considers the very large number of new pharmaceutical preparations which are being developed in this country and abroad and which seek entry to the Canadian market, it is praiseworthy that assessment for safety, if not for therapeutic effectiveness, is carried out as thoroughly and as promptly as it is, despite the fact that not all batches are tested.

The Canadian Medical Association is represented on the Drug Advisory Committee and the Prescription Drugs Sub-Committee, both of which act to ensure that drugs licensed for sale in this country are of a high standard and that drugs unsuitable for self-medication are available only on a doctor's prescription. The operation of one central and five regional laboratories serves to promote safety in foods, drugs and cosmetics, and the Directorate exercises control over the claims made for medicines advertised to the public. Over sixty poison control centres located in hospitals in all parts of the country depend on information supplied through the Food and Drug Directorate. The most recent 1961 amendment to the Food and Drug Regulations establishes a new class of controlled drugs to cover the amphetamines, the barbiturates and methamphetamines. These commonly used and commonly abused drugs are now available only under licence and on prescription.

The Narcotic Control Division administers the Narcotic Control Act, which in 1961 was extensively amended to provide more stringent penalties for illicit trafficking in narcotics and to control the legal distribution through licensed dealers, pharmacists and practitioners. The medical profession is directly involved in the provision to their patients of both controlled drugs and narcotics and although little more than six months have elapsed since the new regulations in both fields became effective it is our impression they are operating well with the full co-operation of practising physicians.

The functions of the Food and Drug Directorate also extend to the supervision of the labelling of proprietary medicines offered for sale and the advertising of such remedies for self-medication. Constant vigilance must be maintained to prevent misleading claims being made in the advertising through a wide range of media.

The Canadian Medical Association is conscious of the fact that a good deal of confusing evidence on pharmacy, the price of drugs, pharmaceutical promotion, prepaid drug plans, generic names and other aspects of a highly technical field is being debated publicly. This royal commission has received from a variety of sources proposals which vary from the establishment of a federal agency to examine the revenue-cost position of individual drugs, to the provision out of public funds of drugs for patients suffering from chronic disabilities. Canadian doctors and their patients are the beneficiaries of the remarkable advances which have been made in pharmacology and it may be said with some justification that new products have revolutionized the treatment of many diseases.

We are interested in providing for our patients at the lowest possible cost these efficacious new remedies, but we are equally concerned that we may be able to prescribe with confidence, knowing that quality and safety have been checked at every stage of the manufacturing process. The reputation of Canadian pharmaceutical manufacturers and the international organizations which they represent is high in this respect, and this very important consideration has been submerged in the attacks to which the industry has been subjected.

We have no panacea for the ills of pharmacy, but from the viewpoint of the medical profession the most urgent needs are—

(a) to provide a means of assuring the doctor that his prescription does in fact contain the stated type and quantity of active drug, even if the generic name is used and no manufacturer specified, and

(b) to provide information on new drugs relating to an objective appraisal of their efficacy and toxicity by an unbiassed body of experts before they are released for general use.

We welcome the recent announcement that the Minister of National Health and Welfare has requested the Royal College of Physicians and Surgeons of Canada to appoint an ad hoc committee to study the existing procedure whereby new pharmaceutical products are evaluated before receiving approval for marketing in Canada.

It is our belief that an important shortcoming in this respect is the lack of facilities and qualified personnel to carry out adequate premarketing evaluation of new drugs at the clinical level, that is an assessment of their effects on humans. The difficulties involved in providing for reliable, properly controlled, clinical trials of new pharmaceuticals are many and complex. The collaboration of the appropriate agencies of government, the pharmaceutical manufacturing industry, and the professions of pharmacy and medicine will be required to devise a satisfactory solution to this problem.

Reference has been made to the good work being carried out by the Food and Drug Directorate, but these precise functions are not now being assumed. It is suggested and recommended that the Food and Drugs Act be amended to provide the authority for the expansion of the work of the directorate to encompass these two functions initially. The necessary finances, facilities and personnel would, of course, require to be provided, but it is felt that the additional expenditure would be modest when the objective is to amplify the existing services of the directorate rather than to establish a new organization. It is our view that the proposed information service would command the ready cooperation of Canadian talent in pharmacy and pharmacology, in research and clinical investigation and in medicine.

The cost of drugs supplied to patients in hospital is lower than the price which applies to drugs purchased in retail pharmacies. Part of the saving is a consequence of bulk purchasing, but another important factor is that federal, provincial and municipal sales taxes are not applied to such purchases by hospitals. As an immediate step to reduce the cost of drugs obtained on prescription it is proposed that this royal commission recommend to the competent federal authority that the 11% federal sales tax on prescribed drugs be eliminated.

Reference is made above to the fact that the then minister of national health and welfare had requested the Royal College of Physicians and Surgeons of Canada to appoint a committee to "examine critically and objectively our present procedures for dealing with new drugs, the requirements of the regulations and any other matters that in the opinion of the committee are relative to this issue."

The Committee on Pharmacy of the C.M.A. presented its views to the Royal College Committee and examined very carefully the findings and recommendations of the committee when they were tabled in the House of Commons in January 1963. Although the chairman of that committee, Dr. F. S.

Brien, has testified before the predecessor of this parliamentary committee, it is appropriate to summarize the main recommendations:

(*a*) the immediate expansion of the staff of the Food and Drug Directorate;

(*b*) amendment of certain regulations under the Food and Drugs Act—

(i) to provide for more adequate clinical trials of new drugs in Canada before they are released for sale, to insure substantial evidence of clinical effectiveness for the purpose intended.

(ii) to create a new classification "Investigational Drugs".

(iii) to provide authority to order the cessation of trials if unexpected toxicity is revealed.

(*c*) the creation of an expert standing drug committee to advise the F.D.D.

(*d*) consideration of the desirability of the division of the present directorate into food and drug sections.

The Canadian Medical Association at its meeting in June 1963 endorsed the report of the committee of the Royal College of Physicians and Surgeons of Canada and we are in full support of its recommendations, many of which have already been implemented by the Food and Drug Directorate.

The reporting of clinical trials of therapeutic substances in the world medical literature is an important means of disseminating information. An account of the investigational use of a new pharmaceutical preparation, whether favourable or unfavourable, by an author whose qualifications are known and respected is perhaps the most satisfactory method of acquainting the medical profession with the merits of new drugs. The Canadian Medical Association *Journal* through original articles contributed by Canadian investigators and through abstracts, case reports and correspondence does its part in the continuing education of the physician. By maintaining high standards of advertising our *Journal* also exerts a salutary influence on the claims for pharmaceuticals made by their manufacturers and conveys to the reader the knowledge that scrutiny has been exercised. We file in this connection the brochure "Advertising in Canadian Medical Association Publications".

Pharmaceutical manufacturers have several avenues open to them in promoting their products after they have been approved for sale in Canada. Advertising in medical journals has been mentioned. Direct mail of letters, brochures, reprints etc. is commonly practised. Medical and scientific exhibits at conventions and meetings of the medical profession are another effective means of disseminating product information and this is closely akin to the work of representatives commonly known as "detail men" in calling on doctors and pharmacists to present the products of their firms. The indiscriminate distribution of drug samples has recently been brought under control in this country and the current situation appears to be satisfactory. The whole matter of promotional activity has been criticized as unnecessarily expensive, contributing substantially to the cost of drugs. Testimony of representatives of the pharmaceutical houses and of the Canadian Pharmaceutical Manufacturers Association will doubtless bring to the parliamentary committee facts and figures on this matter and we prefer that you obtain your information from these authoritative sources. We have made representations to the C.P.M.A. with a view to moderating the flood of direct mail and the apparent wasteful distribution of unsolicited samples which formerly pertained. It is worthy of note that criticism of the promotional methods of the highly competitive field of the industry in North America is represented in reverse in the controlled economy of the Soviet Union where the complaint is that doctors get far too little information

on therapeutic substances. (Ironic Contrast: U.S. and U.S.S.R. Drug Industries, R. A. Bauer and M. G. Field, Harvard Business Review, September-October 1962).

A recent report in the British Medical *Journal* (Survey of Therapeutic information: Wilson, Banks, Mapes and Korte, B.M.J. September 7, 1963) provides the results of a study of the prescribing habits of a sample of physicians in Liverpool in an endeavour to establish the sources of information which led the doctors to prescribe as they did. A table summarizes the findings as follows:

Medical training	34.9 per cent
Consultant advice	8.1 per cent
Textbooks	3.1 per cent
Periodicals	5.4 per cent
British National Formulary	13.3 per cent
Prescribers' Journal	0.5 per cent
Monthly Index of Medical Specialties	3.3 per cent
Drug firms	26.2 per cent
Discussion with colleagues	5.3 per cent

It is quite possible that a similar study in this country might provide approximate data on the prescribing habits of Canadian doctors.

Having decided on suitable medication and having ordered it the doctor and the patient rely on the services of the pharmacists in procuring and dispensing the necessary drugs. Radical changes in the profession of pharmacy have largely changed the druggist from a compounder and a dispenser of complicated mixtures to the custodian of the local supplies of the specific remedies which are available in such abundance. The changes have not lessened the need for wide knowledge and discrimination on the part of the pharmacist and he renders an essential service.

The pharmaceutical manufacturer has assumed a major role in the origination, development and distribution of a wide range of new therapeutic agents without which modern medical practice would be impossible. To illustrate the great benefits which flow from the chemotherapeutic explosion it is possible to assert that 70 per cent of drugs prescribed to-day were uknown in 1935 and 45 per cent of to-day's prescriptions could not have been filled as recently as five years ago because the drugs had not been discovered.* In the chorus of criticism which has been levelled at the drug manufacturer it is often overlooked that without their dedication to research and without their technical skill in product development, morbidity and mortality from many diseases would still be as high as they were prior to world war II. Physicians are conscious that they and their patients have benefited immeasurably from the scientific therapeutic developments which have flowed and which will continue to flow from the laboratories of the much maligned manufacturers of pharmaceuticals. We cannot say that these effective agents are too expensive and it is worthy of note that the Restrictive Trade Practices Commission did not say so either.

We do not propose to discuss in detail the voluminous "Report Concerning the Manufacture, Distribution and Sale of Drugs" prepared by the Restrictive Trade Practices Commission and released in January 1963. It is suggested, however, that this volume should be required reading for members of this

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*References: (a) "The Organization and Economics of Research in the Pharmaceutical Industry"; J. Yule Bogue, Ph.D. The Pharmaceutical Journal (Great Britain) Jan. 13, 1962: pp. 27-32.

(b) Sub-Committee on Anti-Trust, 1962, U.S. Senate, 87th Congress, First Session, Report No. 448, pp. 116-118.

parliamentary committee because it provides essential information on the complexities of the whole field of the origination, development, testing and distribution of therapeutic substances. By the very nature of its task the commission was primarily concerned with the economics of drugs and its investigations commenced with a study of the antibiotic drugs and the ataraxic or tranquillizer drugs although testimony covering a much wider field was considered.

The commission examined the effect of sales tax and the dumping duty provisions of the customs on the price of drugs in this country but made no specific recommendations for changes in the relevant legislation. It is our view, as previously stated, that the elimination of the 11 per cent federal sales tax would represent a practical step toward the reduction of drug prices and a step which is clearly within the competence of parliament.

The most far-reaching recommendation of the Restrictive Trade Practices Commission was "that patents with respect to drugs be abolished". The current position in Canada is that a pharmaceutical product may be patented if produced by a process other than a chemical one, but whenever the process of manufacture is chemical, a patent can be obtained only for the process or for the drug when produced by that process. There is little doubt that the protection afforded by such patent has been a powerful incentive to large investment in research and investigation with the consequent discovery of many useful pharmaceuticals. It is accurate to say that relatively little of this research has been carried out in Canada. There are, however, notable exceptions and plans for the establishment of research divisions in Canadian pharmaceutical plants are going forward.

It is our view that the public interest in Canada is protected from the potential abuse of patent rights by the provision of the Patent Act which provides for compulsory licensing of an applicant who is adjudged to be capable of producing the substance which has been patented. The adverse effect on research effort which would follow the abolition of drug patents constitutes the principal reason why we do not agree with this recommendation. It is suggested that the saving in the price of drugs would be small compensation for the handicap to the discovery of further pharmaceuticals which may be of the utmost benefit to mankind.

Summary

In this submission on behalf of The Canadian Medical Association we have stated:

1. Our belief that the use of insecticides and pesticides does not produce contamination of foodstuffs which we recognize as a hazard to health.

2. Some factors in the process whereby Canadian doctors gain their knowledge of therapeutic agents and their interest in the availability of increasing numbers of efficacious drugs of low toxicity at prices which are consistent with high quality.

3. Our endorsement of the recommendations of the committee of the Royal College of Physicians and Surgeons of Canada on appropriate measures related to the introduction of new drugs.

4. Our appraisal of the work of the Food and Drug Directorate, Department of National Health and Welfare, and our desire that its facilities be strengthened.

5. Some thoughts on the physicians' reaction to the promotional measures adopted by pharmaceutical manufacturers.

6. Our appreciation of the benefits which have accrued from the research and the technical skills of the pharmaceutical industry.

7. Our recommendation that the federal sales tax of 11 per cent on prescribed drugs be abolished in the interest of the reduction of price to the consumer.

8. Our disagreement with the proposal of the Restrictive Trade Practices Commission that Canada should abolish patents on drugs.

The CHAIRMAN: Now, if we could revert and take this brief paragraph by paragraph I think it would be an orderly way of proceeding.

As everyone here is aware we already have reported on insecticides and pesticides, although these matters are still part of our present terms of reference.

Has anyone a question to put in this regard or any comments to make?

Mr. ORLIKOW: I would like to put a question in respect of this very strong and unequivocal belief that the use of insecticides and pesticides does not produce contamination of food stuffs.

Within the last couple of days the Toronto *Globe and Mail* has reported that millions—and I am quoting exactly—of fish in the Mississippi river has been found dead, and according to the experts in the United States this was as a result of the use of dieldrin, which was used to spray sugar cane. Of course, this substance got washed into the river and carried on from there. I realize there is a great deal of controversy and I realize the validity of the statement here, that D.D.T. helped to eliminate malaria. But, at the same time, and in view of the great controversy, along with the expert advice on both sides in respect of the possible dangers as well as the good effects of the use of insecticides and pesticides, I wonder about the almost complete rejection of the idea that perhaps we have to be pretty careful in respect of the use of these things. Would you like to comment on that?

Mr. MCNEIL: We quite realize we seemingly were passing over this portion of your terms of reference quite quickly. However, we did not do this without having researched this problem and this portion of your study considerably. We learned what the national department of health does in this work and we know the responsibilities of the other departments, agriculture, forestry and so on. We have also checked with departments of health in the provinces and across Canada and have received reports from all of these ministries. Also, we referred to the World Health Organization, who supplied us with much material, and we further reviewed the reports that you have received and the opinion which we believe that you have passed on to parliament in an earlier submission. So, we are not passing this over quite so lightly. Of course, dangers also will exist and great care will be required. But, we are satisfied that this care is being taken. We have a number of bodies which are protecting us and we hope the wildlife in our country is being protected also.

Mr. SLOGAN: I think we have a similar problem in the province of Manitoba to that which Mr. Orlikow has referred regarding detergents. A great deal of work has been done in regard to decontaminating the Red river and other waters in that area. I am wondering whether Mr. Orlikow is in favour of abolishing detergents.

Mr. ORLIKOW: I am not in favour of abolishing detergents but I am in favour of the experiments which are being carried out in an attempt to rid detergents of the foaming action.

Mr. MACKASEY: I should like to say one or two words in this regard. I support your statement and realize that in certain states, and perhaps throughout the United States, the form of detergents is changing and have perhaps

less sales appeal because certain ingredients have been removed, but they certainly have been improved in respect of water contamination.

One point in your brief is of particular interest to me. At page 1 you state:

> It is a fact, however, that poisoning may occur by gross overdose of the chemicals which constitute the insecticides and pesticides used in agriculture and in domestic life.

I presume you refer to use by individuals rather than as a result of a generous recommendation of the application? Am I right in assuming that, and that it is something over which the manufacturers have really no control?

Mr. McNeil: The manufacturers have no control over them. There are very definite directions in respect of the use of these chemicals. We lost a pilot in Alberta while he was carrying out his work spraying crops. The dangers I believe lie mainly in the areas of factories where these are produced but I am sure the workers are being protected.

It would seem that the greatest tragedies occur as a result of careless use of these chemicals on the part of individuals who do not obey the instructions.

Mr. Willoughby: I should think, Mr. Chairman, that the criticism, while it is correct as far as contamination in respect of wildlife is concerned, does not apply to the problem that the medical association must consider, namely the question of health matters in human beings. While we recognize that wildlife has suffered from excessive use of some of these insecticides and pesticides, we have never had any proof by evidence from any of the witnesses we have heard that there are any serious results as far as human health conditions are concerned. I think that fact probably answers the criticisms. The medical association deals with health matters only.

Mr. Orlikow: I should like to ask Dr. McNeil one further question. Is it not a fact that there is a good deal of evidence that in products such as those used extensively by younger people, milk for instance, there has been found by experiments, carried out across Canada and in the United States, very appreciable amounts of some of these chemicals?

Mr. Côté (*Longueuil*): Mr. Chairman, I think we have gone through this discussion in respect of pesticides and insecticides and I do not think we should go through it again.

Mr. Orlikow: This subject is covered by the brief.

Mr. Côté (*Longueuil*): I think this discussion should have taken place before we presented our report in respect of pesticides and insecticides. I do not understand why it is taking place in respect of our report at this time.

The Chairman: It is taking place now because this reference is still in our terms of reference.

Mr. Howe (*Hamilton South*): I should just like to suggest that the summary does not correctly reflect the body of the submission in that it is noted at page 2 in the second paragraph that there are relative dangers, yet the blanket statement is made in the summary that there is no produce contamination of food stuffs. The statement appearing at page 2 notes that there are potential dangers, so I would say that this brief has been prepared with complete awareness of this danger but does not reflect that awareness in the summary.

The Chairman: I had the thought that it might be interesting to this committee to ask Dr. McNeil and Professor Wightman, who are both active practitioners in the medical field, whether they have found that the uses of pesticides and insecticides has given rise to diseases or any significant danger of morbidity or mortality.

Dr. K. J. R. WIGHTMAN (*Professor of Medicine, University of Toronto*): I have seen one man who was poisoned through the spraying of one of these materials which produced an illness because he himself had an unusual set up of enzymes in his body and was unusually sensitive to these things. I think other cases of this sort have been described so there are a few instances of poisoning. However, I do not know of any diseases that these things have produced. The fact that one does not know of any of course does not rule out the possibility, but certainly it must be kept in mind that so far the evidence does not show that any disease has been produced by contamination as a result of the use of these materials. I agree with the precautions which are being taken to prevent this sort of thing.

The CHAIRMAN: Is this also true in respect of the situation in Calgary?

Mr. MCNEIL: Yes. I cannot add anything to that statement, I have not seen any evidence of chronic poisoning.

Mr. SLOGAN: Perhaps I could change the subject slightly. I should just like to ask a question in respect of a statement appearing at page 6 of your brief which states:

> —we are equally concerned that we may be able to prescribe with confidence, knowing that quality and safety have been checked at every stage of the manufacturing process.

Do you feel as a medical practitioner when you are confronted by some new drug on the market that you have a tendency to prescribe a drug made by a well known firm with which you have been dealing rather than the new drug which is being offered by a company that is less well known?

Mr. MCNEIL: Are you referring to a new drug?

Mr. SLOGAN: Do you feel that there is a tendency in the medical profession to prescribe drugs supplied by well known reputable firms at perhaps higher prices than perhaps drugs from lesser known firms because you are perhaps worried about the quality of those drugs?

Mr. MCNEIL: Yes.

Mr. SLOGAN: Do you feel that the food and drug directorate could perhaps do more than it is doing to advise medical practitioners in respect of the quality of drugs which are being sold under generic names by different manufacturers, or even the same manufacturer, so that the medical men would be in a beter position of knowing the quality of the drug?

Mr. KELLY: May I say that the hon. member is quoting from a lengthy extract in our submission to the royal commission on health services. We covered that very point at page 6, in our second proposal where we state that we believe a new and very important function of the food and drug directorate would be to provide information on new drugs relating to an objective appraisal of there efficacy and toxicity by an unbiased body of experts before they are released for general use. This is the kind of assurance that is certainly what the doctor wants and requires.

Mr. SLOGAN: How do you think this could be brought about? Do you think this could be brought about through the labelling of a drug, stating that such a drug had passed certain specifications? How do you think this could be brought about for the assistance of those who are prescribing these medicines?

Mr. KELLY: My two companions have had personal experience with the functions of the food and drug directorate and its committees and will be able to speak with assurance on just that point.

Mr. WIGHTMAN: Mr. Chairman, one way of doing this is, of course, to create some system of licensing so that the manufacturing processes are inspected. What you are talking about is really quality control, ensuring that the manufacturing process is done in a uniform fashion so that the drugs will be produced to predictable quality and will be uniform from batch to batch, month to month. This is what one would expect to find in respect of a reputable company which for its own sake is doing its best to produce just such a product. This is what one would hope to see enforced by one means or another in respect of all drug manufacturers. One way of doing this would be by a licensing and inspection system such as is now carried out in respect of biological materials manufactured. It would seem to me, however, to be perhaps impossible or impractical to have the food and drug directorate actually test every batch. I do not think that directorate should take over the function of quality control for the various manufacturers. I think it should interest itself in the procedures of all drug manufacturers.

Mr. SLOGAN: In order that a practitioner in some small backwoods town will know that a drug does meet certain specifications set down by perhaps his own association, do you think the food and drug administration, in co-operation with the bodies that use these drugs, could ask the manufacturers to indicate on the label, once these drugs have passed certain specifications, that they have met certain specifications set down, for example, by the Canadian Medical Association? That doctor would then know that a drug was safe even though it might be sold under a generic name and not be a well known brand.

Mr. WIGHTMAN: Such a program would still involve inspection. Someone would have to undertake to make sure that such was the actual case in the manufacturing plant.

Mr. SLOGAN: Do you feel that the food and drug directorate could carry out such an inspection?

Mr. WIGHTMAN: I think that is a reasonable thing for that directorate to do. Obviously it could not do it as it is set up now, but I would think it a good thing if it could do that.

Mr. SLOGAN: Has your association taken any stand in this regard? I suppose you have taken such a stand in these statements which you have made.

Mr. MACKASEY: I should like to ask a supplementary question. Do you imply in your statements that you believe this type of inspection would only be possible under a licencing system?

Mr. WIGHTMAN: That is really a question for the lawyers. I do not know.

Mr. MACKASEY: In your opening remarks you mentioned the advisability of having manufacturers licensed so that immediately there would be some control in respect of specific drugs.

Mr. WIGHTMAN: That is one way of doing this.

Mr. MACKASEY: I infer perhaps wrongly from your remarks that as long as they are not licensed there is no limitation or standard in respect of the manufacturers operation. Am I right in this regard?

Mr. WIGHTMAN: I think that is true. I think the only standard that is defined under the act is that which provides that a product may be examined from time to time either in a sporadic way or as a result of some complaint and an analysis made to find out whether or not it complies with the specifications. There are certain things which are important in respect of a drug but which are not readily specified. That is to say, in regard to the absence of certain trace materials, the way the tablets are compressed if they are tablets and all manner of other things besides the actual amount of stated ingredients that are present. All these things need to be controlled as well as the amount of drug.

Mr. MACKASEY: At the moment that responsibility remains directly with the manufacturer in following the process from beginning to end?

Mr. WIGHTMAN: Yes.

Mr. SLOGAN: I have one further supplementary question. Do you feel it is necessary to have compulsory licensing, or could some objective be accomplished by the establishment of something in the nature of a drug specification body acceptable to the food and drug administration? It would seem to me that the medical, dental and other professions would restrict their uses to those drugs which had this brand of approval. It would be very desirable from the drug manufacturers point of view to have that approval and I am sure they would invite the food and drug administration to license or inspect them, whichever may be the case. My point is that I do not think it would necessarily have to be a compulsory system.

Mr. WIGHTMAN: I think the very fact that a drug is now sold is in some way an indication that the product has been examined by the food and drug directorate, but this does not do anything in respect of the production methods or quality control. Whether this could be accomplished without some means of continuing supervision or observation of the process of production I do not know. It would be all very well to say that this product had been produced in a way which would comply with any set of regulations but the question is, is it going to be continuously produced in this way? There is a monetary factor involved here and a need for some special mechanism which does not exist now except as a matter of voluntary introduction by some companies.

Mr. SLOGAN: Would you say that the food and drug administration is perhaps doing a great deal of work which is not evident to the average practitioner because he has no way of knowing exactly what sort of specifications these drugs have met and that, therefore, we are spending a lot of taxpayers money for the taxpayers protection in respect of which perhaps he is not getting the benefit in the way of lower prices because the drugs do not carry well known brand names?

Mr. WIGHTMAN: I am not quite sure what you mean. I think one of the things which makes it possible to sell drugs at a lower price is the omission of many of the precautions which are taken in manufacture and which are referred to as quality control. In other words production is cheapened considerably if the long lists of tests in respect of every step of the manufacturing process are not carried out. In other words the man who buys or uses the cheap drug may sort of automatically be throwing overboard this kind of protection. This may not make it different in certain circumstances, but in other circumstances it may be a very critical thing. Again I think the only way of specifying that a method of manufacture is followed which does involve these quality controls involves new regulations and new inspection methods which we do not have. I do not think the work being done by the food and drug directorate is being wasted. I think we are all extremely favourably disposed to the work being done and the attempts being made by that body, but I think it is possible this might be extended to produce more rigid control on manufacturing methods.

Mr. SLOGAN: When referring to quality control Mr. Chairman, I refer again to a point I made earlier. A lot of drug manufacturers may be selling identical drugs under various brand names at different prices, or they may be manufacturing drugs for distributors in respect of which there are exactly the same quality controls and, therefore, the drugs are sold at different prices. However, because of the fact that individuals who buy the drugs do not realize the situation they are more likely to buy the higher priced but better known product.

Mr. WIGHTMAN: That is possible.

Mr. ORLIKOW: You state at page 3 of your brief that doctors gain knowledge in respect of various drugs by reference to publications such as the British Pharmacopoeia and Vademecum International. I am not being critical of doctors or of drug manufacturers at the moment but is it not a fact that a great amount of the information which a busy doctor has in respect of new drugs particularly comes from dealers who have time to spend waiting to see the doctor to provide him with this information about a new product? If that is the case is that not one of the reasons why many individuals prefer to use or recommend well known brand products?

Mr. WIGHTMAN: At page 10 I think there is mention of the influence of prescribing habits of the doctors as far as drugs are concerned. I think this is true. It states there the durg firms, which includes the detail men, advertising material and the other promotional methods and, in that setting, this would seem to produce 25 per cent of the direction in respect of prescribing. So far as the doctors are concerned, I think it is true that the detail men do a lot to acquaint doctors with new products and how to use them. In many instances I think the information which they give is fairly reliable. However, it is not the only source and I would hesitate to say that it is the main source.

Mr. ORLIKOW: I did not say it was the main source. However, the detail men are not often likely to tell you that there are other companies making the same product and that perhaps the other company is selling it at a lower price than their company. Is that not correct?

Mr. WIGHTMAN: Yes.

Mr. ORLIKOW: That would be expecting too much.

Mr. WIGHTMAN: Usually he is trying to interest you in something which no other company has made to date.

Mr. ORLIKOW: But is it not true that a very large percentage of the prescription dollar which the consumer is paying is paid in respect of a relatively small number of products, such as antibiotics, and there is a good deal of overlap? Is it not true that the same or similar product is made by half a dozen companies and as a result, there is a terrific amount of competition between companies?

Mr. WIGHTMAN: Yes.

Mr. ORLIKOW: That is, there is this competition to get the doctor to prescribe their product rather than someone else's?

Mr. WIGHTMAN: I think this is true. There are large areas of overlap in respect of commonly used drugs. The more popular the drug is the more widespread is its use and the more temptation there is to produce a new version of it or new methods of producing it. But, this would not be worth while in respect of other drugs.

Mr. ORLIKOW: Page 3 sets out where the doctor obtains his information, and I am wondering if it is too early to say whether the new regulations in respect of distribution of drug samples, which were worked out last year, have had any appreciable effect on the reduction of the almost indiscriminate flooding of doctors' offices with drug samples by drug companies.

Mr. WIGHTMAN: In my case, it certainly has. I do not know what has been Dr. McNeil's experience.

Mr. MACKASEY: Mr. Chairman, I object to those generalities used by Mr. Orlikow. He referred to the indiscriminate flooding of doctors' offices. I, for one, do not know whether there is or is not, and I do not want to let this remark go unchallenged into the record without first knowing.

I think Mr. Orlikow could phrase his question in a more objective manner. Now, I have no axe to grind in this respect and, I presume, Mr. Orlikow has not. But, I do take objection to this type of flowery phrasing in the beginning of

his questions that presumes something. I do not think it is fair to our witnesses. This is not a McCarthy trial; the witnesses are here to give us information. I do not think it is fair to put on the record that there had been or might be indiscriminate flooding of doctors' offices with samples.

Have you found this literature which has been referred to misleading in any way and do you find that pharmaceutical firms, in pushing their particular brands, claim any performance for their drugs which is not true and, therefore, this is misleading and dangerous to your patients, when taken at face value.

Mr. WIGHTMAN: No. But, in the case of some of the literature from some companies there is a certain amount of generalization, perhaps leaving you with the opinion that it is all the same. But, there certainly is promotional material sent out which is not educational and which does, in subtle ways, overemphasize the place that this particular drug may have, and the value it may have in respect of others. This is a matter of advertising techniques, and this does occur.

If one examines the thing from a scientific point of view I think one might frequently complain there was not enough scientific data for a scientist to satisfy himself. But, I do not think it is very often that you will find misleading information in the obvious sense in which you mean it.

Mr. MACKASEY: In the fourth line from the bottom of page 3 you state:

> Our reaction to substitution at the discretion of the pharmacist is unfavourable.

I would like you to elaborate on that.

Dr. A. D. KELLY (*General Secretary of the Canadian Medical Association*): Dr. McNeil comes from a province where legislation permits such substitutions and perhaps from his own experience he could comment on this.

Mr. WILLOUGHBY: Is this substitution not made after notifying the doctor of the alternative product?

Mr. MCNEIL: It is necessary that a doctor state either the name of the company that produces the drug or the trade name, and it is up to him to state that there be no substitution; otherwise, it is possible for a pharmacist to supply a drug of a similar nature with, perhaps, a different brand name.

In Alberta physicians largely have marked their prescriptions so that there would be no equivalent. They did not agree with this act which allowed substitution.

Mr. WILLOUGHBY: But does not the druggist usually phone the doctor to say he has not this particular product available at the moment and requests permission to prescribe this other product, if it is all right.

Mr. MCNEIL: That sometimes happens, and the doctor might or might not agree. He still has the control of it.

Mr. ORLIKOW: Suppose the food and drug administration was given the responsibility for a much broader testing program than it has carried out to date and they had the facilities for investigating drugs; in this way doctors could be assured when there was a generically named drug available that it was the equivalent, although it might be cheaper. Would you have any objection to this? It seems to me from what you have said up until now you do not think—and I do not think anyone would disagree with you—that the individual druggist really has the knowledge required to be certain that the drug he is going to substitute will do the same thing as the one the doctor prescribed. But, as I say, suppose the food and drug administration tested these drugs, certified or licensed them as suggested, would there be any objection then?

Mr. McNEIL: I think Dr. Wightman already has answered that question. There must be this continued surveillance and the stamp of approval could not be given unless it was known that this testing was constant.

Mr. MACKASEY: On the same point, this sentence does say at the discretion of the pharmacist which, of course, is not quite the same as what Dr. Willoughby said, where a reputable druggist will check with his doctor and obtain permission. Is there anything in the law now that makes it mandatory for a druggist to check with the doctor in case of a substitution?

Mr. WIGHTMAN: Not in Alberta.

Mr. MACKASEY: Do you think a desirable addition to our laws would be that druggists not be permitted to substitute any portion of the compound or prescription without an opinion of the doctor?

Mr. McNEIL: Yes. I know that the physicians—and, I suppose I should not speak for the pharmacists—would welcome this.

Mr. SLOGAN: What is the situation in Alberta when a druggist, without consulting a medical man, substitutes a prescription, as a result of which there is a reaction in the patient and a law suit brought? Is not the responsibility placed on the shoulders of the pharmacist?

Mr. McNEIL: Yes, we have been advised that the pharmacist is liable. He must be very careful. I have been told that the pharmacist, in all probability, would take only a drug which he feels is very safe. He is apt to take a drug which he considers safer and he will not necessarily use the cheaper and inexpensive drug as a substitution.

Mr. WILLOUGHBY: Mr. Chairman, I think I am away out in left field. I wanted to put a question in respect of potency and toxicity, which was brought up initially by Dr. Slogan. However, we got on this other subject of samples and then carried on from there.

May I revert to this matter and ask Dr. Wightman if he does not consider adequate the policy which we had outlined to us here at the last meeting by Dr. Morrell, when he said that no drug is allowed to be sold in Canada without a complete investigation by the department either through its own facilities or, at least, through information supplied from reliable sources which has been presented to the department by the company offering the drug for sale?

I think I, personally, should say at this time that our trip to Montreal was extremely interesting in respect of that subject. There may be smaller companies which are not quite so proficient in their tests. But, after our visit and watching the production of these drugs and the tests they undergo in these reliable firms I do not think we have any fear of any kind in respect of possible toxicity or anything but the highest potency in the drugs produced. I would like to ask again if you do not feel that these precautions are adequate at the present time?

Mr. WIGHTMAN: They are in respect of reputable firms. But, there are many firms which are producing drugs on a very much less satisfactory basis, and the question which keeps coming up is that one can buy drugs cheaply if one wishes, as a result of which we must make sure that what we are saving in money is not made up by less care in the manufacture. This is a thing that frightens one.

Mr. WILLOUGHBY: Is it your feeling that some of these drugs are not up to the potency required?

Mr. WIGHTMAN: Oh, yes. However, it is not so much the matter of potency. There are variations in that. But, there is the question of the care of the manufacturer in the exclusion of minute amounts of toxic materials and the

care which should be taken in the formulation—that is, the way the capsules or whatever they are, are put together, as well as the methods used to protect a drug after it has been packaged and so on. As you know, there are many things which could interfere with the activity of drugs. There are all sorts of curious things which can happen. One might not anticipate that the changing of the amount of an inert material in a tablet to make it look different than before would make any difference, but even though the active ingredient was still present or if a drug was allowed to stand an undue length of time or, in other conditions, changes might come about which would have a different effect on the body which one never heard of before. All these things are unexpected and we must try to protect ourselves by using the greatest care. The same format should be kept in respect of the testing of drugs, the biological activity, clinical tests, and so on.

Mr. WILLOUGHBY: Under the circumstances do you feel the government of Canada should set up a laboratory and equipment for the testing of the potency of drugs which are being manufactured in Canada today?

Mr. WIGHTMAN: No. My suggestion would be that they make the manufacturers do this.

Mr. WILLOUGHBY: They are doing that.

Mr. WIGHTMAN: Some of them are.

Mr. SLOGAN: I believe you referred to the storing and so on of some of these drugs; this sort of thing could happen to the best type of manufacturer and the more specialized drug firms. As you know light and darkness and temperature affect different drugs. In your statement you say that some of the manufacturers are not up to standard. Upon what evidence do you base this?

Mr. WIGHTMAN: Well, I have had experience with drugs that were purchased from these manufacturers.

Mr. SLOGAN: Have you visited any of these small plants that are doing this?

Mr. WIGHTMAN: I have visited only one of them. Some of the others I speak of will buy bulk materials from another country, import them into Canada and put them into capsules, sell them and no one knows anything about the manufacturer. All one particular company may do is fill the capsule and put the capsules into bottles. There are operations of this type particularly designed to capitalize on the success of drugs which are used widely. They want to handle this type of drug because it has a big sale. But, if you handle it in this manner you have not had anything to do with the cost in respect of the finding of the drug, the developing, testing and so on. All you are doing is taking the cream off, as it were. This is one of the ways of getting cheap drugs on generic terms, and we are concerned about that.

Mr. SLOGAN: But are not these firms subject to inspection by the food and drug inspectors at any time, unknown to them?

Mr. WIGHTMAN: Not that I know of, unless the regulations have been changed.

Mr. MARCOUX: Are you satisfied that the difference in price between those small companies and the well known companies represents approximately the difference in care, production or research.

Mr. WIGHTMAN: No.

Mr. CÔTÉ (*Longueuil*): But, is it not true that most of these drugs are usually purchased by people on the recommendation of medical men and is it not the responsibility of the medical men to control that? If this was the case the small companies would not be so popular. In fact, it is not the responsibility of our committee or the food and drug directorate but all the medical men. It is up to them to tell the people at large what drugs to use.

Mr. WIGHTMAN: I think that is true. I do think there is a need here.

Mr. ORLIKOW: I would like to ask the doctor if he has heard or knows of large hospitals which dispense large quantities of prescription items for their patients and which, in fact, are buying drugs in large quantities, many of them from outside the country, thereby saving substantial amounts of money for their patients? Do you not think that hospitals are taking the necessary precautions to make sure the drugs which they are dispensing are safe?

Mr. WIGHTMAN: I can only speak for my own hospital where, when I was chairman of the drug committee, I carried on an unrelenting battle against the hospital administration who wanted to save money, not so much for the patient, but for the hospital services commission. They wanted to buy drugs by tender, specifying various specifications such as would be laid down and then having them tested by an outside agency for these things. In one instance they said this would save $30,000 in buying a certain single drug. Yet, when one came to investigate, one found that the specifications one could lay down were only the things one knew about; there was nothing specified in respect of something one did not know. It turned out that this particular $30,000 drug was one of the ones which could have completely unacceptable adverse effects if it were not properly processed. I must admit that three or four drugs were boxed under these terms by our hospital. These involved bulk purchases, in order to take advantage of this savings. I think this is something in our hospital that has come to be no longer worthy of the trouble involved.

Mr. ORLIKOW: Is it not a fact that very often drugs are produced by some of the primary producers and then sold by companies which are really only packagers and, depending upon the name, there are sharp differences in the prices? After all, we are not dealing with pennies but with the cost of drugs in the tens of millions of dollars. I should like to ask the doctor whether he thinks it important that we try to pass on a savings to the consumer? I think we should keep safety in mind, and no one questions that fact. Do you think that we should attempt to save money for the people of Canada if possible rather than creating a system whereby a company with a well known reputable name can charge two, three or ten times as much for the same drugs as another company?

Mr. WIGHTMAN: I think we must not be penny wise and pound foolish. As we have said in the brief I think we owe a tremendous amount to new drugs and developments which have been accomplished by the pharmaceutical industry sometimes with the help of the medical profession but sometimes completely on their own initative and with their own talents. I think these are things which must also be taken into consideration. I am quite aware of the fact that one must examine the price of anything. I do not know what anything ought to cost in absolute terms but I think that in order to save money on drugs which we presently have we must be very careful not to do anything to prevent the flow of new drugs, because this has made a tremendous difference to our lives during the past ten years.

Mr. ORLIKOW: Mr. Chairman, is the doctor aware of the fact that a large number of new drugs, and I have reference to tranquillizers because of some personal experience in this regard, have been developed in Europe and not on the American continent, but that in the transmission of the drugs from Europe to Canada and the United States the price has jumped by some 60 to 70 per cent? If someone went to Europe and brought the drugs back here and sold them at something close to the European price it would benefit everyone. What is wrong with that concept?

Mr. WIGHTMAN: There is nothing wrong with it as long as the drug is produced properly.

Mr. ORLIKOW: Is it not important to make sure that we have some organization as a result of which we can be certain that products which are being sold, regardless of where they are produced, are produced properly?

Mr. WIGHTMAN: I think that involves half of the problem but the other half has to do with making sure that new products are produced, that research continues, and that further studies are not interrupted. I think there is a possibility here of cutting these things at the roots, or killing the goose that lays the golden eggs.

Mr. SLOGAN: Doctor, do you feel there will be a lessening of research on the part of these companies which have large research facilities as a result of their being placed in a competitive position?

Mr. WIGHTMAN: I cannot tell because it is difficult to know what the acceptance of these other companies' products would be. In other words there have been these companies in operation and in operation now, and I do not know what the effect would be on the original companies' revenues. I cannot answer that question and tell you what the impact would be. I do know that if this were very widespread or condoned by some sort of legislation it would have an effect.

Mr. SLOGAN: Would you say that perhaps a new drug which eventually is placed on the market as a result of research may be developed only after say 100 unsuccessful attempts and, therefore, must bear a larger cost than the cost of the research in respect of that particular drug itself? I use the example of an oil company which drills several dry wells at a cost of several thousand dollars each before hitting one that produces oil, but the producing well must carry the cost of drilling the dry wells.

Mr. WIGHTMAN: Diamonds are not really worth anything except because the supply is held by a few people. There is always the question involved of what is a thing worth to the consumer. We are now getting into an entirely philosophical examination of supply, demand and needs, which is a consideration, actually beyond the medical field. If a producer has something that is extremely good and saves lives and no one else has it then he has the feeling that he has something that people will buy.

Mr. ORLIKOW: That is perhaps true even though the cost of such an item may well be a substantial part of an individual's income. A person may perhaps be living on the old age pension and be required to buy cortisone or one of the new antibiotic drugs which cost a very substantial part of his total income, but permits him to live fairly comfortably. Surely the cost of that item is important.

Mr. WIGHTMAN: That is important, yes.

Mr. MACKASEY: Is it not also important that somebody do the research in the first place to make it possible for these old people to live a little longer through the use of these drugs?

Mr. WIGHTMAN: Yes.

Mr. MACKASEY: I think the case of my boy is typical. I have never regarded the cost of insulin to be unreasonable. Twenty-five or forty years ago people did not have to pay for insulin because it did not exist.

Mr. SLOGAN: May I just ask a supplementary question? I should like to say that it might be wise to point out that many drugs that are produced, and insulin, produced by Dr. Best, is a good example, were not actually patented. Dr. Best made insulin freely available to people without thought of any monetary benefit. I believe there have been many advances in medicine made on the same basis. In fact I think it is unethical on the part of a medical man to do other than what was done in respect of insulin.

Mr. ORLIKOW: Mr. Chairman, I think I should put on the record the fact that insulin is probably alone among many drugs that are being used in respect of which there are no patents, and which is being sold at almost cost. I should be happy to hear any information from any one in respect of any other drugs which were treated in this same way and not patented. I think the example of insulin is probably the worst possible that can be used in terms of comparison.

Mr. MACKASEY: I suggest the difference is that the research done allowing the discovery of insulin was done by a humanitarian whereas research in respect of other types of drugs developed today is done by private industry. I think the time will arrive when the government will have to undertake this research exclusively and private industry must be motivated to seek only a legitimate profit.

Mr. WILLOUGHBY: Before we leave that subject I should like to state that that last statement summarizes very well the whole situation. Until the government of Canada, or any other government, is prepared to spend large amounts of money on research, and we are laging very sadly unfortunately in this area at the present time, we cannot criticize the companies. In fact we should be very thankful to these companies for spending eight to ten per cent of profit on research alone. We should appreciate their efforts in developing things of such great importance to the people of this country.

Mr. MACKASEY: In this regard I should like to suggest that during our trip to Montreal we were privileged to meet a humanitarian, Dr. Genest at the Hôtel-Dieu. I must state that I witnessed the most appalling conditions there that I have ever seen outside of a movie film, and at one stage I jokingly suggested to him that he could raise a little revenue by leasing out the physical aspects of that establishment to a movie company to use as sets. He laughed and said: "we did precisely that last year to the Film Board".

The conditions under which he is working are precisely those which I assume existed 75 or 100 years ago in that particular hospital.

You mentioned potential savings, and you were rightfully interested in saving money for your hospital to the extent of $30,000 by purchasing in bulk. Are you suggesting now that in spite of the fact you are operating a hospital and are able to take advantage of buying in bulk effecting such savings you would think twice about doing so again?

Mr. WIGHTMAN: Yes.

Mr. MACKASEY: You also indicated some of the more practical methods of purchasing used by hospitals. Is one of the main reasons that hospitals are able to buy drugs cheaper than the general public because of the absence of municipal, federal and provincial sales tax?

Mr. WIGHTMAN: Yes, I suppose that is right.

Mr. MACKASEY: Would you say that is the main reason why hospitals can buy so much cheaper?

Mr. WIGHTMAN: The main part of the savings is consequent on bulk purchasing. If one buys large amounts from any company, say in the thousand or ten thousand dollar bracket, the unit cost will be much less.

Mr. MACKASEY: You purchase your bulk supplies from reputable firms?

Mr. WIGHTMAN: Yes.

Mr. MACKASEY: Do you know of any instance of these companies selling below cost?

Mr. WIGHTMAN: I do not know what the cost is.

Mr. MACKASEY: You also mentioned the advantage of the federal, provincial, municipal sales tax relationship to medicines and its effect upon the purchase price?

Mr. WIGHTMAN: Yes.

Mr. ORLIKOW: Do hospital administrators find themselves in a better bargaining position? In other words do you not think there is an advantage in the fact that the hospital administrators can say to the drug company representative that unless they quote such and such a price the drugs will be purchased elsewhere?

Mr. WIGHTMAN: Yes.

Mr. ORLIKOW: I am wondering whether the Canadian Medical Association for example has made any recommendation in this regard. I do not question your right to express opinions and to include them in a brief such as this, but what are your objections to the recommendations of the restrictive trade practices commission? Has a representative of the Canadian Medical Association read the report of the Kefauver commission in respect of the type of competition which takes place allowing hospitals to reduce the price of drugs by two or three hundred per cent?

Mr. WIGHTMAN: I have not read that report.

The CHAIRMAN: You are referring to a report of a United States commission?

Mr. ORLIKOW: Yes, and I am referring to the restrictive trade practices commission report. I should like to place on record the statement that I do not think anyone is suggesting, and certainly I have not made this suggestion today, that the choices we have are between government production at cost and production by drug companies which obviously are going to require a profit. The question to be answered is whether they are going to make a legitimate profit. The restrictive trade practices commission obviously thought their profits were too high, otherwise it would not have recommended changes in the legislation which would reduce the profits. I think this is the point which must be kept in mind.

Mr. WHELAN: Someone made the statement that private firms should have more research facilities than the government, but I am of the opinion that the consuming public pays for the research no matter where it is done. Do you disagree with that sugestion or do you feel that civil servants would be less efficient than individuals working for private industry?

Mr. WIGHTMAN: I do not think the question of efficiency is involved. The question involved is motivation. There is a question involued of interplay, cost and effect. To be useful I think research must go on on all the surrounding planes. I do not think it should be delegated entirely to the private drug firm any more than it should be entirely delegated to universities or entirely placed in the hands of civil servants. Very useful research has taken place in all of those three areas interdependently. Sometimes the drug companies have taken a discovery made at a university or government laboratory and fashioned it into something useful from a treatment point of view. I do not believe in centralization of research to anyone of these three areas.

Mr. WHELAN: Do you think Canadians are contributing enough per capita to research?

Mr. WIGHTMAN: No.

Mr. WHELAN: During a recent trip we made to Montreal we received certain figures by way of comparison in respect of per capita contributions.

If I remember the figures correctly the United States was contributing to research on the basis of one dollar per person, England twenty-five cents per person and Canada ten cents per person.

Mr. WIGHTMAN: I believe that is about right.

Mr. MACKASEY: At the bottom of page 9 of your brief there is a reference to the Soviet Union, and without going into the whole matter, it is my impression that you suggest that doctors in Canada receive too much direct mail information whereas the complaint of the doctors in the Soviet Union is that they receive too little. I think your reference is the Harvard *Business Review* of September—October, 1962. I read that particular article but not having it here to substantiate my remarks perhaps you would assist me. I believe that article made a very strong case in respect of the fact that in the Soviet Union where private industry is practically nonexistent the production of drugs is more costly than it is in democratic countries. Would you care to comment in that regard?

Mr. WIGHTMAN: I will pass that question to Dr. Kelly.

Mr. KELLY: I also read that article with great interest. It was significant that the same kinds of complaints were presented in reverse. Doctors here may say that they receive too much direct mail information whereas doctors in the Soviet Union appear to lack essential information in respect of new products and drugs. We say drugs are too expensive but they do not know the price and use them freely but suggest that they are expensive and perhaps even more expensive under their system. The title of the article of course was "Ironic Contrast". The same complaints were presented in reverse and that is an ironic situation.

Mr. MARCOUX: Do you know of any new drug discovered behind the iron curtain in the last ten or twenty years?

Mr. WIGHTMAN: Yes. New antibiotics have been produced there, for example, and they are quite different than ours.

Mr. ORLIKOW: I should like to ask a question in respect of antibiotics. Is it not a fact that we have had much too wide use of antibiotics for a number of years, and I am thinking for example of antibiotic losenges which were on the market at one time but have now been discontinued?

Mr. WIGHTMAN: Yes.

Mr. ORLIKOW: I understand this limitation resulted from the fact that indiscriminate use of this kind of drug led to the development of a much more resistant strain of the bacteria?

Mr. WIGHTMAN: The indiscriminate use of these antibiotics led to the development of sensitive patients. The patients became sensitized so that when they needed an antibiotic they were allergic to many and required a different kind. I think the indiscriminate use of antibiotic losenges would not produce resistant organisms. I think the use by hospitals of antibiotics may have created this situation.

Mr. ORLIKOW: That involves my next question. Is it not a fact that for a number of years antibiotics were used in cases which did not require their use thus contributing to the necessity to use much greater doses than say 10 or 15 years ago in order to get the same results?

Mr. WIGHTMAN: The answer to your question is again divided into two parts. It is true that antibiotics were used in an attempt to prevent bacterial infection either in advance of or after an operation. This popular use of antibiotics necessitated the use of more and more antibiotics because there was an organism that became resistant, but that use did not make it necessary to use larger amounts of antibiotics.

Mr. ORLIKOW: Are the doses of penicillin, for example, which are now being used, much greater than they were in the past? The doses are now reaching the millions of units stage.

Mr. WIGHTMAN: That size doseage is being used only in cases of a very small number of infections, but not in respect of ordinary use. That size dose is only given to people infected with a certain type of bacteria. This requires the use of doses at these astronomical levels and would have been expensive and difficult to administer 10 or 20 years ago.

Mr. SLOGAN: I should like now to revert back to a consideration of research. I know that atomic energy of Canada has quite a large research establishment at Chalk River. It has been found that it was impractical to continue expanding that establishment, and it has been felt that if this establishment was broken up there would be a certain amount of competition so to speak with more interresearch and results. I understand that is why the new research centre in Manitoba was established. I have the personal feeling that both government and private industry feel there should be interaction in the research field. Do do you know whether the national research council, for example, when it develops a new drug allows companies to produce that drug without paying royalties, or is the price of production affected by royalties paid to the government for the use of such drugs?

Mr. WIGHTMAN: I believe an organization called the national development incorporated patents things for the government.

Mr. MCNEIL: I cannot answer that question.

Mr. WIGHTMAN: I think there is a mechanism in existence which looks after patents in respect of grantees or government employees, if you want to put it that way. I think there is some mechanism of that type in existence.

Mr. SLOGAN: Do you think that if royalties were not payable to the government in respect of drugs produced by government organizations the cost of such drugs to consumers would be reduced?

Mr. WIGHTMAN: I suppose those costs would be reduced, yes.

Mr. SLOGAN: Has your association made any direct recommendation to the government for the abolishment of sales tax on drugs?

Mr. KELLY: Yes, we have made representations to anyone who would listen to us. Perhaps the most recent representation was made to the minister of finance when he was kind enough to invite us to advise him in respect of matters of concern to us. We made that recommendation to him in respect of sales tax as well as to the royal commission on taxation and the royal commission on health services. We have also made such a recommendation to anyone who would listen to us. We sincerely believe that this is one activity within the competence of this parliament which should be exercised in the direction of making prescribed drugs eleven per cent cheaper to patients.

Mr. SLOGAN: Have drug manufacturing firms indicated that they would pass the savings on to the consumer if the sales tax were rescinded?

Mr. KELLY: Actually we have had many discussions with them and I have inferred that they would be just as happy as we if the sales tax were eliminated. I believe this tax is applied at the wholesale level of drug distribution and there are certain complications in respect of abolishing it at the retail drugstore level. I think the pharmaceutical industry would certainly see that the saving was passed on to the consumer.

Mr. SLOGAN: Is there a federal and provincial sales tax on drugs?

Mr. KELLY: That varies from province to province. In some provinces there is an exception in the case of drugs used in hospitals.

Mr. MACKASEY: Am I correct in assuming that when an article which has been taxed eleven per cent gets to the consumer that per cent has pyramided because the eleven per cent is placed on the item before the profit markup?

Mr. KELLY: I have heard suggestions that that actually does occur. The earlier you take off the tax the better it is in the long run.

Mr. MACKASEY: I have not only heard that this situation exists but know that it does, and I refer to the fact that any product in Canada is subject to an eleven per cent tax but unfortunately the supplier does not pay it, the public does. By the time the public pays that tax it has pyramided to 16 or 16 and one half per cent. Perhaps one of the recommendations of this committee should be that the eleven per cent and three per cent tax should be placed on an article at the time of sale rather than earlier so that the profit markup is not based on the cost of an article say $3 plus eleven per cent but rather on the $3. Today a drug which cost $3 to produce cost the wholesaler $3.33 and he marks it up. I think if such were the case there would be a better chance for the elimination of this tax. In all fairness to the public and to the argument put forward by Mr. Orlikow, I suggest that the manufacturer who is pleading, on the one hand, rather sanctimoniously for the elimination of the eleven per cent is using that eleven per cent tax to make a greater profit. I feel that if an article is $4 the eleven per cent should be added on to that $4 at the time of sale, plus the provincial tax, whatever it may be, rather than added into the cost so that the profit markup is related to $4 plus eleven per cent.

Mr. SLOGAN: I think the federal government is just as guilty in this respect. I am not sure whether there is a tariff on drugs, but where tariffs do apply the sales tax is applied to the cost after the tariff is applied and, therefore, the government is actually charging double taxation. I am not sure whether this situation applies to drugs or not but it certainly is true in respect of other things.

Mr. WHELAN: I should like now to revert to our consideration of research. I am not satisfied in my mind with the suggestion in respect of how research should be carried out. In respect of agriculture the greater amount of research is done by civil servants, and they have done a tremendous job. I think we should be doing more in the way of government research.

Mr. ORLIKOW: Mention was made by a member of this committee that we received some figures in respect of the per capita contribution to research in Canada as compared with the United States and great Britain. Is it a fact that one of the obvious reasons why the per capita contribution in Canada is so low is because a great percentage of drug companies existing in Canada in fact are foreign owned and do not carry out research here, but simply take advantage of the developments of their parent companies, whether they take place in the United States, Switzerland, France or Great Britain, and to that extent there is not very much we can do to encourage that kind of research in Canada?

Mr. WIGHTMAN: I would not say that, because the ten per cent figure refers to government spending on research.

The CHAIRMAN: I do not think that figure was quoted in perhaps the right form. I do not think it had reference to research in its entirety. I do not think it included industrial research, for example.

Mr. ORLIKOW: There are very few products to my knowledge developed completely in Canada. I think most of the new drugs put on the market by companies operating in Canada are the result of developments which have taken place in the United States and in Europe and brought here by the parent company under some kind of licencing arrangement.

The CHAIRMAN: You are referring to two different kinds of research. This refers to independent research. You are talking about drug research by drug manufacturing companies. We are talking about research at an independent level, and research in general.

Mr. WHELAN: I think it was pointed out to us that the Ayerst manufacturing company have some of the largest research facilities in the world at Montreal, so I do not think we can say that they do not do any research here in Canada.

Mr. ORLIKOW: I did not suggest that they do not do any research here.

Mr. WHELAN: I think that inference could be drawn by any one reading the evidence.

Mr. ORLIKOW: You quoted the figures in making a comparison between what is being spent in Canada and elsewhere on research.

Mr. WHELAN: I compared the Canadian government contribution to the contribution by the governments of the United States and the United Kingdom. We have spent less per capita on research at universities and government research centres than any other country.

Mr. ORLIKOW: I think that also applies to the drug companies in Canada and we can ask their representatives when they appear.

Mr. SLOGAN: I should like to refer again to something I raised earlier because I am interested in the situation existing in Alberta which was brought about by legislation dealing with the discretion of substituting prescriptions. Was this legislation drafted and initiated by the government after consultation with the pharmaceutical and medical professions?

Mr. MCNEIL: This legislation was initiated by the government without consultation with either the pharmaceutical association or the medical association.

Mr. SLOGAN: The idea was that this legislation would provide a reduction in the cost of drugs to the people of Alberta?

Mr. MCNEIL: Yes.

Mr. SLOGAN: As a result of the reasons you gave earlier in respect of legal implications, is it likely that the pharmacists will substitute higher priced drugs, doing exactly the opposite thing to that which the government of Alberta hoped.

Mr. MCNEIL: I think so.

Mr. SLOGAN: I notice at the bottom of page 6 of your brief you welcome the recent announcement that the minister of national health and welfare has requested the Royal College of Physicians and Surgeons of Canada to appoint an ad hoc committee to study the existing procedure whereby new pharmaceutical products are evaluated before receiving approval for marketing in Canada. Can you tell me what the Royal College of Physicians and Surgeons has done in this regard?

Mr. KELLY: The Hon. member is referring to our brief to the royal commission which was submitted approximately two years ago before the report of the Royal College had been made to the government. At page 8 of our brief we summarize the important findings of the Royal College committee with which we agree. The first recommendation is the immediate expansion of the staff of the food and drug directorate. I believe that the budget for that particular department has been increased and it is endeavour to find competent staff to carry out more detailed work than has been done previously. Secondly, the proposal of the Royal college was to amend certain regulations under the Food and Drug Act to provide for more adequate clinical trials of new drugs in Canada before they are released for sale, to ensure substantial

evidence of clinical effectiveness for the purpose intended. Considerable progress has been made in implementing that proposal and I think it is significant that they recommend clinical trials on new drugs in Canada, because there is nothing more convincing to the Canadian doctor than being able to read reports of trials, whether favourable or unfavourable, of a new drug by the investigators in this country whom he knows and has confidence in.

Mr. SLOGAN: Do you feel that the Canadian medical association might have a greater role to play by perhaps assuming the responsibility of establishing clinical trials? Surely that would be the natural body to carry them out?

Mr. KELLY: There is a question here of whether we should do this or whether it should be done by that very esteemable organization, the medical research of Canada which, as you know, was founded about three or four years ago when it was separated from the general research activities of the national research council. That body is very competent and makes grants to clinical and other forms of medical research. It is doing a very good job. It does not have as much money as it required.

Mr. SLOGAN: Is this a branch of the medical association or of the government?

Mr. KELLY: Actually it is a government creation, shall we put it that way, with representatives from the university and other medical and laboratory professions.

Mr. WIGHTMAN: Much of the medical sphere supports what is called extramural research. The national research council has its own research laboratories and does research in Ottawa on its own premises. The medical research council by and large supports research in universities, teaching hospitals and units of this sort done by people, whether or not government employees in the sense of national research council people who do carry out research at all levels. But it carries out research on all levels, that is basic science and clinical research applied in the medical sphere. So that this research and these clinical trials would actually be done in the community, and probably, in the first instance, the ones that are developing absolutely new drugs would be doing it in universities.

Mr. ORLIKOW: There has been a good deal of writing in the medical journals in the United States about the difficulties which have been encountered in the testing of drugs by drug companies to which these are sent for clinical testing, and by doctors who are very often very busy in their practices and who have no time or real experience to evaluate the actual effect of these drugs. I wonder if the medical association has given any consideration to the question of clinical testing of new drugs in particular?

Mr. WIGHTMAN: We certainly have.

Mr. MCNEIL: You ask if we have given thought to this. The department of clinical therapeutics in a university centre would seem to provide the most reliable information. I do understand that very satisfactory trials have been carried out by busy practitioners right across Canada, and that pharmaceutical houses have felt that they received very worth-while reports from other than the large centres, large hospitals and large universities.

Mr. ORLIKOW: I was not suggesting for a moment that none of the testing done by general practitioners is satisfactory, but I have here an article which appeared in the *American Journal of Public Health* in May of 1961, its subject being the clinical value of drugs, the sources of evidence, where the author raises very clear questions about some of the testing procedures in the United States. I just wonder if we have had any reports of discussions among the medical profession in Canada on this important subject?

Mr. SLOGAN: It would appear to me that a medical practitioner can, I think, give a better evaluation of the clinical effects of a drug than some therapeutic centre because his relationship with the patient may be long standing and he would know the patient personally. I think he would be in a better position to observe the effect of a drug on a patient rather than some therapeutic centre where the patient reports now and then and where there is really no personal relationship.

Mr. WIGHTMAN: We have had discussions with the medical section of the Canadian Pharmaceutical Association which is made up of doctors whose responsibility to the industry is to arrange these tests and trials of drugs. I think it is important to emphasize that tests of new drugs have to go on at various levels, depending on the stage in their development. There is a stage when they must be tested and very carefully controlled by a highly powered, scientific institution, until initial information has been obtained, but as time goes on and more and more is known about the drug and about its risks in application, there comes a time when it must be tested in the community by the practical physician under circumstances similar to those in which it will be used before it is finally introduced and before you know what it is capable of doing and what are its real dangers. So there is a stage of drug testing which is carried out by the general practitioner in a community and which must be done in this way. It might be that certain drugs might have reached this stage too soon, but by and large it is certainly one of the very important phases of drug testing which we could not do without.

Mr. ORLIKOW: Is it not a fact that a very large percentage of the new products are not really new products but variations of other products? In this article they list in the United States 43 new products, of which only 16 were original products, 10 were new sorts of old products, and 17 were derivatives of known drugs. How can the doctor, who is busy in practice, really judge how much better or how little worse the variation is than before? Is this not a question which should be considered by the medical association?

Mr. WIGHTMAN: It has been discussed. The decision as to whether this can be done or should be done by doctors really depends on the circumstances, and it is the responsibility of the person who does the testing. Sometimes it can be done very well, but sometimes it is very difficult.

Mr. MARCOUX: I do not think the committee should have any reason to infer that any doctor is interested in providing a low grade quality of medicine, and, being myself a medical practitioner, I am interested in providing the best quality of drug, and I rely on the most important sources of information I can. Of course, when I am busy, I cannot delve further into the matter as much as I would like, but I have no intention of providing a low grade quality of medicine. Therefore, even though the medical practitioner has not every opportunity to test the drug for himself, I am sure he is doing everything possible. There is no reason at all to imply that he is not interested in providing the best care he can for his patients as far as it is possible.

Mr. SLOGAN: I should like to follow that up. I wonder if Dr. McNeil could answer this question. We, who are general practitioners, are busy men and we do not have time to evaluate these things. Do you think there should be a body in the Canadian Medical Association, or the medical research council, or another body, that could evaluate new drugs and pass some sort of decision on them to the practitioners who use these drugs so that they would have a reliable guide in choosing the drugs and in making sure that they are of sufficiently good quality to prescribe? Perhaps the food and drug directorate should play a bigger part also, but I think in the end there should be a body —and I think it should be a branch of the medical profession—who would pass on this information, and that this should be put on the label, "This meets the

C.M.A. specification number so and so". Every practitioner has a list of these specifications and he knows what these specifications are; he knows whether he can accept this drug or not. This would do a great deal to reduce the cost of drugs to the consumer. I think it would also be a good guide to the profession. I think both the government and the medical profession would have a part to play in it. Do you feel this would be of service to the public and to the profession?

Mr. McNeil: We think that this is the most important part of our presentation, that such a body be set up. That it be entirely in the hands of the medical association we are not certain. This is a tremendous responsibility and it would be very costly. As you have stated, the government, doctors, industry and pharmaceutical men altogether join in this venture. To state that the medical association should carry this out, I think would be impractical.

Mr. Slogan: I do not say they should carry this out on their own, but the medical research council would be the logical body. You have a representation there from the drug manufacturing industry, the government research bodies and the medical association. For instance, in the matter of penicillin, they would draw up certain specifications as far as quality control, the manufacturing end and various things like that, are concerned. They would then say, "This is specification number so and so." It would then be up to the government to see that these specifications are met at the manufacturing end, and that when this was met by the manufacturer he would be given the privilege of putting on the label that the drug met this specification. When I call at my druggist and say that I want a drug which meets these specifications, I am not particularly interested which company it comes from, but I am interested in having it meet certain specifications. The druggist and the doctor would then have a guide, and the government would do something that would reduce the cost of drugs to the consumer. I do not think the consumer is benefiting other than receiving protection as far as the drugs on the market are concerned, but he is not benefiting in the cost of the drugs at the moment. If such a body carried out these procedures, it would do something to benefit the consumer in the way of cost.

Mr. Kelly: I think we agree with that. We stated that there are two deficiencies, as we see them: the doctor must be assured that what he orders is of high quality, potency and safety. That is the first thing, and that is best done by an unofficial agency such as the food and drug directorate. Secondly, the doctor needs information on new drugs, an unbiased objective appraisal of these new drugs regarding what they do and what they want them to do, their dangers, and all the rest of it. Two years ago we thought the second function should be assumed by the food and drug directorate. I think our minds are changing because we have had conversations with such bodies as the Canadian Pharmaceutical Association, the Canadian Association of Hospital Pharmacists, the Canadian Pharmacological Association and our own committee on pharmacy. Between us we would be able to establish that essential drug information. I am not saying it will go precisely that way, but we are talking about it.

Mr. Slogan: You would have to draw up your own pharmacopoeia, and say that these are the benefits and these are the toxic effects of the drug, and so forth. I think it is long overdue. In mentioning advertising and such information, I want to compliment the Canadian Medical Association on its publication. It is a wonderful thing and a good guide. I think it is something they can well be proud of.

Am I to understand then that the different bodies are working towards this end?

Mr. KELLY: We are in the early stages of conversation with each of them because they are all interested and they all believe they have some expert knowledge to contribute to such a body. Our principals have not said that this is the way it is going to be, but we are negotiating and informing ourselves as to whether it can be done better by a voluntary body or whether the original thought that this function should be carried out by the food and drug directorate is better.

Mr. MACKASEY: Do you not feel that a more pressing problem is the licensing of the manufacturers? I keep coming back to the conversation we had that all these are necessary and desirable provided they are applicable to the industry in general. However, there does exist in Canada certain manufacturers who are not up to the standards we would expect from someone producing drugs. For some reason they are finding it quite easy to circumvent policing action or the responsibility that the food and drug directorate puts on them.

Earlier in our conversation a suggestion had been made that all manufacturers should be subjected to some form of licensing. Do you think this is of immediate concern, or is it a long range objective, or else is it an idealistic condition which we cannot achieve? I, as a layman, cannot understand how we can guarantee safety in everything. You doctors mentioned earlier that all these phases are vitally necessary to reduce the cost of producing drugs, therefore the temptation by such operators would be to sell cheaper, regardless of quality. We find manufacturers in Canada who are actually circumventing the food and drug directorate. I am wondering how this can be prevented.

Mr. KELLY: We think licensing is one means of preventing it. It would control the manufacturer in Canada. But of all the fields, perhaps the field of pharmacology is the most international, and it will not control the manufacturers in Naples and other sources of cheap drugs which we find in Canada. It would be applicable only in this country, but it would go in the right direction.

Mr. ORLIKOW: There would not be much use in licensing manufacturers in Canada if you did not at the same time licence distributors so that you could exercise the same degree of control on drugs that are brought into Canada.

There would have to be a parallel action or else the whole job would not have been done properly.

Mr. SLOGAN: Is there now not as much control on imported drugs, because these drugs are being inspected as they come across the border in many instances? Perhaps they do not have all the knowledge at the source where they are produced, but as far as drugs being imported to the country are concerned, they undergo the same tests as any other drugs.

Mr. WIGHTMAN: I do not think so, unless someone asks to have it tested, and then again they have to specify the tests which they want carried out.

Mr. SLOGAN: I understand that if any drug crosses the border, the customs official has to advise the food and drug directorate so that they can go and take a sample of the drug. This is their normal procedure. However, they are not notified of every batch of drugs imported to Canada where there is no food and drug man at the port of entry.

Mr. MCNEIL: I think the food and drug directorate may take this drug and chemically test it and label it regarding its substance, but I do not think we can be quite so sure of its functions, as professor Wightman has said.

Mr. SLOGAN: Do you not think that any large quantities of the drug being imported to this country which are manufactured in another country should be investigated at the source, that the manufacturing set up in that country should be investigated before the drug is sold in Canada?

Mr. McNeil: We understand they try to do that and they make certain trips to the old country to examine the manufacturing facilities. However, this seems like a tremendous job. I understand some of these pharmaceutical houses are nothing more than a small garage, or something.

Mr. Willoughby: Mr. Chairman, as far as I can recollect, Dr. Morrell at the last meeting said that these drugs are not allowed to come into Canada and are not allowed to be used in institutions or any other place without having first of all come up to the standards laid down by the food and drug directorate. If they can prove that they meet those standards, then they are accepted, but not before. He was very emphatic on that, the last time he was here.

The Chairman: If I may say it, the difference here I think is obvious, that the drugs undergo certain tests but they are mostly a quantitive control as opposed to qualitative control. This is the big difference.

Mr. Willoughby: He said they would accept evidence from reliable sources and other such information in the country of its origin and then would not have to submit it to all those tests in Canada, but if they were not satisfied with those tests, they would refuse entry of the drug.

Mr. Orlikow: Surely the point is that if we could devise a system—if we have not got it yet and I do not think anyone would argue that we have achieved the optimum in testing—whereby any drugs which were for sale in Canada, whether they were produced in Canada or outside, could get through the licensing or through adequate testing, the doctors could be assured of the standard which they required and then of course you would be able to get the kind of price competition without reduction in quality which the doctor wants and which the prospective purchaser of the drug wants. Surely that is what we ought to be aiming at.

Mr. Kelly: This comes back to the seal of approval by some reputed authority that what is in the package is as represented and is trustworthy.

Mr. Mackasey: This is precisely what Dr. Morrell said. My question was in respect of drugs being brought into the country. Are there not policing methods to make sure the country of origin is specified as well as the ingredient? And Mr. Morrell said:

> If a drug is brought in, packaged and ready for sale, we have an opportunity to see it at the customs, and we do take samples there and hold it for testing; or we can let it go through customs and go to the distributor.

Further on he says:

> We do not have a food and drug inspector at every customs port. I am not sure how many there are, but there are hundreds of ports, I believe. We do have an arrangement with the customs officers that when a shipment of drugs comes in they notify our nearest inspector who goes out and looks at them. We do have our own inspectors at the largest ports who go right down and look at the manifests, and so on, and take samples at the port of entry.

The point I am getting at is that these are raw materials. After going through the port of entry and into the hands of the manufacturers in this country who may or may not be reputable, what control do we have over these raw materials from that point on to the finished goods if we do not have a system of licensing of all the people who can be using the raw materials and turning them into the finished products?

Mr. Wightman: I think what you are speaking of has to do with drugs packaged for sale, but it does not apply to a substance in bulk.

Mr. MACKASEY: Mr. Chairman, is this the only appearance of the Canadian Medical Association or will they be back on Friday?

The CHAIRMAN: This is their only appearance. This is the presentation of the brief of the Canadian Medical Association. One of the witnesses the steering committee considered calling is Dr. Wightman himself. We will call him as an individual to speak on the clinical aspects of drugs such as safety and side reactions.

Mr. ORLIKOW: I would like to make a suggestion. To me, the important question of the cost of drugs in the submission of the Canadian Medical Association is included in part of their statement on page 12 of the brief where they disagree with the recommendations of the Restrictive Trade Practices Commission. I think that question is likely to take a considerable period of time in discussion. In line with our general agreement I would like to suggest that we should try to separate the two topics, namely the safety of drugs and the price of drugs. I think we should agree that when we come to the question of the cost of drugs we ask the Canadian Medical Association representatives to come back in order to discuss that subject with us. In that light I would be agreeable to letting this go for the time being.

And, while I am on that subject, I think that at some point when we are discussing the cost of drugs we should ask the officials of the restrictive trade practices commission to make a presentation and to appear before us.

Mr. MACKASEY: First of all, I would like to commend our witnesses for such an excellent brief. You have indicated the Medical Association disagrees with the proposal of the restrictive trade practices commission, that Canada should abolish patents on drugs. We will have an opportunity to discuss this later.

The CHAIRMAN: As Mr. Orlikow has suggested, this is such an important topic, and it would be so time consuming, I think at a later date when we are discussing costs we will invite representatives from the Canadian Medical Association for a separate discussion of this one topic.

Mr. WILLOUGHBY: Mr. Chairman, I want to revert back to a statement made by Dr. Morrell when he appeared before us. In respect of new drugs which are offered in the United States, Dr. Morrell said:

> I doubt very much whether the food and drug administration would accept our say so or the say so of any other country in respect of a new drug that was offered in the United States. They would demand it go through the procedures that they require for the introduction of a new drug into the united States and, likewise, although we would accept clinical evaluation if it was adequate according to our requirements—that is, pharmacological and toxicological testing done in the United States—nevertheless, we want to see what was done and we would want to see the complete details of the manufacturers' knowledge of that drug, just as they do. I think it would be unwise to accept blindly any drug without taking a look at the requirements of any particular country, even the United States.

The CHAIRMAN: Dr. Willoughby, would you give the page reference?

Mr. WILLOUGHBY: This is on pages 30 and 31 of proceedings number 2 of this committee.

The CHAIRMAN: If there are no further questions there are three things I would like to say at this time.

First of all, on behalf of the committee I would like to thank the members of the Canadian Medical Association, Dr. McNeil, Dr. Kelly and Dr. Wightman, for appearing before us this morning to be our expert witnesses on behalf of their association.

The second thing I would like to mention is that one week from today, June 9, Dr. Morrell is due to appear before us to continue his testimony in respect of the food and drug directorate. I Just happen to know that during that time the Canadian Pharmaceutical Association is having a convention here in Ottawa and the members are going to be shown through the workings of the food and drug directorate. Would you like me to approach Dr. Morrell and to say that instead of him coming here we would like to go over there to see how his department works. They are already going to be set up to show the workings of their directorate to another body so we would not be inconveniencing them. What is your feeling on that?

Mr. MARCOUX: I move that we take advantage of this situation and visit the food and drug directorate at the same time as this other body.

Mr. WILLOUGHBY: I second the motion.

Motion agreed to.

The CHAIRMAN: Then, I will approach Dr. Morrell to see if we can visit them one week from today. Then, we can have Dr. Morrell back on the Friday instead of Tuesday.

The third thing I would like to mention is that in our last session we passed a resolution dealing with living and travelling expenses of witnesses, together with a certain per diem allowance. Before we can do this we again have to have the same motion, and I would like to have someone move that this committee pay the reasonable living and travelling expenses incurred by Dr. McNeil, Dr. Wightman and Dr. Kelly, by reason of their appearance before this committee, and that a per diem allowance be made to them. I suggest that it be the same as the amount paid during our last session.

Mr. ORLIKOW: I so move.

Mr. MARCOUX: I second the motion.

Mr. WILLOUGHBY: Was that allowance adequate and satisfactory?

The CHAIRMAN: I do not know. We did not have any comment one way or the other.

Mr. MACKSEY: How much was it?

The CHAIRMAN: It was $50 a day.

Mr. WILLOUGHBY: Expenses?

The CHAIRMAN: Yes. It is really a very small amount. I understand this has been the amount which is now accepted by the committee for professional or expert witnesses.

If there are no other problems, gentlemen, we will adjourn.

Mr. ORLIKOW: Is there a meeting on Thursday?

The CHAIRMAN: There is a meeting on Friday at which time the Canadian Pharmaceutical Association will be here. The meeting will commence at 9.30 a.m.

APPENDIX "A"

SUMMARY OF THE INTRODUCTORY REMARKS MADE TO THE PARLIAMENTARY COMMITTEE ON FOOD AND DRUGS WHEN THEY VISITED MOUNT ROYAL CHEMICALS LIMITED AT DORVAL, QUE., ON MAY 28, 1964, BY MR. ROGER LAROSE, PRESIDENT

Mount Royal Chemicals Limited is a typical pharmaceutical manufacturing plant in that it transforms therapeutically active substances into pharmaceutical products. It is owned on an equal share capital basis by two Canadian companies of Swiss origin—Sandoz Pharmaceuticals, Division of Sandoz (Canada) Ltd., and CIBA Company Limited. Mount Royal Chemicals Limited, with its neighbours—CIBA and Sandoz—form a compact which exemplifies the growth of the pharmaceutical industry in Canada. Both CIBA and Sandoz came to Canada in the 20s and started their operations by importing finished pharmaceutical products. They later imported pharmaceutical products in bulk, tablets, ampoules and other pharmaceutical forms and packaged them in Canada. Later still they started manufacturing the tablets, ampoules, ointments and solutions.

In 1957 CIBA and Sandoz incorporated Mount Royal Chemicals Limited for the specific purpose of manufacturing pharmaceutical products primarily for both partners and also, if facilities were available, for other Canadian manufacturers. Sandoz had already settled at Dorval and CIBA was about to. The new company—Mount Royal Chemicals Limited, purchased a piece of land between the Sandoz and the CIBA tracts. Construction of Mount Royal Chemicals Limited was started in October 1958 and finished a year later, so that the production facilities of CIBA, which were already available to Sandoz, were moved from downtown Montreal to the Mount Royal Chemicals Limited plant at Dorval. The available floor space of Mount Royal Chemicals Limited is 56,000 square feet and in 1963 it produced over 200-million compressed tablets, about 70-million coated tablets, 5-million capsules, half a million ampoules, 75,000 litres of liquid preparations, 20,000 kilos of cream or ointment and 4½ million finished packages.

In March, 1960, Mount Royal Chemicals Limited opened a pharmaceutical research laboratory.

Sandoz and CIBA remain completely independent companies both in Canada and abroad. In Canada, while Mount Royal Chemicals Limited has invested 1½-million and employs a staff of 91 persons, Sandoz has invested 1.6 million with a staff of 110, and CIBA 3½ million with a staff of 198.

At Mount Royal Chemicals Limited, pharmaceutical substances emanating from the research conducted by CIBA and Sandoz respectively in Switzerland and in other parts of the world are manufactured into pharmaceutical products. Practically all of the raw material, other than CIBA's and Sandoz active substances, are purchased in Canada. All substances are tested at Mount Royal Chemicals Limited when received and tested again after their incorporation into a finished product.

Mount Royal Chemicals Limited is manufacturing also for a few customers other than CIBA and Sandoz, for instance, Geigy.

APPENDIX "B"

REMARKS MADE BY MR. JOHN B. FROSST AT COMMENCEMENT OF VISIT BY MEMBERS OF COMMITTEE ON FOOD AND DRUGS TO LABORATORIES OF CHARLES E. FROSST & CO. MAY 28/64

Safety of drugs has two chief aspects. One is the ratio of toxicity of a product to its benefits. The other is the accuracy with which a product is made. Today we are primarily dealing with the latter.

We plan to show you production and control in pharmaceutical manufacturing. This will include in—process control as well as control of raw materials and finished products.

We shall not take time to show you all our research laboratories. But because one segment of them, pharmaceutical research, is so closely allied to production we hope you will be interested in a look at this department.

Many companies of this industry in spite of being defined as pharmaceutical manufacturers would be described more clearly if they were called pharmaceutical developers, manufacturers and marketers. This is because many of our companies are much more than manufacturers. Nearly all of them are also marketers of pharmaceuticals and of course many are also basic developers of new products.

Speaking also for the industry there are those companies who have adequate quality control and those who may not. The new laws should soon start having their effects on the latter. A few years ago the Canadian Pharmaceutical Manufacturers Association started advocating the adoption of laws to give greater assurance that Pharmaceutical Manufacturers are equipped and staffed to be capable of assuring quality products—and that they do indeed carry out the necessary procedures. Our Association also asked for compulsory registration of all producers to enable the Food and Drug Division to know of the very existence of each one and thus be able to check up on him.

We have obtained the new regulations on minimum standards but no regulations requiring registration. The well established companies are hoping that the less known organization may not be overlooked from the standpoint of inspection.

Housed in these buildings and stretched across Canada is a group of people representative of this industry that has been nurtured and growing since the turn of the century. This Canadian Company provides work for Canadians and is the means of retaining and developing professional people for the benefit of Canada. This group of people is in reality many teams but because they operate so well together we refer to them as members of one team. Their efforts have been responsible for great relief to mankind here in Canada and elsewhere. They have directly and indirectly saved and prolonged the lives of tens of thousands of citizens of this, and recently past generations. They are supported, of course, only through the sale of our products here and in foreign countries or by the licensing of our processes abroad.

On this display is a summary of some of the things you will see today.

Before we start a tour of the plant and of the laboratories Mr. Earl Dechene our chief control chemist will give you a few more details.

APPENDIX "C"

PHARMACY RESEARCH

by

JOHN F. MILLAR, Phm.B., B.Sc.,
Chief Research Pharmacist, Charles E. Frosst & Co.

I have been asked to outline the function and duties of the Pharmacy Research Laboratory in our industry. The position of this department in the general organizational setup of a pharmaceutical company is best illustrated by reference to a chart. Here we have shown the principal activities and steps that are taken in the development of a new drug product.

I would like to emphasize that this work requires the coordinated efforts of several specialized groups of various kinds.

The three main phases of activity are—Planning, Investigation and Implementation. You can see that Pharmacy Research is involved in both the Investigation and Implementation stages of progress.

First, I will discuss our function in the area of 'Investigation'. Let us assume that a new chemical created by the Chemical Research group has passed through the many tests carried out in the Pharmacology Laboratories using small animals and that data has been obtained to show the potential utility and apparent safety of the material as a new drug.

At this point, consideration must be given to preparing the material in a useful and convenient physical form for further work in evaluation of the drug in larger animals and ultimately in human beings.

Pharmacy Research is accordingly called in as part of the team and assigned the job of formulating the new drug into suitable dosage forms such that further studies can be carried out.

These dosage forms may be capsules, tablets, oral liquids, suspensions or injectable solutions, depending upon the chemical nature of the drug concerned and its pharmacological activity.

The problems encountered in this work are often quite complex, as a great many factors are involved in designing a product that will meet all our requirements for physical and chemical stability, shelf-life and acceptability by the patient, and ultimately lend itself to being routinely manufactured on a production scale.

To illustrate the development of a pharmaceutical product, I will outline the steps involved in an actual project of our own laboratory, concerned with the formulation of an antibiotic suspension.

The project assigned by our research director, was to develop an oral liquid for pediatric use, which would provide a high dose of penicillin in a palatable suspension. The type of penicillin to be used, was a newly developed, tasteless and almost insoluble salt which had been prepared in our chemical research laboratory.

Now one might think that this would be a fairly easy, straightforward procedure involving not too many problems. You have a crystalline powder, just mix it with some water, add a little sugar for flavoring and there it is—a new product. However, things are never quite as easy as they may appear on the surface. On examination of the physical and chemical properties of this

material, one of the first problems encountered by the research pharmacist assigned to the project, was that the drug is extremely hydrophobic—that is, it has little or no affinity for water and can not be easily wetted to form a suspension. Thus the first part of the job was to find a suitable non-toxic and physiologically inert wetting agent which would permit our penicillin powder to be dispersed in water. Mr. Findlay will demonstrate the nature of this problem.

Once a means had been found for dispersing the drug, the next step was to ensure that the dispersion would remain homogeneous and not settle or pack in the bottle. This part of the work involved a search for a compatible suspending agent which would prevent agglomeration and sedimentation. This aspect of a suspension is highly important with potent drugs and here is an example of an unsatisfactory suspension.

The next phase was an investigation of the chemical stability of the drug suspended in the basic vehicle which had now been developed. This involved the cooperation of our analytical laboratory to provide microbiological assays of many of the experimental formulas. In this work, we found that the pH of the suspension—that is, the degree of acidity, was very critical for maximum stability of the drug so that stabilizing agents (buffer salts) were added to control this factor.

Then, a good deal of attention was devoted to the selection of suitable flavoring and coloring materials, so as to obtain maximum palatability and a pleasing appearance for the product. This phase also involved extensive stability testing and analytical work to perfect a final suspension formula which would not deteriorate in terms of activity, flavor or color on long standing.

By the time all these data has been established, several hundred man-hours had gone into the formulation of what was, essentially, a tailor made vehicle to provide the physician with penicillin in the form of a stable, palatable liquid suitable for administration to children.

Problems of similar or more often, greater, complexity are also dealt with in the formulation of other types of dosage forms. For example, the development of tablets is a highly specialized area of technology in itself and approximately half our group are involved in tablet research in the next two labs.

A tablet is a very convenient and useful form to provide the physician with the means for precise dosage of the many potent drugs that are presently in use. It can also be manufactured accurately by mass production methods, with the equipment now available in the industry.

There are, however, many important details involved in the design of a completely satisfactory tablet. The tablet making process in general, comprises mixing the active ingredient with suitable inert diluents, binders and disintegrants, forming the mixture into small granular particles having free-flow characteristics and then subjecting the granules to compressive forces to form a solid object.

The essential requirement in nearly all tablet formulations is that the finished product must be very sensitive to water and digestive fluids, so that when a tablet is swallowed, the original particles of drug are quickly and completely available for absorption in the digestive tract.

It is evident that carefully controlled experimental techniques are required to evaluate and select the proper additives in a tablet formulation to meet disintegration standards and other requirements.

To illustrate the importance of this aspect, Mr. Findlay has a small demonstration of tablet disintegration to show you.

To summarize, it is the job of the Pharmacy Research group to select the combination of ingredients required to accomplish all the required objectives, of a dosage form, carry out the necessary physical and chemical tests in conjunction with the analytical laboratory and then submit the final product to the pharmacology and medical research groups for biological evaluation.

Now, to refer again to the chart. When all the investigational work has been completed, the data from each stage is combined into a new drug submission which is sent on to the Food and Drug Directorate for their examination. If the submission complies with the FDD requirements, the new preparation may then be sold subject to the provisions of the regulations.

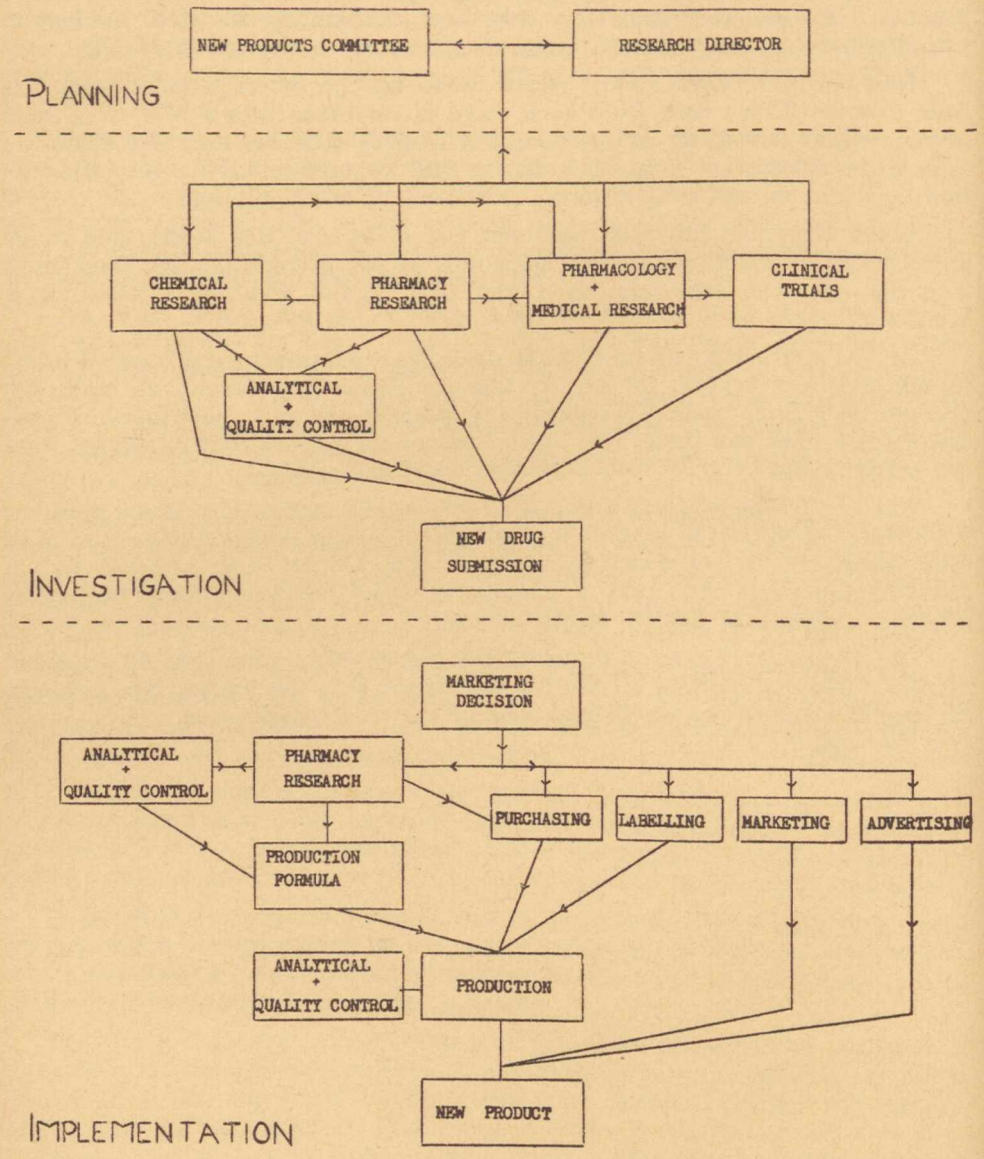
When clearance has been obtained and a decision has been made to go ahead with the manufacture and marketing of the preparation, we then move into the stage of Implementation and here again, Pharmacy Research is involved.

At this point it is our function to draw up a manufacturing formula based on our laboratory work, for use by the production departments to make the product on a large scale. This document specifies the raw materials, the processing directions and the product specifications for quality control and becomes the master record for all future production of the product.

Another function of our group is to continually review and assess products we already have on the market in the light of newer developments that have been discovered in our own laboratory or reported by other workers in the field. In this way, we have a continuing objective to upgrade our older products in terms of quality improvement.

Our Pharmacy Research group at the present time comprises 12 technical people, 8 pharmacists and 4 technical assistants. It is the largest lab. group of its type in Canada and we believe, one of the most progressive.

May 28, 1964.


NEW PRODUCTS COMMITTEE
RESEARCH DIRECTOR
PLANNING
CHEMICAL RESEARCH
PHARMACY RESEARCH
PHARMACOLOGY + MEDICAL RESEARCH
CLINICAL TRIALS
ANALYTICAL + QUALITY CONTROL
NEW DRUG SUBMISSION
INVESTIGATION
MARKETING DECISION
ANALYTICAL + QUALITY CONTROL
PHARMACY RESEARCH
PURCHASING
LABELLING
MARKETING
ADVERTISING
PRODUCTION FORMULA
ANALYTICAL + QUALITY CONTROL
PRODUCTION
NEW PRODUCT
IMPLEMENTATION

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 4

FRIDAY, JUNE 5, 1964

WITNESS:

Mr. John C. Turnbull, B.S.P., Executive Director, The Canadian Pharmaceutical Association, Inc., Toronto, Ontario

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

20849-1—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Casselman (Mrs.)
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jorgenson
Macaluso
Mackasey
Marcoux
Nesbitt
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabriel Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

FRIDAY, June 5, 1964.
(8)

The Special Committee on Food and Drugs met at 9:45 a.m. today. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Côté (*Longueuil*), Enns, Francis, Harley, Howe (*Hamilton South*), Marcoux, Orlikow, Prud'homme, Rynard, Slogan, Whelan, and Willoughby—(12).

In attendance: Mr. John C. Turnbull, B.S.P., Executive Director of The Canadian Pharmaceutical Association, Inc., of Toronto.

The Chairman referred to a letter received from Mr. Claude Jodoin, President of the Canadian Labour Congress stating that his organization has decided not to accept the Committee's invitation to submit a brief on the question of "safety of drugs", but would like to make a submission on the cost and marketing of drugs at a later date.

The Chairman announced that it has been arranged that the Committee visit the laboratories of the Food and Drug Directorate at Tunney's Pasture, Tuesday morning, June 9, at 9.00 o'clock.

He then read into the record the list of witnesses to appear before the Committee up to the 10th of July.

The Clerk of the Committee was instructed to supply copy of this schedule to the Members of the Committee.

The Chairman introduced Mr. Turnbull presenting a submission on behalf of The Canadian Pharmaceutical Association, Inc. It was agreed that the brief be taken as read, and Mr. Turnbull was questioned thereon.

Discussion concluded, the Chairman thanked the witness on behalf of the Committee.

On motion of Mr. Francis, seconded by Mr. Marcoux,

Resolved,—That the Committee pay reasonable living and travelling expenses incurred by Mr. John C. Turnbull, B.S.P. of Toronto by reason of his appearance before this Committee; and that a per diem allowance be made to him.

At 11:00 a.m. the Committee adjourned to Tuesday, June 9, for a visit of the laboratories of the Food and Drug Directorate.

Gabrielle Savard,
Clerk of the Committee.

20849-1—1½

EVIDENCE

FRIDAY, June 5, 1964.

The CHAIRMAN: Gentlemen, we now have a quorum. First of all let me say that I have had some correspondence from the president of the Canadian Labour Congress, Mr. Claude Jodoin, saying that they felt that they would not submit a brief on the question of the safety of drugs but that they would like to appear before the committee when it is discussing cost.

Now, just briefly, I would like to go down our future schedule of meetings. Next Tuesday we have arranged for as many of the members of the committee who wish to go to have a tour through the food and drug directorate. This is located in Tunney's pasture, which is at the end of Holland avenue, above Scott street. It is about a ten to fifteen minutes ride from here. The Ontario Pharmacists Association are going through at the same time and they are starting their tour at nine o'clock, which would mean it would be a little bit earlier than we are used to. I have my car and would be glad to take anybody out who would like to go. We would have to leave here about a quarter to nine. Miss Savard has also a car and would be willing to take anybody out, and I am sure so have other members. So, instead of a regular meeting next Tuesday, we will go out to the food and drug directorate. This will give the members an opportunity to actually see what the department does. If anybody wishes to go, please be in front of the west block at twenty minutes to nine; that will give us more than enough time to get out there.

Mr. ENNS: It is not too far from the new building, is it?

The CHAIRMAN: It is beside it.

On Friday, June 12 we will have Dr. R. F. Farquharson, chairman of the medical research council. I thought he would make an excellent witness. He is an ex professor of medicine at the University of Toronto, and is now chairman of the medical research council. I know a lot of members are interested in research.

On Tuesday, June 16 we have Dr. Morrell of the food and drug directorate again in this room, and we will be able to continue our questioning of the food and drug directorate.

On June 19 we have the Canadian Pharmaceutical Manufacturers Association. On Tuesday, June 23, we will have the Canadian Association of Consumers, Mrs. Plumptre. On June 26 we will have Dr. R. Imrie of the poison control centre. He is paediatrician in charge of the poison control centre at the hospital for sick children in Toronto.

The next two dates are blank. On July 7 our visitor is Lederle research laboratories, and on July 10, Cyanamid of Canada Limited will be presenting a brief here.

I deliberately have not filled in Tuesday June 30 and Friday July 3, because I am not sure what is going to happen on the dates surrounding the holiday of July 1. Mr. Orlikow has suggested that Dr. Cameron should come on one of those two dates, and it is my suggestion we ask him to come on July 3, and perhaps leave June 30 blank until we are sure what will happen on the days surrounding July 1.

What we might do is to have the agenda circulated to the members.

Mr. ENNS: That is a good idea.

The CHAIRMAN: Is it the wish of the committee to do what I have suggested, that we invite Dr. Cameron, who is the gentleman in charge of the psychiatry at McGill University, on July 3, and at the moment leave June 30 blank?

It is agreed.

Gentlemen, I would like to introduce this morning Mr. John Turnbull, executive director of the Canadian Pharmaceutical Association. I am sure you have all received the blue brief. It is a 16 page brief. I am not sure how many of the members have studied it. I think Mr. Turnbull is willing to either take it as read or to read it, whichever the committee wishes.

Mr. ORLIKOW: How much time have we got?

The CHAIRMAN: The house sits at 11 o'clock.

Mr. ORLIKOW: Is it planned that we meet later?

The CHAIRMAN: It was not planned. It really depends on what happens. Usually we have been able to finish with the witness in this length of time. Perhaps today we will not be able to do so. I am not sure whether you are available, Mr. Turnbull?

Mr. Turnbull says he is available this afternoon if the committee wishes him to come back.

Mr. ORLIKOW: Subject to my usual reservation that we have this organization back when we are going to discuss the question of costs, I think we can finish this morning, as far as I am concerned anyway.

The CHAIRMAN: Have the members of the committee read the brief or do they wish it read? We will take it as read.

(NOTE: The brief referred to follows):

We are pleased to present The Canadian Pharmaceutical Association* before the Special Committee on Food and Drugs of the House of Commons. In so doing, it is our aim to make known the views of The Association concerning matters related to drug control and pertinent information respecting the distribution of drugs and the provision of pharmaceutical services in Canada.

Identification and Orientation

1.1 The Canadian Pharmaceutical Association Inc., was founded in 1907 and incorporated by Federal Charter in 1924. It is representative of the Provincial Statutory Pharmacy Organizations in Canada and their over 8,000 registered pharmacists, excepting those of the College des Pharmaciens de la Province de Quebec, which withdrew from constituent membership in the Association effective July 1, 1962. Hence, the Association membership is comprised of pharmacists in all fields of pharmaceutical endeavour in Canada—community retail, hospital, teaching, industry, production control and distribution, government, armed forces, etc. In addition to the representatives of each Provincial Statutory Pharmacy Organization, there are seated on its Council the delegates of the Canadian Conference of Pharmaceutical Faculties, the Canadian Society of Hospital Pharmacists and the C.Ph.A.'s Section of Industrial Pharmacists. For the sake of clarity we would point out that the latter bears no relation to the Canadian Pharmaceutical Manufacturers Association which is an organization of certain companies involved in the manufacture and distribution of pharmaceutical products in Canada.

*NOTE: The initials 'C.Ph.A.' which appear from time to time in this brief refer to the Canadian Pharmaceutical Association, Inc.

1.2 The views of Canadian Pharmacy concerning drug control and related matters having an effect, direct or indirect, on the health and welfare of Canadians have from time to time been made known by The Canadian Pharmaceutical Association in presentations both to legislators and those charged with the administration of legislation. The Association has detailed these in extensive presentations made before various legislative committees and Royal Commissions. In particular, we respectfully draw the attention of the Special Committee on Food and Drugs to the Briefs presented by The Association before hearings and meetings of (1) The Royal Commission on Government Organization, July 31, 1961; (2) The Restrictive Trade Practices Commission, October 24-27, 1961; (3) The Royal Commission on Health Services, May 25, 1962; (4) The Special Committee of the Royal College of Physicians and Surgeons reviewing new drugs, September 27, 1962; (5) The Royal Commission on Taxation, May 2, 1963. In addition, The Association assisted during hearings of the Ontario Select Committee on Drugs and has published views on its Report. Too, Pharmacy's organizations, in every province, have extended the wholehearted co-operation of the profession to provincial legislators and provincially orientated committees.

1.3 This presentation, then, will, in the main, attempt to recapitulate many of the matters which have been discussed previously and, where possible, update the facts and figures believed to be of particular interest.

Pharmaceutical Legislation

2.1 Although the British North America Act clearly designates health matters as a provincial responsibility, drugs, as such, are not specifically mentioned and thus, legislation pertaining to them involves matters of concern to both Federal and Provincial Governments. Federally, legislation based on constitutional power in relation to Criminal Law is intended to protect the consumer from health hazards and from fraud and deception arising from the sale of drugs. Provincial legislation concerns itself with matters respecting property and civil rights and deals more specifically with the actual distribution of drugs and professional control over them.

2.2 It is the belief of The Association that the Food and Drugs Act and its Regulations is conscientiously administered by knowledgeable and capable persons operating within the severe limitations of a restrictive budget of money and personnel. Canada's population is increasing and its manufacturing industry expanding, and, due to the scientific and technical aspects involved, drug production has become most complex. Thus, we have for some time emphasized the need for a well defined departmentalization of food control and of drug control and we are pleased that, to a certain extent, this is taking place. Drug control matters should be specifically handled by those who have a special competence in the field and who can work outside the problems besetting those who are responsible for food control and do so with a complete understanding and appreciation of all scientific, technical and economic aspects. The Association restates its recommendations:

(1) Exclusive of the Proprietary or Patent Medicines Division, the divisions of the Food and Drug Directorate are the Scientific Services, the Inspection Services, the Administrative Services, and five regional divisions. We recommend that in each of these divisions there be a more clear-cut differentiation between the personnel involved and the duties of such personnel in respect to food control and to drug control.

(2) We recommend that consideration be given to the establishment of either or both of the following:

(*a*) In addition to the present Deputy Minister (Medical) there be a Deputy Minister (Pharmaceutical)—qualifications: Ph. D. degree, with undergraduate or graduate training, or preferably both, in a Pharmacy faculty.

(*b*) Either the Director or an Associate Director of the Food and Drug Directorate should possess qualifications as outlined in (*a*) above.

(3) Scientific Services: We recommend (*a*) that the central laboratory services division include, in addition to the present pharmaceutical chemistry section and other existing sections, a pharmaceutics section, and that an essential requirement for technical staff in these two sections be undergraduate, or preferably graduate, training in a Pharmacy faculty and, further, that such individuals be classified within the Civil Service as 'pharmacists'; (*b*) that the technical staff in each regional laboratory include one or more pharmacists, so classified.

(4) Inspection Services: We recommend (*a*) that all members of the central inspection staff whose responsibilities include the inspection of drug manufacturing plants have at least a minimum qualification of an undergraduate degree in pharmacy, and (*b*) that inpection of retail pharmacy establishments at the regional level be carried out by inspectors who have an undergraduate degree in pharmacy. In this connection, we draw attention to the fact that this is the policy followed in the Division of Narcotic Control and that a successful record of enforcement has resulted.

Quality and Quality Control

3.1 Quality related to a drug preparation is something which must be built into it and cannot merely be tested into it. In recent months, stringent regulations have been written so that products being dispensed by pharmacy practitioners will be know as meeting certain minimum quality standards, at least. Full governmental supervision over manufacturing procedures should never be necessary and, indeed, is impractical from a manpower viewpoint but it is the strong view of the Association that only under a system of licensing at the federal level can the authorities be assured that they have the means of scrutinizing manufacturing facilities and control procedures. It may be argued that licensing for such purposes falls within the constitutional right of the provinces. If this is correct, it can be readily seen that a somewhat heterogeneous set of ten different licensing regulations might be written relative to a nationwide problem. We believe that provincial legislators would, in the interests of the citizens of Canada, readily relinquish provincial prerogatives in this regard if made aware of the problem.

3.2 The degree of quality control on drug products that is mandatory under present regulations, is not such as to give absolute assurance to the pharmacist that any given batch of the product of all manufacturers will meet required specifications and indeed, community pharmacies and institutions cannot possibly individually equip themselves to quantitatively examine the multiplicity of drug preparations which they handle nor could they and, in turn, the consumer, finance such operations.

Correction of Potential Hazards

4.1 Secret formula drug preparations sold under the Proprietary or Patent Medicine Act are registered under a licensing procedure administered by the Food and Drug Directorate. The Association continues to recommend that in the best interests of the consumer, the labels of all medicinal preparations should bear the common names of all active ingredients. Further, the Association expresses its extreme concern relative to advertising pertaining to medicinal products which does not give proper attention to the supplying of information which should be known to the consumer of potentially dangerous medications.

4.2 It is recommended that a more rigid screening of promotional claims concerning drugs and drug preparations be instituted. Of particular significance to those involved in the prescribing of drug therapy as well as those who render pharmaceutical services is information concerning toxicity and possible adverse and unpredictable side reactions.

4.3 There is evidence that the ever-increasing number of potent and potentially hazardous products, both drug and non-drug, on today's market, require poison control information to be available on a 24-hour basis from one central source, in addition to the present decentralized locations across Canada.

4.4 There are, at the federal level, various pieces of legislation in addition to the Food and Drugs Act which deal with substances hazardous to health (such as disinfectants, pest control products and additives to veterinary preparations) and which impose certain restrictions concerning same. The failure of these to apply sales restrictions equally to all distributors has contributed to a lack of proper public recognition of the dangers involved. There is a great need in Canada, federally and/or provincially, for legislation—such as a "Hazardous Substances Act"—which properly controls all the many substances which do not fall naturally within the scope of existing control legislation or which may be used for purposes other than those for which the legislation is intended (e.g.—distribution and control of methyl hydrate, an extremely dangerous poison having common consumer, business and industrial uses, is controlled by the Excise Act).

4.5 The C.Ph.A. supports the recommendation of the Canadian Medical Association to the effect that information regarding toxicity hazards be closely associated with advertising material and further suggests that basic information regarding dosage and toxicity might well appear on all labels and/or inserts of the manufacturer's package of drug preparations.

4.6 The recent unfortunate occurrences which necessitated the recall of certain drugs from the Canadian market, point up the need to initiate procedures not presently in force whereby the Association and, in turn, the associations of the provinces across Canada will be informed at the earliest possible time when the matters regarding the questionable safety of a drug arise subsequent to its release for general therapeutic use. Also, it has been well demonstrated that there is a need for some central agency to which physicians in private practice as well as in institutional practice may informally or otherwise report untoward drug reactions. In this way a toxicity information centre may receive, collate and distribute information on such reactions and effects of all drugs as well as industrial and household agents.

Review Committee and Boards

5.1 The Association, through its constant and long-standing liaison with the federal authorities and in particular the Food and Drug Directorate, is well aware of the need for a constant review of all matters respecting drugs in Canada. It is the firm belief of The Association that all matters and recommendations pertaining to drug control measures should be implemented by moves arising from consultation with groups such as the Canadian Drug Advisory Committee of the Department of National Health and Welfare. This Advisory Committee, meeting at more frequent and regular intervals, could, we are convinced, serve a much expanded role. It is essential, too, that ad hoc committees and expert committees and similar bodies working with reference to the Canadian Drug Advisory Committee benefit from the availability of information dealing with technical and professional aspects of Pharmacy.

5.2 Expressions of opinion concerning pharmaceutical matters by those possessing no special competence in Pharmacy cannot be accepted as expert. The Association is of the firm belief that if the public good is to be fully served, pharmacists must be appointed to serve in advisory, administrative and staff capacities on committees and boards charged with the health and welfare responsibilities.

New Drugs

6.1 Canadian drug legislation is well respected throughout the world. Procedures relative to the introduction of new drugs are sound. The Food and Drug Directorate quite rightly does not function as a certifying agent for the efficacy of drugs which it approves for marketing in Canada. A criterion as to effectiveness should be that the manufacturer of a new drug be required to support, with substantial evidence, the claims to be made for it. It would be desirable for such evidence to result from clinical investigations conducted under Canadian authorities.

6.2 A serious deficiency, however, in the legislation and/or its regulations is the failure to require a manufacturer to first hold a license from the federal authority before he may market a new drug. It is believed, too, that specific authority should be provided by the Regulations to enable the Directorate to cancel a 'certificate of compliance' and to immediately stop all sales of a drug.

Sources of Drugs

7.1 Canada, drugwise, is a primary source of very few materials or substances. Its primary supplies, at least, must be imported for further processing or packaging. The drug products stocked by pharmacists are mainly those mass-produced according to standards which equal or surpass the standards laid down in official reference texts. Drugs today are potent and highly specific and, hence, play an important and significant role in the therapy of the ill and diseased as opposed to the mere palliative effect expected of them in yesteryears.

Patents

8.1 We cannot share the opinion that has been expressed by some that patents respecting drugs be abolished. The Association is of the strongest opinion that Canada's patent legislation must be such as to provide for the enhancement of an active, self-sustaining and ever-growing pharmaceutical industry within our boundaries.

8.2 Canada's patent legislation recognizes that the inventor of a drug is entitled to the same protection as is accorded to originators in other fields, provided that the usable end product of his invention is freely available to meet the needs of Canadians. It is the opinion of the Association that patent protection should extend to a drug's production process regardless of its country of origin and provided, also, that in due course, but not exceeding a period of three years or other suitable period made necessary by the nature of the drug, it should be produced in Canadian-based manufacturing facilities. As at present, patent holders should have the right to license other producers. Compulsory licensing provisions of the Patent Act should continue to be exercised to facilitate legal production by Canadian companies.

Nomenclature

9.1 The present system of naming drugs can result in a single entity having at least two non-proprietary names—a chemical or botanical name, as well as a common, generic, proper, official name—and in addition, the brand, trade or proprietary name registered by a manufacturer or distributor.

9.2 The C.Ph.A. believes that the originator who successfully establishes his right to a process patent should be accorded the privilege of a proprietary or brand name. It is suggested, to remove confusion arising from a multiplicity of proprietary names, other manufacturers who subsequently market the same entity, whether by license arrangements or otherwise, be restricted to the established, non-proprietary name or the originator's brand name by license.

9.3 The choice of proper names for new drugs is very important and it is recommended that Canada maintain the closest possible liaison with the World Health Organization and with the United States Pharmacopoeia Nomenclature Committee. The latter periodically publishes "United States Adopted Names" (USAN). Preparations which combine two or more drugs possibly present a difficult problem; nevertheless, their naming according to a common reference designation should be studied.

9.4 The physician and the pharmacist judges a product firsthand in the light of the established goodwill and reputation of its maker, his method of doing business and his ability to market products which meet certain standards of purity and potency, be they their official minimums or standards of excellence exceeding such minimums. To the practising pharmacist, the reputation and "ability to perform" of the manufacturer is extremely important. The name of the manufacturing distributor and his brand-name designations are convenient, sound reference points.

Brand Versus Generic Names

10.1 The Canadian Pharmaceutical Association does not subscribe to nor accept the thesis that drugs having the same generic name, with or without an added brand name, are necessarily therapeutic equivalents. There is a great variety of dosage forms in which modern medicinals can be presented for use. While many physicians may be inclined that a drug is satisfactory as long as it is pure and present in the requested amount, it, unfortunately, is a fact that the efficacy of a prescribed drug may be markedly altered by many circumstances. This arises from factors, mainly pharmaceutical, such as the physical state of the drug, the vehicle in which it is present,

variables in compounding procedures, methods used to reduce irritability or to slow down rate of absorption or cause the drug to be released at certain levels of the gastrointestinal tract. 'Availability' of the drug merits as much attention today as we have been accustomed to paying to its purity and potency. A physician must be able to anticipate consistent results in keeping with his evaluation of a drug as observed in his previous therapeutic uses of it.

10.2 To the pharmacist, prescribing by chemical or common name designations permits dispensing of known reliable brands or non-brands, enables him to better utilize his own professional training and, at the same time, permits him to carry a less extensive inventory. However, it is completely fallacious to assume that all prescriptions or even the majority of prescriptions could be written by generic terminology. One survey of 844 actual prescriptions shows that 7% were written using generic terminology while, of the remainder, 45.56% might possibly lend themselves to the supplying of a non-proprietary product although 13.61% were for brands for which no other preparation was available. (ref: C.Ph.Jnl., 94,5,p.22) In another analysis of almost 3,500 actual prescriptions, it was found that in only 6.69% did the prescribing physician see fit to write using generic terminology. (ref: R.T.P.C. Drug Hearings, p.1008)

10.3 Although a statistical review of the Association's latest edition of "Compendium of Pharmaceutical Specialties (1963)" has not been undertaken, such a review of the 7,776 pharmaceutical products monographed in the first edition indicated that only 25.85% represented single ingredient products available in customary dosage forms which are marketed by more than one company and which could conceivably be prescribed by generic designations. 430 different active ingredients were represented by these 2,010 products.

10.4 Hence, it is erroneous to conclude that even one-third of all prescriptions could be written in generic terminology, as no figures related to potential utilization of the drugs so classified are known.

Advertising, Promotion and Information Services

11.1 Many promotional methods are utilized by drug manufacturers and distributors to place their names and those of their products before practitions in the health professions. The distribution of samples, now legal only under certain specific circumstances, is of continuing concern to pharmacists, inasmuch as members of a profession having specific knowledge of, and legal responsibilities concerning drugs have no control over this aspect of their distribution.

11.2 We feel that a clear distinction should be maintained between the promotion of a drug during the initial or introductory stage and its sales promotion after it has come into widespread use. The proper type of promotion during the introductory phase can constitute a very useful service to the prescribing physician and to the dispensing pharmacist. We believe, however, that such promotion requires a special competence and should only be carried out by knowledgeable persons having special training in Pharmacy or Pharmacology. Possibly some type of certification should be considered.

11.3 Sales promotion, on the other hand, may vary widely as to the method. Because a considerable degree of dissatisfaction appears to exist regarding

present methods, it would seem reasonable that an effort be made to establish certain minimum standards and we believe that medicine, pharmacy and industry, working together, can study and bring forth an acceptable code.

11.4 While advertising and promotion account for a goodly promotion of the cost of drugs, we believe that such activities have, in turn, influenced eventual economies brought about through mass production to meet greater demands.

11.5 Information on drug preparations is available from many sources and in a great variety of forms ranging from purely scientific to consumer material. First class, factual information in summary form concerning every drug specialty preparation available on the Canadian market, is contained in the Association's publication, "Compendium of Pharmaceutical Specialties (1963)" and the Supplements thereto. Thus, in this complete reference text, a busy physician and pharmacist is able to find essential information on all products.

11.6 Previous mention was made of the need for a central clearing house from which information respecting hazardous substances could continuously flow. It is obvious, too, that a complete "Drug Information Service" which would bring together every piece of available information on each and every drug would serve a great purpose in Canada. Such a service is being advanced by the Canadian Society of Hospital Pharmacists. That Society has carried its discussions beyond Pharmacy's organizations and is reviewing its proposals with medical and hospital organizations. It will not be inexpensive to create or maintain, but for such a worthy and essential purpose, it is believed that its creation would prove to be an investment in the betterment of drug safety and in therapeutic efficiency in Canada. This proposal merits the attention of foundations and governments which have money available for its development.

Economics and Drug Safety

12.1 There are many matters of economics which are, of course, of significance in any study related to drug safety. This Special Committee on Food and Drugs is aware that other groups and committees have given advanced, specific study to 'dollars and cents' matters pertaining to the manufacture, distribution and sale of drugs in Canada. Quite rightly, the Committee is concentrating its attention on the solving of problems which will provide for greater safety respecting the use of drugs and respecting the protection of the public against the misuse and abuse of them.

12.2 The Association will not, therefore, in this brief detail its opinions regarding the undesirable and unfair 11% federal sales tax which is applied against sales of drugs prepared for use by individual citizens at a time when their earning power is often reduced. Nor shall we detail the government's responsibility to share the purchasing of needed health care by providing 100% personal income tax relief relative to such purchases.

12.3 Pharmacy in Canada—as practised by those who have assumed professionally orientated, individual responsibilities and who have not allowed themselves to be subjected to the adverse influences of outside, non-Pharmacy pressures—provides and will continue to provide a first class, readily available, ethical service with built-in, inherent safety procedures day in and day out.

12.4 From the commercial retail viewpoint, a retail pharmacy is not 'big business'. The community pharmacist has a particular stake in good business policies. Any tendency, influenced by indiscriminate merchandising practices or otherwise, toward the lowering of standards must be resisted by organized Pharmacy in that such would not be compatible with pharmacists' efforts to instigate minimum standards of pharmaceutical practice and, most certainly, lower standards should not be tolerated by the public. The modern-day range of 'other merchandise' which one may find in a retail pharmacy subsidizes the economic wellbeing of the pharmacy practitioners therein and, in turn, provides for a most essential 'no compromise' standard with regard to the selection of drugs and the manner in which the professional, pharmaceutical services will be rendered.

12.5 A prescription is not an ordinary item of commerce or trade, nor is it a merchandising commodity. It is the tangible, end result of pharmaceutical services ordered for a specific patient to meet a specific need as diagnosed by a medical practitioner. It is the pharmacist's primary responsibility in all areas of practice to render a complete prescription service, including the many activities which fall within the important area of personal, professional judgment related to the drug therapy which has been ordered or which the consumer may deem to request for purposes of auto-therapy.

12.6 Academic standards required of pharmacists before registration to practice in one or another of Canada's provinces equal and, indeed, surpass those of most other countries. Hence, pharmacists working in our communities, in retail or in hospital, or in industrial endeavours and in government service, are well qualified to provide an ever-increasing high standard of service which makes the wonders of modern drugs safely and efficiently available in our nation.

12.7 The Canadian Pharmaceutical Association firmly believes that the Canadian scene and way of life must be fully acknowledged in any discussion related to drugs and pharmaceutical services, their safety, their quality, their efficiency and their economic aspects. The raising of present high standards to encourage greater industrial development without undue, burdensome regulation of procedures conducted within the confines of ethical, professional principles, will prove to bring development advantageous to the general public. Simultaneously, safety procedures, already highly developed will undoubtedly be bettered and we shall continue to benefit from the rather fantastic pharmaceutical 'explosion' of recent years in which our free enterprise system has given us specific means of successfully fighting many deadly diseases.

13.1 The Government of Canada, representative of the individual citizens of our nation, the officials charged with the administration of our laws respecting the professions and respecting commercial activities, and the public, generally, are assured of the desire of the Canadian Pharmaceutical Association, representatives of the profession in all of its aspects to be of continuing assistance in all matters having to do with the enhancement of health and welfare, particularly with regard to the safe and economical availability of drugs required by the ill and diseased.

13.2 We have welcomed this further opportunity of discussing drug matters. We deem it a privilege to work with this Special Committee on Food and Drugs of the House of Commons. Of necessity, the representative problem cannot be discussed in depth in a brief such as this, but you are assured

that the Canadian Pharmaceutical Association would be pleased to assist in the obtaining of further information which may provide desired clarity of any particular point.

THE CANADIAN PHARMACEUTICAL ASSOCIATION, INC.

PRESIDENT:	J. K. Lawton, Ph. C., Halifax, Nova Scotia
PAST-PRESIDENT:	A. W. Matthews, B.S.P., M. Sc., Ph.D. Vancouver, British Columbia
FIRST VICE-PRESIDENT:	J. L. Summers, B.S.P., M.Sc., Saskatoon, Saskatchewan
SECOND VICE-PRESIDENT:	C. R. McClean, Ph. C., Rothesay, New Brunswick
EXECUTIVE DIRECTOR:	J. C. Turnbull, B.S.P., Toronto, Ontario

The CHAIRMAN: The meeting is open for questions.

Mr. ENNS: On the first page, Mr. Chairman, in the terms of identification of the group you mention the Quebec association has not been a member since 1962. Is there any liaison between the Quebec group and the rest of the association?

Mr. J. C. Turnbull, B.S.P., (Executive Director, the Canadian Pharmaceutical Association, Inc.): Almost certainly, sir, there is a liaison with our colleagues in Quebec, but they are not officially represented on the Canadian Pharmaceutical Association council at the present time.

Mr. ENNS: Would their views have been any different than what is contained in the brief as far as this subject matter is concerned, or is this an unfair question to ask?

Mr. TURNBULL: I do not believe I have the right to say that their views are the same or are not the same. Possibly it is best to say that they would probably agree, but I am unable to make such a statement.

Mr. ENNS: I did not really want a committing statement. I wondered if there would have been any difficulty with them. However, you have not been in any way in consultation with them regarding the presentation of this brief?

Mr. TURNBULL: Not on this brief.

Mr. SLOGAN: On page 3 you say:

> We recommend that in each of these divisions there be a more clear-cut differentiation between the personnel involved and the duties of such personnel in respect to food control and to drug control.

What are the difficulties you are encountering now, and why do you make this recommendation?

Mr. TURNBULL: This is a long standing recommendation. We are very pleased to see that many moves are being made towards a definite differentiation between food control and drug control. This is on the basis that only those people who have specific responsibilities for a specific problem can give

it the necessary attention day in and day out. This is not to say that drug problems are not receiving their share of the attention in the food and drug directorate organization because there is evidence that they have given very fine attention to it. However, the personnel involved up until a few months ago have had to wear two hats, they have had to look after drug control and food control. As we well know, if a food problem comes up in Canada or in an area of Canada, it must be looked at very quickly. If it is a problem of poisoning or contamination, or something of that nature, it has to be dealt with very quickly. Personnel have to be placed on such a problem immediately and they therefore cannot continue with their work on drug problems. Also, we feel very strongly that people who are properly orientated in drug problems and in pharmacy problems should be asked to look after those particular problems in Canada.

Mr. ENNS: Would these problems not go together? If there is contamination of a food product would not the person who has a background in pharmacy also be knowledgeable in food contamination, and similarly the person who is training in the other area would not he also have a pretty good competence in both areas?

Mr. TURNBULL: He may have a degree of competence in both, but this does not, in our opinion, allow him to devote attention to both. We are suggesting, just as the Department of National Health and Welfare has found it necessary to have a deputy minister of health and a deputy minister of welfare, that it is necessary to subdivide some of the divisions, in other words, these men do have a competence in both fields. It would be very difficult for them to devote sufficient attention and to work efficiently in both fields.

Mr. WILLOUGHBY: Mr. Chairman, do you wish us to try to follow this page by page, or do you want me to jump from here to the back pages all in one question? I think it would be better if we dealt with it page by page. In respect of page 4, paragraph (4) you mention an undergraduate degree in pharmacy. What do you mean by an undergraduate degree in pharmacy?

Mr. TURNBULL: I hold a bachelor of science and pharmacy degree from the University of Saskatchewan, and this is considered as an undergraduate degree. It is not a masters degree or a directorate degree. So, the undergraduate degree we are indicating here would be a bachelor's degree.

Mr. WILLOUGHBY: Is that not really a graduate degree? You do have your degree in pharmacy?

Mr. TURNBULL: Yes. I believe, university-wise, they term it as an undergraduate degree. It is not a degree obtained in a school of graduate studies.

Mr. SLOGAN: Do you not feel that there are sufficient personnel in each of these divisions so that presently these inspection services are adequately separated at the present time.

Mr. TURNBULL: It is my understanding that inspection services presently are being expanded tremendously, and we are pleased to note that many pharmacists are being employed to undertake this work. Up until the past while the food and drug directorate has worked under a very severe restriction in respect of both personnel and money and we just have not been able to get across the story that more pharmacists should be looking after the drug problems in the directorate.

I do not know whether or not that answers your question, Dr. Slogan, but I believe now there are something like 70 new inspectors. I am not quoting this number from a factual knowledge of the situation but I do believe there is something like that number, and many of them are pharmacists, who are undertaking the pharmacy activities of inspection and control.

The CHAIRMAN: Are there any other questions up to half way down page 5?

Mr. ORLIKOW: Yes, Mr. Chairman. On page 5, paragraph 4.2, it is recommended that a more rigid screening of promotional claims concerning drugs and drug preparations be instituted. What do you mean by that statement? Where are these promotional claims usually found? Are you thinking in terms of advertising either in the printing media or T.V. for the general public or in terms of advertisements beamed toward the doctor, who is the one that writes the prescriptions?

Mr. TURNBULL: Possibly that sentence best goes with the preceding paragraph, Mr. Orlikow, and relates more specifically to the modern type of consumer advertising, the advertising which is promoting, shall we say, the uninitiated consumer to take more and more medication on a self medication basis without properly presenting a message which instils a bit of caution into the mind of the public relative to the consumption of drugs generally.

That paragraph goes on to discuss the promotion and promotional claims related to drugs generally and, particularly, those which might be prescribed by a physician and dispensed by a pharmacist. In this respect we firmly believe that some way must be found to provide the physician with essential basic information relative to each and every pharmaceutical product and that some information and precautionary statements should be available very readily to the practising pharmacists.

Mr. ORLIKOW: What I am trying to get clear in my mind is this. Are you concerned with the advertising which is available, say, in the daily newspapers or on T.V., to the public in general or are you referring to prescription drugs?

Mr. TURNBULL: Both, sir.

Mr. ORLIKOW: That is, prescription drugs which the public can only get if the doctor writes a prescription?

Mr. TURNBULL: Both.

Mr. ORLIKOW: In each case this is the advertising of promotional material which goes to doctors.

Mr. TURNBULL: Well, in both instances. Let us remember that the patent medicines are available in any outlet whatsoever. They are not restricted to retail pharmacists; they are available from the supermarket shelf and from the smokeshop. You can take it on and on and on. Also, there is the type of television advertising, for example, which you see, that creates the urge to buy and buy immediately, and this is being watched by our young people and our children. These people are passing by the low shelves in the supermarket. There is something in their minds that is gradually creating almost a disrespect for medication and the dangers of medication.

Mr. ORLIKOW: Could you give us some illustrations?

Mr. TURNBULL: I do not think that I would care to name any products as I think this is rather unfair. However, can I take it on a general basis?

Mr. ORLIKOW: Well, without naming a company can you give us an example of the type of product to which you are referring?

Mr. TURNBULL: These products which contain bromides, for example; they should not be on the consumer market. There was a time—and I can recall this from my university training, and I am sure the physicians who are present here this morning will also bear me out in this connection—when bromides contributed to possibly one fifth to one quarter of the patients who were hospitalized in mental hospitals. But, I do not think these figures stand up today, thank Heavens.

Mr. ENNS: My question ties in with your point on quality control and the recommendation you make for licensing. It seems to me that we should not pass over this section without some reference to your recommendation in this regard. When you recommend licensing does this mean that you are reluctant to see the continuing availability of drugs and patent medicines in such places as supermarkets and such other places other than established drug houses.

Mr. TURNBULL: The two matters are not related. I would answer your last question possibly first. Yes, we in pharmacy are reluctant to see the continuation of patent medicines on the supermarket and smoke shop shelves. This is not from any desire to obtain a monopoly in the sale of such items; far from it, but we are becoming increasingly concerned with a number of potent drugs that are now part and parcel of the formula of some of these preparations. And, as I said earlier, the type of advertising which is being used and the creative advertising which is now being done is beginning to create in the minds of the consuming public the thought that these are very innocuous preparations from a danger point of view, having considerable value, and they are beginning to look upon all drugs in the same light. Possibly this is the reason we have come in on these studies which you are undertaking in respect of safety. It is our thought the consumer is not looking upon them as being anything serious.

Mr. SLOGAN: I think this same section applies to something I was advocating and on which I was putting questions to the other witnesses who appeared before us. My contention is that the food and drug directorate is doing a very good job so far as protecting the public is concerned, but that the benefits of this work is not getting down to the individual pharmacists and the individual practitioners who follow medicine. My contention is there should be a body, perhaps a medical research council or some like body, which represents all pharmaceutical associations, manufacturers and the medical profession, which would set out specifications for each drug so far as quality control is concerned and so forth, and that they then do license the manufacturers and apply closer inspections so that they see that these specifications are met; also, that they allow the manufacturer to place on the label that these certain drugs meet specification numbers so and so, thereby enabling the brand name because they would be assured of the quality of the drug. Do enabling both to prescribe products more on their generic name than just on the brand name because they would be assured o fthe quality of the drug. Do you feel that such a body would be of assistance to the individual pharmacist and practitioner, and perhaps would do something to reduce the cost of drugs?

Mr. TURNBULL: May I deal with licensing first, because I believe this ties in with the whole thing. There have been many discussions regarding the licensing of manufacturers of pharmaceuticals in Canada. Our views on this are supported, in the main I believe, by the pharmaceutical manufacturers in Canada, with certain exceptions of course. It has been indicated to us that there are certain constitutional problems in respect of federal licensing of a person manufacturing drugs. We find this very difficult to understand because certain areas of the business may be licensed; for example, the Food and Drugs Act does provide for the licensing of that part of the manufacturing which produces injectibles and biologicals, and that type of thing. Also, we find it very difficult to believe that the provinces should be forced to undertake a licensing procedure by which they, shall we say, could control industry that is not in their particular province but is represented by branch offices, or employees of the company.

Also, very readily you can see that if the ten provinces were to come up with some kind of licensing regulations, we would have a real hodgepodge,

and a very heterogeneous set of regulations which undoubtedly would hamper good regulating procedures in Canada, and also add to the cost of same.

Therefore, we feel, even if it is truly a constitutional problem, if it is properly described to our provincial legislators, they would be pleased, in the interest of the Canadian public, to give over their rights, or temporarily farm them out in a manner similar to the manner they gave over the income tax commission rights, and that type of thing, a few years ago.

We feel that only in this way can we honestly expect authorities such as the food and drug directorate to be able to identify each and every manufacturer of drugs in Canada, and in turn take the necessary steps to ensure that the minimum specifications as outlined in the Food and Drugs Act, for example, are being met by all these people who place drugs on the Canadian market.

I am not too sure of our view concerning a specification label. The Food and Drugs Act lays down certain minimums which a drug must reach quantitatively. Specified in that act there are various references which contain minimum standards which a drug must reach. So, physicians and pharmacists know that quantitatively drugs on the Canadian market do reach a certain minimum standard.

Qualitative standards, I think, are something different, and it would be almost impossible for any directorate, or any committee, or board, to rule on the qualitative part of a specific drug. These are not peas where we can label them as fancy, choice and standard, for example, so that the housewife knows what type of can of peas she is buying or what she can expect to find inside the can.

I think the onus should be placed on the manufacturer to continue to market the best possible drugs. If he chooses to go above the minimum standards that already are set, I believe this should be left with the manufacturer; indeed, as one manufacturer puts it, this is the priceless ingredient of his particular products.

Mr. ORLIKOW: Are you suggesting it would be virtually impossible for an organization like the food and drug directorate, given staff and using a licensing system, to be able to ensure, not for the benefit of the public because the public is not directly concerned, but for the benefit of the doctor and pharmacist, that the product of any manufacturer—provided he has the facilities for inspection, producing, let us say, reserpine tablets, or promazine—meets the standards required for safety and health.

Mr. TURNBULL: I am suggesting that this presently exists; but it should not be necessary for a government agency to have to certify that everything the manufacturer puts out is fit and proper. This responsibility quite rightfully should rest with the manufacturer. If he is unable to maintain such standards of periodic inspection, that manufacturer should not have a continuing licence.

Also, if I may say so, I do not think it is humanly possible for any agency to certify that the basis of evey drug appearing on the Canadian market is up to a certain standard. I do not think they can do that any more than the policy force can certify that every car going down a street is staying within the 30 mile an hour speed limit.

Mr. ORLIKOW: That is not the point at all. No matter how much staff you have, no agency is going to see that every product put out by any drug company is perfect. However, the issue which we come back to every time we have witnesses here is—and I am not being too critical of the doctors or the pharmacists—

An hon. MEMBER: Why not?

Mr. ORLIKOW: I will be when I want to. One of the reasons given that doctors prescribe a brand name of a product is that they believe that product produced by a large company is of a quality which they honestly can recommend to their patients. I am not questioning that. The question is, if we had adequate inspection and licensing, would that not give protection to the patient?

I have here some examples of the kind of thing which is going on right now. I do not wish to become involved in a long discussion about prices, although we will do so at some future time; I just wish to put to you that this is important. Here we have a promazine product put out by Wyeth which they call sparine. It is listed at $10.50 a hundred for a 25 milligram tablet. Then, there is a similar product put out by a company named Empire which lists at $1.50 for 100 tablets. My point is that this is a product which is being used very widely, and I am speaking from personal knowledge. Doctors are prescribing it. Surely a saving of this proportion would be very important to a patient or customer. I do not blame the doctor if he does not know whether or not Empire is a reliable company, if no facilities are provided by anybody, including the government of Canada. I do not blame the doctor for writing a prescription calling for the Wyeth product. However, this is the type of thing which can cause difficulties and is the question we are trying to come at.

Mr. RYNARD: We are getting into the matter of costs now. Surely today the committee is discussing the matter of safety and not the matter of costs. You are introducing a new factor. Surely this committee today is dealing with safety.

Mr. ORLIKOW: I only raise this—

Mr. RYNARD: This is only wasting time. You are raising something which will come up later.

Mr. ORLIKOW: Mr. Chairman, I do not agree at all.

Mr. RYNARD: I did not expect you to.

Mr. ORLIKOW: Mr. Chairman, the point I am trying to make is, if there are any legitimate, honest arguments which this organization or any other can bring forward against licensing for any reason, I would like to hear them, and while I am here I am pointing out one of the reasons why licensing might be a good idea.

Mr. SLOGAN: There may be a slight misunderstanding of what we mean. We feel the food and drug people are doing a good job; but this is not getting down to the large pharmacists and doctors. I understand there is a body which presently is looking into the possibility of what I suggested; at least the medical men intimated that. Are you acquainted with any discussion which is going on in that direction at the present time?

Mr. TURNBULL: There are many going on, sir. I am not too sure of what specific group you are thinking.

Mr. SLOGAN: I am not sure what the group is called, but I understand that the medical men told us there are discussions going on between the food and drug directorate and the medical profession, the pharmaceutical association, and so on, regarding the matter of specifications, or something like that.

Mr. TURNBULL: Yes, this is true. Presumably you are referring to the Canadian drug advisory committee which is appointed to work with the food and drug directorate. Also, of course, there is the government organization known as the Canadian standards organization which deals with drugs and many other items such as paint, tools, and anything else purchased by the government.

The C.G.S.B. has brought forth specifications for the manufacturer of drugs, and has very stringent rules on the acceptability of the drugs that they will obtain from the manufacturer, and in turn, with the acceptability of that

manufacturer for future drugs, if he does not come up to the expectations of the government. This is the government, and possibly we should indicate that it is a regrettable situation, to have standards for purchasing by the government and not to extend the same standards to the drugs which are going to be purchased by those whom the government represent, namely, the public.

Mr. SLOGAN: Do you feel that the pharmaceutical association would be assisted if such specifications were made? There would be a certain element of quality control in those specifications which could be ultimate, but there would have to be a certain range. When the Canadian Medical Association was before us they told us about a situation in Alberta where apparently without regard to the medical or the pharmaceutical associations the government there passed a law whereby the individual pharmacist could substitute in a prescription a generic name of a drug without consultation with the physician who wrote the prescription.

Mr. TURNBULL: The legislation in Alberta is basically as you outlined it, yes, except that you used the words that he might substitute what we have come to know as a generic drug if he so see fit. He may substitute a drug either by generic name or brand name, if he so sees fit. However under normal procedure or practice of the profession there have been very few difficulties encountered in this respect; and the pharmacist is very well aware that the physician's choice of a drug by company or by brand name is usually based on some very definite idea, and he will meet the physician's order where possible.

Mr. SLOGAN: Where would this place the pharmacist should he in fact substitute another brand name for the one specified if there should be a reaction in the patient and the patient should bring a law suit against the individual pharmacist who has substituted a drug without reference to the medical doctor? Does this not lay him open to a legal charge?

Mr. TURNBULL: I do not believe there has been any test case or any such situation arise which has gone to the courts. There has been a test case because of a substitution itself, but under the particular circumstances it was successfully prosecuted.

Mr. SLOGAN: You mean that the pharmacist was found guilty?

Mr. TURNBULL: Yes.

Mr. SLOGAN: The other point I was trying to make was that apparently the action of the government in Alberta in bringing out this law, was, in their opinion, to lower the cost of drugs to the patient; but because of the onus placed on the individual pharmacist in making a substitution, the medical association seemed to feel that if the pharmacist was going to make a substitution, he would certainly make a substitution of a better brand name or of a higher cost drug, because he would not want to take the responsibility of substituting a drug with the quality of which he was not perhaps as confident. Could this be true?

Mr. TURNBULL: If I were in practice and I ran into a situation of that nature I would be inclined, where it was necessary to substitute and the physician could not be contacted, to dispense a product which in my opinion could be suitably substituted and cause no difficulty, and indeed perform as I felt the other drug would perform. This would not necessarily mean that it was a more expensive preparation, and indeed I do not see any particular reason why it should be. The criterion is not one of dollars and cents. The criterion is the pharmacist's faith in the product of a particular company.

Mr. SLOGAN: The fact is that it is only normal, as you and I know, for the individual practitioner, whether he be a pharmacist or a doctor, to choose a brand which is better known and in which he has more faith. Usually these

brand names are higher priced than some unknown brands. I think that the law passed in Alberta is perhaps having an opposite effect to what the government there intended it to have.

Mr. TURNBULL: I do not believe that there is any indication of it having the opposite effect. That is the experience up to date. I believe that it is not possible to attain the purpose for which it was designed, namely, that of driving down the cost. It does provide the means for freer activity in the practice of pharmacy and in the use of medication.

Mr. SLOGAN: If there were placed on all these generic brands which have been passed by the food and drug directorate the fact that the specifications have been set up by the pharmaceutical and medical assocations, do you not feel that individual druggist would feel far freer to prescribe some of the lesser known brands which might be substituted?

Mr. TURNBULL: Those specifications are already written in the Food and Drugs Act.

Mr. SLOGAN: Speaking as an individual dentist, I know that I have a preference, because I want to prescribe what I feel would do the best job for my patient, and I want the drugs that have the highest quality. Without those specifications on the label do you feel that the individual pharmacist is in a position to substitute a lesser known drug? Because if he does know about it, and does not know all the quantitative standards, would this not seem the case? He does not know the importance more or less of the quality controls in the production of the drug, and he is not aware of anything other than by consulting with the food and drug directorate.

Mr. TURNBULL: To express a personal opinion here, I honestly do not believe that any board or group could act as a certifying agent for drugs. The minimum standards as specified in the official references which are legal in Canada provide for the basic minimum standards in a drug preparation. Every practitioner in medicine, every pharmacist or dentist is assured that these minimum standards, these quantitative standards are being met to the best of the knowledge of the authorities, who are continually taking samples—several thousand samples across the country—and testing them each year, and quantitatively testing them.

This makes no reference to the efficacy of the drug preparation and the availability of the active ingredients of the formula, nor can it make any reference to the fact that product "A" and product "B" which contain the same drug are going to produce the same expected physiological reactions, in the same patient, or in the patient being treated by the physician. This is because of the character of the pharmaceutical formulation, the various means used to reduce the rate of absorption, or to create intestinal irritation and that sort of thing, by the use of that drug in the human body.

Mr. SLOGAN: Do you not think that the food and drug directorate should get into the field of the clinical study of drugs, and that they could have an inspection of and access to the results of the research done in the individual companies, and that they would know the rate of absorption, and could set certain standards for qualitative analysis? I do not mean that they should be exactly the same, but they could prescribe some range within which they could approve the specifications?

Mr. TURNBULL: First of all, my answer to your first question is no, I do not believe the food and drug directorate should become a certifying body as to the efficacy of any particular drug preparation and any particular drug manuafcturer or distributor.

Secondly, yes, the directorate could provide a great service in the clinical investigation and study of a drug.

And thirdly, the present regulations are fairly new, governing the introduction of new drugs in Canada and are such that the qualitative control procedures are pretty well outlined in the new drug submission made by the introducer, the manufacturer introducer of a particular new drug.

And these, coupled with the new regulations governing the physical facilities and to some extent the personnel who must oversee the drug production, get into qualitative control, and they do cover all the needed minimum standards in keeping with the rest of the food and drug legislation.

Mr. SLOGAN: In other words, you suggest the food and drug directorate is presently perhaps doing this? I still maintain that pharmacists and medical doctors prescribe well known brand drugs. I think we could ask the individuals around this table and find that that is so, but how can we overcome this situation? How can we assist the individual doctor and pharmacist who would like to prescribe a particular drug, in this regard? I do not want to be involved in the question of cost, but I refer to a drug which is less costly but of the same quality, but in respect of which he has no way of being familiar. He does not want to accept the responsibility himself in this way. How can the government assist in this regard so that these less well known drugs become known in spite of perhaps the lack of publicity or staff on the part of the manufacturing company? These drugs may be qualitatively superior to something the doctor is presently prescribing.

Mr. TURNBULL: I do not know the answer to your question, sir. All I can say is that I think it would be a terrible thing for us to undertake, as possibly you suggest, to find a way in which we can help the individual practitioner to prescribe other than the products of the leading research-orientated manufacturing companies if the individual practitioner does not wish to do so or does not wish to move away from relying upon those people in whom he has the greatest faith.

Mr. SLOGAN: The reason the individual practitioner has the greatest faith in certain companies is the fact that the government has failed to convince the professions of pharmacy and medicine that the quality is there. The government has failed miserably in this way and the difference which exists in respect of the cost of drugs is a direct result of that failure. Perhaps the government is convincing itself that the quality does exist but it is failing to pass that information down to the level where it could best be used. I feel for that reason that the government should get into this field. I do not think there is any problem in this regard. This involves a matter of increasing the staff and co-operation between the various professions. I am sure the individuals involved want to co-operate in this direction now, and I think they have indicated that they do want to co-operate. I do not think this would be a terrible thing. I do not think anyone has to be forced to do this.

Mr. TURNBULL: I do not believe that this information is not known to the profession of pharmacy, for example.

Mr. ORLIKOW: Mr. Chairman, I have been trying to break into this discussion. It seems to me as a result of my experience as a pharmacist that pharmacists at least in the cities—I do not know about the rural areas—really play a very small, if any part at all, in this regard. The situation may have changed during the last ten years, although I doubt it, but pharmacists ten years ago certainly never or hardly ever used any product except exactly that product which the doctor prescribed, not just as a drug but by the brand name. No pharmacist would make a substitution without referring to the doctor. Am I right in this regard?

Mr. TURNBULL: Yes, I believe you are right. It is a fact that the pharmacists do this for many reasons, some of them ethical. In addition, the prescribing physician in 90 per cent of the cases at least has some reason for stipulating

a certain drug as opposed to another product. We know this. He knows the results he obtains with brand A, let us say, as opposed to popular brand X. He knows what to expect, what chain of reaction he is going to see in his patient, and if he does not see it he knows why he is not getting this reaction. We know this fact is in the physician's mind. We know also that a man may prescribe even some penicillins in injectable forms in an aqueous substance or in oils, whatever it may be, and it is going to react differently. I can recall from my own practice that one physician always prescribed a particular penicillin in an aqueous substance because he knew exactly what he wanted. We knew the company product that he wanted, and knew that he wanted it because he could not get the necessary and expected reaction by using another company's product.

Mr. SLOGAN: Is it not a fact that one of the reasons why a doctor prescribes a brand name is that he has received some samples in the mail or because someone has visited him and explained the glories of that particular brand?

Mr. TURNBULL: Certainly someone has taken the trouble to outline to him all the advantages of a particular product that he has to sell. It may well be that that individual does not outline some of the disadvantages or potential hazards or dangers of that product, but this is gradually taking place and I hope as a result of this committee's study there will be more emphasis placed on the safety and side reaction phase of the situation.

Mr. SLOGAN: The doctor really does not have an objective judgment which he can make in respect of various brand names because he is not in a position to judge.

Mr. TURNBULL: That is true except that the doctor does know something about the product as a result of his personal experience in using it.

The CHAIRMAN: Doctor Slogan, I do not think it is fair to ask the witness to answer for the medical profession.

Mr. SLOGAN: I should just like to make one further statement. My contention is that because the individual practitioner is not in a position to make an objective judgment there should be a body in Canada in which he has faith to make that judgment for him and put the information on the label so that he is prepared to accept it. At the same time that practitioner would still have a choice after using the drug but at least he would be prepared to use the lesser known ones.

Mr. TURNBULL: I believe that I would support your proposition tempered with the thought that I cannot see even three expert minds agreeing on the decision that one man might make in respect of a product manufactured by any individual company, or group of products of all companies. In other words, I do not think that anybody could reign over such a situation. I truly believe that to be the situation, sir. This is a very involved situation.

The CHAIRMAN: Dr. Willoughby I think you indicated you had a question?

Mr. WILLOUGHBY: Before I ask my question, Mr. Chairman, I should like to say that I think the difficulties involved in the subject which has just been discussed could very briefly be answered in this way. Only the very large companies can possibly afford to do the testing and checking of toxicity and potency of drugs and make them as reliable as the medical man desires. I think, therefore while some of these unknown companies could possibly sell a substance cheaper it would be very difficult for them to compete with the research departments operated by the long and larger established companies. I think that is one fact the medical man must keep in mind. I think the medical man does keep this fact in mind in recognizing a specific firm when writing prescriptions in respect of so called reliable drugs. I think that situation probably indicates some of the reasons for the situation that has been discussed.

Before we move to another subject I should like to refer to something that was mentioned in passing in respect of the hazards attendant in selling drugs over counters in non-licensed establishments such as ordinary stores which are not under the supervision of pharmacists. I should like to know whether or not, and I think this is extremely important, this situation comes under federal or provincial jurisdiction.

Mr. TURNBULL: This is under both jurisdictions. Under federal legislation there are certain products, and these are products which are governed by the Food and Drugs Act, which may be sold under pharmacy control only. This legislation is supported by provincial legislation. In federal legislation there is also a Proprietary or Patent Medicine Act. All these products are licensed and basically are of the same formula preparation. You will find in the majority of provincial pharmacy acts a blanket exemption extended to these particular products allowing them to be sold in pharmacies and in non-pharmacy outlets.

Mr. WILLOUGHBY: As far as the retailing of these products is concerned it is a provincial question?

Mr. TURNBULL: Yes.

Mr. WILLOUGHBY: We as a federal committee cannot suggest legislation which would effect the provinces as far as these outlets are concerned?

Mr. TURNBULL: If you agree with us that this is a definite problem, then I think that the work of the provincial people, who are most anxious to do something about this problem, could be supported by a statement by this committee. You cannot write the legislation yourself, no.

Mr. WILLOUGHBY: We could not recommend that the House of Commons institute such legislation?

Mr. TURNBULL: No, but you could recommend that the necessary steps be taken at the provincial level to provide the necessary protection for the consuming public in respect of these items.

The CHAIRMAN: I think it is true that we can make any recommendations we wish. We certainly made recommendations in our report on insecticides and pesticides. We recommended certain things to the provincial governments, recognizing them as the authorities, but hoping that they would follow our suggestions.

Mr. WILLOUGHBY: I recognize that there is a problem in respect of pesticides and insecticides but I referred more specifically to patent medicines which are being sold.

Mr. ORLIKOW: Mr. Chairman, I think at some stage of our proceedings we are going to have to have a look at the advertising which is permitted in this field. I believe that advertising comes under federal jurisdiction. Certainly advertising comes under the jurisdiction of the B.B.G. in some respect, and if in our investigations we find that the type of advertising in existence tends to promote the use of a drug which is dangerous, we have the right to at least recommend to the B.B.G. that it tighten up its regulations.

The CHAIRMAN: Yes, advertising does come under the Food and Drugs Act.

Mr. ORLIKOW: Certainly we could do a great deal in that regard.

Mr. MARCOUX: I certainly agree with Mr. Turnbull when he suggests that it would be impossible to check every item and every batch produced by every drug manufacturing company in Canada, but does he think that perhaps by way of licensing or in some other way it would be possible for the food and drug directorate to indicate to physicians and pharmacists in Canada that a company is equipped and is effectively carrying out all the required tests from the point of view of security in the sale of these things? This list of companies

could and should be given to the doctors and dispensing pharmacists across Canada. For example, we know that some companies will buy ingredients from a well known company and will either sell them or only dispense them under another name; and this is supposed to be good. Of course, the big company, the manufacturing company, will take a profit for the loss of profit they make with their own products; but this should be known to pharmacists and doctors. Those companies who use products not tested for quality and that sort of thing should notify the doctors and the pharmacists. The prescribing doctor should know which companies are complying with the regulations and which are not complying with the regulations.

What is your opinion about that?

Mr. TURNBULL: I firmly agree with you that this would do the job. I think only through a system of licensing can the necessary control be exerted because, in the first place, it requires that the manufacurer or distributor identify himself very positively with the federal authorities. Possibly we do not have to get involved in licensing; it could be a registration requiring an annual report.

I think another recommendation that we have been inclined to make for some years is that the name of the primary producer of the drug, as well as the manufacturing distributor, should appear on the label. Only in this way can the pharmacist have any indication that one primary producer is conducting the technical tests of production of a certain drug that may be marketed under another distributor's label. This has certain shortcomings in that even those companies who are large in Canada may have subsidiary companies or parent companies producing their drugs for them in, let us say, United States plants, in English plants and in Swiss plants. Where this does occur, I think, it should be so stated on the label. Only in this way can the pharmacist know what responsible manufacturer has produced this drug in its first stages.

Mr. ORLIKOW: What would the pharmaceutical manufacturers think of that suggestion?

Mr. TURNBULL: They would be extremely unhappy, sir. This all ties in with economics. Economics are part and parcel of drug efficacy and drug efficiency and safety, but we can say in Canada that all drug preparations, subject to spot inspections, are reliable, as Dr. Willoughby indicated; but they are not all the same.

Mr. SLOGAN: I noticed on page 14 that you state your association is not giving its detailed opinions regarding the unfair 11 per cent federal sales tax. Obviously, you oppose it. Do you suggest the government remove it?

Mr. TURNBULL: Most definitely. We have led the parade in this suggestion for some 12 years and we are very happy that other organizations have seen fit in the past two, three or four years to advance the same recommendations. We make this recommendation on the basis that Canada is the only country in the world, I believe, that taxes drugs required by the sick and ill.

We, in pharmacy, make this recommendation knowing that pharmacy practitioners actually make a profit on the 11 per cent tax, because the mark-ups are added after the sales tax is added at the manufacturing level. If it is abolished pharmacists across Canada will lose many many millions of dollars every year.

Mr. SLOGAN: Are there any tariffs on drugs being imported in bulk?

Mr. TURNBULL: Generally there is a 15 to 20 per cent tariff. It varies, of course. The taxes or excises are applied now to the finished packaging of the particular product. This we feel is correct in that it influences Canadian based industries. A company which imports, shall we say, a barrelfull must, I understand, declare the method in which it will be distributed, and the tax is put upon it at the package level.

The CHAIRMAN: This is getting into the question of cost.

Mr. WILLOUGHBY: Am I correct in my understanding that chemical materials available in Canada of high standard are protected by a tariff from similar products being brought in from other countries, but that where there is no chemical available in this country that import has practically no duty on it?

Mr. TURNBULL: This I believe is correct.

Mr. ORLIKOW: We should get the tariff board down here to give evidence on this.

Mr. TURNBULL: Some of these are imported as chemicals, not as drugs.

Mr. FRANCIS: I understand that drugs used for agricultural purposes are exempt from sales tax. Is that right?

Mr. TURNBULL: Not to my knowledge. If drugs used for agricultural purposes are exempt and if those used for human purposes are not exempt a ridiculous situation would exist.

Mr. FRANCIS: Is it not so?

Mr. TURNBULL: Not to my knowledge.

Mr. FRANCIS: It is my understanding that certain drugs used by veterinarians are exempt from sales tax and customs duties.

Mr. TURNBULL: I am not too certain about sales tax but in so far as customs duties are concerned there are only six drugs—not six classes, but six drugs—which are exempt. They are cortisone, ACTH, liver injection for pernicious anaemia, vitamin B-12, insulin and radium.

Mr. FRANCIS: I just wanted to make this observation at this time. I will look into it at some further point.

Mr. WILLOUGHBY: At page 12 in paragraph 11.1, you make a statement in regard to the distribution of samples. You state that:

> The distribution of samples, now legal only under certain specific circumstances, is of continuing concern to pharmacists, inasmuch as members of a profession having specific knowledge of, and legal responsibilities concerning drugs have no control over this aspect of their distribution.

I would question whether or not that is correct on the basis that the medical men themselves are responsible for the distribution of those drugs once they are received as samples. What is the difference between distributing them as samples and prescribing them through a drug store?

Mr. TURNBULL: Bill No. C-3, as passed by parliament some two years ago amending the Food and Drugs Act, provided that no sampling of drugs would take place except under certain prescribed conditions. Some time later the regulations were passed providing that sampling could be undertaken by the manufacturer to physicians, dentists, veterinarians and pharmacists. Bill C-3 also provided that no redistribution of samples could take place except under prescribed conditions, and there are no prescribed conditions in the regulations which indicate that redistribution can take place by anyone.

However, in the administrative procedures governing the administration of the regulations it has been indicated that such redistribution could be undertaken by physicians, veterinarians and dental practitioners.

Under the pharmacy acts of our legislation governing the practice and profession of pharmacy, pharmacists have the primary responsibility to control and look after drugs. In this particular instance they may receive samples of drugs; regardless of how dangerous they may be or how innocuous a

particular preparation may be, as for example in a cough drop, but defined as a drug because of the use to which it is to be put, the pharmacist may not redistribute that particular preparation which is under his control as a sample.

We are of the opinion that the necessary control has been somewhat short-circuited by these interpretations and that the people who had a legal responsibility to control them have had that prerogative taken away from them by a piece of federal legislation.

The CHAIRMAN: Are there any other questions, gentlemen?

Mr. SLOGAN: I move adjournment.

Mr. WILLOUGHBY: There is one other question that is not too relevant to our discussion here, but I would like to put it forward because I get a great many complaints from individuals about this. I am told that individuals can obtain their prescriptions more cheaply at the departmental stores which have pharmacists than at regular pharmacists. Is this just a cutrate situation? How do you account for it?

Mr. TURNBULL: Every person, including those involved in the practice of pharmacy, has his own awareness of the value of his services. If one pharmacist, for example, who is an individual in private practice chooses to downgrade, dollar wise, the services which he feels he is rendering, that is a prerogative of his, I am afraid, and if a man chooses to charge what he feels the services are worth, in keeping with the control that he is exercising over the drugs and the type of service that he is rendering in a community, then I feel he is quite right. It is not what so many think it is—that anyone is necessarily profiteering and someone else is cut rating.

Mr. ORLIKOW: At some time we will have this organization back and we will then be able to discuss the aspect of cost.

I would like the pharmaceutical association to know that I for one am interested in what happens to the price of drugs when they move from where they get the drugs to the consumer.

Mr. TURNBULL: We have on many occasions appeared before the committee in discussion groups, commissions, and what have you, during the past few years to review these particular problems, and indeed I had initially prepared myself to come before this committee this morning on that basis. We are only too pleased to have the opportunity of discussing these matters if the committee sees fit to do so.

The CHAIRMAN: Gentlemen, there is just one small question. We would require a motion that the committee pay reasonable living and travelling expenses incurred by Mr. Turnbull to appear before us and that the usual per diem allowance be paid to him.

Mr. FRANCIS: I would be glad to move that this be done, and I would also like to incorporate our thanks to him.

Mr. MARCOUX: I will second that.

Motion agreed to.

The CHAIRMAN: We thank Mr. Turnbull for coming here, and we look forward to having him here again when we discuss the question of costs.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 5

FRIDAY, JUNE 12, 1964

WITNESS:

Dr. R. F. Farquharson, M.B.E., M.B., D.Sc., LL.D., M.D., F.R.C.P., F.R.C.P.(C), F.A.C.P., F.R.S.C., Chairman, Medical Research Council.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

20851—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Gauthier	Orlikow
Asselin (*Richmond-Wolfe*)	Horner (*Jasper-Edson*)	Prud'homme
Basford	Howe (*Hamilton South*)	Roxburgh
Casselman (Mrs.)	Jorgenson	Rynard
Côté (*Longueuil*)	Macaluso	Slogan
Enns	Mackasey	Whelan
Francis	Marcoux	Willoughby—24
	Nesbitt	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

CORRECTION (English copy only)

MINUTES OF PROCEEDINGS AND EVIDENCE NO. 3—Tuesday, June 2, 1964

On Page 63, the sentence on lines 39 and 40 should read:

Of course, dangers *always* will exist and great care will be required.

VISIT TO LABORATORIES OF THE FOOD AND DRUG DIRECTORATE DEPARTMENT OF NATIONAL HEALTH AND WELFARE

TUESDAY, June 9, 1964.

The Special Committee on Food and Drugs visited the Laboratories of the Food and Drug Directorate at 9.00 a.m. this day.

Dr. L. Greenberg, Chief of the Biologics Control Laboratories, made some introductory remarks, after which the members went through the laboratories of the Food and Drug section where explanations were given and questions asked about the work done by the Directorate to safeguard the health of consumers.

Publications of the Consumer Division of the Food and Drug Directorate were distributed to the members.

At 10.30 a.m. the visit was concluded and the members returned to the House of Commons.

Gabrielle Savard,
Clerk of the Committee.

20851—1½

MINUTES OF PROCEEDINGS

FRIDAY, June 12, 1964.
(9)

The Special Committee on Food and Drugs met at 9.40 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Francis, Harley, Howe (*Hamilton South*), Macaluso, Mackasey, Mitchell, Roxburgh, Rynard, Willoughby—(9).

In attendance: Dr. R. F. Farquharson, M.D., M.B.E., Chairman, Medical Research Council.

The Chairman welcomed Dr. Farquharson and invited him to comment on the present status of medical research in Canada.

Dr. Farquharson made a statement about the various aspects of medical research; he was questioned thereon, on the status and functions of the Medical Research Council, and on related matters.

The Chairman thanked the witness on behalf of the Committee for his interesting and knowledgeable presentation, and at 11.05 a.m. the Committee adjourned to 9.30 a.m. Tuesday, June 16.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

FRIDAY, June 12, 1964.

The CHAIRMAN: Gentlemen, we have a quorum. There is no business before the committee this morning to I will get right on with the introductions of our witness for this morning.

I would like to introduce to the committee Dr. Ray Farquharson, who at the present time, is the chairman of the Medical Research Council here in Ottawa.

Dr. Farquharson is a most qualified gentleman. I think several of the people here in this room, including myself, had the pleasure of having Dr. Farquharson as our professor of medicine at the University of Toronto. Therefore, we would like to welcome you, Dr. Farquharson, and to thank you for coming.

I wonder if I could start off the questioning by asking Dr. Farquharson if in his present position he would like to comment upon the present status of medical research in Canada.

Dr. R. F. FARQUHARSON (*Chairman, Medical Research Council*): Mr. Chairman, there is always some medical research wherever good doctors have practised, and every doctor that thinks hard about his work does some research as he goes along.

In many of the fields of medicine the research done by the doctors as they practice in their every day work advances knowledge greatly. But, beginning before the turn of the century people began to do more and more experimental research and this experimental research has grown and grown.

The first most striking research in Canada came with the discovery of insulin. You notice I said "the most striking research" because insulin could not have been discovered if there had not been a great deal of research done along that line before Banting and Best came along with the experience acquired in extracting tissues and the like. And, they made an insulin that could be used in diabetes for the first time, a treatment that was highly effective in diabetes.

Since that time there has been a tremendous amount of work done on diabetes. It is growing and growing because the diabetic patient, living on and on, gets a number of complications that are more common in diabetes than in any other condition.

The discovery of insulin in Canada was a tremendous stimulus to medical research and a number of private persons gave money to support medical research in our country just as they have been doing in the United States. But, ours was a less wealthy country and our wealthy men were slower in getting started in giving money for this purpose. Between the two wars there was quite an extension of medical research but relatively little was done with federal government money. The federal government in one department or another gave some money for the study of tuberculosis but it was not until 1939 that the research council organized what is called an associate committee on medical research which was placed under the chairmanship of Sir Frederick Banting, who chose as his fellow members of the committee a number of people prominent in medicine in Canada.

The initial budget in 1939 was $59,000—and this was rather interesting—the American National Institutes of Health which now have such tremendously large sums for medical research gave also in 1939 to first grants for extramural

medical research i.e. in universities and hospitals, beginning with a budget of $90,000. This American budget was not nearly as large proportionately as that of the Canadian N.R.C., we were spending a good deal more per capita and still more per gross national product than N.I.H. was doing. But N.I.H. increased rapidly and our government slowly increased its money for research.

In 1947, the National Research Council changed the associate committee on medical research to a division of medical research, and by that time it had a budget of about $200,000; its budget proportionately was about the same as the budget of the N.I.H. By 1955 our budget had risen to several hundred thousands of dollars and the N.I.H. was giving about 50 per cent more on the basis of gross national product than our country was doing. In the last ten years the N.I.H. has zoomed up its grants, so that is giving very large grants for research all across their country and some money for research in Canada, when they feel that giving this money for research in Canada really will help the research effort of the United States and of the world. That is, they do not give it just to help Canadian research; they give it because they beleive that it is worth their while to pay for this research to be done in Canada by competent men. The amount of money they gave to Canadian research reached to a maximum of about $1,800,000 per year in 1963. But, their whole budget for support of research in their own country outside of government institutions had by this time amounted to about $800 million a year, a very large sum.

By this time they were giving on the basis of the gross national product of the two countries about six times as much for medical research as was being given by federal granting bodies in Canada. Our Canadian budget for medical research had increased steadily. The associate committee on medical research had become the division of medical research; and in 1960 the division of medical research of the N.R.C. was replaced by the Medical Research Council which is still closely associated with the National Research Council. Our budget has increased from $890,000 in 1957 to $5,100,000 last year, and it is just under $7 million for the current year. Now, that is a very significant increase in the budget and it has resulted in a tremendous increase in research effort in Canada.

There are large research laboratories in most of our universities and hospitals; and increasing numbers of men of high quality are engaged in medical research in Canada. Our medical research effort is very much greater than it was. But, medicine is advancing at a great rate and every new discovery, such as the discovery of insulin which, as I said, came along in 1922, when I was in my final year in medicine, results in additional needs for research.

I saw the first person to be given an injection of insulin. This research on diabetes led to so much more research that there are now thousands of people in the world working on problems of diabetes.

The same thing happened with every new discovery. Each opens doors for research that will at first increase knowledge and, later, sometimes after a year or two and sometimes after a generation will lead to great improvement in the treatment of the patients with various diseases. There are many diseases for which we have no good treatment. But, fortunately, we have now many effective remedies.

However, there is no method of treatment which is not capable of causing harm. And, one of the things that has to be done with all medical research is to study not only the value of the treatments that are being given but also the dangers. Fortunately, the dangers are not numerous in most instances. But, one never knows when beginning to use a new drug, what danger there may be. I will give an instance of that later. But, I am answering the chairman's question and I am wandering a bit afield.

I pointed out that the research funds of the M.R.C. have increased greatly at the Medical Research Council. It is now up to almost $7 million. The department of National Health and Welfare, through a different system of support

for research in universities and hospitals limit its support to work that is more connected with immediate health problems and public health problems and the like. It gives about $3½ million a year for medical research and the defence research board gives about $500,000. So, in the current year there will be used for medical research in the universities and hospitals of our country about $11 million from federal funds. At the same time, the Americans will have on the basis of their national research product spent just about six times as much.

Of their funds in the past six years N.I.H. have awarded to Canadian workers increasing funds reaching about $1,800,000 per year by 1963. Since then they have started not, because of lack of value of the research, but for reasons of their own, which include some unwillingness to give funds outside their own country, to reduce the funds that they have been giving to workers in Canada and other foreign countries. This creates quite a problem for our research-granting bodies because when some people have had large funds from N.I.H.—one research worker has had considerably over $100,000—and when such sums are suddenly cut off it becomes an embarrassment to the research worker and a responsibility of the M.R.C. to try to make a first class worker as much as possible of the American grant that is being discontinued in order that he may carry on with his work.

We knew that the N.I.H. funds awarded to Canadians were going to be reduced and we have tried to have available the necessary funds to keep the work going. How much can be given to make up for loss of American grants, remains to be seen. Our critical problem is that whereas our research support has increased greatly, and is increasing, the need for research is increasing and the number of people who are highly qualified and capable of doing good research also is increasing; it has been increasing more rapidly than are our funds.

You might put it this way: the success of our government in stimulating and supporting research has been great enough that it has increased the number of workers doing good research and has increased the demand more rapidly than the funds have increased. That is the financial side of it.

I mentioned some of the problems about the diabetic. When insulin was discovered, naturally every doctor that was using it thought that diabetes would no longer be a great problem; but they did not know that the diabetic who had some hereditary tendency to become a diabetic also had hereditary tendencies to suffer from certain degenerate diseases, and when insulin was given to maintain a fairly normal blood sugar, the patient might still go on to have related complications in the eyes, kidneys, blood vessels and many organs. Similarly, treatments for other disorders which at first seem to give virtually complete recovery, may later be shown to be inadequate in some respects.

It is one of the interesting things in medical research that insulin was discovered in Canada in 1922, or, rather, became available in 1922. Dr. Minot of Boston who discovered the liver treatment for pernicious anaemia was a diabetic and not likely to live very long. Insulin kept him alive and well enough to discover liver treatment for pernicious anaemia in 1926 and also for many years after that.

When the liver treatment for pernicious anaemia was discovered, it was thought there might be some dietary defect. Soon it was shown that the stomach of these patients could not absorb a particular essential substance. After 15 years it finally was found that the substance in the diet that needs to be absorbed was a substance called B-12. The amount of B-12 actually needed to relieve the disease is extremely small. It is necessary to give only one microgram per day by injection to keep a person completely free from pernicious anaemia. This now can be given by injections about once a month. It is customary, however, to give much more than that. There are 1,000 micrograms

in one milligram and 60 milligrams in one grain, and five grains in an aspirin tablet; a quantity of B-12 the size of an aspirin tablet given per day would be enough to keep 300,000 people free from pernicious anaemia. One can hardly imagine anything working in a smaller amount.

This discovery of Minot's that liver contained a substance which would cure pernicious anaemia gave a tremendous stimulus to the research of the blood forming organs and associated disorders so that now there are thousands of people all over the world working in this big field. Disorders of the blood forming organs occur in a small proportion of people given certain drugs, and this is important when new drugs are used. One never knows whether a given person may become sensitive to a given drug. Every person will not do so; if every person became sensitive to a drug it would never come into use.

To give you an example, around the turn of the century a drug called 606, or salvarsan, was introduced in the treatment of syphilis, and for a very long time was the best treatment. After using this drug for a period of between 20 and 25 years, it was found that a few people suffered a very peculiar condition of the blood. The white cells would be reduced, and then there were certain changes in the bone marrow. A number of people died of this disease because they had developed this type of sensitivity to salvarsan.

Any new drug may have the potential ability to cause allergic diseases of one kind or another in a small proportion of people. When penicillin was discovered by Fleming—and later produced in larger quantities by Florey and his associates, the British found they were unable to manufacture it in the quantities that were needed during the war. They brought over their knowledge to America and the United States pharmaceutical industry co-operated with them wonderfully. During the war they produced it in such quantities, beginning in 1943, that sufficient amounts were available for the treatment of the allied soldiers wounded or suffering from many illnesses and diseases in the Normandy campaign.

We all thought that penicillin was a wonderfully safe drug—and it is. It is also a wonderfully efficient one; it did not take any length of time to learn that you could treat pneumococcus pneumonia, streptococcus infections, and many others, with remarkable results. It immediately cured a number of persons; there was not the slightest doubt of its efficacy. It has been the greatest discovery of the age for the treatment of infection but it does not cure all infections. It has led to a tremendous increase in the search for other antibiotics which are substances derived from the growth of organisms, they come from living organisms and are useful in the treatment of infections because they either destroy or prevent the growth of the bacteria which cause disease. There are not antibiotics for all diseases, but the number of effective antibiotics has increased tremendously. The pharmaceutical houses are the only places where this search can be conducted on a large scale. It is tremendously expensive to do it, and the universities neither have the men nor the wherewithal for it. However, that is another story.

What I started to talk about in respect of penicillin is that first we thought this drug was an entirely safe drug; but gradually we found some persons became sensitive to it. Sometimes the sensitivity took the form of a skin eruption; a dermatitis developed which might last for six or eight weeks, but it was not very serious. However sometimes when penicillin is given by injection to people who have become a little bit sensitive to it, it creates what is called a severe anaphylactic reaction, a type of reaction to proteins which had been recognized many, many years before.

Penicillin can kill a sensitive person in a very few minutes. For example, a certain patient was being treated with penicillin for a skin infection caused by staphylococcus. He became a little sensitive to it and treatment was stopped.

He went to a doctor who was thoroughly competent and who performed a skin test on him with penicillin, by putting a little penicillin in a small abrasion in the skin to find out whether the patient was sensitive. The test was negative. Then the doctor gave an injection of penicillin whereupon the patient died in five minutes. Such sudden death comes only once in several thousands of persons being given penicillin.

This situation was not recognized till several years after penicillin had been introduced and thousands of lives had been saved. That is an example that I would point out about a new drug. One does not know whether it is safer for sure, just from the result of testing it on animals. One does not know if it is safe, for use, even when it is given to a thousand human beings. One is always on the lookout for any adverse reaction which is peculiar to a particular patient when any new drug or even an old drug is administered. It took twenty years to ascertain that "salvarsan" did this sort of thing, and it took only a few years to find instances in connection with penicillin.

But any allergic reaction requires not only an individual who is capable of reacting, but also exposure for a certain length of time to the drug in question or to other offending substances. For example, in this part of the world we are all exposed to ragweed pollen beginning about the middle of August each year. About ten per cent of the people in this country ultimately suffer from hay fever from exposure to it. A few begin to be sensitive to it in their early childhood. Some people have to be exposed to it for very many years before sensitivity appears. Some people never become sensitive to it.

For example, one of my colleagues became sensitive to it when he was 40 years of age. He had never had ragweed fever before. But now at well over 60 he is no longer sensitive to it.

Any new drug may have a capacity to produce some type of allergic reaction. Such allergic reactions may be as mild as hay fever, or as serious as acute anaphylaxis. Research must be continued in this field to study the sensitivity reaction in all its aspects. It is one of the very big problems of medical research today. This problem is tied in with another problem where at first it might not appear to have any similarity. I refer to the transplantation of tissue from one body to another, for example, blood may be regarded as a tissue; there are certain blood groups; and if blood is transfused it is necessary to give blood from persons of the appropriate blood group, or the patient will react against it. That is one type of adverse reaction.

Suppose one wishes to graft skin. It is almost impossible to give skin from another person, and to have it grow on the person who is receiving it—and some of my colleagues in this committee know this well—the surgeon must take healthy skin from some other part of the same body with which to cover the denuded area.

Another study much to the fore now is the transplantation of a healthy kidney to a person dying from advanced kidney disease. If this could be done easily, it would be a very wonderful thing. Most people can get on for many, many years, sometimes until old age, with only one kidney. But when kidneys were first transplanted, every transplanted kidney finally shrank up and died. The surgeon can make an excellent transplantation and join up all the arteries and veins, the kidney will live and may do its job for a little while, only to shrink up later and be of no use.

Then it was found by a famous Englishman and others that if certain cells of the body are destroyed or greatly reduced, particularly those that have to do with development of reactions against transplanted tissues, namely the lymphocytes the ability of the body to react against transplanted tissues is decreased. These cells can be greatly reduced by X-ray treatment and by the use of certain drugs.

Attempts to transplant kidneys have been successful in a few instances, sometimes for as long as six months, and sometimes for a longer period, but the problem is to find some way of keeping the lymphocytes and similar cells reduced and keep the person alive. There is a great deal of work to be done. Hundreds of thousands of dollars are being spent on this one problem of trying to find some way of gradually getting the body to accept a kidney from another person. The best results come when kidneys from an identical twin is transplanted into his fellow.

That is an example of the type of fundamental research which must be done in this very broad field. I do not know how much of our money in the medical research council goes to the study of such transplantation problems, but it is a significant sum. All great research progresses slowly, a step at a time. It is done by imaginative people being given money and freedom to study as they see fit, given a chance to try one approach after another. It is surprising how wonderfully knowledge has increased by this slow process. Usually important practical applications come after the basic understanding has been achieved. Sometimes it comes about as the result of good luck, as in the case of the discovery that eating large amounts of liver would cure a patient with pernicious anaemia.

The point I am making with this rather long discussion is that when you have competent people to do research it is important to give them funds, to give them the freedom to work, to give them places to work and to hope that they will have the breadth of understanding to realize that they can learn a great deal by talking to people engaged in practice. It is a great thing for people to learn from one another. Even medical research workers who are most informed in special fields and have great knowledge can learn by association with good practitioners who tell them of their problems.

I could go on like this, but I think I have gone on too long. I will now be happy to answer any questions the members wish to ask.

Mr. MACKASEY: Doctor, I appreciate your very excellent examples. As most members of this committee know, I am not a doctor or a druggist but I am interested in your remarks in respect of diabetes for a personal reason.

I might say that the first time in many, many years I was ashamed to be a Canadian was during the trip we took to the Hotel Dieu, at which time we witnessed the deplorable conditions under which Dr. Genest works in respect of his clinical research on hypertension. I think they are bloody disgraceful. I do not know whether that is parliamentary language or not, but I know I would be the first Liberal to cross the party bonds if I thought I could support some motion from anywhere in the House of Commons which would do something to put funds at the disposal of humanitarians such as Dr. Genest. We have no excuse for this situation because we have one of the highest standards of living in the world.

The facts you gave us and the facts given to us by Dr. Genest were calculated on a per capita basis. It is time we took our heads out of the sand and realized the value of research and the deplorable conditions that exist. I do not know whether the drug companies are contributing enough to clinical research for men such as Dr. Genest, but one thing that struck me during Dr. Genest's remarks was the fact, as he suggested, when history is written for each century, such as the industrial revolution, the humanities, cultural advances, the 20th century will be referred to as the greatest century for medical discoveries. Dr. Genest indicated in very choice language, which I appreciated very much, that Canada will be way down on the list in respect of what it has accomplished. I think perhaps if this Food and Drug committee does nothing else but forcibly bring these deplorable conditions to the attention of the people who have money,—whether that involves the Department of

Health and Welfare or some other department—, so that they place more money at the disposal of these research laboratories, we will have done something great.

Mr. FARQUHARSON: That is a very good point you have raised because the research councils up to this time have not had funds available for buildings. That has been considered the responsibility of the Universities and Hospitals. Requests have been made that funds be supplied by the federal government for buildings at universities but this request has not been met as yet.

Dr. Genest, of course, receives funds from the Medical Research Council for the operational support of his research. It is only fair, however, to point out that even in the United States, which has much larger funds available to support operational research, only in the last year or two has it given any significant funds for buildings at either hospitals or universities. When the United States government was increasing the funds by leaps and bounds it did not increase the amount for buildings.

There is a peculiar circumstance in United States government policy which does not exist in our government policy. When the N.I.H. puts in its budget to the United States government it asks for a given sum of money. The request goes before the House of Representatives and the Senate and very often the amount of money has been increased to a point that it is greater than can be used well at once. One year the amount granted was increased by $100 million which was about 30 or 40 per cent more than the N.I.H. had requested. That situation could not happen with our system of government.

The point is that even with those large funds they do not give funds for buildings. They feel that this is the responsibility of the local universities. Last year the N.I.H. budget included $50 million for buildings but there are almost 90 medical schools in the United States and if that amount is spread around them all it would not spread very far.

That government has given huge funds for other facilities including tremendously expensive equipment that is now needed in certain types of research. For instance, in medical research, electron microscopes are becoming very important. An electron microscope costs $40,000 and may be out of date in five or ten years.

I feel that our government has come along further than some others. The United States has gone very much further than we have. Sweden has always been ready to give from its relatively small income a great deal for research. Great Britain gives somewhat less, not much more than we give. It is very hard to compare these things. Some of the smaller European countries are very great in their support of medical research. We have to keep in mind that this effort has been made in the last ten years. Ten years ago the United States gave about as much for research through the government, as we did. But through local foundations and their wealthy corporations, they were giving far more than did Canadians.

When I came back from Boston in 1928 to take my position at the University of Toronto I was tremendously struck by the difference between Canadian corporations and United States corporations in respect of their willingness to give money for medical research. There was a little federal money available in Boston but there were many corporations that would give money freely.

Mr. MACKASEY: I have just two more questions to ask and I promise then to remain silent. I have received letters from men in the research field who

indicate some alarm about the fact that they have had to rely almost exclusively, or primarily, on contributions toward research made by our friends in the United States. As a Canadian I am perhaps a little ashamed again in this regard.

Mr. FARQUHARSON: That is true.

Mr. MACKASEY: These people are afraid that perhaps these research funds are not going to be as readily available next year as they have been in the past. I wonder whether you people are aware of this situation. I am sure you are but I should like to know what steps have been taken to compensate or offset the possible damming up of the revenue?

Mr. FARQUHARSON: I made mention of this fact in my earlier remarks. Most of those funds come from the National Institutes of Health. I use the initials N.I.H. because that is common parlance. There are a number of institutes which direct their efforts toward certain types of research such as cancer, heart and general science as well as mental, childhood and maternal diseases etc. These different institutes are under the direction of Dr. James Shannon with whom we have full communication. As I pointed out, they gave about $1.8 million a year ago and we have cut that figure by approximately $300,000 to $400,000. We have not been able to compensate entirely for that cut but we are looking after as large a part of it as we can. We have confidence that the government will come to our assistance.

Mr. MACKASEY: That who might come to your assistance?

Mr. FARQUHARSON: The government.

Mr. MACKASEY: On what do you base this confidence?

Mr. FARQUHARSON: Maybe I have more confidence than you.

Mr. MACKASEY: I ask this subjectively because I am part of the government; we all here are part of the government, and we either pay lip service to this committee or we become involved in it, as I am afraid I have become involved in it, regardless of party lines. I am not interested in party lines; I just want to see more money put at the disposal of research.

Mr. FARQUHARSON: This is a difficult question for me to answer in my position now, but last year our budget increased from $4.3 million to $5.1 million. For the current year our budget has increased from $5.1 million to $6.93 million. I think the trend is for more money, and I think responsible people understand the needs.

Mr. MACKASEY: Who prepares the budget? This may seem to be a rather ridiculous question, but who sets the ceiling on the budget? Do you people ask for more than you want, in the traditional manner? Who sets the limit?

Mr. FARQUHARSON: This is a function of the treasury board. Up till last year, as you know, the treasury board was chaired by the Minister of Finance but there has been a change in that organization. I am not just sure how it will work. However, the officials of the treasury board have the difficult job of trying to fit in all the increasing budgets of all departments. It is natural that the medical research council, looking at its situation and its needs, would like to obtain great increases. Our case is presented each year and I think it may receive increasingly favourable consideration.

Mr. MACKASEY: My only comment is that we seem to be able to find money for bridges, world fairs, and fancy things like that, but when it comes to research there is insufficient money. It is possible that within the government there are insufficient people lobbying or insufficient people who are dedicated.

Mr. FARQUHARSON: Perhaps I can answer your question by quoting Dr. James Shannon, head of N.I.H. He pointed out in an address given some ten years ago at the CIBA conference on medical research in London that in the United States many influential people became aware that their government lacked funds for medical research and that they were behind many other prominent governments, such as the government of Great Britain. He pointed out that between the two wars there became an increasing awareness throughout the people of the United States that all research was important, and particularly medical research, and that the government had responded to the increased desire of the people to have medical research.

Mr. MACKASEY: Thank you very much.

Mr. MITCHELL: May I ask a supplementary question arising from that?

The CHAIRMAN: Mr. Mitchell.

Mr. MITCHELL: I would like to get some background from Dr. Farquharson. You and your staff are part of the national research council or the Department of National Health and Welfare?

Mr. FARQUHARSON: We are the medical research council. This was formerly part of the national research council but in 1960 the government, by order in council, established the medical research council as virtually an autonomous subsidiary of the national research council.

Mr. MITCHELL: Your funds, therefore, come through the national research council?

Mr. FARQUHARSON: We appear before treasury board at the same time as the national research council appears and our budget is listed with their budget.

Mr. MITCHELL: May I go on from there? What staff do you have in your research department and what qualifications do your research men have in different lines?

Mr. FARQUHARSON: I should like to point out first of all that all our funds for research are spent through the universities and associated hospitals and institutions. We have no laboratories of our own at the present time.

Mr. MITCHELL: That is what I am getting at.

Mr. FARQUHARSON: That may come later, but we have none at the present time. Our money is given as grants in aid of research which are applied for by people from Halifax to Vancouver working in universities and hospitals, and some other institutions. Our job is to distribute our funds to the best advantage of medical research. This is done by a council which is appointed to do so, and this council has representatives in different fields of research across the country. The council also obtains the aid of committees of experts in many different fields.

Mr. MITCHELL: Would you obtain any grants, doctor, from any pharmaceutical houses when a new product is being marketed and on which they would ask your research experts to work clinically?

Mr. FARQUHARSON: They do not give money to the M.R.C. for distribution, but some pharmaceutical houses give money to different workers in different university centres, hospitals, departments of pharmacology and so on, which deal with drugs, as you know.

Mr. MITCHELL: But, would you say, not to any particular volume?

Mr. FARQUHARSON: It is not a large volume, no. It is usually for a highly specific purpose that is not broad in its research efforts. The real research that will matter in the long run is broad research which tries to find out about the body and its functions in health and in disease, and that is expensive

research very often. The expenses are growing because instruments that were unthought of a few years ago are wonderfully valuable and equally expensive; and more men are trained to use them.

I am not worried of the Canadian research effort provided it receives the support it requires. We have people who are competent and interested in doing it, people who want to do it in Canada. I am not afraid of some people going to the United States because the transfer to the United States some persons of this type of person is one of the best things that has happened. These people are our best ambassadors abroad, and we are beginning to get some very good ones in return. We are getting more Americans who want to come to Canada than was the case in the past.

The CHAIRMAN: Dr. Willoughby.

Mr. WILLOUGHBY: Dr. Farquharson, in your original commission report you suggested that our expenditure in research is only one to ten in comparison with the United States, but now we have raised it to one to six. Is that correct?

Mr. FARQUHARSON: Yes.

Mr. WILLOUGHBY: In other words, for us to be competitive with the United States we should increase our research money to $45 million from $7 million—if we are to compete in the same calibre of research.

Mr. FARQUHARSON: If we were to have the same amount of funds as the United States we would have to increase by about six times. I said the medical research council budget was just under $7 million. In this calculation I used also the funds given by the Department of National Health and Welfare and by the defence research board; and those funds, together with the funds of the medical research council, come to about $11 million, and we would need approximately six times that figure.

Mr. WILLOUGHBY: You have answered one of the questions that I was going to ask you and that is in reference to the relationship between the medical research council and the national research council. You have said that the medical research council is almost autonomous. Why do you say that it is almost autonomous?

Mr. FARQUHARSON: The report of the committee I chaired recommended that there should be established a medical research council, an autonomous, independent medical research council. The thought was to have a medical research council act. The government went this far: by order in council they set up a medical research council as a virtually autonomous body. The medical research council makes its own decisions but it uses National Research Council buildings and services.

Mr. WILLOUGHBY: Are the funds controlled by the national research council?

Mr. FARQUHARSON: The funds are placed at our disposal entirely.

Mr. WILLOUGHBY: At the disposal of which council?

Mr. FARQUHARSON: The medical research council.

Mr. WILLOUGHBY: So you have complete control of the finances?

Mr. FARQUHARSON: Yes.

Mr. WILLOUGHBY: You spoke of a figure of $15 million, or something like that, that should be donated to assist in the construction of buildings for research areas.

Mr. FARQUHARSON: I think in my report, which was given in 1959, it was recommended that in the next three to five years there should be $39 million given for buildings. That need has increased. This has never been regarded as a federal function. Our committee reported to the federal government. We were

set up by the federal government. That was before I was chairman of the medical research council, but I was already the director of the medical division. We recommended that this money should be provided.

Mr. WILLOUGHBY: You have not received any grants of that type?

Mr. FARQUHARSON: We did not recommend that it be necessarily given through the medical research council. There are certain difficulties in government. We recommend that some way be found to give it for this purpose. We were willing to take it if the government wished to give it to us but we were willing that it should be given through the Canadian universities foundation. We were willing that it should be done in any way, but we were not stating the political method; we were describing the need.

Mr. WILLOUGHBY: You still have not received it?

Mr. FARQUHARSON: No. Locally, many buildings have been built but the needs are great and the cost of equipping these buildings with modern instruments is going up by leaps and bounds.

Mr. WILLOUGHBY: If you did have a building program that would provide buildings, is there a proper co-ordination between the different centres so there would not be duplication and overlapping in one subject?

Mr. FARQUHARSON: That question is often asked. If one had no overlapping it would be bad because people need colleagues working in their field; two people cannot really work in exactly the same way. Let us suppose that some person makes an application to carry out a certain project, then one of our committees—and we have very capable committees consisting of members from the universities and hospitals—may say that this project has been carried out three times and has been well done. The question is answered. We give that information to the man and he does not obtain the grant for that purpose.

Mr. WILLOUGHBY: I see; there is a control.

Mr. FARQUHARSON: It is not complete control but there is advice, if you like. We do not give money to do something we know has already been done. In cases of people working on the same subject, we sometimes suggest that they collaborate with one another.

Mr. WILLOUGHBY: I have one last question. Do you feel, in the circumstances, that actual drug research should be left to the pharmaceutical companies and that the clinical side should be carried out by the universities?

Mr. FARQUHARSON: I would never stop a man in a university from discovering a new drug, but when it comes to the job of getting that drug produced it is often very difficult to do in quantity, as was penicillin. In the case of penicillin, no person had ever been in the field before and it was difficult to produce it in quantities, but the drug houses have tremendous plants for doing this, plants that no university or hospital could equal. The same thing has been the case for producing other new drugs from growths of minute organisms, i.e. antibiotics. The universities cannot begin to cope with it. However, the universities and people in the hospitals have to try out those drugs; they have to try them on animals first and then they have to try them on human beings where it is justified to do so. I make a great point about that. I as a doctor—although I am no longer in practice—would not try any drug, no matter how good it promises to be, which any pharmaceutical house or any other person asked me to try unless I think my patient may gain something by getting that drug, and neither would you. This is one thing that a lot of people do not appreciate. No self-respecting doctor is going to try one drug after another. No matter how eminent a worker he is and how valuable he thinks a drug is, there are always potential dangers in its use. I do not believe in giving a drug that might not help my patient, and

therefore I will not submit my patient to being a guinea pig. This is one of the difficulties of getting proper tests done. Every man who is responsible for the care of patients must make sure that he does what is best for his patient from his own point of view. I am willing to test a new drug that promises a lot and to test it very carefully, but I am not willing to spend my life testing one after another.

Mr. WILLOUGHBY: The point I was making was that the cost of producing drugs is so great that the money now allotted for the medical research council should not be spent to such a great extent on that angle but more on the clinical angle.

Mr. FARQUHARSON: The good drug houses do it so wonderfully well.

Mr. MACALUSO: Dr. Farquharson, talking about medical research at universities, McMaster University has a nuclear reactor. This department has been involved in medical research dealing with atomic research. Does the medical research council contribute funds to their research?

Mr. FARQUHARSON: Most of their money comes from the national research council because they have no medical school. Some funds do go from the medical research council to them as well.

Mr. MACALUSO: Is there a difference in priority of funds from the medical research council, because that university has no medical school as yet and is doing quite a bit of medical research, in fact it is pioneering in the field of nuclear medicine?

Mr. FARQUHARSON: There is a good deal of collaboration between the two councils, and sometimes the national research council says, "We think you should take this over", and sometimes we do it, and sometimes we do not. Sometimes we say, "We think you should take this over". There is much collaboration. I know McMaster university very well and I know that everything that Dr. Thode does he does well.

Mr. MACALUSO: I concur with that wholeheartedly. I know that the university will very shortly be putting up its own medicine school. The pioneering work they are doing, as far as the nuclear field in medical research is concerned has broken ground in this country.

Mr. FARQUHARSON: They made tremendous advances there.

Mr. MACALUSO: Connecting that with, say, drug research, the drug houses themselves have more facilities and more personnel to carry this out on a large scale than a university. In this field of nuclear medical research which McMaster is carrying on, what part would drug research play?

Mr. FARQUHARSON: I do not think they are doing much. The whole field of radio biology is one that needs greater development in Canada. In the United States huge funds have been allotted for that purpose, and much of the work that they do does not need to be done over again, but in every country there must be people who are working on the effects of radiation; there must be people who understand it not only from the point of view or defence but from the point of view of industry. There are going to be accidents, and the study of changes induced by radiation and how people may be affected and how they may be helped is very important. We have a good deal of work in Canada going on, on that subject, and as we train more people in that field there will be many more working on this. It is one of the fields that will progress and which needs highly trained people. This is a very good point.

Mr. MACALUSO: It is, at the present time, one of the fields where more funds can be directed from the federal government.

Mr. FARQUHARSON: Men are being trained for it, and there is as much trouble in getting good trained men as there is in getting the money. If we gave

all the funds in the world, we would still be held back by the lack of highly intelligent, highly gifted in imagination and highly trained people.

Mr. MACALUSO: Right now personnel are coming from universities that are conducting that type of research.

Mr. FARQUHARSON: They are increasing in numbers every year. Up to this time the opportunities for trained men have been increasing more rapidly than the funds for their support or buildings for them to work in.

Mr. RYNARD: First of all, I would like to compliment Dr. Farquharson on presenting a complex and complicated problem in layman's language.

Mr. ROXBURGH: Hear, hear.

Mr. RYNARD: I think all of us in the professional field can learn a good lesson from him.

I would also like to ask him what the top researchers are paid in Canada?

Mr. FARQUHARSON: That is a very good question. Those who work in universities and are paid by the universities at their own scale which varies in amount. An approximate figure—not the absolute top but an average figure for a well established man in full time work in university, doing a great deal of research,—would be $15,000 a year; there are many working for a good deal less. There is a great variation in the United States, as there is in Canada. In the United States, in some universities, the salaries are as low as any in Canada, but there are some salaries which are very much higher than any in Canada. There are a few heads of departments at universities who get $20,000 or more, and a very few getting substantially more—but there are very few indeed.

Now, regarding what the medical research council pays, the M.R.C. began eight years ago when it was a medical division, to pay the salaries of a limited number of research workers. This was before the N.I.H. began to do so. They have expanded their programme much more rapidly. Our present scale has a top of about $16,000. No person has reached that top yet because the men we pay, are still relatively young. We call them medical research associates. They are applied for by the university, the university undertakes to provide the facilities, and M.R.C. offers according to their age, experience and excellence, if you like, a given salary. They are not appointed until they have several years experience after their six year course, and it varies from about $9,000 to $16,000. The one who was appointed first, a highly eminent person who has been there longest, is getting just under $15,000.

Mr. RYNARD: You have noticed, Dr. Farquharson, that there is great unanimity in this committee, and my friend, Mr. Mackasey, stated that very well when he said that we were all together here to support anything that would add to research. I am just wondering if we should not as a group support increased pay for those researchers. Here is Dr. Farquharson's stating their salaries. I am not picking out any one man, but, for instance, Mr. Ouimet gets $40,000, and yet all of those fellows who are in medical research have a tough time. A lot of them work alone with their own problems. It would seem to me that those people are grossly underpaid. I think we as a group here, regardless of politics, ought to support increased pay for those researchers.

Mr. FARQUHARSON: May I interrupt, Dr. Rynard? We make it a rule that we offer our scale to the universities and the university may say, "This should be higher", and they may pay more, or they may say, "We do not want them to be paid this much" because there are a number of universities which have a scale considerably lower and they say it would disturb relations in their universities if the M.R.C. scale were paid. Then we pay on the scale they ask us to pay. If they ask us to pay more we do not pay more than our scale but we do not mind if they increase it. In the United States the scale goes up

to $25,000 and in Canada it goes up to $16,000. But, they do exactly the same thing with regard to the university and sometimes they give people as little as our lowest. If one is working in a university it is necessary to keep roughly within the university scale. I may say that our scale going up has helped the universities to raise their scale. You have raised a very good point there, Dr. Rynard.

Mr. RYNARD: I remember when Dr. Waltham Walters was head of research for some ten years in the United States. This is about 10 years ago and he said that they were experiencing great difficulty in obtaining competent researchers. I am wondering if this same condition exists today in Canada and in the United States?

Mr. FARQUHARSON: Well, our present rates appeal to many people who are dedicated to research; they do not ask for large salaries but they do ask for security. And, M.R.C. on behalf of these people pay the universities all the costs in respect of their pension fund.

Mr. RYNARD: Do you experience any problems where you have a researcher working and he has a very definite plan you have approved of, and then he wants to go off on a side plan, something he feels that it is necessary to do? And, in this connection is there any red tape which holds this up?

Mr. FARQUHARSON: No. We tell him to go wherever he wants to go and to tell us after he has done it. But, we say, "Do not delay; go wherever your research leads you."

In the medical research council we have a great advantage which is not enjoyed by the department of health. We have free use of our funds without any restriction on accounting. I should say these funds have to be accounted for but we can do this after they are used.

Mr. MACKASEY: Do these funds have to be accounted for to you or to treasury board? For example, take Dr. Genest; if he wanted to deviate and suppose he was going to hire two girls at a total salary of $5,000, which was approved, and then he wanted to change his mind and have just one man at $5,000, would this be in order?

Mr. FARQUHARSON: Do you mean if he wanted more money?

Mr. MACKASEY: No, but he wants to take the money which has been approved and use it in a different way?

Mr. FARQUHARSON: We tell him to use it in any way he likes. Treasury board does not make any such restrictions on us.

Mr. ROXBURGH: Mr. Chairman, I just want to ask one question because the bell is ringing.

In dealing with medicine we are dealing with the people of the world and that means people in every country in the world. I want to say very definitely that I am in full agreement with plenty of money being provided for research in every line, especially in medicine; but you made a statement earlier that the United States, which is a wealthy country, gives so much, and Canada gives only so much. You went on to say that Great Britain did not put the effort into research which it might in proportion to the wealth of that country.

Mr. FARQUHARSON: I did not mean that. I said they did not spend nearly as much as the United States.

Mr. ROXBURGH: This concerns the peoples of the world. We have NATO.

Mr. FARQUHARSON: Yes.

Mr. ROXBURGH: Has any effort been made to have a world wide organization into which all countries would put their money according to their national product on a percentage basis, because this affects every person in the world,

every little country, and every large country. If there is not such an organization, would not such an organization be able to do more if the wealthy countries would contribute according to their means. This would be a world wide organization. The experiments, whatever they may be, would be carried out in the different countries of the world. Has any thought been given to such an organization?

Mr. FARQUHARSON: NATO has given some special scholarships, and some funds have been given through the World Health Organization. However, research in general has to be continued on a national basis, except that the United States, through its National Institute of Health, has distributed funds to many countries in the world.

Mr. ROXBURGH: This has to do with all of the people of the world. Do you not think that every country should be involved, such as Africa and others? Here we have all the different countries, such as Great Britain, France, Russia, and Germany all doing a certain amount of research within their own countries. Do you not think there might be a world wide organization where every country could play its part in this?

Mr. FARQUHARSON: I would like to say one thing about that. Finally, the most important thing is to have the men who can do the research, and in so many of the countries there are no persons trained to do it.

Mr. RUTHERFORD: They could be trained with the extra money that the other countries are not putting in at the present time.

Mr. FARQUHARSON: They could be trained but it takes time to train them.

Mr. RUTHERFORD: I am thinking of the future. NATO has started it in one direction, and we were forced into it.

Mr. FARQUHARSON: The first thing is to obtain men who are trained. We train a lot of persons from those countries.

The CHAIRMAN: If there are no further questions, I would like to thank Dr. Farquharson for his appearance and for giving us his time and his knowledge.

The meeting is adjourned until Tuesday, when we will have with us Dr. Morrell of the Food and Drug Directorate.

HOUSE OF COMMONS

Second Session—Twenty-Sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 6

TUESDAY, JUNE 16, 1964

WITNESSES:

Dr. C. A. Morrell, Director, and Dr. L. I. Pugsley, Associate Director, both of the Food and Drug Directorate, Department of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

20853—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Casselman (Mrs.)
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jorgenson
Macaluso
Mackasey
Marcoux
Nesbitt
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, June 16, 1964
(10)

The Special Committee on Food and Drugs met at 9.45 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Asselin (*Richmond-Wolfe*), Francis, Harley, Macaluso, Mackasey, Mitchell, Roxburgh, Slogan, Whelan (9).

In attendance: From the Food and Drug Directorate, Department of National Health and Welfare: Dr. C. A. Morrell, Director; Dr. L. I. Pugsley, Associate Director; Dr. Frank Lu, Head of the Pharmacology and Toxicology Section; Dr. R. C. B. Graham and Dr. D. C. Jessup, Pharmacologists; and Miss E. M. Ordway, of the Consumers Relations Section.

At the opening of the meeting, it was moved by Mr. Francis, seconded by Mr. Macaluso, and

Resolved (*Unanimously*)—That this Committee pay reasonable living and travelling expenses incurred by Dr. R. F. Farquharson, M.B.E., M.D., by reason of his appearance before the Committee.

The Chairman read into the record a letter received from Dr. Jacques Genest, M.D., F.A.C.P., F.R.C.P. (C), Director, Clinical Research Dept., Hôtel-Dieu de Montréal, and referred to another one from Cyanamid of Canada Limited with reference to the visit of the Committee to the Lederle Laboratories at Pearl River, New York, on the 7th of July.

The Chairman then welcomed back Dr. C. A. Morrell and thanked him for having his department show the members of the Committee the laboratories of the Food and Drug Directorate.

Dr. Morrell was questioned about the facilities of the Directorate to carry on its work, the quality control of the raw material in the manufacturing of drugs, the inspection services, the qualifications and training of personnel, licensing, labelling, sale of patent medicine, regulations on quality control, etc.

The questioning concluded, the Chairman thanked Dr. Morrell and the officials of his department for their appearances before the Committee.

At 11.00 a.m. the Committee adjourned to 9.30 a.m. Friday, June 19th.

Gabrielle Savard,
Clerk of the Committee.

20853—1½

EVIDENCE

TUESDAY, June 16, 1964.

The CHAIRMAN: Gentlemen, I believe we now have a quorum.

Before we move on to our witness this morning, as you all remember we had Dr. Farquharson with us last week, and Dr. Farquharson, while being the chairman of the medical research council and therefore a civil servant, did have to make a special trip up here to Ottawa. I would therefore like to have a resolution that we pay the expenses of Dr. Farquharson for this trip.

Mr. FRANCIS: I would so move.

Mr. MACALUSO: I second the motion.

The CHAIRMAN: All those in favour?

Motion agreed to.

It is agreed that Dr. Farquharson's expenses will be paid.

Before we continue with our examination of Dr. Morrell, there are two letters I would like to bring to your attention. The first one is from Dr. Jacques Genest which reads:

> Dear Doctor Harley:
>
> I want to tell you how pleased I was to have the occasion to meet the members of your committee and to show them our clinical research department where part of our activities is devoted to the evaluation of new drugs.
>
> I wish also to thank you for your kind invitation to testify before your committee in Ottawa. I am at your entire disposal if you feel that at any time I can contribute something on any aspects of evaluation of new drugs, the protection of the public in relation to it and the appropriateness of using trade or generic names for drugs.
>
> I wish you success in your work and please convey to your members my best regards.
>
> (Signed) Jacques Genest, M.D.,
> F.A.C.P., F.R.C.P. (C)
> *Director, Clinical Research Department.*

The second letter is from Cyanamid of Canada Limited giving a brief outline of our trip to Pearl river. We will be leaving Uplands airport at eight o'clock on the morning of July 7, and we will be returning here at approximately 9:30 p.m. on the same day.

There is a letter in the mail to every member of the committee asking whether they do or do not intend to be on that trip. We have to clear our trip with the Department of External Affairs, and therefore it is important that we know fairly soon how many are going. It is a courtesy for our government to let the United States government know that one of our committees is going down there.

Gentlemen, I would like to welcome back Dr. Morrell, the director of the food and drug directorate. I would just like to thank Dr. Morrell for having his department show our members through his food and drug laboratory at Tunney's pasture. We enjoyed the trip very much, and we thank you for allowing us to go through it when it was already set up for visitors.

Dr. C. A. MORRELL (*Director, Food and Drug Directorate, Department of National Health and Welfare*): You are welcome. We should have asked you down sooner, I think.

The CHAIRMAN: Gentlemen, the meeting is open for questions. We will go on from where we were approximately a week to ten days ago.

Mr. MACKASEY: Mr. Chairman, I have a series of questions which I would like to introduce immediately because they are fairly lengthy. I have based them on my study of three or four reports we have had, including, of course, our very informative meeting with you a week or two ago. I know that you will not necessarily have all the answers at your fingertips. If I can get them today, fine, if not, too bad. With the Chairman's permission, my first question would be: How many manufacturers or distributors of prescription drugs are there in Canada?

Mr. MORRELL: By prescription drugs you mean all drugs excluding the proprietary or patent medicines? There are 485 manufacturers and distributors of this type.

Mr. MACKASEY: I am not familiar with the terminology, but how many of the others would there be?

Mr. MORRELL: You mean of patent medicines? I do not know. I can find that out for you, if you wish.

Mr. MACKASEY: Yes, if I could have this information. I know it is not your department which deals with it.

Mr. MORRELL: Yes, it is. We register proprietary or patent medicines.

Mr. MACKASEY: My second question is: How many drug businesses have been inspected by the food and drug offices?

Mr. MORRELL: We do it by the calendar year. If I could give you the number that were inspected in 1963, would that satisfy you?

Mr. MACKASEY: That would be ideal.

Mr. MORRELL: The quality control regulations which are now in the Regulations of the Food and Drugs Act were introduced in March 1963, and during the calendar year 1963 there were 183 plants inspected.

Mr. MACKASEY: With the personnel at your disposal, is it possible to cover all these people at least once a year?

Mr. MORRELL: You mean the 485 manufacturers? No, it would not.

Mr. MACKASEY: What increase in personnel do you think you would need to do this job adequately, or would you say that once a year is too frequent?

Mr. MORRELL: It is not adequate in my opinion, Mr. Mackasey. When you go for the first time and you find that things are reasonably satisfactory, that there is no serious deficiency, you might well let that one go for a year or two, but I must point out that we are just starting and there is a good deal of corrective work to be done by a good many manufacturers, so that more than one visit a year is certainly necessary at this time. I do not know whether double the number of staff would be adequate or not, but it would be something in that order.

Mr. MACKASEY: You agree that at the moment you do not have sufficient staff, numerically at least, to police and inspect them at least once a year?

Mr. MORRELL: Definitely not.

Mr. MACKASEY: In your inspection of the 183 plants, did the facilities of any of these manufacturers or distributors fail to meet the standards that you have set out?

Mr. MORRELL: Yes, quite a few. I want to point out to you that we have a marking system. There are a number of points which are critically examined

and a certain mark given to them if it is a major point, and then the inspector judges from what he sees how many marks he shall give for that. For a manufacturing plant to be considered satisfactory, they must get 90 per cent of the total marks assigned, and there are a good many below 90 per cent.

Mr. MACKASEY: Dr. Morrell, has there been any attempt made as yet or has there been any opportunity as yet to compile the basic reasons for failure to meet your standards? Are they categorized into any common deficiencies, or are they a wide range of deficiencies?

Mr. MORRELL: The most common deficiency is apparently the lack of adequate analytical controls over the raw or crude drugs coming into the plant, and in some cases the lack of adequate analytical control of the drug from the raw product to the finished product. In addition to that, perhaps running a close second, are deficiencies in sanitation, in the qualifications of the personnel, in the adequacy of the records kept, and that type of thing. These are the areas in which the manufacturers are losing the most marks, if I can put it that way, or are failing most often.

Mr. MACKASEY: Am I fair in assuming, therefore, that those manufacturers or factories which do not have proper analytical control must rely on their source of supply?

Mr. MORRELL: They rely on their supplier. Sometimes they have relied entirely on the supplier. One of the requirements in the regulations is that they check their crude material in line with the specifications that they may have set up or that are in pharmocopoeias. The identification of them is essential.

Mr. MACKASEY: If these raw materials came from Europe and then went to a manufacturer that does have analytical control, what safeguards are there other than in your offices, for instance?

Mr. MORRELL: That manufacturer may check his final product even though he does not check his raw materials. I would think, however, that this is not really adequate. The greatest concern we have, I think, is with raw materials coming from abroad. I do not want you to think that Canadians are that much better than anyone else, but we do know about Canadian production, and I might say that most raw materials do come from abroad—I am including the United States and the United Kingdom when I say "abroad" because they are outside of our jurisdiction. The majority of our raw materials for pharmaceuticals in Canada do come from outside of Canada. In cases where the drugs are not checked our concern depends, of course, on the country from which they come. If they come from countries where we have some reason to suspect and to believe that the controls are not as good as they should be, then we are greatly concerned. If they come from the United States, the United Kingdom or Switzerland, or some such place where there is a very reasonable, or even excellent, manufacturing drug industry, we are not quite so concerned. However, we think that as a matter of course, anyone who is putting up crude drugs into a finished pharmaceutical form which is going to be administered to a patient should check his raw material before he compounds it into a pharmaceutical drug.

Mr. MACKASEY: You agree that there is a possibility of some of these raw materials coming in from areas in Europe, other than the United Kingdom, whose sources you are usually concerned about, being used in conjunction with ingredients that do not meet your standards and have no analytical control. That would be double-barrelled trouble.

Mr. MORRELL: It compounds the difficulties.

Mr. MACKASEY: Again you will have to lead me because I am not too familiar with the process. I am not a doctor but I am trying hard. The one thing

that struck me at the meeting when we toured your place is something that a doctor explained to us—and he did an excellent job. He said that a finished product can also be very dangerous if for instance it does not dissolve at a rate at which it is supposed to dissolve. To come back to these people who do not have analytical control, who depend on the appearance of the finished product, we cannot really use that as a sole standard, can we?

Mr. MORRELL: The finished product itself? Oh no, I do not think we can because even if you have a pharmacopoeial drug—by that I mean an official drug for which a standard and a monograph is laid down in British and United States pharmacopoeia—even though the tests that are laid down, and with which the drug must comply if it is to meet the standards, are complete, you must know something about the manufacturing processes in order to anticipate or predict the possible impurities that may occur in the manufacturing process, and these do not always show up in the tests that are laid down in pharmacopoeias; you must go beyond that to be absolutely sure.

Mr. MACKASEY: To get away from that point, we could say therefore that this is one area of control that is lacking owing possibly, and very probably, to your shortage of staff, and secondly to the lack of proper facilities which you discovered within these manufacturing plants.

Mr. MORRELL: We have discovered, as we anticipated, that some of them do not carry out the tests, and our efforts are now directed to getting them to correct this.

Mr. MACKASEY: What action have you taken so far against these types of manufacturers whose facilities are unsatisfactory?

Mr. MORRELL: This being the first year in which they have had to comply with these regulations, we have followed the usual procedure of inspecting and first of all pointing out to the management where they are deficient in our opinion. Discussions are held with the management by the inspector who makes the study of the plant, and he points out to the management what he thinks is wrong. That is the first step. Then, if there are more significant and serious deficiencies, we have sent a warning letter. Where these deficiencies are significant, a second visit has been made following fairly shortly the first one, to make sure that the manufacturer is correcting the deficiencies that we have found. I can say from the reports that I have had that a great deal of progress has been made. They know that they must eventually do this and they get right down to it.

Now, this coming year—this would be the second year—our attitude will be very much different because they will have had time now to correct these deficiencies. It takes time to remodel a building, which had to be done in some cases, and to get new equipment and money. They should have had time to do this by now and we will be much stiffer this coming year than we were in the first round last year. This may lead to prosecutions.

Mr. MACKASEY: I have two more questions. One was pretty well answered but I will repeat it. Are schedules of inspections of premises and facilities of manufacturers and distributors of drug products set up, and if so how frequent are the inspections? Obviously from your original answer it appeared that you had nine months to visit 183 plants out of 485.

Mr. MORRELL: It was really 11 months. We had made some inspections before the regulations came into force. Some manufacturers were consulted in setting up these regulations. We had many meetings with them, so that they were aware of exactly what was coming. We started it 11 months ago rather than nine months ago.

Mr. MACKASEY: That makes it a little worse. What would the ideal schedule be, in so far as you are concerned? How frequent should be the inspections?

Mr. MORRELL: We lack two things: we lack numbers and we lack experience and qualification in inspectors. We have had to hire them. We are trying to get pharmacists, but when we offer them $5,000 and they can get $6,500 in a drug-store, you can see that the competition is very tough. We have even taken a man right out of the school of pharmacy. You cannot expect him to know everything and he has to learn it after he comes into our employ. I can say that the manufacturers have been very helpful in this respect by agreement and discussion with us. A number of the larger companies have said, "You can put a man in our plant for two or three weeks to study our methods of quality control, and then he can go on to another company to see what they do".

Mr. MACKASEY: My last question is: How many inspections of drug manufacturers facilities outside of Canada which supply drugs to Canadian manufacturers have been carried on by inspectors of the food and drug directorate?

Mr. MORRELL: We have done none so far in the pharmaceutical field. I want to be sure that when we send an inspector to Europe he really knows his business, because I think he would have to. In terms of other drugs under the Food and Drugs Act, the biologics for example, we have an inspection scheme. The manufacturer is licensed to produce a biological product. This requires a yearly inspection, and I think we have 17 European plants, including the British, and 17 United States plants which have been licensed, so that there have been 34 inspections. This has been going on for many years because we have had licences for many years, and so we have inspectors who are quite familiar and well qualified. I have no hesitation in sending them to Europe. I hope that in a year or two, if we can, we will have someone over there looking at the pharmaceutical industry.

Mr. MACKASEY: Thank you very much, Dr. Morrell.

Mr. MACALUSO: Dr. Morrell, you mentioned 485 manufacturers and distributors. What inspection, if any, has been made with respect to these distributors and what type of inspection has been made?

Mr. MORRELL: We want to find out what they are doing. A manufacturer, in our terms, is a man who really does some processing and puts it into dosage forms. If you or I wanted to put up a drug under our names, we would be called manufacturers in terms of the definition under the regulations, although we might hire someone else to do it for us. There are a number of custom manufacturers in Canada to whom we could apply and get them to produce our product in capsule form or other dosage form according to our specifications. They would be willing to do that for a price. We would then put it under our names. However, we would be the manufacturer although we did not do the manufacturing ourselves. Those, in a general sense, are distributors, and I think you would probably not call them manufacturers but distributors. In the case of distributors, we want to know what they do, who does their custom work for them and how it is done. We want to know as much about them as we would like to know about a firm such as Ayerst which have their own compounding facilities. We want to know who does what, where, and so forth.

Mr. MACALUSO: I am thinking of one distributor in Hamilton with whom I am familiar. This gentleman obtained some of his products, drugs, pharmaceuticals or whatever you wish to call them, from the West Indies or from Jamaica, or some place like that. He has brought some in and I believe he has run into some trouble with the food and drug directorate. Is there any type of inspection carried on in regard to drugs coming from the West Indies or from Jamaica, and are they checked by the food and drug inspectors when they come through customs?

Mr. MORRELL: We would check them if we have a laboratory man available. We do not check all of it. Again, we are short of staff.

Mr. MACALUSO: You agree that in a case like that there is no analytical control or inspection and there is therefore a danger there?

Mr. MORRELL: Yes, there is a danger there.

Mr. MACALUSO: In these inspections that are carried out, or that have been carried on since last year, what type of inspection is involved, what is the process of this quality control, does the inspector check the machinery and all the steps in the processes, or are there certain standards that must be met, does he analyse the product?

Mr. MORRELL: Perhaps I could give you in general terms what I am reasonably certain an inspector does when he goes to a plant. He may find out what they are manufacturing that particular day, what is being run through their machinery. He will start at the beginning. He will want to know from where their raw materials are received and the room and place where they are received. He will start from there. He will find out, for example, whether the raw materials are what we would call quarantined, that means the raw materials are brought into a room and they are not allowed out of there until the plant chemist or the control people are satisfied that they are what they are. This is one of the things we are trying to get over to all manufacturers, that is, to bring their materials in and keep them in a certain place, and not allow them out into the plant at all until the quality control people are satisfied they meet the specifications or standards under which they have been bought—these may be pharmacopoeial standards or some other standards, but they should be checked. This is one thing the inspector will inquire into, and he will want to see the actual release for the particular drugs that are being used in the manufacture of the pharmaceutical that is going on that particular day.

Then he would want to see a formulation card. The manufacturer should have a card or sheet of paper telling exactly how much of each ingredient will go into that finished drug, and it will all be calculated on the size of the batch that he is making. Our inspector will want to see that, and he will want to see who signed it or okayed it. He will want to see who made the weighings, he will want to talk to him and he will want to know how he made the weighings, for example.

When he is satisfied with that, he goes on to see how the various ingredients of the products are sent out into the plant. They should be marked separately. You have so many white powders, and it could be very easy to make a mistake and put in more of one powder than another, so each container of the ingredient should be marked.

Then it comes to the point where it is mixed. He will want to follow right down through the production line to the finished product all of the operations concerned with the production of that particular pharmaceutical. He will want to know if they take off samples from the production line at this stage. He will want to know what they do about their labels, who keeps track of the labels. Strangely enough this is a very important point of the manufacturing process, because we have found drugs on the market which have been mislabelled. This is a fault of the man who looks after the packaging and labelling. The labels should therefore be only released by someone with knowledge, experience and authority. You do not send a workman to get you 5,000 labels. They have to be counted out, and if they are not used they should be returned in case they are mixed up with some other bottle or dosage. This is important.

Then, of course, they want to know what controls there are on the finished product. There should be a test of the product as it is in the bottle or the dosage to be sold. That will take him again to the analytical laboratory.

This is a good way of seeing all the things around the plant. He will see whether, for example, there is a lot of dust rising from the mixing machines. If there is dust, he will see whether it is confined to a room and whether the

dust cannot get into some other drug. He will have a chance to look at the sanitation, cleanliness and good housekeeping of a plant. This is very important. If you have good housekeeping, everything is arranged in an orderly manner where the manufacturing supervisor can tell you, "I know exactly what that is; it is always kept there", then there is less chance of accidents or errors.

Then, of course, he wants to know what package inserts, and so on, are put in the package. He wants to see everything about that particular drug which he has followed through. He then takes a look at the records in the general office, what records are kept of that product. The new regulations require that records be kept, and if there are not any records for that particular batch because they have not been sent out yet, he will say, "Let me see last year's batches". The records are spelled out in the regulations.

Then, he will want to know what are the qualifications, technical or otherwise, of each supervisor—is he a pharmacist, is he an engineer, is he a chemist? He will want to know how many years experience he has had, how long he has been on his job. All of these are important. He will want to know whether he is a bacteriologist, if he is on parenteral drugs which are injected. He will want to know what is done about parenterals, are they filled into vials, are they sterilized, what tests are made to show whether they are sterile, what tests are made to show that the area in which they are filled is proper and adequate—this is a ticklish business.

These are in general the procedures followed by an inspector. It will take two inspectors a couple of days or more to go through a plant, depending on how big it is—it might even be longer.

Mr. MACALUSO: Inspection is made as far as the containers are concerned. Would a product be filled into containers in a separate room?

Mr. MORRELL: The injectables are filled in a separate special room.

Mr. MACALUSO: What about the pills being put into bottles?

Mr. MORRELL: You mean a pill to be taken by mouth, or a capsule? They have machines which make tablets by the millions. We want to know, also, whether these machines have been cleaned since the last operation which may have involved totally different ingredients. We will want to see this and to see what they do and who does it, because you might carry over some other material into your first lot of tablets until it got sort of washed out with the incoming material. That would not be very good. So that the mixing machines, or the granulation as they call it, must be carefully cleaned before they are used for a different type of product.

Mr. MACALUSO: I have just a few more questions. You mentioned before that you are lacking two things in the inspection field, that is there is a lack of personnel and a lack of experience and qualifications. You said you are obtaining pharmacists who had just graduated. Take, for instance, a graduate pharmacist who comes out of a pharmacy college. He has to be trained in this type of inspection work. What type of training is carried on? How is he trained for that type of work in the directorate?

Mr. MORRELL: There are two kinds, as I mentioned before. Some of the larger pharmaceutical manufacturers have offered to train our men, or to give them experience for maybe two weeks in their own plants. Then he will go on to another plant for perhaps another two weeks. That is one type of training on the job. Then, following that, he will go with a more experienced inspector, and watch him conduct the inspections. It is again on-the-job training. There are very few special courses that are available. I do not suppose there are any in inspection. There are courses in pharmaceutical manufacturing, and I think some of the pharmacists on the committee can check me, but I think all pharmacists must take some courses in their university education dealing with pharmaceutical manufacturing. There are therefore some basic principles that

they already know, but most of it is on-the-job training and experience. In our laboratory here in Ottawa, we can give them some hints and some short courses. We have them once a year. They spend two weeks, or sometimes longer, going from one laboratory to another. Our own scientists can tell them things to look for, things that they have found in their analytical work, and things to watch for when they are in the plants, so that there is also that form of training.

Mr. MACALUSO: From what I hear, there is quite a vacuum here, not only in the lack of personnels' experience, but also I understand that one of your restrictions is the low salaries which you are able to offer them. If you were able to offer them from your budget a greater salary, would this help to alleviate the lack in numbers?

Mr. MORRELL: You would undoubtedly get more applicants, and you could recruit more.

Mr. MACALUSO: I was wondering whether the following thought occurred to you—as I am sure it has—of starting inspection on a planned basis. This is really a new field for the directorate, in a sense. For instance, the health and welfare has inspectors in food and meat processing plants where there is a veterinarian on duty. We have government inspectors who see to it that food does not go out of there unless it is stamped as government approved. My thinking is that perhaps this is what is needed here. I do not know whether it is practical. At the present time it is not practical because of he lack of personnel. However, has it ever been discussed that in each manufacturing plant there should be a government inspector who would study it at all time?

Mr. MORRELL: It has been suggested. I think there has been much discussion pro and con regarding the feasibility of this. There is no question that even in meat inspection this is helpful, but you cannot guarantee the absolute safety of the product even if there are resident inspectors. I am loath to have people say that a drug is guaranteed by the Food and Drug Directorate. I do not see how we can guarantee it. There are many subtleties, and we have not the facilities to detect differences.

Mr. MACALUSO: I do not mean a guarantee of the safety of the drug as to its side effects.

Mr. MORRELL: But you cannot put "government approved" on a drug.

Mr. MACALUSO: I was thinking more of the inspection of general precautions which you outlined, such as analytical control to see that tests are made, that labels are not misplaced, to see there is quality control as far as raw materials are concerned, that sanitary precautions are taken, that machinery is cleaned, and that analytical inspections are made. I agree it is impossible to put "Canada approved" on a drug and that therefore its safety is guaranteed.

Mr. MORRELL: My own personal opinion is that if we were able to send an inspector into every plant without specifying the exact date or time—every two weeks for example—we would accomplish the same thing.

Mr. MACALUSO: That is not possible because of the lack of personnel. Would you suggest that your problem there would be solved if you could give higher salaries and obtain more personnel?

Mr. MORRELL: I think our main problem is lack of numbers. We need trained people, and that is our biggest obstacle. Of course, salaries are involved.

Mr. MACALUSO: How would you suggest going about obtaining this type of personnel?

Mr. MORRELL: We must get the authority to have positions for them. Secondly, we must get salaries that will attract them and keep them. Certainly, we must provide them with adequate training. Training takes time. The

laboratory people cannot take a day or two off to train personnel without that day or two being taken away from other work.

Mr. MACALUSO: Maybe a training school should be set up in the directorate?

Mr. MORRELL: We have really made serious and desparate efforts in the last few years to have our own training programs, and I think we have made some progress. I do not call it a school, but I think we should have a training program that is more formal, that is more systematic, and that is more thorough than we have had over the past years.

Mr. WHELAN: First of all, Mr. Chairman, I think that some mention was made here, and my impression was, that we had inspectors in all our food processing plants. This is not correct.

Mr. MACALUSO: I did not say that.

Mr. MORRELL: We do not have them in our meat processing plants, either. When a meat processing plant does an interprovincial trade, they must have federal inspection.

Mr. MACALUSO: I did not intend to convey the impression that each food processing plant has government inspectors.

Mr. MACKASEY: It is nice to hear Liberals arguing like that.

Mr. WHELAN: Mr. Chairman, it is annoying to me to hear a repetition of everything we heard and saw in Montreal. I myself have found time to leave Ottawa to go to Montreal to see these drug manufacturing plants, and it does not please me to listen to a repetition of all this.

Mr. MACALUSO: There are those of us who perhaps did not attend that meeting because of sickness. You do not get as much information from looking at the physical structures as you do from questioning someone who is experienced.

Mr. FRANCIS: I do not think we have to go into all that.

Mr. WHELAN: We went into more than the physical structures. Everything was explained to us in complete detail on that trip. All this was very educational, and even someone from the legal profession would have found it educational.

There are seven committee meetings this morning, which is the height of idiocy as far as I am concerned because it is impossible for us to attend committee meetings twice a week as well as carry on our other responsibilities.

Mr. FRANCIS: There will be seven on Thursday.

Mr. WHELAN: The Chairman should work it out with chairmen of other committees so that we do not have people running around looking for members to make a quorum. Pretty soon we will have to reduce our quorum to three.

The only question I really wanted to ask is whether the drug manufacturers themselves do not do a certain amount of manufacturing in their own drugstores?

Mr. MORRELL: Yes, in a small way.

Mr. WHELAN: Is there any inspection there at all?

Mr. MORRELL: It is very slight. There is a check of prescriptions at times.

Mr. FRANCIS: This is declining.

Mr. MORRELL: We may know the percentage of compounded prescriptions.

Mr. FRANCIS: Is it one per cent?

Mr. MITCHELL: I would say that we still make plenty of compounded prescriptions, probably 10 per cent.

Mr. MORRELL: A couple of years ago I saw that 80 per cent of the prescriptions were not compounded. That would leave 20 per cent for something.

Mr. MITCHELL: I was playing a little safer than that.

Mr. WHELAN: Do you not think, Dr. Morrell, that most of the drug firms themselves are really responsible people and very conscious of their responsibility to the public they are serving?

Mr. MORRELL: Many of them are, there is no doubt about that. You saw some who were.

Mr. WHELAN: I know this is true in the food processing industry. There is not an inspector there at all times when food processing is under way, but they do not know when one is liable to pop in on them. The cans are marked in such a way that they can check them right back to the product's origin through the serial numbers. These people can come in and test samples out of cans at any time. The manufacturers are conscious of the fact that the packs can be ruined by unsanitary conditions.

Mr. MORRELL: There are all kinds of people in business, just as there are all kinds of people everywhere. I suppose we are there to check the wrong type. Our purpose is to see that they accept their responsibilities.

Mr. WHELAN: What I meant was that I do not think it is really necessary to have full time inspectors on the job.

Mr. MORRELL: No. I also feel that way. There may be some plants where a full time inspector might be useful, but not in the bigger plants. I think that if we drop in on them much more frequently and at unspecified intervals, this would do the trick as well or maybe better than having a resident inspector.

Mr. ROXBURGH: I have missed a number of meetings and possibly this information may have been given before. How long has inspection of chemicals in production plants been going on?

Mr. MORRELL: We have only had the regulations which would give us the authority to do something for a year. Our inspectors have seen plants before and been in them, but if we felt uneasy about them our only recourse at that time was to take some of the products and see if we could find anything wrong with them.

Mr. ROXBURGH: You had no right to go into a plant?

Mr. MORRELL: I think we had the right to go into a plant and we could tell the manufacturing superintendent that that was not good enough. He would say, "That is your opinion. In my opinion, it is all right". We could not get any further than that argument.

Mr. ROXBURGH: Did you ever enforce the right to go into a plant?

Mr. MORRELL: We have enforced the right to go into a plant. I am now thinking of a food plant.

Mr. ROXBURGH: I am talking about drugs.

Mr. MORRELL: I do not think we have ever had to do that. We have been accepted by all drug plants. I have no recollection of our inspectors having been refused entrance into a drug plant.

Mr. ROXBURGH: In other words, as far as Canada is concerned, it was pretty much of a hit and miss affair up to within the last year, and even within the last year, because of lack of personnel, it is pretty much of a hit and miss affair.

Mr. MORRELL: I do not like the expression.

Mr. ROXBURGH: If you had enough money and if, as Mr. Macaluso suggested, you had a training program, how long would it take you, do you honestly think, to acquire a full complement of inspectors who could do the job without going to excess?

Mr. MORRELL: My guess would be maybe three years.

Mr. ROXBURGH: Those are all the questions I have to ask.

Mr. MITCHELL: Mr. Chairman, I would like to ask Dr. Morrell one or two questions. Earlier in our conversation there was a hint that some of these manufacturers do not get the blessing from the department. I am speaking of pharmaceutical manufacturers. What would your feeling be towards licensing of pharmaceutical manufacturers to enable them to live up to your standards, and those who do not, would not have the privilege of selling their products to the Canadian public?

While you are answering that question, what would be your feeling towards provincial licensing against federal licensing?

Mr. MORRELL: It is easy enough for me to answer the first one. I am all for it. Firstly, one reason is that at least it should provide us with a means of knowing just who is in business. Now, we have to scout around to find out who is in business. Secondly, it gives a great weight of authority to whatever we do when we have a licence. I am all for it. Whether it is legally possible, I do not know, but if it could be done, it would solve more problems than it would create for us.

Mr. MITCHELL: You would prefer federal licensing rather than the hodge-podge of overlapping different provincial licensing, is that correct?

Mr. MORRELL: Do I have to answer that, Mr. Chairman?

The CHAIRMAN: I would say to the committee that we are anticipating the calling of Mr. Curran who is the legal adviser to the department. He has already been before this committee at one other time and he went into some detail on the aspects of provincial and federal licensing. It would probably be better to leave that question to him.

Mr. MORRELL: However, I believe that it would be possible to register or license the manufacturer of particular drugs. We already have that authority in biologics. I am told that to license an industry raises some constitutional problems. We have had comments from the industry that a good portion of the industry wants it, and their legal adviser said he thought it was possible. However, there is apparently disagreement among the legal people on this, as on everything else.

Mr. MITCHELL: What would be your feeling, Dr. Morrell, on the labelling of the ingredients of a manufactured product going as far back as the supplier of the ingredient rather than the finished product under that manufacturer's name?

Mr. MORRELL: Let us suppose the manufacturer put his name down as Smith and Company, but bought his ingredients from Jones and Company and they were processed by Brown and Company. All that would be on the label—manufactured from material supplied by Brown and Company and by Jones and Company for Smith and Company, or something of that sort. I have had that question put to me and I have thought, "What would this look like?" Maybe it would be useful, never mind what it looks like, I do not know.

Mr. MITCHELL: We will not pursue that any further.

I have another question, Mr. Chairman. This committee is set up for the control and safety of food and drugs. This question has to do with the safety of patent medicines which come under the food and drug directorate. What is your feeling towards making mandatory the labelling of ingredients in a patent medicine which is for free sale over any drug or grocery counter? The reason I am asking that is that some distressed mother can call me or a poison centre or her pharmacy and say, "Little Mary has taken a handful of these pills, what are they, what can I do, are they injurious? Shall I rush her to the hospital or should I just give her a glass of hot milk or something like that?" This puts the person who is being asked the question in a difficult position if he does not

know what is in the pills. If the manufacturer were forced to show the complete amount of the products, not necessarily the dosage per pill but the names of the drugs on the label, it would make it much easier to give a complete and satisfactory answer to some mother who was very worried about the product which had been taken. I know this has been mentioned before probably, not in this committee but in certain meetings that you have been attending, and I know that the people who manufacture these products would probably be very much against this. I also know that your department has the formula at hand of any of these drugs before a licence is granted. Do you feel it would be an advantage to the general public and to the persons who would like to get this information correctly?

Mr. MORRELL: Mr. Chairman, I think it is archaic to have any secret formula medicines today. I think the great bulk of manufacturers of these products would not resist a change. There are some smaller ones who might resist it simply because they are not aware of things that are going on, but we have, and I think we will this coming year, recommend to the Minister a change in the Proprietary or Patent Medicine Act. This will be one of the features which would remove this so-called secret formula. As you know I think, Mr. Mitchell, there is a schedule under the Proprietary or Patent Medicine Act of drugs which are possibly dangerous which requires that the composition of these drugs must be on the label.

Mr. MITCHELL: Only that one drug?

Mr. MORRELL: Or two, if there are two. There is a limited dosage, of course, beyond which they cannot go in these particular drugs. In other words, there are many patent medicines on the market which have a secret only with respect to one ingredient. I think that is foolish. Secondly, all of the poison control centres in Canada have been supplied by us with a list of all potentially hazardous ingredients in all patent medicines, so that if a mother calls the poison control centre they have just to look at the card to see what is in there. It may not be on the label but it is on that card.

Mr. MITCHELL: You mean the product by name?

Mr. MORRELL: Yes.

Mr. MITCHELL: For instance, "Mrs. Murphy's chowder?" The formula would be at your disposal and at the disposal of the poison control centre?

Mr. MORRELL: It would indicate that it would contain ingredients A, B or C which could be harmful. It does not say it contains chalk, sucrose or lactose because they are not harmful, but the poison control centres will know it contains A, B and C.

Mr. MITCHELL: There are not enough poison control centres readily at hand.

Mr. MORRELL: It depends on where you are. There are a lot of poison control centres in some provinces and not so many in others. This is for the province to do. We have merely provided information to them and we collect information from them on the poisonings.

Mr. MACALUSO: Dr. Morrell, I have a question on patent medicines. As you know, there are many stores which sell nothing but patent medicines. When a prescription comes in, they just take it to the pharmacy up the street which fills it out, and then they give it to the customer. I am familiar with a couple of those. Personally speaking I am against anyone selling patent medicines in a store where prescriptions are not filled out unless they have a responsible pharmacist available. That is my personal view. What is the view of the directorate and of yourself as far as the selling of patent medicines in such stores is concerned where all they do is retail patent medicines? Some of these people represent themselves as pharmacists. Some of the customers

do not know any better and they do not know that their prescription is filled elsewhere. Is there any inspection made with respect to this type of vending operation?

Mr. MORRELL: With regard to your first question, the Food and Drug Directorate has no authority to say who shall sell drugs in a province or a city. This is provincial responsibility. Only the provincial pharmacy act, or the regulations thereunder, can exempt proprietary or patent medicines from sale in drugstores. This is exempted by provincial law, not by the Food and Drug directorate. We could not do it even if we wanted to. It is a provincial matter. My personal opinion is that there are places in various provinces where a drugstore is not very handy, so that there is a store which sells such things as simple headache remedies, or a simple laxative, or something that is supposed to settle an upset stomach, or something which you use to rub on your sore back. These are what I think of personally as home remedies, and I feel that there ought to be some provision, and there is of course under the provincial pharmacy act, for the sale of these in areas where a drugstore is not convenient. I think that the provincial authorities feel this also.

Mr. MACALUSO: I am referring to patent medicines over and above these home remedies.

Mr. MORRELL: These are really patent medicines that are supposedly home remedies. There is pressure to get other drugs in there which we are resisting as well as we can, but the great majority of them are what I describe as headache remedies, or laxatives, or drugs to settle an upset stomach, or something to put on a sore back or muscle or sprain. They are rather simple things that most people do have in their households. You can get these in pharmacies. Patent medicines are also sold in some pharmacies.

Mr. MITCHELL: They are sold in all pharmacies.

Mr. MACALUSO: What happens when a prescription is filled elsewhere?

Mr. MORRELL: I did not know this was going on.

Mr. MACALUSO: I know a particular case where it does go on. This is what I am referring to. I think this should not be allowed.

Mr. MORRELL: This man to whom you are referring does not fill the prescription?

Mr. MACALUSO: He takes it elsewhere.

Mr. MORRELL: But he gives it to the customer?

Mr. MITCHELL: I would suggest that should be up to the inspector of the licensing body under any provincial pharmacy act. The inspection is being done but not as well as it should be.

Mr. MACALUSO: I have one last question with respect to regulations as far as safety precautions which have been underlined in the Food and Drugs Act at the present time is concerned. Were not these regulations which are now in force brought about also with the co-operation of the manufacturing associations or the larger firms which really helped draw them up themselves?

Mr. MORRELL: And anyone who wanted to comment on them. They were sent out in a letter to many hundreds of them, not just to one group, but to many hundreds.

Mr. MACALUSO: Do you feel the regulations, as far as safety is concerned, are adequate, or should they be enlarged?

Mr. MORRELL: I am talking about these new regulations on quality control. We will know in a year or two whether there are loopholes in them that we did not foresee. You can only tell by experience. Looking at them now, I think they are pretty good.

Mr. MACALUSO: They better be because that is all we have.

Mr. MORRELL: They are pretty good anyway in comparison with what occurs in other countries. We are better off than some of the big countries nearby.

Mr. MITCHELL: I have a question for you, Dr. Morrell, but you do not have to answer this if you do not wish. It may come under your department or it may not. What do you think of the recent act in Alberta having to do with allowing the pharmacists to substitute products on prescriptions? You do not have to comment on that but please do, if you like.

Mr. MORRELL: I think I will not, if you do not mind.

Mr. WHELAN: I have one question I would like to ask you, Dr. Morrell. When any druggist fills a prescription, is the person who receives that prescription supposed to be able to trace that right back to the pharmacist?

Mr. MORRELL: There is a prescription number on it and the name and address of the store. It must be on the prescription label.

Mr. MITCHELL: That is correct, also the number must be designated of the type of medication that is prescribed. A prescription item in schedule G indicates that it cannot be repeated anyway.

Mr. WHELAN: How can a store selling patent medicines get away with fooling people that they are filling the prescription?

Mr. MITCHELL: A patent medicine and a prescription are two different things.

Mr. WHELAN: Mr. Macaluso says that they get their prescription filled out elsewhere. The customers would be able to tell where the actual prescription was filled.

Mr. MITCHELL: Yes, and the persons who are party to that can be prosecuted.

The CHAIRMAN: Are there any other questions?

Mr. SLOGAN: I have just two follow-up questions to Mr. Mitchell's questions a while ago regarding ingredients on the label or the name of the producer. This was suggested by the pharmaceutical association in their presentation to us. In some way this might be a suggestion which has been made regarding specification numbers but I do not think this has to be quite as complicated as you explained. For instance, in the case of any pharmaceutical item that has one major ingredient or one active ingredient, could it not just have the generic name with the producer in brackets behind it? This would enable the individual pharmacist to tell the medical doctor where the main ingredients came from. There might be flavourings and other items in it which would not necessarily affect the action of the drug. I believe the pharmaceutical associations are advocating this. Do you not think this would be a good idea?

Mr. MORRELL: I think this could be done.

Mr. SLOGAN: I know it is complicated where you have a lot of main ingredients, but most of them have one main ingredient. It would certainly be a lot more enlightening to practitioners.

The CHAIRMAN: Are there any other questions, gentlemen?

We would like to thank Dr. Morrell for coming back. This is his third visit, plus one visit of the committee to his laboratory. We would like to thank him for giving us his time and the time of his department.

In closing, gentlemen, let me say that next Friday we will have the Canadian Pharmaceutical Manufacturers Association. They have presented a 50 page brief which they will be summarizing on Friday. I hope the members will have a chance to read a portion of it. It is my understanding they will

have many witnesses here, approximately 10 witnesses, to comment on any specific portion of the brief they have written. This may be a very good morning. We hope members of the committee will be here on Friday. There will not be too many other committee meetings on that day.

Mr. FRANCIS: Would you accept the suggestion of Mr. Whelan that the committee try to avoid Tuesday mornings? There are far too many meetings on that day.

The CHAIRMAN: The steering committee will be pleased to consider this. What other day would you suggest?

Mr. FRANCIS: Monday morning.

The CHAIRMAN: A good many members are not here on Monday morning.

Mr. MACALUSO: It is fine for those in Ottawa but not for those who have to fly into Ottawa.

Mr. WHELAN: I believe you can hold these meetings when the house is in session. There are not many meetings in the afternoons.

The CHAIRMAN: There are some.

Mr. WHELAN: This morning I saw in the elevator the list which showed seven meetings in the morning and only one meeting this afternoon.

The CHAIRMAN: If you get enough members interested in the debate in the house, they will not come until the end of the orders of the day, which would be 3:30 or four o'clock. It is unfair to the witnesses when you cannot tell them what time they should appear.

Mr. ROXBURGH: Surely we could get eight people here on Monday at 11 o'clock.

The CHAIRMAN: At 9:30 a.m.

Mr. ROXBURGH: You could call it later on Monday morning, at 10:30 maybe. You would not have to stop at 12 o'clock. There are no meetings on Mondays at all.

Mr. SLOGAN: The reason there are none is that you cannot get a quorum.

Mr. ROXBURGH: There are only eight members needed.

Mr. MACALUSO: If you made sure that only those members who are interested in the subject are members of a particular committee, the difficulty could be obviated.

The CHAIRMAN: It would be impractical to change the dates now. We have our witnesses lined up on specific dates until the end of July.

Mr. WHELAN: I do not see how in the world members in the house can absorb these committee reports. When you finalize your submission to the house, how can they possibly digest all these committee meetings and seriously understand what is going on at these meetings when eight people decide what should be done for the other 257 people?

Mr. MACALUSO: That is not the problem here, it concerns the whip's office.

The CHAIRMAN: The meeting is adjourned to 9.30 Friday, June 19.

HOUSE OF COMMONS

Second Session—Twenty-Sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 7

FRIDAY, JUNE 19, 1964

WITNESSES:

In attendance: Representing the Canadian Pharmaceutical Manufacturers Association: Mr. Stanley N. Conder, General Manager, Ottawa; Dr. Arthur D. Grieve, Ph.D., Director of Quality Control, Ayerst, McKenna & Harrison Limited, Montreal; Dr. William K. MacDonald, M.D., Vice-President and Medical Director, Schering Corporation Limited, Montreal; Mr. F. R. Hume, Q.C., C.P.M.A. General Legal Counsel, Toronto; Mr. George C. Shannon, Director of Manufacturing, Parke, Davis & Company Limited, Brockville; Dr. Roger Gaudry, D. Sc., Vice-President and Director of Research, Ayerst, McKenna & Harrison Limited, Montreal; Dr. J. D. McColl, Ph.D., Assistant Director of Research, Frank W. Horner Limited, Montreal; Dr. John M. Parker, M.D., Ph.D., Director of Research, Charles E. Frosst & Company, Montreal; Dr. C. Walter Murphy, M.D., Medical Adviser, CIBA Company Limited, Montreal; Dr. Peter H. Nash, M.D., Assistant Director of Scientific Division, and Medical Director, Abbott Laboratories Limited, Montreal; and Dr. Sidney A. V. Deans, Product Development Manager, Pfizer Company Limited, Montreal.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21029—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Gauthier	Orlikow
Asselin (*Richmond-Wolfe*)	Horner (*Jasper-Edson*)	Prud'homme
Basford	Howe (*Hamilton South*)	Roxburgh
Casselman (Mrs.)	Jorgenson	Rynard
Côté (*Longueuil*)	Macaluso	Slogan
Enns	Mackasey	Whelan
Francis	Marcoux	Willoughby—24
	Nesbitt	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

FRIDAY, June 19, 1964
(11)

The Special Committee on Food and Drugs met at 9.50 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Mrs. Casselman and Messrs. Armstrong, Francis, Harley, Howe (*Hamilton South*), Mackasey, Marcoux, Mitchell, Prud'homme, Rynard, Slogan (11).

In attendance: Representing the Canadian Pharmaceutical Manufacturers Association: Mr. Stanley N. Conder, General Manager, Ottawa; Dr. Arthur D. Grieve, PhD., Director of Quality Control, Ayerst, McKenna & Harrison Limited, Montreal; Dr. William K. MacDonald, M.D., Vice-President and Medical Director, Schering Corporation Limited, Montreal; Mr. F. R. Hume, Q.C., C.P.M.A. General Legal Counsel, Toronto; Mr. George C. Shannon, Director of Manufacturing, Parke, Davis & Company Limited, Brockville; Dr. Roger Gaudry, D.Sc., Vice-President and Director of Research, Ayerst, McKenna & Harrison Limited, Montreal; Dr. J. D. McColl, Ph.D., Assistant Director of Research, Frank W. Horner Limited, Montreal; Dr. John M. Parker, M.D., Ph.D., Director of Research, Charles E. Frosst & Company, Montreal; Dr. C. Walter Murphy, M.D., Medical Adviser, CIBA Company Limited, Montreal; Dr. Peter H. Nash, M.D., Assistant Director of Scientific Division, and Medical Director, Abbott Laboratories Limited, Montreal; and Dr. Sidney A. V. Deans, Product Development Manager, Pfizer Company Limited, Montreal.

The Chairman introduced Mr. Stanley N. Conder who, in turn introduced those in attendance, stating that they were at the disposal of the Committee to answer questions in their particular fields.

On behalf of the Canadian Pharmaceutical Manufacturers Association, Mr. Conder presented an extensive brief concerning Drug Safety in Research and Manufacturing.

He then read a prepared summary of the submission.

Mr. Conder, Dr. Grieve, Dr. MacDonald, Mr. Hume, Mr. Shannon and Dr. Gaudry answered questions thereon, and on related matters.

At 11.00 a.m. the Committee adjourned to 2.00 p.m. this day.

AFTERNOON SITTING
(12)

The Committee reconvened at 2.10 p.m. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Côté (*Longueuil*), Francis, Harley, Mackasey, Marcoux, Mitchell, Slogan (8).

In attendance: Same as at the morning sitting.

21029—1½

The Committee resumed consideration of the submission of the Canadian Pharmaceutical Manufacturers Association.

Dr. Nash, Mr. Conder, Dr. Parker, Dr. MacDonald, Dr. Murphy, Mr. Shannon, Dr. Gaudry, Mr. Hume and Dr. McColl, supplied information to the members of the Committee in relation to the manufacturing and sale of drugs.

Dr. McColl tabled two papers entitled: "INFLUENCE OF PATENTS ON DEVELOPMENT AND DISTRIBUTION OF INSULIN", by A.M. Fisher, and "INSULIN: ITS ACTION: ITS THERAPEUTIC VALUE IN DIABETES, AND ITS MANUFACTURE" (The Insulin Committee of the University of Toronto); it was agreed that they be reproduced and distributed to the members of the Committee. He read part of the first one into the record.

At the conclusion of questioning, Mr. Mackasey moved, seconded by Mr. Mitchell,

Resolved,—That the submission of the Canadian Pharmaceutical Manufacturers Association concerning Drug Safety in Research and Manufacturing be printed as an appendix to today's proceeding. (*See Appendix "A"*)

The Chairman complimented the Canadian Pharmaceutical Manufacturers Association for its excellent brief; on behalf of the Committee he thanked the associate members for having sent experts to supply information to the Committee, and through the Association, the Companies involved who took part in this effort.

At 3.15 p.m. the Committee adjourned to 9.30 a.m. Tuesday, June 23, to hear the representations of the Canadian Association of Consumers.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

FRIDAY, June 19, 1964

The CHAIRMAN: Gentlemen, we now have a quorum.

We have with us this morning the Canadian Pharmaceutical Manufacturers Association and their representatives. I think the easiest thing for me to do as Chairman is just to introduce the general manager of the Association, Mr. Conder, who has his office here in Ottawa, and let him introduce the other witnesses.

Mr. S. N. CONDER (*General Manager, Canadian Pharmaceutical Manufacturers Association*): Mr. Chairman and members of the special committee on food and drugs, on behalf of our Association, I wish to thank you for the opportunity of appearing before you on this important subject of drug safety.

We have as our delegation, a number of medical, scientific and technical personnel, who are authorities in their respective fields of endeavour. All are employed by our member companies. These, our expert witnesses, are as follows: Dr. Roger Gaudry, vice-president and director of research, Ayerst, McKenna & Harrison Ltd., whose subject is basic research and metabolism; Dr. J. D. McColl, assistant director of research, Frank W. Horner Ltd., whose subject is pharmacology; Dr. John M. Parker, director of research, Charles E. Frosst & Company, whose subject is toxicology; Dr. C. Walter Murphy, medical adviser, CIBA Company Ltd., whose subject is clinical pharmacology; Dr. Peter H. Nash, assistant director, scientific division and medical director, Abbott Laboratories Ltd., whose subject is clinical investigations; Dr. William K. MacDonald, vice president and medical director, Schering Corporation Ltd., whose subject is concluding remarks on the clinical aspects of drug trials; Dr. Sidney A. V. Deans, product development manager, Pfizer Company Ltd., whose subject is product research and development; Mr. George C. Shannon, director of manufacturing, Parke, Davis & Company Ltd., whose subject is pharmaceutical manufacturing; Dr. Arthur D. Grieve, director of quality control, Ayerst, McKenna & Harrison Ltd., whose subject is analytical development and end product control; and Mr. F. R. Hume, Q.C., who is counsel to our Association.

Mr. Hume and I are here to assist your committee wherever possible with matters of a general or legal nature. However, the other members of our delegation are the ones expert in the area of drug safety as it applies to the pharmaceutical manufacturing industry. They are prepared to answer and discuss any questions you may have concerning their papers and respective fields of endeavour.

As you know from our written submission, copies of which were delivered to you last Monday, it consists of a series of papers prepared by the members of our delegation. In view of its length, and to conserve your time, I will merely read a summary of the salient points contained in the submission.

Before doing so, however, I wish to apologize to the French speaking members of your committee, for the delay in sending to you the French language version of our submission. This should have been in your hands at the same time as the English version but, unfortunately, we had considerable trouble finding competent translating assistance.

The Canadian Pharmaceutical Manufacturers Association represents 55 companies engaged in manufacturing and distributing drugs sold on doctors' prescription. Our interests are those of domestic industry, in that the drug products we represent are made largely in Canadian plants, by Canadian

workers. It is estimated that our Canadian industry now employs some 12,000 Canadians at an annual wage bill of about $48,000,000.

Ours is one of the oldest trade associations in Canada. CPMA was founded in 1914 and, this year, is marking its 50th anniversary.

Much has been said, and will be said, on the subject of drug safety before your committee, by government and professional representatives. Our submission deals exclusively with drug safety as applied to pharmaceutical manufacturing, research, and control, within the Canadian industry. In this area, we are expert.

It will be seen from our written submission that the art and science of pharmaceutical manufacturing, in its broadest sense, is not a casual process. In fact, few other products in the general field of manufacturing must meet the exacting requirements which are the very foundation of the modern drug. The medical science involved is such that the conditions of safety can be determined only by trained personnel in manufacturing, in medical practice and in the food and drug directorate.

As was mentioned in the preamble to our submission, we understand that one of the primary decisions for your committee is to determine whether adequate safeguards now exist to ensure that the community at large is protected against unwarranted side effects, but is not prevented from access to required medication.

Regarding this aspect of public protection, it may be said that the government and the House of Commons decided, in 1962, to establish a parliamentary committee, to investigate drug safety, as a result of the concern about the introduction of new drugs arising from the unfortunate thalidomide incident. Since then, the department of National Health and Welfare and its regulatory agency, the food and drug directorate, have studied the situation in detail, and have revised the directorate's procedures and regulations concerning new drugs. This, in turn, resulted in the recently promulgated new drug regulations.

Accordingly, the food and drug directorate now has in effect the legal and procedural methods needed to ensure the degree of safety required to protect the public interest. Equally important, it has also established the legal machinery with which to withdraw from the market drugs which are shown to be unduly toxic. This has been accomplished since the first special committee was formed in December, 1962.

In studying the adequacy of these safeguards, care must be taken to ensure that future discovery is not inhibited. In other words, an overly restrictive approach to a life saving substance might well protect the general public against some adverse side effect, but it might also prevent a patient from having a medicament that is essential to his life.

In this respect, it must be recognized that potency is the very keynote of modern drugs. Every drug which carries with it a biological value must in some way have an effect on the body. Consequently, it is impractical to expect a potent chemotherapeutic substance to be effective and yet be without side effect in susceptible individuals.

The earlier scientific breakthroughs, such as penicillin and the sulfonamides, may have very serious side effects in those who are sensitive to these substances. It is a matter of medical record that some patients have died from these drugs as a result of such side reactions. Yet countless thousands more would have died had these products been withheld from medical use through legislative edict. It may be said, and rightly so, that withdrawal has not been necessary in these cases, as a result of the recognition and knowledge of the side effects by the medical profession.

If we as a nation become overly restrictive in our legislation, and attempt to replace the knowledge of the medical profession with too restrictive government controls, we may well keep from the market the sulfonamides, penicillins

and cortisones of tomorrow. Dramatic though this may seem, we must nevertheless recognize the fundamental principle that science and medicine can thrive only in a comparatively unfettered climate. If we bind too tightly the hands of our researchers, scientists and manufacturers, the result will be a loss of initiative, incentive and willingness to undertake experimentation. The ultimate loser will be the patient who is now suffering from an ailment or disease for which medical science has not as yet found the answer.

Profound knowledge, judgment and integrity are required to determine at what time and under what circumstances a drug should be withheld from the practice of medicine. While the burden of this decision is being shared to an increasing degree by the food and drug directorate, the pharmaceutical manufacturing industry must still bear the major responsibility for balancing on the one hand the need for public protection and on the other the need for the continuing progress essential to new discoveries.

The individual papers contained within our written submission indicate that our member companies are aware of this responsibility, and that every effort within the limitations of modern science is being made to ensure drug safety at the company level. The required balance between efficacy and potential toxicity is well considered from both the medical and scientific standpoints. It is also apparent that careful standards have been developed and are being implemented in manufacturing and control.

As the focal point for industry action in the area of drug safety, our association is striving to meet the increasing demands of what has become our new era of pharmaceutical development. Through conjoint effort by specialists from our companies, we:

—have spent considerable time and effort to assist the special committee of the Royal College of Physicians and Surgeons during its investigation into the safety aspects of new drugs;

—are continuing to co-operate with the Food and Drug Directorate in developing new drug regulations and other safety precautions;

—are establishing a special Recall Service to provide a prompt and effective means of recalling pharmaceutical products which must be withdrawn from medical use;

—have taken concrete steps, through establishment of the Canadian Foundation for the Advancement of Therapeutics, to improve and refine the methods of evaluating drugs in Canada;

—will continue to work through the various sections within our association to disseminate general information and that covering new procedures which have a bearing on drug safety at the company level.

In this respect, we submit that our domestic pharmaceutical manufacturing industry, certainly that part of it comprising the members of our Association, is working in the best public interest by ensuring Canadians of the newest and most effective medication available, consistent with medical safety.

It is essential to drug safety, however, that the gevernment maintain a record of all those engaged in manufacturing and/or distributing pharmaceuticals in Canada. To achieve this objective, we recommend that the food and drug directorate be enabled to institute a form of certification or registration of manufacturers, distributors and agents as a prerequisite to doing business in this country.

Finally, we submit that adequate safeguards now exist in Canada in relation to the original drug products discovered and manufactured by the members of the Canadian Pharmaceutical Manufacturers Association.

In summation, we respectfully suggest:

(1) That the food and drug directorate now has in effect measures required to protect the public interest in respect to the introduction of new drugs, and older compounds which may be found to be unduly toxic.

(2) Care must be exercised in extending these measures on the grounds that over-restriction may retard future discovery, and curtail the introduction of needed medication.
(3) It must be recognized that a potent drug invariably carries with it some form of side effect, and the decision for the use of such drugs must be vested in the medical profession.
(4) In place of overly-restrictive legislation, it is recommended that the decision as to the required balance between efficacy and toxicity can best be determined through the present relationship between the manufacturer, the food and drug directorate, and the medical practitioner.
(5) And that the food and drug directorate be permitted to institute a form of certification or registration of manufacturers, distributors and agents.

All of which is respectfully submitted by the Canadian Pharmaceutical Manufacturers Association.

The CHAIRMAN: Thank you very much, Mr. Conder.

We all have a copy of the brief. Anyone who has any questions to address to the witnesses may address them to the Chair, and whichever of the experts before us in whose field the question falls will answer it informally from where he sits.

Mr. RYNARD: Mr. Chairman, the drug parnate is recalled. Do you feel we have adequate machinery set up to check this drug so it can either be discarded or brought back onto the market?

Mr. CONDER: I would say that the legal machinery to implement the recall is adequate as it now stands. However, an additional system is needed to implement the machinery with which to recall the drug. Machinery is being implemented through what we call our recall service, in respect to a drug which may be recalled from the market and placed under schedule H of the Food and Drugs Act. Arrangements will be made through our companies to pick up these drugs and have them returned.

Mr. RYNARD: I do not think that you have fully grasped my question. Do you think our machinery is adequate to get that drug back or to have the drug recalled and taken off the market entirely, or to get it back into usage? I have particular reference to parnate. There are other drugs involved too. Parnate was called off in the middle of February and here we are now in the middle of June. Surely for a drug which has been in use as long as this there should be more adequate machinery to assess it, and to assess it more quickly, because there has been a great deal of hardship. There is a great deal of hardship caused not only to the medical profession but to the patients who are taking the drugs when they are recalled. I do not believe we have taken adequate notice of this.

I have had people calling me up from all over with respect to the drug parnate. I know of a physician who was taking it. This causes great hardship when people are depressed. I do not think we have taken adequate notice of this. Why in the world should it take a period of almost five months? We still do not know after five months whether this drug is coming back or not.

Do you feel our machinery can be improved so we can get a much quicker answer than we are getting today?

Mr. CONDER: In other words, you are asking whether machinery can be improved to permit the re-use or release of a drug which has been recalled?

Mr. RYNARD: Yes.

Mr. CONDER: I would say definitely yes, it could be improved. It could be speeded up because when we are dealing in the area of medication for patients—

and my professional colleagues may have further comments to add to this—administrative time should not be a problem.

Mr. RYNARD: This is the point. I feel it is entirely too long and it should not take so long at all. I would like to hear some more comments on this.

Dr. ARTHUR D. GRIEVE (*Director of Quality Control, Ayerst, McKenna & Harrison Ltd.*): There is a process under the new drug regulations for new drugs which may be regarded as being in dispute to be referred to an impartial body which can be created to study the matter.

Mr. RYNARD: This is exactly what was done with parnate.

Dr. WILLIAM K. MACDONALD (*Vice-President and Medical Director, Schering Corporation Ltd.*): On this particular point, if I am not mistaken, an ad hoc committee was set up by the Food and Drug Directorate to study the particular question you raise. They have met, I believe, on several occasions. This is a committee from outside the industry. Their decision on whether a particular product should again be made available has not been brought down.

I think, sir, that there might be many situations in which the value of a drug to the medical profession and its potential problems with certain patients might be difficult to evaluate. I would like to say that if I was on such an ad hoc committee I would want to take a reasonable length of time to reach this decision. After all, if they were to decide quickly to return it and then the problems, let us say, for any drug became magnified, they would be in the same position as they were before; they would have to withdraw it once again. I do not think it is a decision which can be made quickly in this particular situation.

Mr. RYNARD: Mr. Chairman, certainly with the speed of communication today they could get in touch with every psychiatric hospital across Canada—and this is a psychiatric drug—and with every professor of medicine in 48 hours. This drug is used extensively in England and it was not recalled there. It was recalled in the United States but I believe it has gone back on the market. This idea of waiting five months seems to me, and it certainly seems to the public, to be an unduly long time. It also seems to be unduly long to quite a number of doctors who have spoken to me; and this is why I have brought up the matter.

The CHAIRMAN: As I say, Dr. Rynard, I think the point that is being made is that this decision to either restore it or put it back on is not to made by the industry itself; it is a decision of Food and Drugs. These gentlemen really have no part to play in the decision whether it goes back on the market.

Mr. RYNARD: I was just trying to get an opinion. This is something we should know.

Dr. MACDONALD: The decision to withdraw this particular drug was taken by the company in question after consultation with the food and drug directorate, and I think they have acted in extremely good faith throughout. They certainly at this point will wait until the ad hoc committee, which is set up to judge this from a completely outside point of view, has rendered a decision. Once again, I think it is a manifestation of the desire of the member companies of this industry to leave no stone unturned to be sure of the safe usage of the products they produce.

Mr. RYNARD: I realize this and I want to thank you for that answer, but this is a drug that is life saving and substitutes are much more severe. I do not know whether you have agreed with me that this is a long, long time and that it seems unreasonable to the public and to doctors, too.

Mr. MITCHELL: Mr. Chairman, I was going to ask questions on the same subject, but Dr. Rynard seems to have covered it pretty well.

After having read a news release of this particular product being available again, or being considered to be available again by United States authorities, I had wanted to comment upon it. Even though it had been withdrawn in Canada, it was available to psychiatrists, and so on? Is that correct?

Dr. MACDONALD: It was available to hospitals.

Mr. MITCHELL: For clinical use and so on?

Dr. MACDONALD: Yes.

Mr. MITCHELL: The reason for which I bring this up is that one of the doctors in my area is being bugged by his confreres to release some of it to them, but he did not wish to take the responsibility of doing so; it was available to him. I asked him to write to the directorate and see what their answer would be, but I have not heard any more.

An another subject, Mr. Chairman, I asked a question of Dr. Morrell which I would like to ask of Mr. Conder and his group. In your brief you mention that licensing should be agreeable to the pharmaceutical industry. I think today the industry is represented here by the leaders in the industry, but there are many who are not leaders and I feel that licensing would be preferable to the industry at large. Just what form it would take I am not prepared to say, but it would control drugs at the stage at which we are trying to decide whether they are safe or not. I think the leaders in the industry would have no objection to this licensing

Another question is whether licensing should be looked after by the federal government or the provincial governments. I favour the federal government inasmuch as there would be an overlapping or hodgepodge of different regulations if it were handled by a province or by all the provinces. What are your comments on that, Mr. Conder?

Mr. CONDER: It would not be practical, sir, to institute a form of licensing, certification, registration, or whatever word you wish to use, in this connection at the provincial level because, as you point out, there would be considerable overlapping of regulations. The laws concerning this form of legislation should be uniform, and it should be implemented at the federal level. We have made submissions to the Department of National Health and Welfare to the effect that all companies should be registered. This includes not only manufacturers but also distributors and agents, in fact anyone carrying on the supply of drugs in Canada, aside from the pharmaceutical profession itself. We say this not because registration, licensing or certification actually guarantees or ensures the safety of the preparations issued by these companies, but because it does in fact give the food and drug directorate a means of knowing absolutely everyone who is engaged in the business of supplying drugs in Canada, and this is what we are aiming at. We feel at the present time that the food and drug directorate does not have this. It does not know everyone who is engaged in the business in Canada today. This is no criticism of the food and drug directorate; they would like to implement this themselves but they have been advised legally that they do not have the right to do so.

We have approached the food and drug directorate with our own counsel, Mr. Hume. We brought him to Ottawa and he made a considerable plea to the food and drug directorate's legal staff to the effect that it could institute a form of drug registration. Their lawyer said, based I believe on a decision of the Department of Justice, that it could not be done; that it was impractical. It is not a fault of the food and drug directorate; I am sure they would like to see this accomplished. The reason why it is not done is because of the difficulty in overcoming what you might term a legal and administrative matter.

The CHAIRMAN: I was wondering if Mr. Hume would like to comment on this.

Mr. F. R. HUME, Q.C., (*General Legal Counsel to C.P.M.A.*): The difference of opinion, if you could call it that, simply was the view of whoever was reviewing it and had his interpretation of the statute and recent amendments to its regulation section, the section which gives the minister or the department or the governor in council the right to make the regulations. Our view was that the wording of the section was wide enough to include such a regulation. It was perhaps the more cautious view of someone in the Department of Justice that this was not necessarily true. So I think the point merely is a question of interpretation of that section. If it were wide enough—and parliament could certainly make it wide enough if it decided it was in the public interest—then this could be done.

Mr. MITCHELL: We will try to remember that in our recommendations from this committee.

The CHAIRMAN: We will call the legal adviser from the Department of National Health and Welfare for his opinion and also possibly someone from the Department of Justice.

Mr. CONDER: I might add, Mr. Chairman, in connection with the view of the Department of Justice that the food and drug directorate cannot do this legally under the present set-up, we suggested earlier that the Department of National Health and Welfare approach the ministers of health at the provincial level in order to get their concurrence to transfer this responsibility to the federal government.

Mrs. CASSELMAN: Reverting to Dr. Rynard's question, Mr. Chairman, on the speed of returning withdrawn drugs to the market, may I ask if there is an immediate effort by the companies involved for further research or any assistance to the committee in coming to some conclusion?

Dr. MACDONALD: There is no question that they would participate in providing information to the ad hoc committee. I am sure that no company in the position of the type outlined would hesitate a minute to provide the ad hoc committee with every single piece of evidence they have with regard to the cituation. They are just as anxious if not more anxious than anyone else in this regard.

Mrs. CASSELMAN: Is there any emergency approach? Dr. Rynard mentions the need for such drugs. Is there any emergency approach for getting them back into use?

Dr. MACDONALD: Not to my knowledge.

Mrs. CASSELMAN: Could there not be something done to speed things up in this way?

Dr. MACDONALD: I think one thing that has not been perhaps completely settled as yet is the manner in which a company or a group outside could apply to get a rapid consideration of the problem by an impartial group. If the machinery were available, it might be helpful to establish a committee for hearing such considerations in this type of situation. This does not exist at the present time.

Mrs. CASSELMAN: Or perhaps there could be a standing committee for emergency purposes.

Dr. MACDONALD: In my opinion this would certainly have virtue. I would like to hear some other comments on it.

Mr. RYNARD: That was a recommendation of our committee a year ago. Dr. Brien in his last presentation to this committee suggested that there should be a special committee set up. We now wait a whole month approximately be-

fore a committee is appointed and then the committee goes on for month after month. This is very disturbing. In view of the comments we have heard this morning I think something should be done to bring this to a head. For instance, we have heard what Mr. Roger Mitchell has said. A patient can be put into a hospital and he can be given the drug; then surely a qualified psychiatrist is capable of giving that patient the treatment outside the hospital. Those are things that should be cleared up. If a doctor is qualified to treat a patient in hospital, he is surely qualified to treat him out of hospital.

Mr. MITCHELL: Is there not a committee now? I am sure Mr. Conder would know. There is a drug advisory committee which is from outside the industry and which is at the call of the department at various times. Could not that committee be used for that purpose?

Mr. CONDER: Possibly it could, but the Canadian drug advisory committee is quite a large one. It has a pharmaceutical advisory subcommittee, however, which might do this, but that comprises only a few people with diverse interests. This whole situation would have to be looked into in considerable detail from the administrative standpoint, and also from the technical and scientific standpoints, before a decision could be made as to the correct method of approaching the problem.

Dr. GRIEVE: When the latest regulations of drugs were under discussion and the composition of the referee body, board or whatever you want to call it, to which I referred a moment or two ago, the question was also discussed whether this should be a permanent body—and by that I do not mean a body in full time employment but one which is a fixed group of people—or one which should be composed of specialists appropriate to the case that was up for consideration at a given time. Both of these alternatives were considered, and the trend of the discussion was that the second alternative was preferable because in one instance the drug in question might be one in the field of psychiatry, and in another instance it might be an anaesthetic, and so on. Consequently, the discussion ran along the lines that it was better to constitute this referee body specially, choosing those specialists appropriate to the case in hand.

Mr. SLOGAN: Mr. Chairman, first of all I would like to congratulate the association on the amount of work they have put into this brief. It is a very comprehensive brief, a very good one. My only regret is that we will have insufficient time to do it justice. I would have preferred to have gone through the various sections one by one, because there are some most capable men here who should have the opportunity of expressing their views.

I would like to ask Mr. Conder how many members they have in their association?

Mr. CONDER: We have 55 manufacturing companies, or companies engaged in manufacturing and/or distribution.

Mr. SLOGAN: To your knowledge, how many companies are there in Canada which are occupied in the manufacture or distribution of drugs?

Mr. CONDER: I do not know the exact number engaged in this field, and I doubt whether there is any source in Canada that does. I would venture that there are approximately 75 to 80 companies which you might term as multi-line companies, which distribute drugs and manufacture drugs for distribution to the national market. In addition to this, there is a considerable number of what one might call small regional companies, in which the company manufactures certain forms of medication for a small section within a province or across a province as a whole.

The CHAIRMAN: If my memory serves me correctly, Dr. Morrell said in his testimony that in their opinion there were 485.

Mr. SLOGAN: This is strictly a voluntary association?

Mr. CONDER: Yes. I might add one point. It is estimated that we represent approximately 85 per cent of the drugs manufactured in Canada.

Mr. SLOGAN: This is a voluntary association? Are there any standards or regulations or qualifications required for anyone becoming a member of your association?

Mr. CONDER: Yes. You will notice in our submission in appendix B that we give a brief review of our association.

Mr. SLOGAN: For the record perhaps you could just tell us about that.

Mr. CONDER: It reads:

> The most important single requirement for membership is proper quality control facilities. Our bylaws state in part that ". . . membership is open to firms which manufacture in Canada, under proper conditions for control of quality and standards, pharmaceutical preparations. . ." In the case of a non-manufacturing subsidiary, then the parent company must meet this requirement. In order to determine the company's qualifications in this respect, 11 of the 21 questions on our membership application form deal with quality control.

These questions are itemized at this particular juncture.

10. State name and qualifications of person in charge of control.
11. State name and qualifications of person authorized to release finished products.
12. State number and qualifications of chemists in control department.
13. Broadly describe control laboratory and give approximate floor area.
14. List principal equipment in control laboratory.
15. Check type of laboratory analysis made: a. physiological, b. biological, c. chemical, d. bacteriological.
16. State whether each product batch is identified by code throughout manufacture and distribution.
17. State extent to which raw materials are analysed to assure their integrity.
18. State extent to which finished products are analysed to assure their integrity.
19. State extent to which products requiring biological tests are so examined, and state reasons for any omission of such tests.
20. Name those who do outside control work for you and describe it.

When these questions have been answered and submitted by the applicant, the form is then turned over to our membership committee for processing. Two directors are then required to visit the premises of the applicant to determine whether the statements made are correct. If the applicant does not meet these requirements, then he is not eligible for election to membership.

This is based on the ethical responsibility of our association. In this case applicants for membership are also required to sign an agreement that they will abide by the principles of ethics of the association. These include:

1. The calling of a pharmaceutical manufacturer is one dedicated to a most important public service, and such public service shall be the first and ruling consideration in all dealings.
2. The pharmaceutical manufacturer must produce his preparations only under proper conditions and with scrupulous faithfulness to required standards of quality.

3. Preparations must be labelled and merchandised only in a manner free from misrepresentation, misleading practices of all kinds and in entire harmony with the highest standards of commercial morality and professional ethics.
4. Pharmaceutical manufacturers must constantly and conscientiously strive to advance the science and elevate the calling of manufacturing pharmacy to the highest plane of public value, to the end that it may best and most completely serve the medical profession and the public.

I might add that these principles of ethics are not lip service. Our companies are required to adhere to them, and if any company, for any reason whatsoever, takes a course of action which is contrary to these principles of ethics, it is called up on the mat.

Mr. SLOGAN: Have you ever refused membership to any applicant?

Mr. CONDER: Yes.

Mr. SLOGAN: To many?

Mr. CONDER: It would be difficult to say without going back to our records. I would say a considerable number.

Mr. SLOGAN: Have you ever had occasion to throw out a member that you had accepted previously?

Mr. CONDER: It has happened on occasion.

Mr. SLOGAN: So that these companies would still of course be operating in Canada?

Mr. CONDER: Yes.

Mr. SLOGAN: By your own standards, therefore, there are manufactureres in Canada who are not really meeting the qualifications which you set for drug manufacturers?

Mr. CONDER: That is correct. We are also reviewing these requirements in complete detail to adjust them in line with the new requirements of the food and drug directorate and to determine how we in turn can strengthen our requirements for membership within our association.

Mr. SLOGAN: This was a very small proportion of the drug manufacturers in Canada. Would there be any financial barriers for any of the smaller companies joining your association? I was wondering how you set your membership fee.

Mr. CONDER: Most definitely. It is becoming increasingly more costly these days to manage and operate a trade association, particularly one in our field. I say this without being in any way facetious, but to prepare presentations before an inquiry such as this costs us a considerable amount of money. The cost of this must be borne by the members of our association in the form of membership dues. These dues are now fairly high. They are based on a percentage of the company's gross annual sales. So, in other words, a large company would automatically pay more for a membership than a small company.

Mr. SLOGAN: How would you do this for a relatively small company? You say there is a certain barrier. Actually, if it is a small company, there would not be a barrier if you are ruled by a percentage of their sales.

Mr. CONDER: We have examined this closely. There has to be a minimum when you establish a membership fee schedule for any association, ours or in any other field of endeavour. You have to establish a certain minimum fee. We took a very close look at this and felt that there were certain companies, particularly small firms, which believed the membership dues were too high. As a

result we took a good look at this and, at the very lowest level on our membership dues schedule, reduced them to a figure which we felt would be reasonable for companies which wished to join us. Still some of the smaller companies believe that it is too high and that they do not want to pay it at this time. I might add that we do not represent only the large companies. We also represent some small companies, which are members of our association.

Mr. SLOGAN: So there would be small companies operating which would meet your standards except that they feel the financial burden of joining you is perhaps too great for them?

Mr. CONDER: Yes, I know that does occur.

Mr. SLOGAN: What sort of a service would you give? I imagine the services that you give would be more than beneficial to the small companies, which do not have some of the facilities which you have in the association, than to the companies which have probably more facilities than the association. Are you making an effort to try to attract these small companies into your association?

Mr. CONDER: We are now studying our membership requirements in full detail, and this includes a review of our membership dues. Following this we will probably inform some of the smaller and highly reputable companies in this country, which are not now members of our association.

Mr. MACKASEY: I must apologize for coming and going. Possibly some of the questions or observations which I will make will be repetitive and have already been expressed this morning. I apologize indeed for it.

I would like to make an observation and say that this meeting is an ideal one in that it gives all members an opportunity to sum up what has been taking place in the last few weeks. I am reluctant to express the opinion that this meeting should have been held on a day when we had more time at our disposal because the extent of the brief and the number of witnesses indicate the seriousness with which the pharmaceutical association have accepted our invitation to co-operate for the general safety of the public. I did not realize the costs involved. It suggests we should have a further meeting when we have more time so as to do a little more exhaustive study of the brief.

I have a few questions which I would like to ask. Dr. Morrell last week indicated there are, I believe, 485 firms in Canada considered as manufacturers and distributors. You say you have only 55 members. For the record I would like to ask a question, and I think I know the answer to it. There is no barrier to the other 430 firms joining your association if they can meet the quality standards and the financial standards which you say have been designed to make it possible for all firms to join? Am I right in saying this?

Mr. CONDER: That is correct. As long as the company can meet the requirements. For quality control, if it is a manufacturer and also if it is prepared to meet the requirements of our principles, then that company is eligible for membership in our association.

I might just add, when I am speaking of dues in this respect, that our lowest membership fee, which we established specifically for smaller companies, is $300 per year.

Mr. MACKASEY: Which is nothing. This is a very small sum. Remarks were made sometimes in the past about the profits of the industry. Three hundred dollars is no problem, and I wonder why every manufacturer is not a member of your association.

You mentioned quality control as being one of your own main objectives. Are you assisting the food and drug directorate on a voluntary basis by helping to set up quality control among your own members?

Mr. CONDER: Yes, and internally within our association. We believe quality control is absolutely essential in the manufacturing of medication. It is not something that can be added on at the end; it has to be built right into the product during its manufacture. If the members of our association are doing so, and they incur costs involved in this aspect of manufacturing, then we feel everyone else should do it.

Mr. MACKASEY: Dr. Morell admitted in response to a series of questions I asked him last week, based principally on the resumé of the proceedings, that of the 485 manufacturers in Canada he was able, with the added staff we had put at his disposal, to inspect only 185 on a yearly basis, indicating that there are 300 manufacturers in this country who have not been inspected for over a year. He also indicated that some 185 have violated some regulations of the food and drug directorate. Do you know of any that are at the same time members of your association?

Mr. CONDER: Absolutely. There has been a great shakedown following the introduction of these regulations by the food and drug directorate. It is not merely a matter of saying that the manufacturing plants shall do this and that. Quite often it depends on the interpretation placed on a specific regulation or recommendation of the directorate by the inspector concerned.

Mr. MACKASEY: Am I right in presuming therefore that many of the features of your buildings which, to the public, may seem to be an extravagance regarding their roominess and airiness, are basically built-in methods of safety control?

Mr. CONDER: It definitely has a bearing on it. The housekeeping within a plant must meet certain standards—this is absolutely essential. I believe someone mentioned before one of your recent hearings, for example, that dust on a beam over a tablet making machine is a hazard, and this is certainly true.

Mr. MACKASEY: I have one other thing on which I would like to get your viewpoint. We questioned Dr. Morrell on it quite extensively. I am speaking about the importation of raw materials from Europe. I made this point, and I would like to hear your remarks on it. If there are 300 firms which were not inspected last year, we, the public, are therefore at the mercy of these 300 firms and we depend on them to maintain a certain standard, at least between visits. However, it seems to me that the risk is compounded by the fact that many of these 300 firms are using products coming in from Europe that have no source of inspection at that level. Dr. Morrell agreed this is compounding the problem of safety. Have you any recommendations on how we can do something about these raw materials to protect the public? Dr. Morrell is obviously helpless owing to lack of finances and lack of staff. He would like to inspect these plants right at their source of origin.

Mr. CONDER: That is a very difficult thing to do. I can appreciate Dr. Morrell's problem, particularly insofar as the locations of the plants abroad are concerned. We know from experience, based on our own knowledge of how companies operate, that there is no major problem insofar as plants located in some major pharmaceutical countries are concerned, and by this I mean the United States, the United Kingdom, and Switzerland. There is no problem in this area. However, when you get into certain other countries, it becomes a problem. For example, you as an agent in Canada might purchase a drug from a company in Italy. The name of the Italian company may appear on the product, but the drug may not have originated in the plant in Italy at all. It may have been transshipped from Bulgaria or from some other country. You might go into the Italian plant—I am using this Italian reference merely as an example, there is no slight intended—and you might inspect their premises and say they meet your requirements exactly. But the products being shipped

in may not even be made in that plant. So certainly it is a problem. We feel that in the final analysis manufacturing of the product as such requires sound quality control facilities, and these facilities and the control procedures involved must be built into the product during its manufacture. You can have the finest looking plant and equipment in the world, but unless these quality control procedures were maintained during the complete line of the manufacturing process, the manufacturer would not be ensuring safety to the best of his ability. The products that are turned out depend primarily on the reputation of the manufacturer, and the reputation of the manufacturer is based on that manufacturer's integrity.

Mr. SLOGAN: Can you tell us approximately what percentage of the products going into the drugs manufactured by your members are imported into Canada?

Mr. CONDER: I would like to clear up something first. Manufacturing in our particular field is a form of processing whereby you take one or more active medical ingredients and put them into a dosage form so that the dose in turn can be used by the medical practitioner. The chemicals themselves—there are exceptions to this but not many—would not be usable in dosage form by the doctor. They have to be processed or manufactured into dosage form.

Mr. SLOGAN: In other words, what percentage of the drug, the ingredients of which have been manufactured in a foreign country, would be imported into Canada by your own members?

Mr. CONDER: I did a survey on this about three years ago and I understand from our member companies—I am speaking of the manufacturers in this country—that they were manufacturing approximately 85 to 90 per cent of the products which are being distributed in Canada by these companies. This would vary. Some companies do 100 per cent, that is, everything they manufacture is turned out right here in Canada, while other companies might be doing 85 per cent. This depends primarily on the products.

Mr. SLOGAN: Would you say this percentage is substantially higher among companies which are not members of your association?

Mr. CONDER: I would say this percentage is high among the companies which are not members of our association.

Mr. GEORGE C. SHANNON (*Director of Manufacturing, Parke, Davis & Company Limited*): I might say that because of the small size of the Canadian chemical industry, many of the raw materials which have to be imported from the United States are basic materials. As Mr. Conder says, we compound 85 per cent of the products we put on the market.

Mr. MACKASEY: I have a question along the same lines. Would you tolerate within your association a firm that had the reputation of constantly importing these raw materials not from the United States, from the United Kingdom or Switzerland but from firms of disputable character? You mentioned that in many ways you are helping out Dr. Morrell and duplicating his work, but would you go so far as to penalize your own firm or recommend that it cease its practice?

Mr. CONDER: If we found a member of our association taking a course of action which we felt was detrimental to safety, or to the sound manufacturing principles within our own industry, that member would be taken to task.

Mr. MACKASEY: You cannot have it both ways. If it is not sound to the outside firms, it cannot be sound for those within your association.

Mr. CONDER: You are looking at the basic raw material that goes into a drug. Even this basic raw material comes from a reliable source, the manufacturer must check the material to determine that it is in fact what it says on the label. Invariably it comes in large drums. If this substance meets the

requirements, then it goes into the manufacturing process. It is during the manufacturing process into dosage form that the safety factor becomes highly important. I am not saying it is not important for the active ingredient; the active ingredient is equally important.

Dr. GRIEVE: I can only supplement what you have just said. One of the requirements for membership is adequate facilities and sufficient staff for maintenance of quality control. One of the functions of the quality control department in our companies, among several others, is the testing and accepting or rejecting of any raw material, active or inert, domestic or imported, so that with these measures there is then adequate control of the raw materials that are being used.

Mr. MACKASEY: May I finish my own questions and then let someone else start his questions?

Mr. SLOGAN: May I ask one question before we go on to another topic? Do your companies send any of their representatives abroad to check on the companies which supply the raw materials from abroad?

Mr. CONDER: The majority of our companies, partically all of them, certainly do this when they arrange to purchase raw materials from other sources. They do manage to check out those sources, and invariably they send someone to visit the source of their raw materials.

Mr. MACKASEY: Most of us in this committee were privileged as the result of your organization's invitation, to visit not only some of your excellent firms but also to visit the clinical research department of Dr. Genest. This, I think, was the logical step in the visit, in that it brought to the attention of a layman—because I am neither a doctor nor a pharmacologist—the fact that in the final analysis all the products must be tested on humans over as long a period as possible so as to get their precise reactions. Frankly, I was appalled at the conditions under which Dr. Genest operates. I have said so. I know you realize that Dr. Genest is performing a function that in the final analysis is necessary to the eventual marketing of your products. I am wondering to what extent you people help Dr. Genest. Dr. Genest's answer to my question—he was a very reluctant but polite witness on this point—left me with the thought that the sole financial assistance he is getting from the pharmaceutical industry on the particular research he is doing is the sum total of a salary of one particular person who followed this product through. I could not help but think that you people would have to spend thousands of dollars to set up a duplication of this man's effort. Do you people morally feel you are contributing your share towards this medical research?

Mr. CONDER: Dr. Genest's operation is not the only one in this country. Our companies contribute considerable amounts of money to organizations such as Dr. Genest's, to universities and other research organizations across the country. I believe that Dr. Gaudry may be able to comment on this.

Dr. ROGER GAUDRY (*Vice-President and Director of Research, Ayerst, McKenna & Harrison Limited*): I think that all the companies that have new drugs that need to be tested clinically will go to see Dr. Genest and people like him who have facilities to do clinical testing under very precisely controlled conditions. When companies go and see him for work such as that they always carry all the costs involved, and sometimes more. Over and above that, many companies help him with research without any strings attached. This is a fact I know very well. I do not know that it is the function of the companies to support basic investigations which he and people like him are carrying on. I would not want to speak for Dr. Genest because he will probably appear before you, but it is true that you saw some rather appalling conditions there which will be changed very soon. He has been granted a large amount of money by

the provincial government to build a new institute. When he has those physical facilities, I am sure he will find more money for a much larger and more efficient staff. However, most of the big companies are supporting him or others like him to carry on the fundamental work. Of course, it may not be enough.

Mr. MACKASEY: I have one last question, Mr. Chairman. Dr. Morrell has indicated a preference for the licensing of all manufacturers. It is one which —I might as well be honest—I approve of because it is safety in which I am interested. Could you give me your viewpoint on what you think the advantages would be to the Canadian public of a system of licensing, if we can get over the federal-provincial problems and demand that any manufacturer be licensed before he starts?

The CHAIRMAN: This question has been gone into fairly intensely, and we did have Mr. Hume, the lawyer, talking about this.

I wish to say that I understand the gentlemen who are before us are available this afternoon if the committee wishes to go on with further questioning.

Mr. MITCHELL: I would so move, and I would suggest four o'clock this afternoon.

The CHAIRMAN: I would say two o'clock would be preferable, if it is possible for the members of your group, Mr. Conder, to come back and finish answering questions of the members. Can all members be here so that we will have a quorum?

Mr. MACKASEY: This could be quite informal.

The CAIRMAN: Would two o'clock this afternoon be suitable? It is agreed.

Mr. SLOGAN: I am very interested in what goes on with labels on drugs. I feel that a lot of the labels are not very helpful to the general practitioner. Since your association is analogous to a professional association—you say you have your ethical standards in various things of which we certainly approve—I was going over the list of your members and I know I patronize a number of them, although some of them are not known to me. Do you think if your members would put on their labels that they are members of this association that this would be of assistance to the general practitioner when choosing a drug?

Mr. CONDER: It very well could be. This would be a point which we would have to examine in detail. There has been considerable talk about what should go on a label of a pharmaceutical preparation. We must realize some of these labels are quite small in size and that we are limited by space.

Mr. SLOGAN: The initials at the bottom would be sufficient.

My other question is as follows: as you know I have been suggesting that in order to be of assistance to practitioners and pharmacists on the local level there should be a body set up in which specifications for certain products would be set up and numbered, and that on the label of these drugs it be put that it meets certain specifications which would be set up by this body. What is your opinion of that suggestion?

Mr. CONDER: I think it has merit, sir. You would have to examine the legal implications of a body guaranteeing in effect medication that is distributed by companies over which it may have no direct control.

Mr. SLOGAN: But it would have to have a certain amount of control. The prerequisite would have to be licensing, and also some sort of check on quality control. There could not be an absolute guarantee—this is impossible—but I think the medical and other professions would be satisfied with the knowledge that at least a certain basic qualification was met by the drug, which we do not have at the present time.

Mr. CONDER: You have it primarily through the reputation of the manufacturer himself, and that is about as far as it can go in that area. An organization such as this would have to first of all examine the company, examine its products and say that this company does meet certain standards which were laid down for it. This is fine; if the company is manufacturing here and you have control over the company, it can be done. But what happens in the case of an agent who, for example, might go to a hospital and get a tender and then go out and find out from which foreign country he can buy the medication. This often happens. Sometimes people calling or answering tenders feel that they can get it from one of three or four different companies in Europe. They will put in a tender on a specific product and then shop around for the best price they can get from their sources.

Mr. SLOGAN: What do you think of the suggestion of the pharmaceutical association that the name of the original producer be put on the label, such as the producer of the most basic ingredient or of the most active ingredient?

Mr. CONDER: There are pros and cons. I would venture to say it would not affect materially the members of our association.

Dr. GRIEVE: There is another aspect. I am not quite sure of your point but let me please make this one. If you recall Dr. Morrell's testimony, he pointed out that under the Food and Drugs Act there is a schedule which lists seven different reference works, pharmacopoeias as formularies. These are thereby declared to be official pharmacopoeias in this country. He named them from the Canadian formulary the British, and United States pharmacopoeias and the rest. These reference works set the standards for very many drugs—the most important drugs that are on the market in this country and in other countries where these compendia, as we call them, are official.

The Food and Drugs Act and the regulations made under it require that if one labels a drug with a name that is official in one of these compendia, one is automatically deemed to be claiming that the drug conforms to the specifications of strength, quality, purity and safety that are called for in these respective pharmacopoeia. Therefore, the mere use on one's label of the official name for the drug automatically defines what the drug might be.

Mr. SLOGAN: The specification angle for it exists at the time except at the quality control manufacturing?

Dr. GRIEVE: There is now more than there was. There was recently added to the regulations under the Food and Drugs Act a section which I choose to call, though I do not think it is labelled thus, the good manufacturing practice section. It sets out to define, in so far as one can define, what are deemed to be good manufacturing and quality control practices; and it includes requirements of cleanliness, physical facilities, competence training and experience of staff. These are all then subject to inspection by inspectors of the food and drug directorate when they visit a pharmaceutical plant.

I might add something Mr. Chairman, in that connection which perhaps in part applies to a question of Mr. Mackasey a while earlier when he asked whether our association was participating with the food and drug directorate in raising standards and achieving higher aims along these lines. This so-called good manufacturing section is just one example of many in which the representatives of this association have participated through working parties with Dr. Morrell and his staff, working through successive drafts of such regulations as this to try to devise regulations which are meaningful and which would achieve these desired purposes and be workable, and so we felt that we each knew what th other was trying to express.

The CHAIRMAN: Gentlemen, Dr. Nash also wishes to make a statement on this. I suggest we adjourn the meeting now and come back at two o'clock this afternoon when Dr. Nash can make his statement. I think Mr. Francis also has some questions.

AFTERNOON SESSION

FRIDAY, June 19, 1964

The CHAIRMAN: Gentlemen, we now have a quorum. Let us start at the point where we left off this morning. Doctor Nash had a few comments to make on the questions brought up by Mr. Slogan and Mr. Mackasey.

Dr. P. H. NASH (*Assistant Director of Scientific Division, and Medical Director, Abbot Laboratories Limited, Montreal*): There have been various suggestions made to the committee that some type of group such as a testing agency should be set up to examine and test all drugs with the idea of comparing them against a set of standards, and to say this one agrees with the standards, and therefore some kind of stamp, seal or something should be put on the label to show that this drug is all right. I say that such a system would be extraordinarily difficult to put into practice because while a drug may have passed the requisite quality test at one time, it might not always have such a quality.

For instance, a manufacturer who lacked adequate facilities for quality control, could readily employ such facilities from outside and submit a batch for testing which proved to be excellent in all respects. But how could it be assured that in the following month, the following year, or in several years time this drug with the seal on the label would still be of this acceptable quality? I would think that such a task would be almost impossible when one considers the thousands and thousands of inspections and tests which would be ncessary.

I think a more basic way to insure this would be through registration, certification, or licensing of manufacturers, because once that is done, and once the food and drug directorate know who all the manufacturers are in this country—at the present time they have no means of knowing this—but once they do know this, then through their spot checks, if a manufacturer persistently produces a drug of inferior quality, or one which does not measure up to the required standards, then of course some process may presumbaly be brought to bear to remedy such a situation.

The CHAIRMAN: Dr. Marcoux:

Mr. MARCOUX: Without any inference on the cost of drugs, is it possible for a company which furnishes materials to supply one company, and this company in turn to supply another smaller distributor, and this one in turn to sell the product on the market? Would it not be that the security side of such an action might be maintained if the small company knows that the bigger company is buying its raw materials from another even bigger company which is a rival? Are you getting my question?

Mr. SLOGAN: I think the point is that it is common practice in all fields, even in the manufacturing, that the same product may be sold under different labels, although it is the identical product, and that it could be sold at different prices. This may be getting away from the subject, but it has to do with the factor of safety. They would want to have a bit of protection, but how is the individual pharmacist, or how is the individual doctor to know? How can he be put in a position to identify a product as coming originally from a reliable producer?

Mr. MARCOUX: Let us take for example meprobamate which is produced by very few companies, yet it is distributed by many companies under different names. According to what I have heard the original product comes from only one or two companies.

Dr. NASH: Again I think that proper registration of companies should go a long way to solve such a problem, because if the original manufacturer who sells it to several others has adequate quality control, that is in respect of the ingredients, then the drug would be all right. And if it is going to be placed

in a formula, then of course the second company which places it in the formula also would have to be licensed, or whatever procedure is decided upon, and equally it will be subject to spot checking by the directorate.

Mr. SLOGAN: I think it all boils down to the fact that we need licensing and more inspection at the level where the product is used. There may be only this mark to show that there is quality control.

Mr. CONDER: That is all very fine in principle, but not in practice. To license a company cannot guarantee the quality of the product. Moreover, inspecors cannot guarantee that all products coming from a company are efficacious, or that they come out with sound quality behind them.

It was mentioned earlier this morning that Dr. Morrell had said there were 480 odd manufacturers in Canada. I would question that statement from our point of view, but not the point of view of Dr. Morrell. I have a feeling that in this particular case he must have been using the term manufacturer to include everyone, such as the distributor, the agent, and possibly someone who might make a compound in a room at the back of his shop. When we speak of manufacturers as such we speak of those who are actually engaged in the manufacture of a product starting with the raw materials.

The group may number 480, but it probably also includes some proprietary manufacturing companies who do not manufacture prescription drugs. It would also include—and I would imagine this would be the great majority—all those firms which fall into the category of what term in the industry, subdividers, those who buy a product in bulk and then package it and put it out in smaller sized packages.

Mr. MACKASEY: I was the one who mentioned this subject. I have looked at my notes since then and I see that Dr. Morrell did include manufacturers and distributors, but he did not have the figures for the different categories with the people involved who would possibly require inspection. The potential membership in your organization is not accurate. But nobody has challenged Dr. Slogan's suggestion that it is a well known fact or common knowledge for companies to produce the same material under different labels and at different prices. I think that is a rather sweeping statement. One has the feeling that it is probably quite prevalent in many fields. But perhaps some of you might care to review it.

Mr. CONDER: I am prepared to comment on it. I say that the statement is basically correct, but there are certain qualifications which must be added to it. Granted, there are many products which fall within the same general therapeutic classification on the market today. They might carry the same basic ingredients, but this does not necessarily mean that they are to be considered as equivalents and that they will perform precisely in the same way in the human body. Perhaps some of my professional colleagues with me would be able to comment on this aspect of it in more detail.

Mr. MACKASEY: I know the bells will be ringing soon, but perhaps I might add a little more strongly there is a feeling around the country that we can buy precisely the identical drug with different labels, coming from the same manufacturer, one bearing a brand name, and another without the brand name, but with a considerable difference in the cost.

Mr. CONDER: You say by the same manufacturer?

Mr. MACKASEY: That is the inference I got from Dr. Slogan.

Mr. CONDER: I would doubt it very much. I do not know of a company engaged in this type of practice. There may be one, but I do not know of it. If you are thinking of a stencil line product for durable goods, that is another matter; but it does not happen in our industry, because generally speaking our companies have only one thing to offer, and that is the product name of

the company, behind which stands the prestige of that company and the quality of its products. By using the same name, the company implies that the product will always be consistent, batch by batch, or bottle by bottle, if it goes out in a bottle.

Mr. MITCHELL: Would not patents have some bearing on the situation we are talking about? We know it to be common knowledge that certain manufacturers will, under a patent, sell their patented preparation to another distributor, and he in turn will put it out under his own label, yet it is controlled by the original manufacturer. I am not mentioning the price at all. I am mentioning the article.

Mr. CONDER: What can happen in that case, is that the original manufacturer licenses several other manufacturers to sell a specific drug, and this, of course, adds to the competition which exists in our industry.

Dr. J. M. PARKER (*Director of Research, Charles E. Frosst & Company*): I should just like to say in that regard this does not mean, even though they start out with the raw ingredients, that the finished products tablets, liquids, capsules or what ever they may be—will be identical in their behaviour on a patient, even though they may state the same thing on the labels, because there are differences in manufacture.

Mr. SLOGAN: I am referring to a product after it is manufactured.

Mr. CONDER: I see.

Mr. SLOGAN: To give you an analogy, you could buy an Electrohome stereo and an Eaton's stereo, and the working parts in the Eaton's stereo are made by the Electrohome Company. They are exactly identical except one has a Viking label and the other has an Electrohome label, and there is a difference in price.

Mr. CONDER: No. In our business this is not the general practice at all. I mentioned also the aspect of quality, integrity and reputation of the manufacturer. The point is that a company or manufacturer may be well known for its integrity, quality and reputation and it places a name on its product which will be accepted by the medical practitioner. The medical practitioner, in turn, will recognize the contents and the effect the product will have on his patient by the information contained through the name of the product. If the manufacturer changes that name and puts a different name on the product he will defeat that purpose.

Mr. CÔTÉ: You suggested earlier, and correct me if I am wrong, that a company could not guarantee its product, or would not give a guarantee in respect of a product; is that right?

Mr. CONDER: I said that a reputable manufacturer must in fact guarantee the contents of his product.

Mr. SLOGAN: Perhaps I could ask two or three questions in respect of another topic. When the Canadian Medical Association appeared before us each member of the committee was given a set of rules in respect of advertising which I think probably have been sent to the manufacturers. I think those rules were very well composed and no doubt the association follows them very closely.

I know of a specific situation which occurred in my office last week when I was visited by one of the representatives from, I suppose, one of the biggest and most reliable companies in this field. He was discussing a particular tetracycline class of antibiotic. This antibiotic has a specific effect in a pregnant woman on the enamel of the teeth of the child. I presume it would have the same effect if administered to a child. I happened to be aware of this fact but during his presentation to me he completely ignored this fact and it was only

Now, the responsible members in this industry, certainly the ones who are members of our association, make it a practice to send an exact copy, either through the detail men or through the mail or through both, to any physician who might conceivably be going to use that product. I think you will concede that if we had a product for use in dermatology, it would be ridiculous to send information on it to an obstetrician. This would be impossible because it would not be within economic bounds to provide every physician with all the details on every single drug, and it would be useless. However, to the extent that we feel a physician may use our products, we make available to him through one source or another complete information regarding indications, precautions, side effects, and so on, that are available. The detail man, in the limited time that he gets in many doctors' offices, cannot possibly get this whole message over. Most companies will tell you that it is part of their policy to try to leave a file card or a summary, such as I have described, with the doctors so that it will be available. They cannot possibly get all this information in a two-minute discussion.

The other point I would make is that it is the responsibility of a physician who plans to use a product for the first time to know what he is using. It is always available to him, even if he has not received a summary, to find out from the company by writing to them and asking for such information. It is impossible to cross all the t's and dot all the i's, but the industry members recognize thir responsibility very clearly to get the physician as familiar as possible with the proper way to use their products. If we fail to do this, then in the long run we are the ones who suffer.

I think you would concede that we are not in business for today but that we are in business forever, and we must give the physicians the information that would provide for the proper use of our products.

Mr. SLOGAN: I think maybe my point was lost sight of. I agree you do provide good service and you do provide all this information. What I am saying is it is only natural—that the detail man—I have met quite a few of them—should place less emphasis perhaps on the side effects and on the toxicity of these drugs. It seems to me these factors are glossed over by them, and it seems to me that in their case it is not just a matter of forgetting but it is quite deliberate and natural for them to emphasize all the positive aspects and gloss over the negative aspects of a drug. There should be a little more emphasis placed on the safety of the drugs which they are promoting.

Mr. CÔTÉ (*Longueuil*): Is it not possible that the reaction to some of the drugs are not known? We had never heard before about reactions to antibiotics but now we hear a lot about it. Many people have all sorts of reactions to them. The reactions to the first antibiotics such as penicillin were not known by the company which put it on the market and they only became known later. Is that not right?

Dr. MACDONALD: This is certainly true. At the time you introduce a product you do not know everything about it. One of the other points that was made in our brief was that we recognize the importance of continuing evaluation of the product even after it is on the market. We are just as anxious to find new things about it and to try in whatever way we can to make sure that the medical profession are aware of these side effects.

You made the point, I think sir, that you felt that at times the emphasis was not put in the proper place, that in certain situations the side effects should be emphasized in detail. I would agree with you on this, and I am sure any responsible company would also agree with you that in certain instances, with reference to certain products where the side effects are apt to be a permanent part of their use, they should be emphasized, and I think in actual practice where a serious side effect may accompany the use of one of our

drugs, the detail man as well as those who prepare promotional material, make an effort to be sure that this particular side effect is well understood. Certainly we would do this, and I think many companies would also do so. I have in mind a particular statement of directions or summary which we put out some years ago in which the first paragraph in the summary was a statement of precautions. This is not a normal procedure, as you can well imagine. When you have something that you hope to put into use, you would tend to state its uses and advantages, but the circumstances were such that we agree this was good policy. I am not just speaking for our company; I am sure every one of the member companies of this association would take similar action.

Dr. C. WALTER MURPHY (*Medical Adviser, CIBA Company*): When unexpected side effects are discovered one of two things will happen, and that is that the physician will receive a detailed memo on the drug, and if the side effect is of sufficient seriousness, then a letter will be set to all physicians in Canada. This is quite common. We have had several instances of this in the last three years.

Dr. NASH: Mr. Chairman, I will explain how the side effects are made known to the medical profession. Under the new food and drug regulations we must inform the directorate of all the side effects which come to our attention and which are of an unexpected nature. It is something hitherto unknown. Naturally, when we have a number of these, we decide that we must incorporate these in our literature and we therefore inform the food and drug directorate and say that we think those doctors must now be cautioned about this. They agree, and the literature is changed. If it is something unusually serious, we may well suggest that we also send an informational letter or drug warning letter to every doctor in the country, or the food and drug directorate may suggest this to us. But however it is done, these things are finally printed and it does not take very long, in the new revised company literature.

I am sure that if you had asked this detail man for his file card or brochure, whatever it is, you would have found this side effect in there. The fact that he did not tell you about it at that time was certainly an omission. It should have been mentioned particularly considering your profession. We do go to considerable trouble to train these detail men. In fact they are trained by these gentlemen you see here. We always emphasize that they must warn doctors about these side effects. Generally, I think this is done, but obviously there are occasions when there is no time, or for some other reason it is not done on that occasion.

Dr. MACDONALD: Could I make one other comment relative to the statement you made about C.M.A. advertising policy which you reviewed with the C.M.A. people? It should be known that at the time that policy was created, three members of the medical section of this association and three members of the marketing section of our association sat down with the board of the C.M.A. and helped to formulate this exact policy, and we endorsed the principle behind it 100 per cent.

The CHAIRMAN: Any other questions, gentlemen? Now, if I may, I would like to put a question to Dr. Parker. I was interested in a question I was going to put and I did not ask it when we were at the plant.

One of the best ways to tell me whether a drug would or would not be dangerous would be whether or not they have any trouble in manufacture of it in their plant. In industry do you have much trouble with the personnel who actually are manufacturing drugs? Perhaps you could say a word on the handling or usage of them and what check you keep on it.

Dr. PARKER: I think Mr. Shannon also would like to comment on this.

You will recall this morning that we mentioned the value of good housekeeping in any kind of manufacturing procedure. In addition to that a periodic examination of people is important. We keep a check on those who are working in a dusty atmosphere and, therefore, might inhale large quantities of fumes, caused through the manufacturing of these drugs through faulty ventilation and so on. And, even the small masks which are worn over the nose are checked. I could give an example of something which occurred in our company. We were considering certain substances for coatings and, of course, it came to the point where we had to make a choice between two substances. One of these substances could be dissolved and used in an aqueous or oil solution while the other had to be used in a solution dissolved in carbon tetrachloride, even though there was none of this substance left in the finished tablet. But, during the process of coating it would be used. So, we decided in favour of the other substance.

I think everyone continually should review their processes with this type of thing in mind and we should ensure that our people who are working in the plants are not placed in hazardous situations.

The CHAIRMAN: You have had no trouble with diseases of one kind or another over the years?

Dr. PARKER: In the industry there have been cases of feminization of men working with female sex hormones in the making up of tablets and so on.

Mr. MITCHELL: Would some dermatitis creep into that?

Mr. SHANNON: We have had cases of that come up in respect of people working with the company and either through the company or their own doctor we found out what item it was which was affecting them and we took them off that work. Also, in the making of nitroglycerine tablets we found that we had to use the tall girls to do that work because even with a hood, the fumes would come out and after working a couple of hours they would get a bad headache. We usually rotated the girls. We tried to rotate them every hour so that they do not acquire bad effects.

Mr. MACKASEY: After working in the House of Commons for a couple of hours we have headaches too. And, we are against the rotating system.

Mr. CÔTÉ (*Longueuil*): Might there not be certain sicknesses develop in your plant, not because of the fact the employees are working with the drugs themselves but because of the way they work. I noticed when we visited the plant that a number were working on the filling of bottles and they were engaged in the same operation all day long. I do not know how they can stand it without having a nervous breakdown or developing some type of mental illness. Cannot something be done for these people?

Mr. SHANNON: In most companies girls who are employed in the finishing of the product are rotated from one place to another. They may be capping bottles for an hour and then may be put on the counter for the next hour, after which they may be putting the product in cartons. To my knowledge, they do not work continually eight hours a day on the one spot.

Mr. CÔTÉ (*Longueuil*): I noted one girl in one company always worked at the same thing. You could see that she had been kept in this particular type of job because of the different muscles she possessed from other girls.

Mr. MACKASEY: It could be that she was interested in this type of work and that she wanted to stay with it because it was a matter of pride with her.

Mr. CÔTÉ (*Longueuil*): Well, she had much different muscles from other women. I have never seen anything like it.

The CHAIRMAN: Perhaps this is a rather unusual occupational hazard.

Are there any further questions?

Mr. MACKASEY: My question, Mr. Chairman, does not relate to safety. However, I would like to hear a capsule comment on the pros and cons of patents. I understood from some of the witnesses before us that possibly the drug companies would be even more eager to do some of the badly needed research in Canada if they could get some type of protection on their end results. We have heard the other side of the story, that this encourages abnormal pricing. Before I make up my own mind in this connection I would like to hear a frank prejudiced opinion from you people, if necessary, because I am sure it will be helpful in making up our minds.

Dr. PARKER: In reading through the transcript I noticed that a statement was made that insulin was not patented, and Dr. McColl has documentary evidence on this. But, insulin was patented and one of the benefits of this was that the university of Toronto derived royalties.

The insulin committee during the war kept the widow of Dr. Minkowski, who had diabetes and who was the first one to receive the treatment. They kept her alive all during the war and she was saved from the concentration camp.

Mr. CONDER: I gather from that statement in question that this is an example of how a product was brought out by a nonprofit enterprise and made available without patent. But, as Dr. Parker said, it was patented. It was also a fact that a large percentage of the money that resulted in the production of that drug was supplied by a manufacturing company.

I might say also that insulin is not unique in that respect. There is a research scientist by the name of Dr. Waksman, who discovered streptomycin. Two or three months ago he made a statement in the United States to the effect that streptomycin was produced by the Merk company. He discovered streptomycin while working on a grant from the drug industry. Dr. Waksman stated if Merk had kept streptomycin to itself, the company would have made a fortune out of the drug. I understand that Merk made streptomycin available generally to anyone who wanted to produce it. So, you see, it does happen in other areas.

Mr. MACKASEY: Are you advocating that this be a policy?

Mr. CONDER: It would be impossible to adopt a policy in that respect because a company must make money not only to ensure further investment from the shareholders but also to ensure that there is enough money on hand for future development and to pay research expenses as well. But, you have asked for a very brief statement on the subject of patents and I would ask our counsel, Mr. Hume, to give you a very brief statement on that situation as it exists in Canada today.

The CHAIRMAN: May I break in here? This is getting a little off the subject of safety. We are breaking into the question of costs. If the committee wishes to do this, I have no objection, but Mr. Hume may not be prepared because he was not asked to come here to discuss patents today. This body will undoubtedly be invited back to discuss costs and patents if they so wish, but the gentlemen here may not be prepared to discuss it now. The CPMA at a later date may decide they have a different set of experts to be heard on this topic.

Mr. SLOGAN: My understanding is that it is unethical for any medical, dental or other person of a professional nature who develops a drug to patent it himself. Have you any examples of professional men who have developed an invention on their own, outside of institutions? Insulin, for example, was developed at the University of Toronto and I imagine it was the University of Toronto which patented it, not the inventor.

Dr. GAUDRY: I am a member of the national research council and in that council there is a company called the Canadian Patent and Development Company which takes patents on behalf of investigators throughout Canada

who cannot afford to take patents themselves. I have to say that taking patents can be a very costly business, and most of the private investigators just do not care to spend the money, even if they have it, because the chances that a valuable commercial product might come out of their investigations are not great. A company such as Canadian Patent Development Company takes patents for them and will get royalties if the product becomes of commercial value.

Mr. SLOGAN: Is this from private individuals or just people in government?

Dr. GAUDRY: Private individuals working in all the universities and practically anywhere in Canada, but mostly university people. In fact, two days ago I was told that most of the patents filed on potential new drugs by private individuals as so-called discoveries are from university people. I do not know a single university in Canada that has a clearcut patent policy in that they would decide to take patents and pay for the cost of filing. They are only too pleased to let the investigator go to a crown company such as this company which takes patents, and foots the bill at least to some extent. Then the royalties are split between the universities and the investigators and the crown company if there are any profits. Of course, this crown company has been in existence for about 20 years, I think since just after the war. They have only one or two patents that are bringing in money. The company was in the red for many years and it is now beginning to make money, much money, but through only one out of many many patents they have obtained.

Mr. SLOGAN: But it was probably set up originally to patent government discoveries?

Dr. GAUDRY: Partly that and partly discoveries coming from other research departments and discoveries made by university professors working under grants from the government, from the National Research Council.

Mr. SLOGAN: It would deal with discoveries which were made by people working under National Research Council grants, but apart from those—

Dr. GAUDRY: They go further than that too now.

Mr. SLOGAN: If John Doe on the street invents something, could he go to that company and have the patent taken out?

Dr. GAUDRY: Yes.

Mr. MITCHELL: What is the life of a pharmaceutical patent?

Mr. HUME: The same as any other.

Mr. MITCHELL: There has been a suggestion, Mr. Chairman, that the period be cut down as far as pharmaceutical products are concerned.

Mr. HUME: A comment was made earlier about patents and we were asked for a five minute resume on the subject. I am not prepared to deal with that because I did not realize that this would be even part of your considerations, but I would like to say that the whole question of patents has received some careful study from the Ilsley Commission, and the subject is being considered now, I know, as a result of recommendations made by the restrictive practices commission. I respectfully suggest for the information of the committee, through you, Mr. Chairman, that it is not a subject that can be discussed in five minutes. I think this industry, like others, is in favour of patents; but as far as the industry's point of view is concerned—while I think this association would be very glad to prepare something on it if you want it—I would hate to try to sum up the views of the industry in five minutes or a little longer without preparation.

The CHAIRMAN: I think it would be fair to say that this committee would be very interested in that and we would welcome such a brief but, at this time, we are not really considering the question of cost. Until such time as we are considering that subject we would not be prepared to go into patents, but we

would undoubtedly invite your organization back at the time when we are considering cost, at which time patents would be one of the points to discuss.

Mr. CONDER: We would be very pleased to come back at that time.

Dr. J. D. McCOLL (*Assistant Director of Research, Frank W. Horner Limited*): Despite your observations about subsequent debate on this subject, in connection with the comments made by Dr. Parker about insulin, I recall reading something of the discoveries of insulin and, being a Toronto graduate I should be up on this. I recall at the time Dr. Von Mering had decided not to file a patent—and perhaps for the reason that Dr. Slogan mentioned, that it was unethical—but he was advised legally at the time to file a patent which was duly done "for the sole purpose of preventing any other person from taking out a similar patent which might restrict the preparation of such extract". I take that quotation from a paper on the "Influence of Patents on Development and Distribution of Insulin". The rights were turned over to the governors of the university.

I would like to submit to the committee two articles which I have obtained from the University of Toronto, the one I have just mentioned, which is written by A. M. Fisher of the insulin committee of the University of Toronto, which appeared in May of 1963, the other entitled "Insulin: its action: its therapeutic value in diabetes, and its manufacture", also issued by the insulin committee of the University of Toronto. If these are of any help to your committee, Mr. Chairman, I would be happy to leave them with you.

Mr. SLOGAN: If they are not too long perhaps they could be added as appendices.

Dr. McCOLL: All the details may not be pertinent. The history of insulin is given and the development of the entire situation is outlined, but just to point up patents in this particular area I thought it might be of interest to your group.

The CHAIRMAN: The articles Dr. McColl has handed to me are "Insulin: its action: its therapeutic value in diabetes, and its manufacture", printed in July, 1923. The other is "Influence of Patents on Development and Distribution of Insulin", May, 1963.

What is the feeling of the committee with regard to these? Would you like these to be appended and held until we discuss costs and patents?

Agreed.

Mr. MACKASEY: I would not like to see our report held up for the appendix.

Mr. FRANCIS: They could be tabled perhaps.

Dr. McCOLL: Perhaps you would care to read into the record one particular point from the summary of Dr. Fisher's article on the effects of patents. In his summary he says:

> In the case of insulin, Canadian patents, whether owned in Canada or abroad, have had a favourable effect upon research and the distribution of insulin in Canada.

I think this may perhaps be most pertinent to your deliberations.

Mr. SLOGAN: The best way to solve this, without involving a lot of costs, may be to have the secretary photostat these articles for the benefit of the members of the committee. This might be of assistance at a future date.

The CHAIRMAN: I will have these photostated for every member of the committee and distributed to them.

While we are speaking about this I would like to ask for your guidance on the submission presented by this association. The brief, including the appendices, is approximately 100 pages. What is the feeling of the committee with regard to printing this? The summary of the brief, of course, is contained in the context of today's proceedings because it was read by Mr. Conder.

Mr. FRANCIS: I think the summary should be included in our minutes, as you indicated, and that the rest of the brief could go into our individual files.

Mr. SLOGAN: There is a great deal of interest in this question. I think it is a very comprehensive brief from the people concerned. It is double spaced. I think for the benefit of those across the country who are not on the committee this would mean a great deal, and we should include it.

The CHAIRMAN: The problem I foresaw was one of printing.

Mr. MACKASEY: Possibly we could review the record and determine the people who are interested and who wrote in, and send them a copy.

Mr. SLOGAN: Perhaps they should write directly to the Canadian Pharmaceutical Manufacturers Association.

The CHAIRMAN: At 90 Sparks Street. What is the general feeling? Should it be included as an appendix, or should we include merely the summary?

Mr. ARMSTRONG: I suggest we include only the summary.

Mr. HUME: This is a summary of the work of some very learned people whose qualifications appear at the chapter headings. If your proceedings are as widespread as I assume they are, and because of the widespread interest in this problem in Canada, I think there might be a great number of people who would be interested in reading this brief.

Mr. CÔTÉ (*Longueuil*): In that case it should be added as an appendix.

The CHAIRMAN: It was not the economic considerations that I was thinking of but rather that the reports take such a long time to prepare.

Mr. HUME: I thought you were asking for our opinion on whether it should be included in your proceedings. There are people across the country who would read it subsequently with great interest.

Mr. SLOGAN: There are a lot of sections in it we have not even touched on.

The CHAIRMAN: Would someone care to move that it be included in today's minutes?

Mr. SLOGAN: I so move.

The CHAIRMAN: All in favour? Those contrary minded?

Motion agreed to.

I declare the motion carried. I am sorry, gentlemen, that we were temporarily interrupted by these questions of procedure. Are there any further questions, gentlemen?

Mr. MACKASEY: I am timid about bringing up another question, but I would like to get to the question of parnate, which has had a bit of a cloud hanging over it. However, following consultation between the pharmacists' association and the department, there were limited conditions put on its use, or rather certain conditions placed upon its usage. After looking at the thalidomide question, perhaps it was a very wise decision. Perhaps my question should have been directed to Dr. Morrell as to whether he has the facilities for bringing the matter of this particular question of parnate to a satisfactory conclusion, and whether the cloud should be removed from it and that it go back to the original use for which it was intended. I do not think it is fair to anybody that the drug should be mentioned by name. I wonder if the pharmaceutical association could give us the type of drugs in which it falls, and in which this type of question would inevitably fall. Do they feel that the directorate has acted fairly in this matter? Is the time element too great, or do you feel that the department is overtaxed and must necessarily shelve investigation of such drugs as parnate, and hold up their usage?

Mr. SLOGAN: Have we anybody here representing the manufacturer?

Mr. MACKASEY: Is it not a question to be decided between the manufacturer and the directorate?

Mr. CONDER: I do know that the manufacturer concerned is working with the food and drug directorate on this particular problem. I myself am not qualified to give a specific answer with respect to parnate.

Dr. PARKER: I think the ad hoc committee appointed a year ago to serve with the food and drug directorate has worked very well. It is true they have taken a long time to bring down a decision, but perhaps since this is the first time such a committee has been formed to act, it might well be considered to be reasonable, because they certainly want to make the right decision and give the best advice they can to the food and drug directorate.

Dr. MACDONALD: I think that the terms of reference of the ad hoc committee should not specify the product, but rather should refer to the classes of drugs, of which there are a number. I think the terms of reference should review the purpose of this group of drugs and make recommendations about them as a group. This would explain why they have taken longer than might normally be the case.

The CHAIRMAN: The chairman of the ad hoc committee has also appeared before this committee. I refer to Dr. Wightman from the University of Toronto who was here on behalf of the Canadian Medical Association. I asked him if he would care to come back as an individual to testify, and he said that he would be delighted to do so in his position as chairman of the committee as well as professor of medicine at the university.

Are there any other questions? If not I would like to thank the Canadian Pharmaceutical Manufacturers' Association and their associated members for sending us their experts today. We have taken up a good part of their valuable time, and at considerable expense to them to come here before this committee. I think their brief is an excellent one. It has been very well prepared. I read it yesterday, and I found that it brought out many points that I did not realize. But also its preparation was very time-consuming. I know that they have spent a great deal of time over it. I would like to thank your association and through you the companies involved who have taken part in this effort. Thank you.

The meeting is now adjourned until Tuesday next at 9.30 a.m. when we will have before us the Canadian Association of Consumers.

APPENDIX "A"

SUBMISSION

to the

SPECIAL COMMITTEE ON FOOD AND DRUGS
House of Commons
Ottawa

concerning

DRUG SAFETY IN RESEARCH AND MANUFACTURING

by the

CANADIAN PHARMACEUTICAL
MANUFACTURERS ASSOCIATION

* * *

Ottawa, Canada
June 19, 1964

21029—3½

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The Special Committee on Food and Drugs,
House of Commons,
Ottawa, Canada.

Mr. Chairman and Members:

This submission is respectfully presented to your Committee by the Canadian Pharmaceutical Manufacturers Association, an association of manufacturing companies founded in 1914 and incorporated under the Dominion Companies' Act in 1959.

The Association represents 55 companies engaged in manufacturing and distributing ethical pharmaceutical preparations in Canada. The term "ethical" refers to pharmaceuticals dispensed on doctors' prescription and those not advertised to the public, as different from proprietary or patent medicines which are advertised to the public.

As might be expected, some of our companies also make proprietary medicines to varying degrees, but our Association does not represent this field of medication.

This submission deals exclusively with drug safety as applied to pharmaceutical manufacturing, research and control at the industry level. It comprises a series of papers on these subjects by expert medical, scientific and technical personnel employed by the Association's member companies. These expert witnesses are prepared to answer and discuss any questions you may have concerning their papers and respective fields of endeavour.

It is our hope that the contents of this submission will be of some assistance to your Committee in its deliberations concerning drug safety in Canada.

Respectfully submitted,

Stanley Nesbitt Conder,
General Manager.

Ottawa, Ontario.
June 19, 1964

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PREAMBLE

Consideration of drug safety carries with it a twofold responsibility. The first is to ensure that a medical substance is not released for general use until it has been proved to be safe for human consumption. The second responsibility is to ensure that a substance valuable to the medical armamentarium is not withheld from use.

It is here that scientific evidence and medical experience must be the determining factors. Rarely does a potent therapeutic substance lack toxic or side effects. For this reason, it is the degree of value of the substance and the degree of toxicity which must be considered.

An improved form of acetylsalicylic acid which produces convulsions as a side effect, obviously would not be marketed regardless of the improvement. However, a new and effective treatment for carcinoma, even with serious side effects, might be made available to the medical profession. The decision in this case would be based on whether the value of the preparation in medical use is more important than the toxic effects produced. Here the one must be weighed against the other, and the consideration must be purely a medical one.

One example of this was the drug thalidomide. Following synthesis, the drug was tested extensively in animals and then in humans. It was found to be highly efficacious as a sedative-hypnotic and a most useful substitute for the barbiturates. The animal experiments and clinical testing further indicated that thalidomide had an extremely low toxicity. Thus it had a value in medical use.

The drug's subsequent and unexpected teratogenic activity resulted in its withdrawal from the market. From the scientific standpoint, however, the untoward experience with thalidomide created for the first time a greater awareness of the need to study new drugs in respect to teratogenicity. Prior to this time, experimental teratologists had known for some years that antimetabolites and steroids could induce congenital malformations in mammals. But the science of mammalian teratology was then young and the number of scientists working in the field limited.

For one thing, reactions to a teratogen may vary from mammal to mammal. A drug producing one effect in rats may not produce the same effect in mice. This implies, therefore, that animal experiments are not necessarily applicable to human conditions, and helps to explain why drug effects on animal embryos cannot be transferred uncritically to man. Even within a species, a drug may have different teratogenic effects upon the embryos of different strains.[1]

Briefly, this was the situation at the time of the thalidomide incident. It may be said that this medical tragedy occurred primarily because at that time scientific evidence and knowledge concerning drug induced congenital malformations was minimal. No test method on animals then known could have revealed its teratogenic effect on a small percentage of women in a certain period of pregnancy.[2]

It might be added that while thalidomide was subsequently withdrawn from the market, it may still be used experimentally in animals in approved institutions. The reason for this is that thalidomide has such a strong influence on life processes that the substance may evenutally produce a boon for medical science, such as in the area of carcinoma.[3]

As a result of the need for greater understanding of teratogenicity in relation to drugs, the leading research houses throughout the world have embarked on extensive investigations into this area of scientific endeavour. Similar research is being done in our universities, and medico-scientific conferences have been held for much the same purpose.

Through this work, much more is now known about this problem than was available prior to 1961. However, we have by no means found the complete

answer and it may be several years before this is forthcoming. Consequently, as a direct result of its untoward effect, thalidomide produced three effects.

Firstly, it created the awareness which is leading us towards overcoming still another scientific barrier to medical progress. Secondly, it has highlighted from the medical standpoint the precaution that, in prescribing drugs for pregnant women, the potential benefit of the substances must be weighed against the possibility of any untoward effects they may induce.[4]

The third post-thalidomide result is the rash of similar complaints which have been applied against other forms of medication. In a few cases, these have been warranted; in the majority, they have not. The classic case, of course, involved the concern that penicillin among other antibiotics caused death in certain patients. It had been recognized long before the advent of thalidomide that penicillin could produce severe toxic effects in those having a sensitivity to the drug. This was well understood in medical practice. Yet the statement, coming as it did after the thalidomide incident, aroused unwarranted concern at the lay level.

To a large extent, this concern in the public mind about adverse effects of the more potent substances is in one sense a tribute to the development of modern drugs. The problem rarely arose years ago because many therapeutic substances then available had little pharmacodynamic effect. The past two decades have ushered in a revolutionary era in medication where potency, the essential ingredient in effective medicine, has become the keynote.

It is recognized that every drug which carries with it a biological value must in some way have an effect on the body. Living organisms can be damaged to an extent, even though this extent may be transitory. Consequently, it is impractical to expect a chemotherapeutic substance to be completely effective and yet be completely without side effect.

In the words of George Brownlee, Professor of Pharmacology, King's College, University of London: "The non-toxic drug . . . is a contradiction in terms. The anaesthetist daily uses a battery of potentially toxic drugs with safety. The permissible amount of damage to living tissue, not always reparable, is accepted as a calculated risk of greater need."[5]

We respectfully submit that the decision for this Committee is to determine whether adequate safeguards now exist to ensure that the community at large is protected against unwarranted side effects, but is not prevented from access to required medication. We further submit that such safeguards now exist in respect to new drugs.

Federal Bill C-3 established enabling legislation which permitted the Food and Drug Directorate to broaden controls over the introduction of new drugs and, at the same time, to prohibit the sale of certain drugs such as thalidomide. Following this, an extensive study of the requirements of the Food and Drug Regulations, and the then current procedures for dealing with new drugs, was undertaken by the Royal College of Physicians and Surgeons of Canada, at the request of the Federal Government.

As a result of the College's report, published in December, 1962, the Department of National Health and Welfare completely revised the Food and Drug Directorate's procedures and regulations concerning new drugs. This, in turn, resulted in the recently promulgated new drug regulations. We will not review the regulations here, as this information is now available to the Committee.

However, it may be said that the government has now instituted regulations concerning the safety of new drugs as required by the public interest. It has also established the legal machinery with which to withdraw from the market drugs which are shown to be unduly toxic. But in studying the adequacy of these precautions, care must be taken to ensure that drug research and development, and consequent new medical discoveries, are not hampered by an overbalance of restriction.

As you will see from the ensuing pages of this submission, the industry maintains sound standards in relation to research, manufacturing and control. The required balance between efficacy and toxicity is well considered from both the medical and scientific standpoints. In addition, the industry has taken a strong interest in the administration of safety measures through the leadership of our Association.

Our Medical Section, which comprises the medical directors of our companies, worked closely with the Royal College of Physicians and Surgeons during its investigation into the safety aspects of new drugs. Following this, our medical and technical people co-operated with the Food and Drug Directorate in developing the new drug regulations.

While the government has enacted legislation permitting the recall of drugs from the market, under Bill C-3, it was realized that administrative machinery was inadequate to meet emergency situations. To fill this gap, our Association is in the process of establishing a Recall Service. Object of this service is to provide a prompt and effective means of recalling pharmaceutical products which the Food and Drug Directorate in an emergency, wishes to have withdrawn from medical use. It will be administered by our Association through our member companies.

In another area, those in charge of clinical investigation for our companies recognized a need to improve the standards for evaluating new drugs. To initiate interest and research in this field, our Association established a Canadian Foundation for the Advancement of Therapeutics. Our companies contributed more than $61,000 to the support of the Foundation's work during its first year, and will continue contributions for at least five years.

The Foundation operates independently from our Association and member companies. It provides financial support for the training of clinical investigators in the methodology of drug investigation and research into the study of methodology itself, with the aim of improving and refining the methods of evaluating drugs.

In concluding this preamble, we wish to offer for your consideration the words of E. B. Chain, Ph.D., F.R.S., Professor of Biochemistry, Imperial College of Science and Technology, London, and Nobel Laureate in respect to the discovery and application of penicillin:

"Another, more serious accusation frequently made against the pharmaceutical industry, particularly since the thalidomide tragedy, is that the industry launches drugs too rapidly on the market without adequate toxicity controls. Whoever is familiar with the painstaking and elaborate system of pharmacological testing of new drugs practised in industrial laboratories of repute before it is released for clinical use, knows that there is no substance in this accusation.

"The thalidomide events were undoubtedly a tragedy, but the experts are in general agreement that no pharmaceutical test method on animals then known could have revealed its teratogenic effect on a small percentage of women in a certain period of pregnancy. Further progress in the sciences of toxicology and pharmacology will help us to devise tests to prevent the occurrence of similar incidents, but it is impossible to eliminate risks altogether with absolute certainty.

"As in all spheres of human activity there have undoubtedly been failings and abuses in the pharmaceutical industry. This is unavoidable, due to human nature. However, when one draws up the balance sheet of the positive achievements of the pharmaceutical industry and the negative aspects, there can be no doubt that the credit side overwhelmingly overbalances the debit side and the writer, for one, prefers to have an active pharmaceutical industry and life saving drugs, accepting in the bargain a few abuses, than to have a system in which theoretically no abuses are possible, but which produces no drugs."[6]

INTRODUCTION TO THE SUBMISSION

This submission deals exclusively with drug safety as applied to pharmaceutical manufacturing, research and control at the industry level. Its primary objective is to explain in detail the various stages through which a new discovery passes, from its birth in the basic research laboratory to its availability as an effective therapeutic substance.

Much has been said and written on the subject of drug safety in general. The important factor at this juncture from our standpoint is to determine whether the steps taken in the development of a drug at the industry level are based on the meticulous care and caution required by modern scientific medicine. This can only be determined by a careful review of all procedures involved.

These procedures come within three stages. The first stage includes what might be termed the determination of a substance's biological value to medicine. This is found through basic research, pharmacology, toxicology, and the study of metabolism.

The second stage covers the testing of the substance in humans to evaluate its therapeutic effect. This introduces clinical pharmacology and clinical investigation. These first two stages explain the scrientific and medical considerations involved in developing a new drug.

The third stage includes the study of the product's entry into manufacture, and the safety precautions required to ensure efficacy and quality. The elements here are pharmacy research, pharmaceutical manufacturing, and analytical development and end product control.

In total there are nine procedures involved in these three stages. To ensure that this information would be presented to your Committee in the most efficient yet comprehensive manner possible, we have asked nine prominent specialists representing each of these fields to prepare papers on their respective specialties.

Accordingly, this submission comprises a series of papers, presented in chronological order, on the procedures involved in the research, investigation and manufacturing of pharmaceuticals. They have been written by expert medical, scientific and technical personnel employed by our Association's member companies.

Following presentation of their papers, these expert witnesses will be prepared to answer and discuss any questions your Committee may have concerning their papers and respective fields of endeavour.

While the three stages in the development of a pharmaceutical are treated separately within this submission, it will be realized that there must necessarily be an overlapping and in all cases coordination of activity.

For instance, the clinical pharmacologist in stage two will have worked closely with the laboratory pharmacologist and toxicologist in stage one. Similarly, the pharmacy research department covered in stage three will have assisted the clinicians in stage two with the preparation of dosage forms for clinical trials. However, we believe that a clearer perspective of the work involved in industry will be provided by treaty these three stages separately.

STAGE 1: BASIC RESEARCH, METABOLISM, PHARMACOLOGY AND TOXICOLOGY

Basic research is the endeavour to discover through scientific study potential new medical substances, and to determine the course of critical investigation required to achieve the objective. In the pharmaceutical industry this is the beginning, the point from which all work evolves.

When the scientist has isolated his discovery and produces a substance which appears to have potential, it must then be referred to the pharmacologist for consideration. Pharmacology in this sense might be termed the scientific study of the action of therapeutic agents on living tissue in man or animal.

The object of this work is to determine whether the substance does in fact possess a biological activity. To evaluate this, the pharmacologist must necessarily have recourse to techniques used in the biological and physical sciences. His methods will include studies in vitro, which refers to isolated tissues, and in vivo, which refers to living animals.

At this stage, careful consideration must be given to whether the effect of the substance on man or animal would be hazardous or injurious. In short, will the substance have toxic or side effects so serious that it cannot or should not be used in man, regardless of the medical value of the substance. Thus, the science of toxicology enters the picture.

If the initial findings of the toxicologist are favourable, then experiments will be conducted to determine other information such as the quatitative aspects of toxicity in relation to dosage and duration of therapy, among others.

Basic research, pharmacology and toxicology are considered the vital stage in the birth of a pharmaceutical. It is here that the potential substance has the greatest chance of being abandoned. When we consider that only about one in from 3,000-5,000 substances tested becomes a new drug, and the great percentage of these are discarded within this stage of evolution, the value of this initial triumvirate to medical science becomes evident.

The following three papers cover this important area of development.

BASIC RESEARCH AND METABOLISM

by Roger Gaudry, D.Sc., F.R.S.C.

An organic and biological scientist and a recognized authority on amino-acids, Dr. Gaudry is Vice-President and Director of Research, Ayerst, McKenna & Harrison Ltd., Montreal. A Rhodes scholar, he received his D.Sc. from Laval University in 1940 where he remained on the faculty. He subsequently became Professor of Chemistry, Faculty of Medicine, Laval University in 1950. He has been guest lecturer at the Sorbonne, Paris, and was recipient of the Pariseau Medal, "Association Canadienne Française pour l'Avancement des Sciences". Dr. Gaudry is a Fellow of the Royal Society of Canada, and served as President of the Chemical Institute of Canada, 1955-56. He is a member of the National Research Advisory Council and of the Defence Research Board of Canada.

The purpose of this paper is to discuss the origin of new drugs and to summarize all the steps that are being taken by the modern pharmaceutical research laboratories to evaluate the biological activity of drugs and ensure their safety and determine their mode of action in animals before being submitted to clinical testing in man.

To set the problem in its proper focus, it is necessary to remember that modern drug research is of recent origin. In 1903, the oldest barbiturate (Véronal) was introduced as an hypnotic. It took nine more years for the second one (Luminal) to appear on the market. At about the same time (1909), the first anti-syphilitic drug (Arsphenamine) was discovered. Between that time and the discovery of the sulfonamides, around 1935, except for a gradual increasing number of barbiturates, almost the entire drug catalogue was made up of substances extracted from natural sources, and almost exclusively from plant material.

These plant extracts go back to the remote antiquity and the study of the effects of these drugs on man has been carried out very slowly but continuously, as medicine began to become a science. It is therefore only with the advent of substances made by the chemists in the laboratories that it became necessary to evolve methods for the pharmacological evaluation of new potential drugs.

The developments of modern chemistry suddenly made it possible and practical to prepare thousands and thousands of new substances which could possibly have great therapeutic value, but as is often the case, the development of methods of screening new compounds for activity and safety did not exist when the possibility of these new substances was first realized. Today's pharmaceutical research involves mainly either of two things:

(1) The extraction and purification of biologically active material from plant and animal sources, the determination of their structure, the precise estimation of their biological activity for uses which are suspected according to the nature and the source of the original material. The discovery and development of the alkaloid reserpine from the Indian plant Rauwolfia is a good example of this type of pharmaceutical research starting from naturally occurring material. Another very important naturally occurring drug obtained from animal source is insulin, discovered in Canada, and without which thousands of diabetic patients would not be alive today. I should also mention the vaccines which are drugs in their own rights and can only be prepared using living material.

(2) However, the main trend today is towards the partly or totally synthetic substances. In such fields as steroid hormones, the scientist still depends heavily on plant sterols which are extracted from certain tropical species. These sterols are not immediately useful as drugs, but have to be submitted to many chemical transformations before they can be classified as drugs. Therefore, the naturally occurring material is not a drug in itself but is just used to prepare drugs by usually complex series of chemical transformations. Here again, the number of drugs derived from such sources is limited although very important because most of the modern anti-inflammatory drugs have to go through this complex procedure.

By far, the largest number of so-called modern drugs, meaning drugs discovered during the last 25 years, are synthetic drugs. Here I mean drugs made of new chemicals in large numbers in the laboratories by completely synthetic or chemical routes. Very often, these structures bear no resemblance to any known biological material. The activity of these drugs is usually at the beginning found by a so-called broad screening for activity.

Once a potentially useful biological activity has been discovered by the pharmacologist, the chemists go back to work to try to improve the properties of the compound by various chemical transformations or structural changes, in order to increase the activity on one hand and reduce the toxicity on the other.

The number of these new compounds made is very large. It runs into thousands each year. It is difficult to estimate precisely how many of these are made in drug research laboratories within one year, but I would venture to say that this number today, speaking for the whole world, exceeds one hundred thousand. The number of these which would actually become a drug is very small, and the often quoted figure is that not more than one in 3000-5000 would ever reach the market.

Describing the origin of new drugs, I mentioned the substances extracted from natural sources such as plant material. There is another natural source of new drugs which is very important in therapy. I am referring to the modern antibiotics which are usually extracted from fermentation media where certain micro-organisms have been growing.

At the beginning, these substances were used without any chemical transformation but only after an adequate degree of purification. One can name here penicillin as the best example. Here again, through modern drug research, attempts have been made to increase the value of these antibiotics by submitting them to various chemical modifications. For example, certain new

penicillins that are specially useful against staphylococcal infections are made from substances that are first produced by fermentation but which are then transformed further by purely chemical means so as to produce the desired end-product.

It remains to state that there is no simple, well defined road to follow but that modern drug research proceeds mainly through the difficult process of trying to discover new useful activities in therapy in the largest possible number of new chemicals that modern science can produce.

Metabolism

Once the precise biological activity of a new drug has been established, and when one is reasonably confident that the drug is safe for administration to human beings, it is very important to try to determine the fact of the drug in the body. In other words, it is important to try to find out for how long the drug remains active, to find out if it accumulates anywhere in the body, to find out how easily the drug is absorbed and how easily it is excreted or rejected. Some drugs circulate through and are excreted unchanged, but the majority of drugs are transformed and this is normally referred to as the metabolism or as the way the body transforms a drug so as to be able to inactivate it or get rid of it.

This study is usually very difficult. When a drug is excreted unchanged, it is often relatively easy to follow it because its very activity remains. Penicillin for instance, is excreted mostly unchanged, and its activity can be determined in the urine. When, however, a drug is chemically changed by the body, it is sometimes almost impossible to know exactly what happens to it. Fortunately, modern techniques such as the one using radioactive elements, now make it sometimes possible to follow a molecule or sometimes part of the molecule through many transformations.

While this study of the metabolism of drugs is not essential to prove the efficacy and safety of drugs, it is becoming increasingly important to the clinical investigator to know as precisely as possible what happens to the drug once it is absorbed, so that he can more precisely give to the patient the right dosages at the right time and in the right way. In other words, this knowledge increases very much the usefulness of the drug to the clinician.

One cannot emphasize too much the fact that metabolism studies done in man are also essential to confirm or disprove the results obtained in laboratory animals. The importance of clinical pharmacology is obvious because every one here realizes that man is different from other animals and that results obtained in any animal species do not necessarily apply to man. One can give an obvious example of this, in the new drugs designed to help mental patients. While it is possible to obtain fairly precise indications of activity with the help of a battery of animal tests, the true usefulness of a drug to mental patients can only be determined when testing it with these patients themselves.

Pharmaceutical research carried out by industry has produced a large number of outstanding advances in therapy and many drugs developed by industrial research laboratories have proved to be life-saving drugs. One could name among such successes: the sulfonamides as anti-bacterial agents, and the diuretics which permit control of heart edema and salt retention. The potent anti-inflammatory sterols of the corticoid type are among the most useful and the most necessary drugs affecting the metabolism of the whole organism. The phenothiazines have led the way to the discovery of the first really useful drugs for treating mental patients.

The most dramatic results of modern therapy have, without doubt, been obtained with antibiotics. While penicillin was not originally discovered in industrial research laboratories, its development and its successors are definitely the products of industrial pharmaceutical research and there is no doubt

that today the majority of the major advances in therapy are made possible because of the existence of modern industrial pharmaceutical research. This becomes quite obvious when one realizes the complexity of the work involved in putting a new drug on the market. This is so because of the many steps requiring the training of specialists in many fields. Such teams very rarely exist today outside the industrial laboratories.

PHARMACOLOGY

by John Duncan McColl, M.Sc., Ph.D.

A pharmacologist by profession, Dr. McColl is Assistant Director of Research, Frank W. Horner Ltd., Montreal. He graduated from the University of Western Ontario with an M.Sc. in biochemistry in 1950, and gained his Ph.D. in pharmacology from the University of Toronto in 1953. From 1950-51, he served as assistant research chemist at Parke, Davis & Company, and in 1953 joined Frank W. Horner Ltd. as a pharmacologist.

The science of pharmacology, in its broadest sense, is the study of the action of chemical agents, or drugs, on living tissue whether it be microorganisms, animal or man.

The ultimate aim of pharmacology is the development of new agents for the prevention, diagnosis or treatment of disease. As a science it is concerned with fundamental pharmacology or pharmacodynamics, the action of drugs, and with toxicology which is the study of dangerous or toxic doses and effects of drugs. From this it can be appreciated that pharmacology encompasses three large areas of scientific endeavour:

(1) action of drugs on animals (pharmacodynamics)
(2) action of toxic doses of drugs on animals (toxicology)
(3) action of drugs in man (clinical pharmacology)

I intend to confine my remarks to the first of these areas but would like to point out that all are interrelated and in practice overlap. In this way the division is arbitrary, as the information gained from one area may be of value in another.

During the 18th and 19th centuries the science of pharmacology became more than a description of the effect of crude drugs on animals. The isolation of pure drugs from natural products enabled the pharmacologist to use compounds of known physical properties and to define the action of a compound in terms of a mass of chemical per mass of living tissue.

This led inevitably to the quantitative science of pharmacology that we know today. One of the fundamental concepts of the pharmacologist is the quantitative relationship between drug dosage and biological effect. This is known as the dose response and implies that for each increase in dose there is a corresponding increase in effect, or vice versa.

Despite its long history as a qualitative or descriptive science, pharmacology as a quantitative discipline is relatively new. Trevan, a consultant for a pharmaceutical firm in the U.K., described the mathematical basis for these dose responses for therapeutic ratios. This statistical concept has enabled the laboratory and clinical pharmacologist to define precisely the action of a drug and to compare the effect of one agent with another or with a placebo.

It is of interest to note that much of the development of pharmacology was due to the increasing demands of the medical profession for drugs of standard and known activity. Indeed Sir Henry Dale, the distinguished British pharmacologist, who might be called the godfather of industrial pharmacology, was employed early in his career by a pharmaceutical concern to "do something about the assay of ergot."

The next important development of pharmacology was the use of synthetic organic chemistry which made available a host of new chemical compounds—barbiturate, antihistamine, local anesthetic, sulfonamide, anticonvulsant, and others, all with previously undefined biological properties. Faced with the endless creativity of the synthetic chemist, the industrial pharmacologist has devised a technique known as "screening procedures" to determine the presence or absence of useful biological activity of a chemical substance.

Because knowledge concerning the relationship between chemical structure and pharmacological activities is limited, as is the knowledge of the mode of action, the search for new and better drugs appears to have many illogical features. These appear in the procedure called "screening" or "blind testing". It does not preclude, however, that the procedures should not be as systematic and accurate as possible. Screening deals with what may be termed a qualitative question and answer. "Is an interesting activity present or absent." This question is different from "How much drug is required to produce a given effect" or "How active is the drug". A variety of test methods or "screens" may be employed and cover a wide range of pharmacological activity. The procedure only attempts to answer the problem whether a candidate drug does or does not possess certain biological activity and is not concerned with the relative effectiveness of the compound in relation to a standard agent. The discovery of diphenylhydantoin (Putnam and Merritt) for the treatment of epilepsy was the first success of what might be called the modern screening process.

If a candidate drug is observed on screening to possess activity, it is then subjected to a more definitive and quantitative study of its properties in different animal species, and may ultimately result in its being tested in man. The compound is compared quantitatively with the actions of another compound of the same general type. For example, an analgesic agent may be compared with morphine, or a hypotensive agent with a ganglionic blocker, an antidiabetic agent with insulin or tolbutamide. Such tests are designed to define the potency or activity of a new drug in relation to a known standard agent.

If the results indicate a possible advancement in therapy, further study of the compound as to its site and mode of action, its effect on metabolism and on different organ systems will be undertaken as the investigation of the drug proceeds. Such studies are designed to learn as much of the action of the drug as possible in order to predict its usefulness in the human species. Such predictability is not only concerned with primary pharmacological action of the drug but also with its secondary and toxic effects. A study of the absorption and metabolism of the new agent will also be undertaken.

It is worthwhile noting that a possible advance in therapy may be indicated by increase in potency, a decrease in toxicity or secondary effects, a different or more precise mode of action, or a combination of these.

It will be of value to describe at this stage some of the diverse methods employed to investigate a new drug. Pharmacology as a science borrows heavily from all biological, and indeed some of the physical, sciences. Physiology, biochemistry, experimental pathology, embryology, physics, mathematics and chemistry are all called upon for techniques by which the pharmacologist may investigate a new drug. The same techniques may be used in screening and in definitive studies. If a technique is not available from other sciences, an entirely new one may be devised. In general the methods include studies on isolated tissues (in vitro) and in living animals (in vivo).

A classic example of the isolated or in vitro method is the study of compounds on a strip of intestinal tract suspended in a nutrient bath. Various agents can produce contractions of the intestinal strip and these can be suitably recorded; other compounds can produce antagonism. Such a method is

used in the testing of antihistaminic agents. Histamine produces a contraction of a smooth muscle, and antihistamines, such as those employed in the treatment of allergic conditions, will antagonize this contraction. The relative potency of a given compound against histamine can be measured and defined on a mathematical basis. The effect of digitalis on the isolated heart can be measured by means of contraction of the heart muscle, or by the spread of the electrical impulse over the surface as recorded by the electrocardiograph.

The effect of a drug on the blood vessels may be readily determined by studying the effect of these compounds in an isolated hind limb or ear of animal. Small rings of tracheal muscle can be used to determine the effect of an antiasthmatic agent. Arteries, isolated from an animal body, may be used as is the intestine in a bath to evaluate a new agent for the treatment of disease. The isolated eye suspended in a nutrient bath may be used to determine the effect of a compound on the eye muscle. In general, a vast variety of isolated organs which boast some particular advantage in the description of a pharmacological property have been and may be employed.

With intact living anesthetized animals, the effect of a new drug on the entire cardiovascular system may be evaluated. It is by this means that agents which may be useful in the treatment of high blood pressure are tested. Or in an opposite way, agents which may be valuable in antagonizing shock characterized by a pronounced fall in blood pressure may be examined. Similarly the effect of a drug on respiration of an animal may be investigated. Through the use of the intact anesthetized animal, the action of drugs on the gastrointestinal tract may be measured, thereby permitting an evaluation of agents useful in the treatment of ulcers or other gastrointestinal diseases.

By using some of the new advanced methods of investigating the central nervous system, agents useful in treatment of mental disease may be evaluated. Such procedures include a recording of electrical activity of various portions of the central nervous system and study how this activity may be modified by chemical substances. In the intact animal the rate of excretion of various endocrine organs in response to the stimulus of a new compound may be directly measured. It is in the intact animal that the rate of absorption and excretion of a new drug and its metabolites are studied.

These studies are all undertaken in the normal animal. Many other procedures may be undertaken in the animal in which a pathological or diseased state has been produced by experimental means. A classic example is of course the description of the antidiabetic action of insulin in the diabetic dog as studied by Banting and Best. New antidiabetic agents are constantly being evaluated in animals in which diabetes has been experimentally produced.

Blood pressure lowering agents are further evaluated in animals made experimentally hypertensive. Methods exist by which experimental peptic ulcers may be produced in different animal species, and the curative value of new agents tested.

Compounds useful in treating endocrine disorders may be evaluated in animals made deficient by experimental means. The same approach has been used for the description of various nutritional factors such as vitamins and essential food components.

Lesions or damage may be produced in specific portions of the central nervous system producing many of the neurological symptomatology encountered in man (e.g. Parkinson's Disease), and permitting the experimental evaluation of new drugs for these conditions.

Various methods have been employed for the development of chemotherapeutic agents. Again such evaluations are done both in the living animal and in isolated organisms and tissues. Antibacterial and antiviral agents are studied by producing experimental infections in the living animal. Agents intended for the treatment of cancer may be studied in animals in which a tumor has been induced or grows spontaneously.

Similarly, antibacterial agents are studied by using cultures of pure microorganisms and determining the sensitivity of these agents on the bacteria. New antitumor agents may be studied in tissue cultures which permit the growth of a single cell type.

The successful transposition of results from the laboratory to the clinic presupposes that the characteristics that determine both action and elimination of the compounds in other animals and man are not significantly different. As in any branch of science there are shortcomings in the methods employed. A competent scientist recognizes these problems and evaluates his results in this light.

By themselves in vitro testing results are apt to be misleading as an indication of clinical utility or, for that matter, efficacy in the intact experimental animal. There are numerous examples that can be cited to demonstrate the unreliability of predicting results from in vitro experiments alone. This is not to minimize the value of such tests, but they should be viewed as an indication of the order or type of activity of a compound in a more or less rigidly defined system. There is also the risk that the in vitro system shown to be inhibited by a series of compounds does not bear a definitive relationship to their action in all animals. In vitro methods serve to reveal interesting magnitudes of activity among compounds. Actually they bear only a superficial relationship to the clinical application. Certainly such tests give no insight into the metabolic action.

A few examples. The potency of chlorthiazide diuretics bears no quantitative relationship to their in vitro carbonic anhydrase inhibitory action, even though they must possess this or what must be a very similar attribute to be effective. The importance of sulfanilamide was appreciated not so much on the basis of the in vitro antibacterial action but in experimental infections in the mouse. To determine just the in vitro antibacterial actions of the compound is to disregard the fact that an agent may increase significantly host resistance to experimental infection without being antibacterial itself. Indeed this was one reason put forth to explain the delay between the synthesis of compounds like arsphenamine and sulfanilamide and their clinical use (i.e. 1907-1910, 1932-1935).

One of the most important reasons for the limitations of the predictability of pharmacologic actions—animals to man—is the factor of species difference. Various species of animals react differently to the same drug. For example, morphine depresses man, rats and dogs, but stimulates cats, goats and horses. A drug may be active in one or more animal species and yet be relatively ineffective in man. The converse is also possible. A drug slightly active in animals may be highly effective in man. In fact an effective drug may be overlooked since compounds with low activity in animals are rarely selected for clinical trial. This, I can assure you, keeps the pharmacologist awake at night. It also emphasizes that the pharmacologist, and the toxicologist, must constantly revise and improve methods.

The action of phenylbutazone, an antirheumatic drug, was first observed in man. It is so rapidly metabolized in rats that relatively enormous and near toxic doses are needed to induce an anti-inflammatory effect. Biscumacetate, an anti-coagulant, was originally studied in the rabbit, an animal which metabolizes the compound at about the same rate as man. In contrast, the dog inactivates the drug by the same reaction as man but so slowly that if screened in this animal it might have been discarded as inactive.

These problems highlight the importance in drug development of testing a drug in man as soon as feasible to see, among other things, whether its rate of metabolism makes it clinically practicable. The practice of studying the physiological disposition of a drug in man only after it is clearly the drug of choice in animals may not only prove shortsighted and time consuming but may also result in relegating the best drug in man to the shelf.

Despite these limitations in interpretation these methods have resulted in the availability to the medical profession of a variety of agents in the last 50 years. The newer thiazide diuretics, useful in treatment of hypertension and edema states; the variety of potent steroid agents for treatment of rheumatic diseases; the synthetic antibiotic agents with greater activity towards "resistant strains"; the antihistamines, themselves useful in allergic conditions, gave rise to the phenothiazine tranquillizers and other central nervous system agents which have changed the picture of mental disease; the anesthetic agents which permit the skill of the surgeon; and others which have all been the subject of intensive investigation by the pharmacologist using many of the diverse skills I have mentioned, and many which I have not.

In summary, the aim of animal pharmacology is to define the activity and to predict the usefulness of a new compound, synthesized or isolated by the organic chemistry, in the treatment or diagnosis of disease, using a wide variety of pharmacological methods in isolated tissues and in test animals; to predict secondary pharmacological actions or side effects in man and to anticipate some of the toxic effects which might be encountered with excessive doses in man.

TOXICOLOGY

by John Mulvin Parker, M.D., Ph.D., D.P.H.

A toxicologist and pharmacologist, Dr. Parker is Director of Research, Charles E. Frosst & Company, Montreal. He graduated in medicine from the University of Manitoba in 1941, received his Diploma in Public Health from the University of Toronto and, in 1953, gained his Ph.D. in pharmacology from the University of Toronto. During World War II, he served in experimental medicine with the R.C.N. Medical Research Unit and later, in 1948, was engaged in pharmacology and toxicology at the Defence Research Board. In 1953, Dr. Parker became head of the Toxicology Section of Defence Research Medical Laboratories and, in 1956, joined Charles E. Frosst & Company.

Toxicology is here considered as the study of the hazardous effects of drugs and chemicals. In the pharmaceutical industry, toxicological investigations are made in an attempt to predict any hazards which might result from the use or misuse of drugs. Toxicology is also a science with other ramifications. For example, it is useful in forensic medicine. These other aspects will not be considered in this submission.

In order to predict hazards from drugs, information is obtained in three general fields—acute toxicity, subacute and chronic toxicity studies and information on the pharmacodynamics of a drug. This latter may be defined as a study as to how drugs exert their actions, and includes the observation and description of these actions. Thorough knowledge of all the actions of a drug is an invaluable guide in predicting untoward effects. Most of the toxic manifestations of reserpine in man were predictable from knowledge of the drug obtained from the pharmacodynamic studies in the animal.[7] The techniques used in pharmacodynamic studies encompass all those used in physiological and pharmacological investigations.

When such information about a drug is considered along with the way it will be used, that is, the dose and usual duration in therapy, etc., experiments can be designed to obtain quantitative data regarding toxic effects. It has been said there is no such thing as a toxic compound, only a toxic dose, which is merely a way of emphasizing the importance of quantitative aspects. For example the essential components of food—amino acids—NaCl—can be toxic at certain doses.

Toxic or adverse reactions to drugs can be divided into three categories:

1. Those toxic features which are inherent activities of the drug and which are apparent from the pharmacodynamic studies. This is why it is so important to study a drug thoroughly in all aspects of its pharmacology. Not only do pharmacodynamic studies give a good indication of what tests and systems should receive special attention in the acute, subacute and chronic animal studies, they also indicate what to be on guard for, clinically.

Some of these toxic effects which are inherent to a drug may occur concomitantly with its therapeutic effects. An example often cited is the alteration in gastrointestinal function which accompanies the hypotension or lowering of blood pressure by ganglionic blocking drugs. All these effects occur at the same dose and, depending which action is desired, the other will be regarded as a side effect.

Another concomitant type of side effect is that due to higher dosage. Insulin lowers blood sugar in the treatment of diabetes. If the dosage it too high, the blood sugar is lowered too much, this is no longer a therapeutic effect. Now it is considered a toxic effect.

2. The second class of toxic effects are those which are allergic or described as idiosyncrasy.

Allergy means an altered reaction and here individual variation is extremely important. These effects occur sporadically in a few individuals, at a therapeutic dose. These reactions may take the form of skin rash, fever, liver damage, bone marrow damage—the later taking several forms, aplastic anemia, agranulocytosis, thrombocytopenia, etc.

3. The third category, miscellaneous toxicity, includes cataracts, alopecia, retinal damage, fetal and neonatal toxicity, and behavioural toxicity, such as toxic psychoses. These are grouped as miscellaneous because the underlying processes are unknown.

The first group of toxic effects, those related to the pharmacodynamics of a drug, can be demonstrated in animals. The allergic manifestations are almost impossible to demonstrate in this way. In particular the blood dyscrasias which have serious implications for man are impossible to demonstrate satisfactorily in animals. The miscellaneous toxicities have, unfortunately, been observed first in man and only in some cases is it possible to reproduce these effects in animals. The type of paralysis which was seen in Algiers from the use of adulterated cooking oil can be reproduced in the chicken. When a disorder occurs in man, it is relatively easy to search through animal species to try to find a model situation. The reverse is difficult, although much more desirable, but without a clue, there is nowhere to start.

To illustrate the problem of predicting human effects from animal data, Dr. Litchfield reviewed six drugs. [9, 8] These were from the following classes: antibacterial, tranquillizer, glucocorticoid and antialcoholic. All six drugs had been given to dogs for at least six months and to rats for one year. They also had been studied in man, with 500 or more cases for each drug.

Table I lists signs reported only for man. This illustrates the inadequacies of animal testing in the area of allergy. In the area of subjective symptoms elicited by questioning, animal tests can never replace clinical studies. The genetic variability of man may mean that some individuals may have adverse responses to drugs. Some families show a sensitivity to the antimalarial drug, primaquine, and this appears to be a sex-linked inheritance. These patients receive the normal does of the drug, nothing happens for the first few days, suddenly their blood cells being to break down, the urine becomes dark from excretion of hemoglobin, and they may progress to acute renal failure.

There are many examples of these inherited differences. So far suitable strains of animals for testing drugs in this regard have not been developed. Some drugs are metabolized and broken down differently in the body of man

than in animals and again, tests with animals would not reveal toxicity. There is no satisfactory explanation why the allergic manifestations of drugs cannot be duplicated in animals. But the bone marrow damage, allergic liver damage, and skin manifestations do not occur in animals. In spite of these drawbacks, animals are used as skillfully as possible to give warning of side effects in man.

In the design of tests the presumed application of a new drug must be considered. Drugs can be divided into five groups according to their use:

1. Those that are given a few times on rare isolated occasions.
   Example: anaesthetics.
2. Those given for a short concentrated period.
   Example: Potent analgesics.
3. Those given in repeated short courses.
   Example: antibiotics.
4. Those given for long periods of months or years.
   Example: anticonvulsants.
5. Drugs where the administration is relatively uncontrolled:
   Example: Drugs available without prescription.

TABLE I

Signs in Man not Predicted from Dog or Rat.

Skin	—	Gooseflesh
		Dermatitis — rash — erythema — urticaria
		scarlatiform eruption
		bullous dermatitis
		phototoxic dermatitis
		Desquamation of hands
		Pimples
		Pinpura
Fever	—	Chills
Vaginitis		
Bladder Irritation		
Nasal Congestion		
Kidney — Oliguria & Anuria		
Edema		
Interstitial Myocarditis		
Bradycardia		
Trismus		
Increased Food Intake		
Localized Fat		
Blood	—	Aplastic Anemia
		Thrombocytopenic purpura

If tests are to mimic use, drugs in the last category require the longest period of trial. There is considerable evidence that toxicology studies in laboratory animals such as rats and dogs will provide full information after 3 months. No further information seems to result from continuation of trials to 6 months or a year. Nevertheless, this is the usual practice.

Methods Used

Acute Toxicity: This means the toxic effects produced by a single dose of the drug. The acute lethal dose, usually referred to as LD_{50}, is one of the first determinations made in studying the pharmacology of any compound. This is a dose which will kill 50% of animals. It is obtained by setting up groups of animals and giving them a wide range of doses, then with some idea of doses

which would yield death rates between 10% and 90%, the trial is repeated with careful observations of the animals to observe the mode of death.

An estimation of the toxic dose in man is made from doing LD_{50} determinations from several species. Various routes of administration are used. The clinical use is kept in mind but often other routes are used as well, e.g., intraperitoneal. In special situations, information is required about skin or eye toxicity and tests are then done placing the substance on the skin or in an animal's eye. The rabbit is often used for such tests.

Chronic Toxicity: Chronic toxicity refers to toxicity resulting from repeated daily administration of the drug. There is some confusion in terminology at this point in the duration of such trials. Many refer to chronic studies carried out on a 6 - weeks basis as subacute chronic studies. Here this terminology will be used. Chronic toxicity will refer to toxicity studies extending to three months or longer. In order to determine suitable doses, the same ranging type of trial is done as for acute toxicity measurements.

Doses somewhat below the acute lethal dose are used and given to a few animals repeatedly in order to determine the dose which will cause lethal or damaging effects. Once such a dose has been determined, it is then possible to use this and set up the chronic studies with a high dose designed to cause death over a period of weeks. Other groups receive half that dose, and a further group half that dose again. The tests and measurements made during these trials will be outlined below.

There is a considerable body of evidence that suggests that comrehensive testing will elicit more information from short period trials of up to three months than from longer testing.

Designing Chronic Tests

The first essential feature is knowledge of the physical characteristics of the drug to be tested. This includes knowledge of the chemical structure, the purity, the stability and physical properties such as solubility, particle size, etc. It is very desirable to have adequate analytical methods so that assays may be conducted on material used during the trial. It is also useful to be able to measure the concentration of the drug in body fluids.

Subacute Toxicity: This is probably the most crucial toxicity study. Infor-fation obtained will be used in planning the chronic tests. Information obtained will serve as a guide to advisability of proceeding with clinical pharmacology In conjunction with other information the subacute toxicity trials help to establish the exploratory dosage for man. Subacute toxicity trials are done using weanling rats supplemented by dogs. These trials last from one to three months. Observations made are outlined in Table II; rate of growth, food and water intake, behaviour of animals and their general appearance are recorded. Mortality is noted. If toxic effects occur, and animals commence to die, the survivors are sacrified and autopsied. Those surviving at lower doses are treated the same way at the end of the trial.

TABLE II

Tests done during subacute and chronic toxicity trials.

(1) Physical methods—observation—weight gain—food consumption—neurological examination—behavioural changes.
(2) Biochemical methods—liver and kidney functions and measurements—clinical chemical procedures as developed for man are applied to animals.
(3) Hemotological methods—blood morphology—hemoglobin estimation, etc.

(4) Special observations where indicated—eye irritation—skin changes—after eye or skin application.
(5) Pathological procedures—post-mortem—histological examination of tissues.

It is unfortunate but due to species differences and probably other factors of which there is no knowledge, the proof of safety of a chemical for man can never be completely demonstrated in animals. It is for this reason that clinical pharmacology must be undertaken although one of the most important reasons is to see if the compound is useful for man.

To protect the first patients in every way, all the available animal data is brought to bear in designing initial clinical studies. In order that the clinical pharmacologist may be fully conversant with the problem a clinical orientation brochure is prepared. This includes detailed information of the chemistry, the physical properties, such as solubility and stability; the pharmacology and the toxicity data, the proposed indications and usefulness of the compound, as well as estimated safe starting dose for dose response measurements. Naturally, very low doses are used initially and gradually increased. There is often need for a conference between the clinical pharmacologist and members of the research staff. This will be outlined in greater detail in the clinical presentation.

Two special problems in which prediction is inadequate relate to potential teratogenic or carcinogenic properties of drugs. Techniques are being developed in these fields. For carcinogenicity, drugs are applied for a major portion of the life span of the laboratory animal. For teratogenicity, drugs are given to pregnant animals or to fertilized incubated chicken eggs. Another technique is to continue giving the drug to the offspring and breeding these and again giving the drug to the offspring for at least three generations. At the present time there is a very poor correlation between clinical experience and results of these studies. To emphasize these difficulties the following is quoted from Professor F. Clarke Fraser of McGill:

"So, at last, the drug in question has been tried in many strains of all possible species, for a wide range of doses, through all possible stages of pregnancy, by all possible modes of administration, and the offspring have been examined by all the means necessary to detect malformations. I suspect that all pharmacologically active compounds, if tested this way, would be teratogenic in some way. I do not know of any drug tested as thoroughly as thalidomide that has not be teratogenic in animals. But suppose such a drug was found—it could not be concluded that it was safe in man. Admittedly, however, one would be much less likely to worry about the drug's possible teratogenicity in man under these circumstances. But one has also to admit that it would be entirely impractical to attempt to test drugs in all experimental species by various routes, at several dosages and all stages of gestation, and the farther one falls short of this, the more likely one is to miss the teratogenic combination of factors. Certainly one or two species and one or two dosages does fall far short of this, and is not at all a reassuring test for safety.

"Now consider, on the other hand, what happens if the drug in question does produce malformations—a situation which will occur more and more frequently as testing becomes more and more widespread. Let it be said again that there are drugs in current clinical use, some not requiring a prescription, that are very teratogenic. These include adrenalin, ACTH, phenobarbital, progestins, salicylates, oxytetracycline, tetracycline, thyroxine, androgens, caffeine, cortisone, meclizine, prednisolone, estrogens, imipramine, insulin, and tolbutamide. With the exception of some of the sex hormones, these are not recognized teratogens in man—i.e. they do not produce malformations very often, if at all. (It is as yet impossible to rule out the possibility that they may bring about developmental errors occasionally.)"[13]

Summary

The fundamental problem in drug safety is the need for the development of methodology for toxicology studies which would reveal inherent toxicity of a drug by laboratory tests. Pharmacodynamic studies are very useful.

Acute toxicity studies in several species may indicate the possible hazards from an acute overdose in man.

Chronic toxicity studies, teratogenic studies, and carcinogenic studies require development of methods. It is unfortunate that fine details, such as the way of dosing an animal may be considered to such a degree that the fundamental question "is the rat or the dog, etc.?" the animal of choice to predict information for man, become overlooked.

It is unfortunate that studies in methodology have not been considered a fertile field of research by many pharmacologists outside of industry.

Finally, it should be emphasized that adverse toxicity is not the only reason for not marketing a drug. Difficulties in scaling up the chemical synthesis have delayed the marketing and full development of many drugs. Finally, many drugs do not fulfill their promise in the clinic or do not show improvement over existing products and are abandoned.

STAGE 2: CLINICAL PHARMACOLOGY AND INVESTIGATION

The potential value of the new substance discovered by the basic researcher has now passed the stringent scientific requirements of the pharmacologist and toxicologist. But it is still in the experimental stage.

The substance now must go to the clinical pharmacologist and director of clinical investigation, to determine whether it should be studied in humans and, if so, the manner in which these studies can be safely and effectively implemented.

It will be appreciated that the decision here is a vitally important one, requiring the sound judgment of physicians and scientists. All evidence leading to this stage must be carefully sifted and evaluated by the company's medical department. In some cases, depending upon the form of the substance, outside advice may be solicited from specialists in the particular field.

If the substance is passed by this exhaustive and meticulous analysis, the organization of clinical trials then begins. Highly qualified clinical investigators must be considered, the form of initial studies must be determined, and the Food and Drug Directorate must be notified.

It has been said that clinical exploration is to medicine what space travel is to cosmic science. Both depend upon eliminating the joint factor of human and scientific error before the journey may be commenced. The explorations of both are vital to the continued advances of their respective disciplines.

It is this stage of clinical investigation with which we will now deal in the following three papers.

CLINICAL PHARMACOLOGY: INITIAL DRUG TRIALS

by C. Walter Murphy, M.D., M.A.

Dr. Murphy is Medical Adviser, CIBA Company Ltd., Montreal. He graduated with an M.A. from Dalhousie University in 1939, and then attended L'Université de Paris for one year under a French Government bursary. Following discharge from the R.C.A.F. as a Flight Lieutenant in 1945, having spent three years as a prisoner-of-war in Germany, he attended McGill University, graduating in medicine in 1950. He served as President of the Osler Society and Editor of the McGill Medical Journal. He interned at

the Royal Victoria Hospital and the Barrie Memorial Hospital. Before joining CIBA Company Ltd. in 1953, Dr. Murphy was a Senior Research Assistant in Psychiatry, Allan Memorial Institute, Montreal. In 1964, he was made a Fellow of the newly formed American College of Clinical Pharmacology and Chemotherapy.

This presentation will deal with the initial stage of clinical testing in humans, the so-called pilot trials, which are concerned with the clinical pharmacology already mentioned in the previous papers.

By way of introduction several points which have already been made should be emphasized. First of all the study of drug action is a relatively new science, and it is a body of knowledge which, though steadily growing, has in common with many other sciences the fact that much of the territory it embraces still remains unexplored. The procedures which are adopted in the study of a drug reflect the best use that can be made of what we know today, and many of the precautions with which new drug trials are surrounded stem from the results of past experience.

The second point is that the only way to test the action of a drug of suspected therapeutic usefulness is to test it in humans. Much can be learned of the nature of a drug from the animal testing procedures which have been described to you, but not until a new drug is studied in humans can we know what its effect will really be. This is because on the one hand there are some disease entities in the human which have no counterpart in the animal, and, on the other, because man differs from other species of the animal kingdom, just as such species show differences one from the other.

There is clearly a risk involved in this, but, as Dr. F. S. Brien pointed out in his report to the Minister of Health, one of the aims of new drug evaluation should be to minimize this risk, utilizing to the full what is currently known of the science of drug testing, rather than by attempting the impossible task of eliminating all risk, to interrupt all future drug progress. It is only in this way that the search for better treatment of all illness can proceed, with the hope that drug research in the future will make contributions to the treatment of disease that such agents as insulin and the antibiotics have made in the past.

To proceed then to a discussion of how new drugs are first studied in the human, and to detail the precautions that surround such studies, I should like to refer you to Charts A and B, located at the end of the paper, which present in flow-sheet form much of what I wish to say. The first point of departure for a pharmaceutical company is to decide which of the many new chemicals produced by its laboratories are so to be tested. The choice is made by a group composed of research, clinical and management personnel who decide, at the completion of the pharmacological testing of the compound in the animal, whether the activities which these studies have revealed are suggestive of significant therapeutic usefulness. If it is so decided, the toxicity studies are begun, and on the basis of these results, a decision is reached as to whether the activity and toxicity data indicate that a human trial is warranted and likely to be safe. If the decision has been taken to proceed, the following measures preparatory to the initial trial are carried out:

1. A detailed orientation brochure is prepared, covering all the pertinent chemistry, pharmacology and toxicity known at this point.
2. The medical director, responsible for initiating clinical trials, contacts the investigators who have been selected for the initial studies.
3. An investigational new drug submission is prepared in accordance with the recently revised New Drug Regulations, with which you are familiar, and submitted to the Food and Drug Directorate.

In this important phase, only the most highly qualified investigators are considered, such as physicians with clinical and research backgrounds, working in teaching centres and hospitals in their particular speciality, whose experience

in the testing of new drugs warrants their being considered. It is usual at this time to confine the initial testing, or the pilot trial, to one or two investigators.

The investigator (or investigators) who has been approached examines the information provided by the medical director in the orientation brochure in detail, and discusses it with him. It will be recalled that this brochure contains all the information about the drug known to date, including its chemistry, its pharmacologic activity and the results of the toxicity tests. If the investigator considers the drug to have potential clinical usefulness, the first trial is planned, in which the information sought is carefully outlined.

The aspect of drug action to which most attention is given at this stage concerns its potential toxicity in the human, so that decisions are taken relating to the starting dose (always a fraction of that dose on a weight basis which produced the earliest toxic symptoms in animals); the laboratory tests to be performed (routine blood tests, urinalyses and hepatic function tests, with special tests wherever the nature of animal toxicity or previous experience with similarly acting drugs suggests their necessity, such as renal function tests, and others); the clinical signs and symptoms to be monitored, such as the general condition of the patient, his blood pressure, pulse and respiratory rate, together with those signs and symptoms which may be particularly related to the anticipated effect of the drug.

The second aspect of drug activity to which particular attention is also paid during the pilot trial is concerned with its possible therapeutic effect, so that the design of the study takes this into account as well. Patients are selected with diseases considered most likely to benefit from treatment with the new drug on the basis of its presumed therapeutic potential and they are submitted to very careful examination throughout the study by observations and tests selected to define the results of the action of the drug. A third aspect which it is attempted to study at this point is the intermediate metabolism of the drug in humans, that is, the way in which the body absorbs, transforms and excretes it.

As was mentioned above, the prime concern in initial testing is toxicity, so that low doses, generally subtherapeutic, are first administered. These doses are slowly increased, in stepwise fashion, until there is an apparent therapeutic effect, or until significant toxicity appears. If the latter should arrive before the former, the drug is withdrawn. If there is an apparent therapeutic effect, in the absence of significant toxicity, the trial continues, as such features as optimal dosage, nature of the action of the drug in the human, the effect of administration of the drug over several days or months, and the clinical results in a variety of diseases are studied.

During the period of the pilot study, more than one patient will have to be studied in order for any conclusion to be reached, but it must be emphasized that the first studies are carried out on a small number of patients, frequently those who have not responded to other accepted therapy. Occasionally, patient volunteers or healthy volunteers are invited to participate. Such trials are undertaken only on hospitalized patients under the most careful observation, and complete records are kept. Every precaution that is known which will safeguard the patient from potential harm is carefully observed by experienced investigators.

The initial trial stage continues until enough knowledge is obtained on which to base a decision concerning the value of studying the drug further in a larger group of patients. This decision is based on what had been discovered concerning its toxicity in humans, and its clinical activity, both examined in relation to the results obtained from animal studies. The decision taken may be ether that the drug should be abandoned, that further study at the pilot trial level should be undertaken, or that it is safe to proceed with its examination in a larger number of patients. If the last decision is taken the drug then proceeds to the second stage of clinical investigation which will be described in the next presentation.

CHART—CHART—

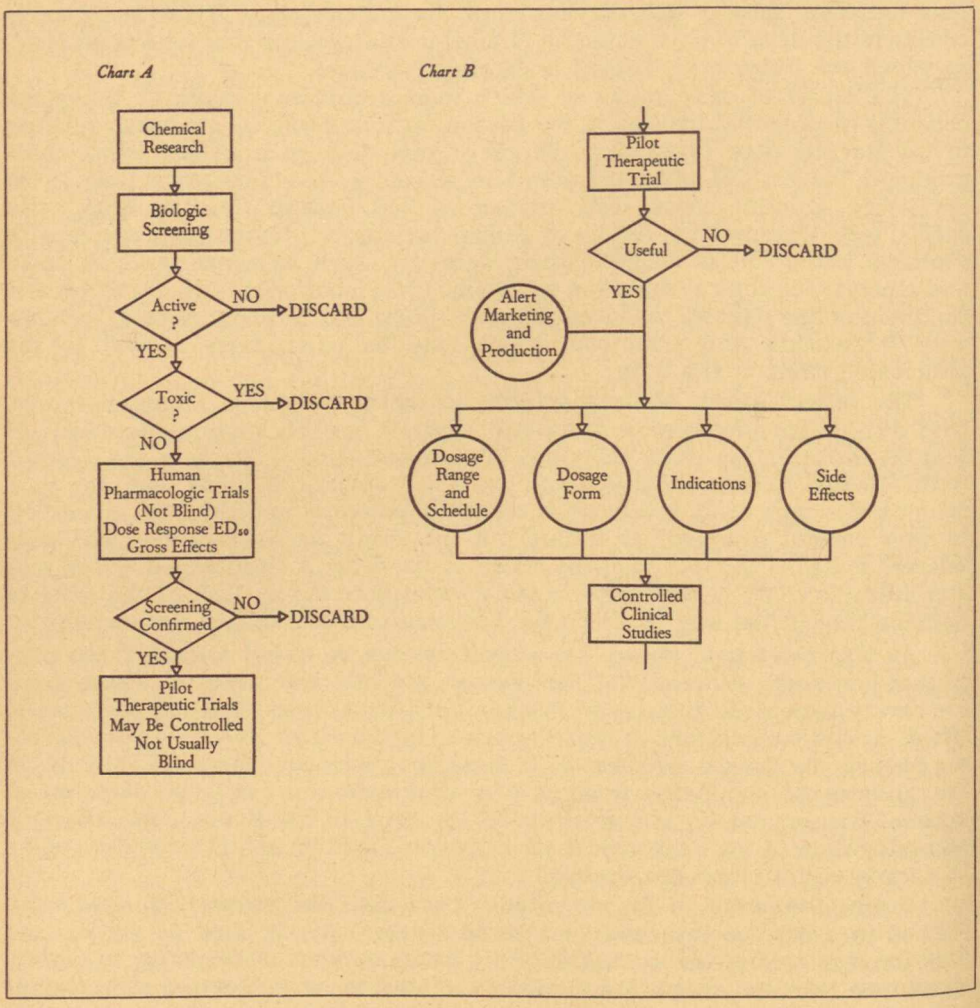


Chart A
Chemical Research
Biologic Screening
Active ?
NO
DISCARD
YES
Toxic ?
YES
DISCARD
NO
Human Pharmacologic Trials (Not Blind) Dose Response ED_{50} Gross Effects
Screening Confirmed
NO
DISCARD
YES
Pilot Therapeutic Trials May Be Controlled Not Usually Blind
Chart B
Pilot Therapeutic Trial
Useful
NO
DISCARD
YES
Alert Marketing and Production
Dosage Range and Schedule
Dosage Form
Indications
Side Effects
Controlled Clinical Studies

CLINICAL INVESTIGATION

by Peter H. Nash, M.D., M.A., D.P.H., D.I.H.

Assistant Director of the Scientific Division and Medical Director of Abbott Laboratories Ltd., Montreal, Dr. Nash graduated in medicine from Cambridge University in 1941. Following service with the Royal Army Medical Corps in Europe during World War II, he received a Rockefeller Fellowship in 1946-48, and subsequently became Research Fellow at Harvard Medical School. He holds Diplomas in Public Health and Industrial Health and is a Member of the College of General Practice. Dr. Nash is also a member of the medical staff of the Royal Victoria Hospital, Montreal, and Consultant in Pharmacology, Department of Experimental Surgery, McGill University.

The initial or pilot trial of the compound, previously described, has now been completed. From it we should obtain an approximation of the dosage of the drug, learn a little about its effectiveness in man as opposed to animals and discover something about its side effects and toxicity, if any.

A drug which is toxic in only a small percentage of people will be quite acceptable provided it is of real value. Examples of this are penicillin, which very rarely can cause a dangerous anaphylactic reaction, the antibiotic chloramphenicol which is most valuable in the treatment of certain infections even though it may on occasion damage the bone marrow, the anti-thyroid drug, propylthiouracil, and the anti-epileptic drug, trimethadione, which may on rare occasions have similar effects. Toxicity in a drug of less value, such as headache remedy would obviously preclude further clinical investigation. Side effects, on the other hand, are often related to dosage and can be reduced or eliminated by giving a smaller dose while still retaining the therapeutic effect of the drug. One always hopes that a new drug will be completely free of toxicity, but some side effects in some patients may have to be accepted.

The purpose and importance of a well-planned drug trial was stated in the brief of the Medical Section of the Canadian Pharmaceutical Manufacturers Association to the Royal Commission on Health Services, as follows:

"The fundamental purpose of the drug trial is to obtain objective assessment of the value and safety of new drugs and to avoid the marketing of worthless or harmful products. The pharmaceutical industry is fully alert to the fact that the acceptance by the medical profession of a new drug is primarily dependent on proven therapeutic efficacy without untoward toxicity, and that claims for a new drug cannot be made without adequate clinical drug trials. Drug trials on new products cannot be conducted without experienced investigators, proper laboratory data, and the appropriate methodology. Thus, the drug trial requires careful planning and control and adequate associated laboratory facilities."

Organization—the full scale drug trial

If the results of the initial trial are such as to encourage further investigation, the drug is then taken to a certain number of well-qualified physicians who are experts in the disease which the drug is designed to treat. Almost always these doctors are attached to medical schools in our leading universities. The objectives of these trials are many. First, more precise information regarding dosage of the drug must be obtained, otherwise, the drug may never be used in such a way as to obtain its maximum benefit. Secondly, an assessment of the effectiveness of the drug is made. Thirdly, further information on side effects and toxicity, if existent, is obtained. To this end the patients are closely observed and questioned, and laboratory tests, of the type indicated by the results of the initial trial, are carried out.

To help ensure the effectiveness of such a trial there is an initial meeting between the physician from the pharmaceutical company concerned and the investigator. At this time the investigator is given an investigational brochure which has been prepared by the pharmaceutical company. This brochure contains a description of the nature of the drug, details of its pharmacology and animal toxicity tests, and particulars of the initial human trials which have been performed. As each new report is received it is included in this brochure which gradually increases in size as the investigations proceed. The trial is carefully planned; such questions as the number of patients to be included, whether or not a control series will be used, if the trial should be blind or double blind (terms which will be explained later), the dosage scale to be employed, which laboratory tests should be done and what side effects should be anticipated, are all discussed.

This meeting is followed by continuing contacts and the results of the trial can be compared with those of others that are proceeding at the same time. Finally, a report is produced by the investigator concerned and, when a few of these have been obtained, a rather complete picture of the drug begins to emerge. This full scale trial is the most important of all in the investigation of the drug, not only because a few such well-conducted trials can supply a great deal of knowledge about the drug, but because it is the results of these trials which most frequently are published and come to form the classic studies of the new drug and the main sources of information for the medical profession.

The clinical profile of the new drug, its action on patients and its effectiveness in disease, have now been defined. But further information as to possible toxicity and the utility of the product in medical practice is needed. If a drug, for instance, should have a toxic effect only occasionally, this may not show clearly until a large number of patients have been treated. At this stage it is therefore distributed more widely to other physicians in university centres and major hospitals.

Again, these doctors will probably be specialists, who are competent to assess the drug, but whose interests lie more in medical practice than in clinical investigation. They will, however, use the drug, maintain reports on forms supplied by the pharmaceutical company, and carry out laboratory tests as necessary. The information obtained from this stage of the trial serves to confirm previous data and bring to light infrequent toxicity, if present. Records are maintained showing the names and addresses of all physicians who have received the new drug, the dates and quantities of shipments and the lot number of the batch from which such shipment originated.

If the drug now appears to be one which may have wide use in medicine, rather than being confined to a specialized area, and to be safe and effective for the purpose for which it is intended, it is finally distributed more freely to practicing physicians, including, perhaps, some general practitioners. It should not be assumed that the latter have no part to play in a clinical drug trial. Quite useful work can, in fact, be done by general practitioners and in the smaller hospitals.[14] The main purpose of such wide distribution is to obtain the opinions of doctors regarding the usefulness of the drug in practice and, by enlarging the experience with it, to confirm the evidence concerning the absence or presence and frequency of toxicity.

It is generally while this stage is in progress that the application to the Food and Drug Directorate is prepared. If this application is found to be satisfactory and the drug is marketed, medical department contacts with investigators and others using the products are maintained indefinitely and the performance of the drug is followed by reports received.

Methodology—the need for refined technique

A properly conducted clinical trial is the most precise method we have for measuring the effectiveness of any treatment. But, largely because we are dealing with living beings rather than inanimate objects, it is full of pitfalls.

So fascinating, however, is the methodology of meaningful trials that a few experts have devoted themselves entirely to this branch of medical research. Only some of the most important points can be presented here.

The method used must first be sufficiently sensitive to detect the changes in patients given the new drug that are likely to occur. An example will illustrate this. A well-known United States investigator gave a group of patients with arthritis acetylsalicyclic acid (A.S.A. tablets) in three different strengths three times a day. The tablets were specially prepared so that neither the doctor administering them, nor the patients, knew which dose was being given, nor if a completely inactive tablet, called a placebo, was being administered.

After a two week period on each dosage, every patient turned in a report card indicating his reaction to the medication during the period. Statistical analysis of the results showed that the patients were unable to distinguish between any of the doses of A.S.A. and the placebo. One might conclude that A.S.A. was inactive or that a larger number of patients should have been included in the trial. Both conclusions would be wrong, for the method used was not sufficiently sensitive to detect the changes which occurred. A second experiment in which a bedside observer recorded the patients' reactions (i.e. relief of pain) as they developed showed that the patients could indeed distinguish, not only between the A.S.A. tablets and the placebo, but between the different doses of A.S.A.[15]

The dose of the drug also has to be carefully considered. If it is too small, the whole trial could be conducted with the drug appearing to have little effect; if too large, frequent side effects may be produced.

There is also the question as to whether or not to use a control series of patients. If the drug is dramatic in its effects, or if the disease which it treats is invariably fatal without treatment, then no controls are needed to demonstrate the effectiveness of the medication. Also, if the disease is a chronic one which will not improve without treatment, the patient can act as his own control—observations being made of his condition when receiving the drug compared with intervals of no treatment.

In many instances, though, effects of drug on disease are less clear cut, or there may be a tendency for the disease to show natural remissions. In these cases a control series of patients, with as nearly as possible the same age and, if necessary, sex distribution as the treated group is given either no treatment or an inert tablet and the results in the two groups compared. Even such an experiment may still be misleading unless the results are assessed statistically. We have to be sure that the results could not have occurred by chance. Statistical significance, therefore, is simply a method of calculating the odds against the results of the experiment happening by chance. If they could not have occurred by chance more than once in 20 times, the statistician considers this a reasonable gamble to take and says the results are "just significant"—if the odds are 1 in 100 or 1 in 1000 against a chance happening, the result is "highly significant".

Obviously, if there is only a small difference between the treated and untreated groups, larger numbers of subjects will be needed to demonstrate the presence or absence of significance than if the difference is large. This factor has to be taken into account beforehand and the number of patients which must be included in the trial to demonstrate successfully the expected difference determined. Often consultation with a statistician is necessary to do this.

A final point which must be mentioned in this very brief summary of the methodology of clinical trials is the matter of the elimination of human bias

from the results. If the patient were to know when he was receiving the active drug and when the inert pill—the placebo—the psychological effect of this knowledge would tend to favour the drug. Suggestion can actually be so powerful that patients who are not told which is which, frequently show curative effects from the placebo and may even go so far as to complain about the side effects of the inactive tablet! Therefore, it is advisable to conduct the trial "blind", the patient not knowing when he is being given the placebo, and to make the group large enough to compensate for differences due to people showing a reaction to the placebo.

The investigator, also, may not be free from bias and may influence the results by conveying to the patient a greater sense of reassurance or enthusiasm when he is administering the medication than when the placebo is being given. To compensate for this the active drug and the placebo can be supplied by the manufacturer in identical forms, distinguishable only by a numerical code, which is not revealed to the investigator until the end of the trial. Often, of course, with a drug showing a marked effect, the code will be broken before the end of the trial, but this fact serves to confirm the efficacy of the drug concerned. This is the famous "double blind" technique about which so much has been written. It is a most valuable tool for the measurement of differences of therapeutic effect, particularly when these would not otherwise be too appreciable.

Ethics of the Clinical Trial

From the time of the earliest beginnings of medicine, among the ancient Egyptians, with Galen and the herbalists, through experience with the early drugs, such as ipecac and quinine, to Ehrlich and more modern times, new drugs have been tested on humans. The only essential difference between earlier times, or between twenty or thirty years ago, and now, is that there are many more drugs to be tested and we have had to develop more sophisticated techniques of investigation. If there were some sub-human species, with physiology identical to man, we could test drugs on them. But existing animals are not sufficiently similar to humans to serve the purpose, so man is used. It is obvious that to advance, medicine needs continually to test and it is probable that without continued research our knowledge would wither away as it did in the Middle Ages and be forgotten until some future renaissance again brought it to light. However, if humans are to be used we must be quite certain that ethically and morally we are justified.

The physician should focus first, last and all the time on the care of his patients, but the good investigator must also be very much concerned with his investigation. There are other loyalties, though, which are common to both these men, such things as responsibility for teaching, for the care of their families, for earning a living, perhaps for public service. The investigator simply has one more loyalty to which he must give correct priority—loyalty to his search for the truth.[16]

A useful guide in all clinical investigational work is that you should not do anything which you would not be willing to have done to yourself or to a close member of your family. Another, which is generally followed by investigators, is that if a patient is deteriorating on the experimental regime he must be removed from the trial and given whatever treatment is necessary, provided that some better treatment exists. Placebo-controlled trials are not carried out under conditions in which the patient's health would be harmed by withholding for a while active treatment. It should be remembered, too, that such trials serve to eliminate useless drugs—an end which could not be accomplished otherwise.

With regard to the use of new drugs by physicians, there are two schools of thought. One cautions with Pope, "Be not the first by whom the new is tried, nor yet the last to lay the old aside." The other, from which most advances

come, feels that "faint heart never won fair lady! Nothing venture, nothing win." Dr. H. Beckman, the noted pharmacologist and physician, discussing the doctor who incorporates few or no new drugs into his practice, notes that he is "a sturdy fellow . . . But it is nevertheless undeniable that some of his patients are not going to receive all the aid that they might get elsewhere." Concerning the use of drugs which are beneficial to many but may on occasion be harmful, he says, "Just being alive even in a healthy state involves great risk in itself. I believe that the physician is justified in adding to that risk in the hope of cancelling out an additional one—if he has reached his decision to do so with full knowledge of what is involved and is sure that he can cut his losses with good conscience."[17] Most throughtful physicians would certainly agree with this view.

The Need for More Canadian Participation in New Drug Trials

The number of investigators in Canada with the training, interest and facilities to carry out the adequate evaluation of new drugs is small. Almost without exception the experience of every member of the Medical Section is identical in the difficulties faced in having good clinical trials of new drugs carried out in this country. This can be attributed in part to the orientation of clinical investigators in this country towards physiology and pathology, as opposed to therapeutics.

The result has often been to relegate drug trials to a position of secondary importance in the research programs of major institutions. It is not being suggested that drug trials should occupy a position of pre-eminence, but rather that Canadian doctors should play a greater part in those drugs which they will later use.

In order to obtain the required information therefore we have to rely to a considerable extent on work carried out in other countries. For this reason the proportion of Canadian work included in New Drug Submissions is small, although the Directorate is on record as saying that it would prefer more reports from Canadian investigators. It is unfortunately true that at the present time new drug evaluation is the Cinderella of medical research—admitted to the program only when all other commitments have been fulfilled.

This state of affairs is also due in part to the lack of training in human pharmacology and in the methodology of new drug evaluation. Since the training of most investigators has not included this branch of research, few are capable of deriving intellectual satisfaction from it. The same can be said of the statistical planning of experimental designs which involve concepts without appeal to the uninitiated.

However, there are some notable exceptions. A few disciplines, psychiatry, for example, have made laudable and successful attempts to set up drug evaluation units, financed by outside help, with the manufacturer covering certain costs in each trial. Some departments of anesthesia have done excellent trials of new agents. The vast majority of drugs, however, fall within the purview of departments of medicine, and to a lesser extent departments of surgery. It is in these areas that the greatest value could be derived from the organization of investigation units. It would not seem unreasonable to suggest, in the light of the present stream of potent preparations from manufacturers, that one unit should be set up in each medical school, and financed in part by the university, in part by the industry and in part from other sources.

The revolution which has occurred in medical treatment during the past twenty years, with more and more effective drugs being made available by manufacturers, may be expected to continue. This carries with it an obligation to test new drugs in humans—a task which the manufacturer unfortunately cannot perform, limited as he is to animal experimentation. This obligation, which is both medical and social, devolves therefore on the medical profession,

particularly in the medical schools and larger hospitals. It is not a new obligation in that the profession has always demanded knowledge of the safety of a drug before using it on patients; what is new is the extent of the problem, and its increasing social significance.

Drugs that are placed on the Canadian market should be carefully scrutinized and tested by Canadian doctors. Tests carried out in other countries are often valid and acceptable to the Food and Drug Directorate, but that Canada should take a greater share in this work, and accord it its rightful place in medical research, should go without saying.

In an effort to play its part towards the above end, the Canadian Pharmaceutical Manufacturers Association, through its Medical Section, has created the Canadian Foundation for the Advancement of Therapeutics. Under the Chairmanship of Dr. F. S. Brien, Professor of Medicine, University of Western Ontario, and the Honorary Chairmanship of Dr. R. F. Farquharson, the Directors of this Foundation are scientists of the front rank. The Foundation's objectives are to stimulate and aid research in the science of drug evaluation and to train investigators in this field. This Foundation has already granted several fellowships to research workers during 1964. It is earnestly to be hoped that the existence of this foundation will stimulate other granting bodies, as well as universities, to take an interest in this field of drug evalution, which is so vital to medical progress.

New regulations under the New Drug Section of the Food and Drug Act have recently made their appearance. In drafting these, the Food and Drug Directorate consulted the C.P.M.A., and the Medical Section, and other parts of this Association gave all possible assistance to the Directorate. If the object of these regulations is to ensure stricter control of the investigational use of drugs without being so restrictive as to retard seriously research and development, then it appears that this objective is likely to be achieved. These regulations, in the drafting of which the industry played a significant part, will contribute toward the overall objective of safety in the testing and use of new drugs in this country.

Finally, the significant observation of the Special Committee on New Drugs of the Royal College of Physicians and Surgeons of Canada, appointed by the Minister of National Health and Welfare, should be noted:

"There is an urgent need for collaboration on the part of all bodies concerned with, or interested in, the clinical testing of new drugs . . . to assess the magnitude of the problem, the facilities presently available, the expansion necessary to enable adequate clinical trials to be carried out in Canada (in terms of personnel and additional facilities) and the roles which each could, or would, be willing to assume in this matter."

CONCLUDING REMARKS ON THE CLINICAL ASPECTS OF DRUG TRIALS

By William K. MacDonald, M.D., M.C.G.P.

A specialist in clinical investigation, Dr. MacDonald is Vice-President and Medical Director, Schering Corporation Ltd., Montreal. He graduated in medicine from McGill University in 1943, and following practice became a Member of the College of General Practice. In addition to his duties at Schering Corporation Ltd., Dr. MacDonald also serves as a member of the Post-Graduate Board of Montreal General Hospital, which includes post-graduate teaching in all of its forms, and is Demonstrator in Medicine and Clinical Medicine at McGill University.

The previous papers by Dr. Nash and Dr. Murphy have outlined for you the careful steps taken to develop as accurately, and as safely as possible, the facts needed to determine whether a product can be released for sale in this country.

When the producers of a drug feel that they have accumulated sufficient information on its qualities to indicate that it will be of value to the medical profession, and the people they treat, they prepare a new drug submission, and forward it to the Food and Drug Directorate for review. The requirements in this connection are clearly laid down in the Food and Drugs Act and Regulations, and I will not bore you with a repetition of the information required.

A feature of the new drug submission is a section in which a summary of all the information of potential use to the physician is listed. It is designed to indicate to the physician as accurately as possible the nature of the product concerned, the indications for which it may be useful, the advantages it may have in certain respects, the dosage range which is recommended, the precautions and side effects to be taken into consideration, the packaging, and, frequently, a bibliography of references for the statements made in the summary.

Such summaries may be comparatively short, where the use of the product is uncomplicated, or may be quite voluminous where its use may be complicated by a number of side effects, or other factors. But, in every instance, the summary must reflect accurately and completely the information which has been developed in the investigations carried out with the product.

If the material required in the new drug submission is complete, orderly and clearly expressed, and if the applicants make themselves available for discussion of any complex areas, we believe that an adequately staffed directorate will not have too much difficulty in determining if the product can be safely released for use by the general public under prescription or otherwise, as circumstances might indicate.

We would emphasize that the practice of providing physicians with an exact copy of the summary which I have referred to above, a practice which is very commonly carried out by responsible companies, is in fact, a very important one. The product information to which I have referred is also available to physicians at any time on request. It is the most reliable source of information available relative to the product in question. I think it is a fair statement to say that if the physician uses the products which have been passed on review by the Food and Drug Directorate in the manner prescribed, and with careful attention to the indications, contraindications and precautions listed in the product brochure (summary), he should not get into difficulties attributable to the product concerned.

May I add one word on the importance of continuing investigations and surveillance of drug actions and reactions after they have been introduced into general use following release by the Food and Drug Directorate. Even drugs which have been in use for many years may demonstrate a new side reaction under certain circumstances. The careful accumulation of such knowledge is recognized as an important phase of clinical drug trials and should be encouraged in every way possible. The medical departments of the pharmaceutical companies can be counted on to participate in any plan which will facilitate the transmission of new information on their products to everyone concerned.

Samples of typical statements of directions issued for new products are attached under Appendix A.

STAGE 3: MANUFACTURING, PRODUCT RESEARCH AND CONTROL

We have now reviewed the scientific and medical considerations involved in our new substance. The next step is to study its entry into manufacture. Even the most effective pharmaceutical from a medical standpoint would be worthless if it could not be manufactured in sufficient quantity to meet the needs of mass distribution.

The object of pharmacy research, not to be confused with basic or developmental research, is to determine the most effective and stable dosage form of the preparation and the best technique for its manufacture. Invariably, this is done in conjunction with or at least commenced during stages 1 and 2.

When the dosage form or forms and production techniques have been determined, and the new drug application approved by the Food and Drug Directorate the product is then ready to be manufactured.

As is pointed out in the following papers, manufacturing of pharmaceuticals is a careful process, requiring caution and know-how. At this stage, the essential element is quality control, to ensure that the product meets label claims and the consistency from batch to batch which is the hallmark of a therapeutically sound product.

Quality is not something which can be determined merely by checking the final product alone. It literally must be built into the product during manufacture. The following three papers explain the work involved in this our third and final stage.

PHARMACY RESEARCH: PRODUCT RESEARCH AND DEVELOPMENT

by Sidney A. V. Deans, Ph.D.

A specialist in what is known as developmental research, Dr. Deans is Product Development Manager, Pfizer Company Ltd., Montreal. He graduated from McGill University in 1939 with a B.Sc. and First Class Honours in Chemistry, and also gained his Ph.D. in organic chemistry and biochemistry in 1942. Dr. Deans has been actively concerned with the development of new products in the pharmaceutical and chemical industries since 1947.

In the development of a new drug preparation from a new drug substance, Pharmacy Research plays a vital role. Before a new drug substance may become a candidate for Pharmacy Research, its safety and biological activity in various animal species have to be established by exhaustive pharmacological studies. Only then, does Pharmacy Research enter the picture. The main functions of Pharmacy Research are the formulation of stable drug preparations, and the development of suitable techniques for their manufacture.

Throughout the development of a new drug preparation, Pharmacy Research draws heavily on the scientific knowledge and experience of a team of pharmacists, chemists, pharmacologists, medical practitioners, bacteriologists, and other specialists. For example, the research chemists who discover the new drug substance, determine its physical and chemical properties before the substance is converted by pharmacy research into a new drug preparation. The medical director, in collaboration with the pharmacologists who screen and evaluate the new drug, stipulates the initial dose and route of administration. Pharmacy Research also relies heavily on Quality Control for the development of specifications and test methods for new formulation ingredients.

Formulation of New Drug Preparations

New drug preparations may take the form of dry-powder capsules, compressed tablets, oral liquids, oral suspensions, parenteral liquids, parenteral suspensions, or other dosage forms. The formulation of some of these drug preparations by Pharmacy Research will now be considered.

If the new drug is a solid substance and has to be converted into a dosage form suitable for oral administration, it may be reduced to a finely divided powder, blended with other ingredients, and then filled by means of automatic, or semi-automatic, equipment into dry-powder capsules. The size of the capsule

chosen for the purpose is usually just sufficient to hold a single dose of the new drug. Many of the broad and medium spectrum antibiotics are administered in capsule form.

New drugs in the form of finely divided powders may also be converted into tablets. The powdered drug is blended with lubricants, binders, disintegrants, or other ingredients, and after further processing, is compressed by means of a tablet machine. Here, as in other formulations, each ingredient serves a useful purpose. The lubricant prevents the drug from sticking to the punches and dies. The binder prevents the tablets from crumbling to a powder after the tablets have been compressed. When acted on by gastric juice, or intestinal fluids, the disintegrant helps the tablet to break down and release its active ingredient. Modifications of these basic tablet and capsule formulations are also required. Some of the modifications are designed to release their medication at a controlled rate, or at a specific site in the gastro-intestinal tract.

Liquid preparations are usually administered to patients who have difficulty in swallowing a tablet or a capsule. In a typical liquid formulation, the new drug is dissolved in water, or other suitable vehicle, to form a clear solution. The new drug preparation may be rendered more palatable by means of various sweetening agents and flavors, and its appearance may be improved by the addition of coloring agents. Preservatives are usually added to prevent mould growth. Drugs for pediatric use are frequently supplied in the form of liquid preparations.

Solid drugs, with limited solubility in water, may be formulated as oral suspensions. The solid drug is dispersed in a finely divided state in a liquid vehicle. The vehicle in this case may contain sweetening agents, flavors, coloring agents and preservatives, as well as suspending agents. The function of the suspending agent is to prevent the finely divided particles of the drug from settling to a solid cake during storage, and to hold the particles in homogeneous suspension during administration. Some of the sulfonamides are formulated as oral suspensions.

If a new drug has to be administered by injection, it may be dissolved under aseptic conditions in a liquid vehicle to form a clear solution. The vehicle may consist of water, buffers, solubilizers, preservatives, and other ingredients with separate functions. Special precautions must be taken to prevent the formulation of pyrogens. A satisfactory method of sterilization has to be worked out for each solution. Provided the solution will withstand heat, it may be autoclaved. Otherwise, the solution has to be passed through special filters designed to remove bacteria and other living organisms.

When a solid drug has a limited solubility in water, it may be formulated as a sterile suspension. The solid drug may be dispersed under aseptic conditions as a finely divided sterile powder in a sterile liquid vehicles. The liquid vehicle in this case will usually contain suspending agents as well as buffers, preservatives, and other ingredients. Procaine penicillin suspension for injection is a typical example.

The new drug preparations formulated by Pharmacy Research usually consist of one, or more drug substances mixed with other ingredients. These other ingredients, called pharmaceutical necessities, are required for the successful formulation and stabilization of the new drug preparation. They include antioxidants, preservatives, coloring agents, flavors, diluents, emulsifying agents, suspending agents, pharmaceutical solvents, and other agents. A pharmaceutical necessity must meet a definite standard of composition, strength, purity, quality, or other property. Some of these standards are set forth in the Canadian Formulary, The British Pharmacopoeia, the United States Pharmacopeia, the National Formulary, and other compendia listed in the Food and Drugs Act.

Stabilization of New Drug Preparations

After the new drug preparation has been formulated, it is examined for the presence of physical and chemical incompatibilities, or other signs of instability. For this purpose, the new drug preparation is exposed for prolonged periods to the extreme conditions of temperature, humidity, light, air, shock and vibration which may be encountered in the manufacture, transportation and storage of the product.

Some of the problems which come to light during the stability studies on a new drug preparation will now be considered. If tablets are not properly formulated, they may split, crack, soften, harden, or bloom. Capsules may dry out and crack, or the contents may liquefy, or harden. A clear solution may undergo a change in color, develop a foreign odor, or give rise to a sediment. The solid particles in a liquid suspension may settle to form a solid cake. The oily droplets in an emulsion may coalesce and rise to the surface to form a separate layer. The active ingredient, added flavor, or coloring agent in an oral liquid may be sensitive to heat, light, air, or other environmental condition.

If problems arise in the stability studies conducted on a new drug preparation, they have to be investigated. For example, the reaction product of a chemical incompatibility may have to be isolated and identified. To eliminate the incompatibility, the new drug preparation may have to be reformulated, and subjected to further stability studies. Buffers, antioxidants, preservatives, or other ingredients may have to be added to stabilize the formulation. The container may also affect the stability of a new drug preparation. The possibility of a reaction between a parenteral solution and the glass vial, or rubber closure, which comes in contact with it, has to be considered.

When the stability studies on a new drug preparation are complete, manufacturing instructions are prepared. These instructions list the ingredients of the new drug preparation, the order of addition, the processing operations, and the precautions to be observed to ensure a quality product. Raw material and finished product specifications are drawn up in collaboration with Quality Control to complete the work of Pharmacy Research in the formulation and stabilization of the new drug preparation.

The initial batch of the new drug preparation is then produced by Pharmaceutical Manufacturing. Its identity, potency and safety are thoroughly checked by Quality Control. Provided the new drug preparation proves to be safe and therapeutically effective in clinical testing, a new drug submission is filed with the Food and Drug Directorate. If the new drug submission complies with the requirements of the Food and Drug Directorate, the new drug preparation may then be sold, subject to the provisions of the Food and Drugs Act and Regulations. It is then ready for full-scale production by Pharmaceutical Manufacturing.

PHARMACEUTICAL MANUFACTURING

by George C. Shannon, B.Sc.

An authority on the intricacies of manufacturing pharmaceuticals, Mr. Shannon is Director of Manufacturing, Parke, Davis & Company Ltd., Brockville. He graduated first with a B.Sc. in chemical engineering in 1932 and then with a B.Sc. in chemistry in 1934, both from Queens University. Mr. Shannon has more than 28 years' experience in pharmaceutical manufacturing.

The manufacture of quality pharmaceuticals, as practiced by the member firms of our Association, is of necessity one of the most exacting manufacturing operations carried on in Canada. Many of the end products are either taken orally by humans or are injected in their bodies.

From the briefs previously submitted to this Committee the members will recognize the importance of teamwork by all concerned in carrying a drug product from basic research through to the end product. At the manufacturing stage we are producing in quantity the product that will eventually be prescribed by the physician, dispensed by the pharmacist and consumed by the patient.

The team at the manufacturing stage must be headed through all phases of manufacturing by persons with professional training. It is essential that these supervisors have degrees in Pharmacy, Chemical Engineering, Chemistry or Bacteriology or their equivalent. These persons are the watchdogs of all processing.

The processors or workers who do the actual labour of compounding should be above average in intelligence and preferably have several years of high school education. Often they must learn to use complex equipment and follow detailed instructions during the course of their work. There are many ground rules of good manufacturing practice they must learn before they are considered to be satisfactory workers.

Continuous education of staff is most important and is carried out by the job training and group instruction methods. Some of the more important principles we instil in all our employees are that they must take time to be right, they must be eternally vigilant, and should an error be made in their work they must immediately report it to their superior. This last point is keenly stressed because the hiding of an error could endanger many lives.

Education in manfuacturing practices is important because even a small change in procedure at one point in a process, though seemingly minor, may change equipment required, method used and conditions further on in the process.

We as manufacturers consider quality and safety in the end product as the vital factor. To provide this quality and safety requires extreme care and checking through all phases of manufacture which to the layman might appear to be painstaking and over cautious.

To describe in every detail each manufacturing method would take many days. I shall describe for you the general procedures followed by all manufacturers, emphasizing the various checks needed to insure the safety of the drug. In our various companies we use different titles for departments, personnel etc., but the end results are the same. I would request that you extract from your copies of this submission Charts 1 and 2 which follow this paper, so that you may study by outline.

1.0 *Sales Forecast* The sales department through a sales forecast is usually the starting point of our cycle. They tell production how much of a product they need and when. After a product is established, sales history tells production when they need to manufacture the product.

2.0 *Pharmacy Research* It has been explained to you how manufacturing instructions and specifications for every product are set up by pharmacy research with the assistance of many departments. The master card is held by this department. When a batch or lot is requested by the Inventory Control Division of manufacturing, as a result of a sales forecast, an exact duplicate of the master card is prepared. The duplicate will differ from the master in only one respect: it will have a batch or lot number that will identify it from any other card for the same product or any other product. A general example is shown in Chart 1.

3.0 This card will represent all the instructions, list of materials, material requisition tickets or orders, required to provide the actual materials used in the manufacture of the product. Each material ticket will carry the batch number and identify the particular material to be used. The batch number is listed in a register which gives the number, the title of the product and the quantity to be manufactured. Copies of the register are distributed to all production departments and are used for checking purposes throughout manufacturing.

3.1 The materials specified by the batch card are assigned by the material control section. Some cards may require ten or fifteen different items, others only one or two. Requisitions are sent to the Purchasing Department to obtain the various materials. The requisitions will carry the stock number, standard title, specifications and quantity of the materials required.

3.2 Purchasing will order the materials according to strict standard specifications from one or many recognized suppliers.

3.3 When the materials are received, each material is given a receiving number which identifies that particular shipment of the specific material. This number, the title, the quantity received and the supplier's name become part of the receiving number register. Copies of this register are circulated to all production departments to be used in checking procedures during manufacture. The materials are isolated in a quarantine area which is separate from other stores of materials. A control checker samples the containers in accordance with definite procedures laid down by the Quality Control Department.

3.4 The samples, along with an analytical request containing all data pertinent to the shipment are sent to the analytical section of Quality Control for analysis according to specific procedures. Should the shipment be rejected it is returned to the supplier with the details.

3.5 When approved, the material involved is released for production use and Quality Control authorizes Material Control Section stores to place the lots received in regular stores.

3.6 The Material Control Records Section now has all the materials required to manufacture the batch. The clerk proceeds to deduct the materials from her records and enter the specific receiving number for the specific material on each ticket printed with the batch card which shows the quantity required.

3.7 When all tickets have been deducted they are sent to Material Control Stores for dispensing along with a summary sheet. The summary sheet has also been printed from the master card; it carries the batch number and lists only the titles of the various materials required. The batch card itself is sent directly to the Manufacturing Department office.

When the material tickets are received in Material Control Stores the control checker checks the receiving number on each material ticket against the receiving number register for accuracy and then they are given to a dispenser. Each ticket for each material is processed separately. The dispenser with his control checker goes to the material containers and each identifies the material from the title and the receiving number which is on the container and also on the ticket. The material is taken to the dispensing area and is

checked for identity by the checker. The dispenser measures the quantity required which is put in suitable containers which are labelled from the title on the original container. The checker checks the measure dispensed and also the label written out by the dispenser for accuracy.

The material ticket has many "boxes" for signature to record the various operations. The dispenser signs for putting up the material and the checker signs the ticket for checking on the original container, checking the identity and checking the measure. The signed material ticket is attached to the container holding the specific material. The material is checked off on the summary slip and assembled in a batch card unit container which will hold all the materials and only the materials for the specific batch. The same procedure is followed until all materials have been dispensed and checked and placed in the isolated container.

The materials for the batch are now ready to be delivered to the manufacturing department materials area.

4.0 The Manufacturing Department now has the batch card and the materials needed to produce the product. They also have received a production schedule for this product from the planning section of the Inventory Control Department. There are, however, some preliminary operations required before actual manufacture can begin.

5.0 A control checker in the Manufacturing Department takes the batch card to the materials area and checks the information on each material ticket against the label on the container. He assures himself that all the materials are there, that all tickets show the same batch number as the batch card and that the receiving number on each material container agrees with the receiving number on the material ticket. As he checks each material ticket he also sees that the measure specified on the ticket agrees with the measure specified opposite that material on the batch card. He then enters the receiving number on the batch card opposite the proper material. When all the items have been so listed he takes the card to the receiving number register and looks up each number to be certain that the title on the register agrees with the title on the card. He then signs the material tickets for checking in the materials and places a tick mark in the column to the left of the receiving number on the face of the batch card (Chart 1). The batch card is ready for actual manufacture when the production schedule indicates it should be started.

6.0 When the actual manufacture is started, the batch card is handed to a processor who goes to the material area and brings the materials to the work area. The processor takes each material from the isolated unit container and arranges them in the work area. The processor is not allowed to have any materials from any other batch card in the same work area.

6.1 The processor calls a control checker who thoroughly inspects all the equipment the processor is to use to be certain it is clean and free of contamination.

6.2 When approved, the processor will weigh or measure the first ingredient to be added according to the instructions and the control checker checks the ingredient for identity, agreement of title and measure with the material ticket and the batch card. He also places a tick mark in the column to the left of the quantity column on the card face. At the time the processor adds the material to the manufacturing container he places a tick mark in the column at the far left of the batch card (Chart 1).

7.0 This procedure is followed through the various steps of the process, the processor ticking off on the instructions at each step as he completes it. The control checker signs each material ticket as he clears it for use and verifies its addition to the mix.

7.1 In many processes it is necessary to have the progress of manufacture checked by the analytical section of Quality Control. When the instructions so state, a suitable sample is taken, labelled, checked by the control checker, and submitted to the manufacturing office, where a supervisor writes on the back of the batch card the test required and sends the card and sample to the analytical section. The test is run and results are entered on the back of the card. If adjustments must be made, they are so specified. If the test is satisfactory, the card is returned to the Manufacturing Department allowing processing to continue. Some batch cards require several checks of this nature and others only one.

8.0 At the end of the instructions, the final yield is checked by the control checker and both the processor and the control checker sign the record section of the card. Samples of final yield are taken, labelled and checked and submitted to the manufacturing office with the batch card.

8.1 The manufacturing supervisor checks all card records and material tickets and as he checks the latter places a tick mark in the column at the right hand side of the card (Chart 1). The sample for final assay is sent to analytical as described above; if adjustment is needed it is specified on the card; if the tests are satisfactory the card is returned to manufacturing. The final control sample with the batch card is then submitted to the Control section with a request for approval for packaging. The approved card is returned to the manufacturing office, office records are up-dated in manufacturing and the supervisor signs a release tag which physically travels with the batch to the Packaging Department.

9.0 The Packaging Department has been performing several preliminary operations while manufacturing has been going on. The planning section of Inventory Control was notified the day manufacture began. In turn, the planning clerk has issued a packaging card which carries the lot number, the batch card number and specifications for the quantity and size of the finished package or packages. The lot number is the final number that appears on all final labels and the packaging card correlates this with the batch number with which we have operated to this point.

9.1 One of the first operations is to procure and have available the proper labels for the product. The label checker checks the batch number on the packaging card with the batch number register for agreement. She indicates in the card how many labels are required. A label room clerk is given the packaging card. The clerk counts from bulk label stores the correct number of the specific labels, allowing a definite excess. The clerk records her name for counting the labels. The lot number is set up in type and checked by the checker against the lot number on the packaging card. The labels are run through the printing equipment which imprints each label. The labels are given to the label checker who recounts the labels, and signs for checking.

The counted labels are placed in a separate container to await actual packaging. Should labels be spoiled during packaging, a control checker can obtain additional labels and the same checking procedure is followed as above. Control of the number of labels is most important to be certain that a loose label is not mixed with the labels of some other product. All unused labels are accounted for, counted and are sent back to label stores for destruction.

9.2 The packaging card is returned to the packaging office and requisitions are placed with packaging stores for bottles, caps, outer cartons, shipping packers etc.

9.3 When all these materials are ready in the specific work area in the packaging department, a control checker will inspect the equipment to be used for packaging; he will inspect the labels and transfer ticket for the bulk batch itself for identity. He will record his name for checking, as have all other persons having anything to do with the product previously. A check bottle identified by the bulk batch number as well as the package lot number is filled to act as a guide for all personnel on the line during the production run. This bottle is checked for accuracy of label, measure, label placement and general appearance before filling is started.

10.0 The packaging operation is begun and a control checker makes periodic checks to see that the product is being filled in accordance with specifications. Each packaging operator is trained to be a checker in his own right. Everyone is looking for any variation from the standard.

11.0 When the run is complete all packaging operators and checkers sign the packaging card in the record section. The card with final samples is sent to Quality Control for final control approval. Inventory Control Department is advised of the final yield and update their stock records.

12.0 Upon final approval by Quality Control the finished lot is sent to Finished Stock.

Description of the above operations is necessarily detailed and is rather difficult to put into words in general terms. It does indicate the exactness of all operations.

There are three main principles that are followed throughout.

1. Permanent records of every operation provide a continuous chain of events, personnel concerned, and assays from the beginning through to final approval. At any time we can follow the line right back to the supplier of any single ingredient that was in the formulation.

2. The principle is followed that it requires two persons to check every transfer of material or every addition of material to a batch. When material is taken from one container and placed in another, there is always a double check.

3. The person maintaining records is not the same person who does the dispensing, and the person who reviews the records does not do the work. There is separate maintenance of records and final inspection.

There are other phases of our operations, which require in addition to the above procedures, special handling, such as Narcotics and Controlled Drugs which are subject to review by the narcotic auditor of the Department of National Health and Welfare at regular intervals.

Another operation requiring special attention is the manufacture of sterile products. These are produced by trained personnel in special rooms which are supplied with purified air under positive pressure. The rooms and equipment are thoroughly cleaned and sterilized after each manufactured lot. Everything that enters the rooms, except the personnel, enters only through the autoclave after sterilization. The personnel wear sterile gowns, masks, gloves, and foot coverings and must enter the room through an air lock. Continual checks of the rooms and equipment are made and records kept of the results of these tests. The whole sterile area and its procedures are subject to approval by the Laboratory of Hygiene of the Department of National Health and Welfare for products covered by Division 3 & 4 Part C of the Food and Drug regulations. The manufacture of all parenteral drugs are prepared under these same conditions.

The equipment used for producing parenteral and other ethical pharmaceutical preparations must be selected with care. In many cases the pharmaceutical manufacturers have made suggestions to equipment suppliers to correct some factor of construction that would present a contamination hazard. In many cases ordinary stainless steel is not satisfactory for constructing equipment in our field. We must often specify stainless steel alloys which are more inert to reaction with the ingredients of our various formulae.

Equipment maintenance in our field is most exacting. Our maintenance personnel must be trained to follow methods that conform with our quality control procedures. Machine bearings cannot drip oil that might drop in the product. This might be all right in a machine shop or an equipment parts plant, but not in a pharmaceutical plant.

Plant housekeeping and sanitation are of prime importance. Maintenance of a clean and orderly plant is most necessary to the production of quality pharmaceuticals.

Because of the care necessary in the manufacture of our products our staffs must be composed of persons with better than ordinary educational backgrounds. Because of our exacting checking procedures we require proportionally more indirect and clerical personnel than other manufacturers. I believe you will agree that pharmaceutical manufacturing is in a class apart from the usual.

INSERT CHART I—

BATCH NO.

PRODUCT TITLE

YIELD

✓	INGREDIENTS	✓	QUANTITY	✓	NUMBERS	✓
	Material A					
	Material B					
	etc.					

Records

Materials checked by

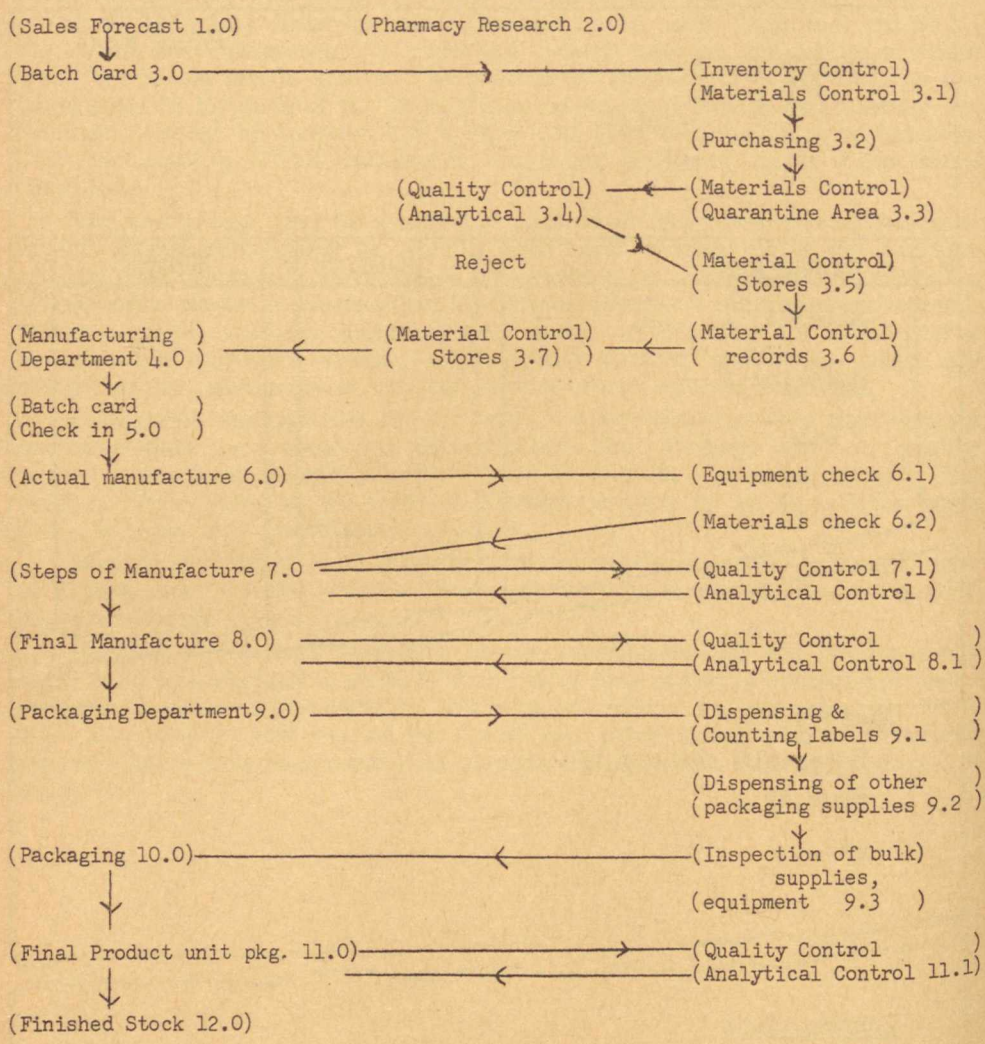
Made by

etc.

Instructions

Quality Control Records
Analytical Records

INSERT CHART II—



ANALYTICAL DEVELOPMENT AND END PRODUCT CONTROL

by Arthur D. Grieve, Ph.D.

Considered Canada's foremost authority on quality control procedures in the field of pharmaceuticals, Dr. Grieve is Director of Quality Control, Ayerst, McKenna & Harrison Ltd., Montreal. He graduated with a B.A. in chemistry from the University of Western Ontario in 1929, following which he achieved his Ph.D in chemistry from McGill University in 1932. Dr. Grieve joined Ayerst, McKenna & Harrison Ltd. in 1932 and was appointed Director of Quality Control in 1947.

This section will describe the function of the Quality Control Department in our industry. It will deal with these functions under two headings:

(1) Analytical Development, which is the development of analytical methods and specifications for a New Drug substance and its dosage forms.

(2) End Product Control, which consists of the application of these specifications and methods to the control of the identity, potency, purity and safety of new (and old) drugs when they reach the stage of routine manufacture for the market.

1—Analytical Development

When a New Drug substance has been developed by the Research Department and found to have interesting physiological action, it is prepared in dosage forms (such as tablets, capsules, injections) for clinical trial in the manner which has been described in other sections of this brief. Before these dosage forms can be prepared and released for clinical trial, it is necessary to establish specifications and analytical methods by which these specifications can be enforced for the New Drug substance and the dosage forms which are to be tried. For this purpose use is made of the physical, chemical and physiological properties of the New Drug substance.

Most compounds have characteristic melting points, color, the ability to absorb light of a characteristic wavelength, either in the visible, the ultraviolet or the infrared regions of the spectrum. Some have characteristic crystal forms, others will fluoresce when exposed to ultraviolet light. These and other similar properties provide the basis for the analytical methods needed to determine the potency and purity of the compound. They also help to define its safety. When additional determinations for safety are needed, the drug substance can be administered to experimental animals to determine if its toxicity is within normal limits.

Using the methods described above, specifications are established to define the identity, potency, purity and safety of a New Drug substance. These specifications and methods are then used to ensure that each lot of a New Drug substance conforms to the desired standards.

The dosage forms made from such a New Drug substance must also be controlled for identity, potency, purity and safety. The same physical, chemical and biological properties can be used as were used in controlling the New Drug substance itself.

The problem is more complicated in the case of dosage forms, however, because in their manufacture it is necessary to add inert ingredients, such as diluents, binders, flavorings, etc. Many of these interfere with the methods which worked successfully on the pure compound. It is therefore necessary to devise methods of isolating the drug substance from the inert materials which it has been necessary to add in order to make it into a platable and convenient

preparation. Sometimes this isolation can be achieved by means of relatively simple extractions, using water or some organic solvent, such as alcohol, ether or chloroform. At other times more elaborate procedures are necessary. Fortunately, in the last few years many new instruments have been devised which greatly assist the analyst in carrying out such separations.

When the separation of a New Drug substance has been achieved, it is possible to apply one or more of the analytical methods referred to above, for the determination of identity, potency and safety of the dosage form.

2—End Product Control

After the analytical development phase has been completed, the clinical trials conducted and the New Drug Submission prepared, filed and approved, as has been described in previous sections of this brief, the product is now ready for the manufacture for sale. What is contained in this section will describe the procedures used in controlling the manufacture of such a New Drug product, but the same procedures are also used with any drug product whether new or old.

Before proceeding with the manufacture of a batch, specifications are re-examined for all of the ingredients of the product, whether they be active drug substances or inactive diluents, binders, flavoring, etc. Purchases of these materials are made against the specifications established. When the shipments are delivered by the supplier, each shipment of each material is sampled, and tested by the various analytical methods referred to in the section on Analytical Development. If each lot of raw material is found to be satisfactory, it is released for manufacturing use and the batch is prepared in the manner described in the section on Pharmaceutical Manufacturing.

When the batch is completed, samples of it are submitted to the Quality Control Department for testing. They are tested for conformity to the specifications which have been established for this dosage form, using the methods which were developed as described in the section on Analytical Development. By this means it is possible to determine that the product will conform to label claim and identity, that it is pure and that it will perform its intended function when used according to the directions.

If the batch is found to conform to all specifications, it is released for packaging. After packaging and before the batch is released for sale, samples of the final packages are tested for identity to make sure that no mixup has occurred during the packaging operation.

With the release of the finished package the control of the product does not cease. It is normal practice to study the stability of drug products to make sure that they retain their potency and purity during normal shelf life. For this purpose samples of representative batches of each product are selected and stored under the normal conditions prescribed on the label (and sometimes under conditions of elevated temperature, humidity, etc.). These samples are re-examined and retested at appropriate intervals to determine if the product undergoes any change in potency or purity which would render it unsuitable or unsafe for use.

In such studies many products are found to be almost indefinitely stable, and therefore have for all practical purposes an unlimited shelf life—say, five years or more. Other products are found to undergo slow deterioration. When this is the case, an expiry date is established. This is stamped on each package. It indicates the date beyond which the product is not recommended for use.

All of these measures are designed to produce products which are true to labeled identity, which conform to the potency claims on the label and which are pure and safe at the time that the batch is released for sale. The stability

studies which have been described are designed to follow the behaviour of the product on the market and to ensure that it is suitable for use during a reasonable shelf life.

SUMMATION AND CONCLUSION

It will be seen from the foregoing that the art and science of pharmaceutical manufacturing is not a casual process. In fact, few other products in the general field of manufacturing must meet the exacting requirements which are the very foundation of the prescription drug. The medical science involved is such that the conditions of safety can be determined only by trained personnel in manufacturing, in medical practice, and in the Food and Drug Directorate. The field of drug safety is not one where the judgment of the uninformed layman has validity.

As was mentioned in the preamble to this submission, we respectfully submit that the decision for your Committee is to determine whether adequate safeguards now exist to ensure that the community at large is protected against unwarranted side effects, but is not prevented from access to required medication. The responsibility here is a heavy one, for an overly cautious approach to a lifesaving substance might well protect the general public against some adverse side effect, but it might also prevent a patient from having a medicament that is essential to his life.

Major scientific breakthroughs, such as penicillin and the sulfonamides, all have very serious effects on those who are allergic to these substances. It is a matter of medical record that some patients have died from these drugs as a result of such side reactions. Yet countless thousands more would have died had these products been withheld from medical use through legislative edict. It may be said, and rightly so, that withdrawal has not been necessary in these cases as a result of the recognition and knowledge of the side effects by the medical profession.

If we as a nation become overly restrictive in our medical legislation, and attempt to replace the knowledge of the medical profession with too restrictive government controls, we may well keep from the market the sulfonamides, penicillins and cortisones of tomorrow. Dramatic though this may seem, we must nevertheless recognize the fundamental principle that science and medicine can only thrive in a comparatively unfettered climate. If we bind too tightly the hands of our researchers, scientists and manufacturers, the result will be a loss of initiative, incentive and willingness to risk experimentation. The ultimate loser will be the patient who is now suffering from an ailment or disease for which medical science has not as yet found the answer.

Profound knowledge, judgment and integrity are required to determine at what time and under what circumstances a drug should be withheld from the practice of medicine. While the burden of this decision is being shared to an increasing degree by the Food and Drug Directorate, the pharmaceutical manufacturing industry must still bear the major responsibility for balancing on the one hand the need for public protection and on the other the need for the continuing progress essential to new discoveries.

It is evident from the individual papers contained in this submission, that Canada's pharmaceutical manufacturers are aware of this responsibility, and that every effort within the limitations of modern science is being made to ensure drug safety at the company level. The required balance between efficacy and toxicity is well considered from both the medical and scientific standpoints. It is also apparent that careful standards have been developed and are being implemented in manufacturing and control.

As the focal point for industry action in the area of drug safety, our Association is striving to meet the increasing demands of what has become our new era of pharmaceutical development. Through conjoint effort by specialists from our companies, we:

—have spent considerable time and effort to assist the special committee of the Royal College of Physicians and Surgeons during its investigation into the safety aspects of new drugs;

—are continuing to co-operate with the Food and Drug Directorate in developing new drug regulations and other safety precautions;

—are establishing a special Recall Service to provide a prompt and effective means of recalling pharmaceutical products which must be withdrawn from medical use;

—have taken concrete steps, through establishment of the Canadian Foundation for the Advancement of Therapeutics, to improve and refine the methods of evaluating drugs in Canada;

—will continue to work through the various Sections within our Association to disseminate general information and that covering new procedures which have a bearing on drug safety at the company level.

We submit that our domestic pharmaceutical manufacturing industry is indeed working in the best public interest in ensuring Canadians of the newest and most effective medication available, consistent with medical safety.

By the same token, Canada's regulatory agency, the Food and Drug Directorate, has established the legal and procedural methods needed to ensure the degree of safety required to protect the public interest. It is our understanding that the details involved are documented in your Committee's records. A study of the regulations now in effect under the facilities of the Directorate indicates clearly that we have now reached the demarcation line between public safety and limitation of scientific endeavour.

It is essential to drug safety, however, that the government maintain a record of all those engaged in manufacturing and/or distributing pharmaceuticals in Canada. To achieve this objective, we recommend that the Food and Drug Directorate be enabled to institute a form of certification or registration of manufacturers, distributors and agents as a prerequisite to doing business in this country.

Finallly, we submit that adequate safeguards now exist in Canada in relation to the original drug products discovered and manufactured by the members of the Canadian Pharmaceutical Manufacturers Association.

Respectfully submitted,

'CANADIAN PHARMACEUTICAL
MANUFACTURERS ASSOCIATION.

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APPENDIX A

TRADE NAME

TRILAFON
INJECTION

Perphenazine

Description

Trilafon Injection is perphenazine, an extremely potent tranquilizing and antiemetic drug.

Indications

Parenteral administration of Trilafon is indicated when a more rapid tranquilizing effect is required than is obtainable with oral administration or when oral medication is not feasible; i.e. as in uncooperative patients or in those unable to retain orally administered drugs. Trilafon Injection is indicated as initial therapy or in the treatment of acute episodes in agitated mental and emotional disturbances, including psychoses, manic states, catatonic excitement, hysteria, senile dementia, panic reactions and acute behavioral problems in mental defectives; acute alcoholism, nausea and vomiting due to various causes; obstetrics; hiccoughs; chronic pain and severe pruritus. The tranquilizing and antiemetic effect of Trilafon Injections are also valuable in surgery.

Action

Trilafon Injection possesses rapid tranquilizing and antiemetic actions. It is effective in alleviating symptoms of anxiety, tension, psychomotor excitement and other manifestations of emotional stress. Trilafon Injection is also highly effective in the symptomatic control of nausea and vomiting due to various causes. Following intramuscular administration of Trilafon Injection a therapeutic effect is evident within 10 minutes with a maximum effect in 1 to 2 hours. The average duration of action of a single dose is 6 hours. Trilafon Injection is more potent, milligram for milligram, than Trilafon Tablets. Therefore an equal or higher dose of Trilafon Tablets is required when a patient is transferred to oral therapy. Side effects with intramuscular Trilafon have been infrequent and transient. Although seen in some cases with lower dosage, extrapyramidal symptoms have been observed more frequently at dosage levels above 15 mg. daily. However, these symptoms are not necessarily seen even when very high dosage, well above the 30 mg. daily suggested limit, is used. These extrapyramidal manifestations have disappeared within 48 hours after a decrease in dosage or withdrawal of the drug. Anti-Parkinsonian drugs have been used concomitantly in some hospitalized patients to control these symptoms. Paradoxical excitement may rarely be seen. Mild or moderate drowsiness has been observed in some patients treated with Trilafon Injection.

Advantages

Trilafon provides a favorable therapeutic ratio. It has a parenteral milligram potency much greater than other phenothiazine compounds without a corresponding increase in autonomic, hemotologic or hepatic side effects. Smaller doses are therefore required both in patients under treatment with older drugs and in those not previously treated. The degree of adrenergic blockage with

Trilafon Injection is considerably less than may be encountered with certain other phenothiazine tranquilizers. Thus significant hypotension has rarely been reported. Deep intramuscular injection is extremely well tolerated; no local reactions, including pain at the side of injection, have been reported. Neither agranulocytosis nor jaundice has been reported with Trilafon Injection.

Administration and Dosage Intramuscular

The dosage of Trilafon must be adjusted to the individual requirements of each patient; i.e., the severity of the condition and the response obtained. As with all potent drugs the lowest dose that will produce the desired effect should be used. The usual initial dose is 5 mg. (1 cc.). This may be repeated every six hours. The total daily dosage should ordinarily not exceed 15 mg. in ambulatory patients or 30 mg. in hospitalized patients. When required to achieve satisfactory control of symptoms in severe conditions an initial 10 mg. intramuscular dose may be given. Intramuscular injection should be given with the patient seated or recumbent and the patient should be observed for a short period after administration. Dizziness or significant hypotension after Trilafon Injection is a rare occurrence. Patients should be placed on oral therapy as soon as practicable. Generally this may be achieved within 24 hours. However, in some instances patients have been maintained on injectable therapy for several months. It has been established that Trilafon Injection is more potent than Tablets. Therefore, equal or higher dosage should be used when patient is tranferred to oral therapy.

Mental and emotional disturbances: While 5 mg. of Trilafon intramuscular has a definite tranquilizing effect, it may be necessary to use 10 mg. doses to initiate therapy in the more severely agitated states. Most patients will be controlled and amenable to oral therapy within a maximum of 24 to 48 hours. Acute conditions (hysteria, panic reactions, etc.) often respond well to a single dose whereas in the more chronic conditions several injections may be required. When transferring patients to oral therapy it is suggested that increased milligram dosage be employed to maintain adequate clinical control. This should be followed by gradual reduction to the minimal effectve maintenance dose.

Acute Alcoholism: Trilafon Injection is indicated in the agitated withdrawal phase and in delirium tremens. The initial intramuscular injection of 5.10 mg. (1.2 cc.) may be followed if necessary by 5 mg. after 6 hours before transfer to oral medication. Surgery: Trilafon Injection may be employed in adult surgical patients to relieve anxiety and apprehension, and to prevent or control nausea and vomiting. Intramuscular administration of 3.75-5.0 mg. ($\frac{3}{4}$ to 1 cc.) approximately one hour prior to surgery and repeated at six hour intervals for one to three doses thereafter will reduce the incidence of vomiting and help to bring about a smoother, more comfortable postoperative course. Although significant hypotensive action or potentiation of depressant drugs ordinarily are absent or minimal when this dosage is employed, the possibility of such effects should be kept in mind.

Nausea and Vomiting: To obtain rapid control of vomiting administer 5 mg. (1 cc.); in rare instances it may be necessary to increase the initial dosage to 10 mg. In general, higher dosages should be given only to hospitalized patients.

Obstetrics: When active labour is established, 5-10 mg. of Trilafon Injection intramuscularly may be given. Analgesic and/or sedative drugs or scopolamine, 0.4 mg. (1/150 grain) may be administered concomitantly if desired. Some investigators when using a 10 mg. dose of Trilafon have found it possible to reduce the amount of narcotic-sedative drugs. Repeated doses of Trilafon Injection ordinarily are not required. An additional 5 mg. may be administered after 6 hours if necessary.

Hiccoughs: A single intramuscular dose of 5-10 mg. will generally abolish hiccough in from ten minutes to one hour. In particularly resistant cases it may be necessary to repeat Injection once or twice at 6 hour intervals.

Chronic pain: The usual 5 mg. dose of Trilafon exerts only slight potentiating effect on narcotics. However, the tranquilizing action of Trilafon makes patients less reactive to their symptoms, thus decreasing the need for full therapeutic doses of depressant drugs.

Severe Pruritus: Single dose of 5 mg. administered intramuscularly is suggested. This may be repeated in six hours if necessary. Patients can be maintained on Trilafon Tablets after severe symptoms are controlled.

Pediatric dosage has not yet been established. Children over 12 may receive the lowest limit of adult dosage.

Administration and Dosage Intravenous

Intravenous administration is not recommended except when absolutely necessary to control severe vomiting, intractable hiccoughs, or acute symptoms such as violent retching during surgery. Its use should be limited to recumbent hospitalized adults in doses not exceeding 5 mg. When employed in this manner, intravenous injection ordinarily should be given as a diluted solution using either fractional injection or a slow drop infusion. Blood pressure and pulse should be followed continuously during intravenous administration. Intravenous nor-epinephrine should be available in the event of a significant blood pressure drop. In the surgical patient, slow drip infusion of not more than 5 mg. is preferred. When fractional administration is used, Trilafon Injection should be diluted to 0.5 mg./cc. (1 cc. mixed with 9 cc. of physiologic saline solution), and not more than 1.0 mg. per injection given at not less than one to two minute intervals. Intravenous injection should be discontinued as soon as symptoms are controlled, and should not exceed 5 mg. The possibility of hypotensive and extrapyramidal side effects should be considered and appropriate means for management kept available.

Important

Side effects with intramuscular Trilafon have been infrequent and transient. Extrapyramidal effects occur with increased frequency at dosage levels above 15 mg. per day, but are not necessarily seen even when very high dosage well above the 30 mg. per day suggested limit are used. These effects, which in some respects resemble the Parkinson syndrome, have been abolished by reduction of dosage or administration of benztropine methanesulfonate. These effects have disappeared spontaneously in less than 48 hours following withdrawal of Trilafon. Paradoxical excitement may rarely be seen. This may be accompanied by tachycardia, an increase in blood pressure and contractions of the shoulder girdle or limb muscles in some instances. The drug should be discontinued and sedation with barbiturates instituted in such cases. Isolated instances of muscle spasm have occurred and have been controlled by benztropine methanesulfonate or withdrawal of the drug. Mild autonomic effects such as dizziness, dryness of the mouth or blurring of vision have been reported infrequently. These generally subside promptly and do not require treatment. Mild or moderate drowsiness has been observed in some patients treated with Trilafon Injection. The degree of adrenergic blockage with Trilafon Injection is considerably less than

may be encountered with certain other phenothiazine tranquilizers. Thus significant hypotension has rarely been reported. Agranulocytosis or jaundice has not been reported with Trilafon Injection.

Precautions

Patients receiving Trilafon Injection should be under observation and the drug should not be used indiscriminately. Trilafon is an extremely potent anti-emetic agent and may obscure the diagnosis of such conditions as brain tumor, drug intoxication, intestinal obstruction. The dosage of barbiturated or other anticonvulsant medications should not be lowered in epilepsy or convulsant states. Though hepatic and hemopoietic side effects have not been observed with Trilafon Injection the possibility of their occurring cannot be excluded since Trilafon is a phenothiazine compound. Significant hypotension has been rarely reported with Trilafon. However, as with other phenothiazines caution should be used when administering these drugs to patients with coronary disease or severe hypertension. A significant rise (above 101° F) in body temperature not otherwise explained may indicate drug intolerance, in which event the drug should be discontinued. Trilafon Injection should not be given to patients in coma or severely depressed states.

Packaging

Trilafon Injection (5 mg./cc), ampuls of 1 cc. boxes of 6 and 100.

TRADE NAME

Pr
CELESTONE

(Betamethasone)

Description

Celestone is betamethasone, a new synthesized derivative of prednisolone which possesses hormonal and metabolic effects common to all anti-inflammatory adrenacortical steroids but exhibits these effects in markedly different proportions. Celestone is available in tablets of 0.5 mg., scored for convenient fractional dosage.

Indications

Celestone is indicated in the management of various allergic, dermatologic, rheumatic, ocular and other conditions known to be responsive to corticosteroid therapy. Celestone is particularly recommended for patients who have shown a diminution in response to other anti-inflammatory corticosteroids and may be useful in those who have developed severe, incapacitating side effects on previous hormonal therapy. Representative conditions responsive to steroid therapy as repeatedly confirmed in the medical literature include: *Allergic Conditions*—bronchial asthma (including status asthmaticus), intractable allergic rhinitis, angioedema, transfusion reactions, drug and serum reactions. *Dermatoses with an Allergic Component*—atopic dermatitis, contact dermatitis, neurodermatitis, allergic eczema, exfoliative dermatitis, urticaria and derma-

titis herpetiformia. *Inflammatory Eye Diseases* (of posterior segment)—uveitis, chorioretinitis, sympathetic ophthalmia, iritis, iridocyclitis, retinitis centralis, herpes zoster ophthalmucus (not herpes simplex), optic neuritis and retrobulbar neuritis. *Collagen Diseases*—rheumatoid arthritis, acute rheumatic fever, disseminated lupus erythematosus, scleroderma and dermatomyositis. *Lymphomatous Neoplastic Diseases* (for remission). *Soft Tissue Conditions*—bursitis, synovitis and tenosynovitis. *Blood Dyscrasias*—idiopathic thrombocytopenic purpura and allergic purpura. *Miscellaneous Conditions*—adrenogenital syndrome, acute gouty arthritis, pemphigus, ulcerative colitis, nephrotic syndrome, pulmonary emphysema, pulmonary fibrosis, nasal polyps and Bell's palsy.

Action

The glucocorticoid activity of Celestone is approximately 2 to 5 times that of prednisolone. Although sodium retention is characteristically associated with older corticosteroids, Celestone has been found in these same animal studies to produce an increase in sodium excretion. In the clinical management of corticosteroid-responsive conditions, Celestone has significantly increased anti-rheumatic, anti-inflammatory and anti-allergic actions. Symptomatic relief with increased vital capacity is generally observed following the use of Celestone in status asthmaticus. Patients with chronic intractable asthma are usually maintained symptom-free on low dosages of Celestone. The anti-inflammatory and anti-allergic actions of Celestone have also proved valuable in the management of Pollenosis (intractable hay fever). Marked relief of symptoms is obtained, and therapy is usually not required for longer than 10 to 14 days.

In dermatologic and ocular disorders, Celestone promotes a rapid subsidence of inflammation, edema and allergy. In rheumatoid arthritis and associated conditions, relief of joint pain, stiffness, swelling and tenderness is usually evident within 24 to 48 hours following initiation of therapy. A sense of well-being and improvement in appetite are usually noted. In some instances, the relief obtained with Celestone has been superior to that seen with other corticosteroids. Lowering of elevated sedimentation rate and temperature and subsidence of joint and skin manifestations are also noted following institution of Celestone in patients with lupus erythematosus. It should be kept in mind, however, that a diversity of complications may be encountered in advanced cases.

Advantages

Celestone possesses certain advantages over older corticosteroids. It affords a greatly enhanced anti-inflammatory effect with the use of lower dosages, and certain undesirable side effects such as abnormal salt and water retention and excessive potassium excretion are not discernible in most patients receiving usual therapeutical dosages.

No new side effects have been observed with Celestone, and steroid effects associated with certain other cortocoids such as anorexia, protracted weight loss, vertigo, severe headaches and muscle weakness do not appear to be characteristic of Celestone. However, Celestone is a potent cortico-steroid and therefore is capable of producing certain effects associated with adrenocortical therapy.

Dosage and Administration

The dosage of Celestone must be determined and adjusted to the individual requirements of the patient, i.e., severity of the condition, anticipated duration of therapy, tolerance to the steroid and response obtained. As with all cortico-

steroids, the lowest dose that will produce the desired clinical effect should be employed. The following chart gives the average daily dosages for initiation of therapy and maintenance of response in the conditions described below:

	Daily Initial Dosage	Daily Maintenance Dosage
Status Asthmaticus	3.5 to 4.5. mg.	As required
Chronic Intractable Asthma	3.5 mg.	0.5 to 2.5 mg.
Intractable Hay Fever (Pollenosis)	1.5 to 2.5 mg.	As required
Allergic Dermatoses	2.5 to 4.5 mg.	As required
Inflammatory Eye Diseases	2.5 to 4.5 mg.	As required
Rheumatoid Arthritis and Rheumatic Disorders	1.0 to 2.5 mg.	0.5 to 1.5 mg.
Bursitis	1.0 to 2.5 mg.	As required
Pulmonary Emphysema and Fibrosis	2.0 to 3.5 mg.	1.0 to 2.5 mg.
Adrenogenital Syndrome	1.0 to 1.5 mg.	As required
Acute Rheumatic Fever	6.0 to 8.0 mg.	As required
Disseminated Lupus Erythematosus	1.5 to 3.5 mg.	1.5 to 3.0 mg.

Precautions

Although Celestone differs significantly in potency and electrolyte effects, it is a corticosteroid and hence is potentially capable of causing any of the reported side effects of other such compounds. The physician must weigh anticipated clinical improvement against the possibility of undesirable effects in certain conditions regarded as relative contraindications to steroid therapy.

As with other corticosteroids, recurrence of complications of peptic ulcer may occur during therapy with Celestone. When it is necessary to use steroid therapy in a patient with a history of ulcer, he should be kept under close observation for signs of adverse effect. The patient should also receive an adequate anti-ulcer regimen such as diet, rest, antacids, anticholinergics, etc. Patients without a history of ulcer who complain of gastric symptoms during therapy should xe x-rayed. Active, questionably healed, or suspected tuberculosis is usually an *absolute* contraindication. Corticosteroids have been used when confronted with life-threatening conditions which may be amenable to the combined use of steroids and appropriate anti-tuberculosis chemotherapy. Although hyperglycemia, glycosuria and increased insulin requirements usually do not occur with Celestone in the controlled diabetic patient, close observation should be maintained during therapy. In individuals exposed to, or in the active phase of, chickenpox or other exanthematous disease, it may be desirable to temporarily reduce or discontinue corticosteroid therapy. Herpes simplex of the eye is usually an absolute contraindication to the use of corticosteroids.

Packaging

Celestone Tablets, 0.5 mg., bottles of 30 and 100.

APPENDIX B

THE CANADIAN PHARMACEUTICAL MANUFACTURERS ASSOCIATION INCORPORATED

The Canadian Pharmaceutical Manufacturers Association was founded in 1914, and was incorporated under the Dominion Companies' Act in 1959. It represents 55 companies engaged in manufacturing and distributing ethical pharmaceutical preparations in Canada.

Membership in the Association is by company, and the categories comprise Full, Associate and Affiliate Member. Full Membership consists of companies which manufacture and distribute under their own names in Canada. Associate membership consists of companies which do not as yet manufacture in Canada, but which are subsidiaries of recognized and reputable corporations. When we introduced this system of membership in 1955, there were several companies in the Association which might be considered suppliers to the industry. These companies would not be eligible today, but we permitted them to retain membership in view of their many years of active participation in Association affairs. These firms come under the Affiliate category.

Quality Control

The most important single requirement for membership is proper quality control facilities. Our by-laws state in part that ". . . membership is open to firms which manufacture in Canada, under proper conditions for control of quality and standards, pharmaceutical preparations . . ." In the case of a non-manufacturing subsidiary, then the parent company must meet this requirement. In order to determine the company's qualifications in this respect, 11 of the 21 questions on our membership application form deal with quality control. These are:

10. State name and qualifications of person in charge of control.
11. State name and qualifications of person authorized to release finished products.
12. State number and qualifications of chemists in control department.
13. Broadly describe control laboratory and give approximate floor area.
14. List principal equipment in control laboratory.
15. Check type of laboratory analysis made: a. physiological, b. biological, c. chemical, d. bacteriological.
16. State whether each product batch is identified by code throughout manufacture and distribution.
17. State extent to which raw materials are analyzed to assure their integrity.
18. State extent to which finished products are analyzed to assure their integrity.
19. State extent to which products requiring biological tests are so examined, and state reasons for any omission of such tests.
20. Name those who do outside control work for you and describe it.

When these questions have been answered and submitted by the applicant, the form is then turned over to our Membership Committee for processing. Two

Directors are then required to visit the premises of the applicant to determine whether the statements made are correct. If the applicant does not meet these requirements, then he is not eligible for election to membership.

Ethical Responsibility

Applicants for membership are also required to sign an agreement that they will abide by the Principles of Ethics of the Association. These include:

1. The calling of a pharmaceutical manufacturer is one dedicated to a most important public service, and such public service shall be the first and ruling consideration in all dealings.
2. The pharmaceutical manufacturer must produce his preparations only under proper conditions and with scrupulous faithfulness to required standards of quality.
3. Preparations must be labelled and merchandised only in a manner free form misrepresentation, misleading practices of all kinds and in entire harmony with the highest standards of commercial morality and professional ethics.
4. Pharmaceutical manufacturers must constantly and conscientiously strive to advance the science and elevate the calling of manufacturing pharmacy to the highest plane of public value, to the end that it may best and most completely serve the medical profession and the public.

APPENDIX C

Canadian Pharmaceutical Manufacturers Association
Member Companies

Abbott Laboratories Ltd.

Ames Company of Canada Ltd.

Anca Laboratories, Div. of The Wander Co. of Canada Ltd.

Arlington-Funk Laboratories Division, U. S. Vitamin Corp. of Canada Ltd.

Astra Pharmaceuticals (Canada) Ltd.

Ayerst, McKenna & Harrison Ltd.

Baxter Laboratories of Canada Ltd.

Bristol Laboratories of Canada Ltd.

The British Drug Houses (Canada) Ltd.

Burroughs Wellcome & Co. (Canada) Ltd.

Calmic Limited

Canada Duphar Limited

CIBA Company Limited

Cyanamid of Canada Limited Medical Products Department

Fisons (Canada) Limited

Charles E. Frosst & Company

Geigy Pharmaceuticals Division of Geigy (Canada) Ltd.

Glaxo-Allenburys (Canada) Ltd.

J. F. Hartz Company Ltd.

Hoechst Pharmaceuticals, Div. of Canadian Hoechst (1964) Ltd.

Hoffmann-La Roche Ltd.

Frank W. Horner Limited

Ingram & Bell Limited

Lakeside Laboratories (Canada) Ltd.

Laurentian Laboratories Ltd.

Eli Lilly & Company (Canada) Ltd.

Mallickrodt Chemical Works Ltd.

May & Baker (Canada) Ltd.

McNeil Laboratories (Canada) Ltd.

Mead Johnson of Canada Ltd.

Merck Sharp & Dohme of Canada Ltd.

The Wm. S. Merrell Company, Div. of Richardson-Merrell Inc.

Mowatt & Moore Limited

Ortho Pharmaceutical (Canada) Ltd.

Parke, Davis & Company Ltd.

Penick Canada Limited

Pfizer Company Limited

Pitman-Moore, Div. of Dow Chemical of Canada Ltd.

Poulenc Limitee

The Purdue Frecerick Co. (Canada) Ltd.

Riker Pharmaceutical Company Ltd.

A. H. Robins Company of Canada Ltd.

Rougier Incorporated

Roussel (Canada) Limited

Sandoz Pharmaceuticals, Div. of Sandoz (Canada) Ltd.

R. P. Scherer Limited

Schering Corporation Ltd.

G. D. Searle & Co. of Canada Ltd.

Smith Kline & French Inter-American Corp.

Strong Cobb Arner of Canada Ltd.

The Upjohn Company of Canada

Henry K. Wampole & Company Ltd.

Warner-Chilcott Laboratories Co. Ltd., Div., Warner Lambert (Canada) Ltd.

Winthrop Laboratories

John Wyeth & Brother (Canada) Ltd.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 8

TUESDAY, JUNE 23, 1964

WITNESSES:

Mrs. A. F. W. Plumptre, National President of the Consumers' Association of Canada, Ottawa; and Dr. C. A. Morrell, Director of the Food and Drug Directorate, Department of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21031—1

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Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, June 23, 1964
(13)

The Special Committee on Food and Drugs met at 9.40 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Francis, Harley, Macaluso, Mackasey, Marcoux, Mitchell, Orlikow, Roxburgh, Rynard, Slogan, Whelan (12).

In attendance: Mrs. A. F. W. Plumptre, National President of the Consumers' Association of Canada; and Dr. C. A. Morrell, Director of Food and Drug Directorate, Department of National Health and Welfare.

The Chairman announced that the witness at the next meeting will be Dr. R. Imrie, M.D., Pediatrician, in charge of the Poison Control Centre at the Hospital for Sick Children, Toronto.

On motion of Mr. Francis, seconded by Mr. Armstrong,

Resolved (unanimously),—That this Committee pay reasonable living and travelling expenses incurred by Dr. R. Imrie of Toronto, by reason of his appearance before the Committee, and that a per diem allowance be made to him.

The Chairman introduced Mrs. Plumptre; before making her presentation, the witness commended the Committee for its report on Pesticides. She read a brief, copies of which had been distributed to the Members the previous day.

With regard to the last paragraph, Mrs. Plumptre referred to the proceedings of the second national congress on medical quackery in the United States.

She was questioned on the brief and produced, for the information of the Members, photographs and the prototype of a new kind of safety bottle.

Dr. Morrell was also questioned. He supplied information with regard to regulations about medical devices and gadgets for cures.

Mrs. Plumptre was further questioned.

The Chairman thanked her on behalf of the Committee, and at 11.00 a.m. the Committee adjourned to Friday, June 26, to hear Dr. Imrie.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

TUESDAY, June 23, 1964.

The CHAIRMAN: Gentlemen, we now have a quorum. We can start the meeting. Before we turn to Mrs. Plumptre, who is with us today, let me say that on Friday we are having Dr. Imrie before us. He is a paediatrician in charge of the poison control centre in the Hospital for Sick Children in Toronto. I would like a motion that his reasonable living and travelling expenses, by reason of his appearance, be paid, and that the usual per diem allowance be made to him.

Mr. FRANCIS: I so move.

Mr. ARMSTRONG: I second the motion.

The CHAIRMAN: All those in favour?

Motion agreed to.

The CHAIRMAN: Gentlemen, today we have Mrs. Plumptre with us. Most of us will remember Mrs. Plumptre from her last appearance, although she did not read the brief herself on that occasion. Mrs. Plumptre is the national president of Consumers' Association of Canada. She has presented a brief. Unfortunately, it arrived only yesterday. I doubt whether members have had a chance to read it, but it is a fairly short brief and probably it is a good idea to have Mrs. Plumptre read it.

Mrs. A. F. W. PLUMPTRE (*National President, Consumers' Association of Canada*): Mr. Chairman, before I start on this, may I make a remark which I hope is in order. I would like to commend this committee on the report on the pesticides section which we were delighted to see. We now hope it will be implemented.

On behalf of the Consumers' Association of Canada, I wish to thank you for the opportunity of appearing before this committee to discuss the safety of drugs. This has been a matter of great concern to our association for a number of years, and we welcome the investigation and examination which your committee is undertaking.

For the consumer, ethical drugs have a unique feature. In purchasing these drugs, the consumer is unable to exercise his usual consumer prerogatives. He is, instead, a captive buyer. He has no choice as to whether or not he should make the purchase. Indeed he has little or no knowledge of the drugs he is buying. He only buys these drugs in times of illness: the doctor orders the drugs and the consumer pays the bill. He makes these purchases because he has confidence in his doctor, and in his doctor's opinion of these drugs.

In addition to these ethical drugs, there is on the market a vast array of preparations which may be sold without prescriptions and in the case of those registered under the Proprietary or Patent Medicine Act, they may be sold in stores, other than licensed pharmacies. Although doctors do, from time to time, order these drugs for their patients, consumers may and do buy these drugs without prescription on the basis of their own desire and choice, and administer them without the supervision of their physician.

In regard to both these types of drugs, our association is concerned with their safety from two points of view—first as to the safety of the drug itself, and secondly as to the attitude of consumers regarding the consumption and handling of drugs.

I would like to say, before I deal with the safety of drugs, that we strongly recommend to our members—and this is a belief which we hold very firmly—that drugs in general are not safe unless they are administered according to the directions of the physician or the manufacturer. In this particular section I am dealing with the contents of the drug, but we do emphasize to our members that drugs in general are not safe.

Safety of Drugs

To begin with, a drug is safe only if it is pure, that is, if it does not contain any matter other than that stated on its formula: if its potency is also stated in that formula and on its label: if it is well-labelled at the time of sale to the consumer, and especially if it has been manufactured under procedures with careful quality control, so that its quality does not vary and meets the requirements of the formula in all respects. The responsibility for this type of safety must lie with the manufacturer. But to make sure that all drugs on the market are neither harmful nor fraudulently represented, government regulation is also needed. Consumers are fortunate in Canada in that both parties responsible for this safety—the Canadian pharmaceutical manufacturers and the food and drug directorate which administers the government controls—accept and carry out their responsibilities and ensure us a supply of safe drugs.

However, events in recent years have pointed up the dangers and unexpected hazards which may result from some of the new complicated drugs being made available and for that reason our association welcomed the amendments to the Food and Drugs Act as passed in December 1962 and the additional regulations and amendments to regulations passed in 1963. We are particularly pleased that this legislation

(*a*) gives the minister power to withdraw a new drug "where in his opinion it is necessary to do so in the interests of public health" (Regulation C08.006);

(*b*) regulates certain requirements for the facilities and controls to be used by anyone manufacturing drugs (both domestic and imported) in their final pharmaceutical form, (Regulation C01.051 to C01.056);

(*c*) limits the distribution of drug samples to specified professions and requires a record of distribution (Regulation C01.048 and C01.049);

(*d*) requires a "pre-clinical" submission from a manufacturer before a new drug may be distributed for clinical trial (Regulation C08.005).

Although these regulations if fully enforced will provide Canadians with better protection regarding drugs, we consider there are four aspects which allow gaps in this protection.

(i) It is still possible for a drug to be sold on the market in Canada without meeting any of the requirements of the Food and Drugs Act. We, therefore, ask that legislation be introduced which will require the registration of all drugs, both domestic and imported, which are sold on the Canadian market.

(ii) Legislation of any kind is only useful in so far as it can be fully enforced. It is our opinion that it is quite impossible for the food and drug directorate with its present limited staff to ensure full compliance with Food and Drugs Act and regulations. The need for more staff for this directorate has been a major concern of our association for a number of years. We drew this need to the attention of the government in 1960 and again in 1962 (at that time the inspection staff totalled 86).

The thalidomide tragedy in early 1962 alerted the public to the seriousness of this situation and this seriousness was emphasized by the opinion expressed by the special committee of the Royal College of Physicians and Surgeons of Canada that "due to the lack of personnel and increasing volume of work, the present staff (of the directorate) is inadequate to meet the demands placed upon it", and... "the responsibilities of the food and drug directorate are almost overwhelming at the present time, in the drug field alone, and that the demands made upon it far exceed its resources". We are pleased to note that the government has taken cognisance of the recommendation of this committee to increase the personnel of the directorate in the medical section and laboratory divisions, and we are aware of some of the difficulties being experienced by the directorate in filling these positions.

We are, however, also concerned that the present inspection staff of the directorate is inadequate to carry out the duties imposed on this body by the legislation covering the fields of food, cosmetics, medical devices and drugs. At the present time the inspection staff (field and headquarters) totals 151. Can Canadian consumers be sure of adequate protection in all these fields with so few men and women available for this work? Let us consider the drug field alone. The directorate is charged with the inspection of all drugs sold in Canada to ensure that the standards of purity and quality (as stated in the Food and Drugs Act) are met by manufacturers, both domestic and foreign. We do not wish to detract from the excellent control standards maintained by reliable manufacturers to ensure the high quality of their products, but not all firms maintain the same standards. This was indicated in the 1960 annual report of the food and drug directorate by the following statement "there were 410 inspections of drug manufacturers and distributors, with special attention being directed to those firms whose control procedures had been determined by previous inspection to be less than the optimum". The recent legislation asks for stricter manufacturing procedures. Surely this calls for stricter inspection and yet we understand that in the past year only 185 of the 485 manufacturing and distributing firms in Canada have been inspected by officers of the directorate. Can we as consumers then be sure (and now I refer to the requirements of the regulations) that all drugs sold in Canada have been "prepared, manufactured, preserved, packaged, processed, stored, labelled, and tested under suitable conditions", that is under sanitary conditions by qualified personnel, with adequate testing of bulk materials, and of each batch of drugs in quality controls and with records of all procedures, of dosage form tests and of measures taken to ensure rapid recall of any lot for the market?

This is a matter, gentlemen, which we consider needs your serious consideration and we strongly urge that the qualified inspection staff of the Directorate be increased to enable this body to carry out the duties required by legislation.

(iii) We are concerned that there is insufficient control of the quality of the promotional material which floods the medical profession. We are aware that the food and drug directorate controls the advertisement (what might be termed the directions for use) which manufacturers insert in the packet of the sample of a new drug, but there appears to be little or no control over the more spectacular promotional literature which does not always stress the limitations of the product. We have noted that in its brief the Canadian medical association states that "from the view point of the medical profession" one of "the most urgent needs" is "information on new drugs relating to an objective appraisal of their efficacy and toxicity by an unbiased body of experts before they are released for general use".

We wish to repeat a suggestion made in our presentation to the restrictive trade practices commission in 1961, that regular, concise and objective reports on new drugs should be compiled by a committee of representatives from the medical profession and the food and drug directorate basing their reports on clinical tests of the manufacturers as reported in their submissions and of the food and drug directorate. We ask that this committee give consideration to this suggestion.

(iv) Stricter control over the retail sale of drugs. It is encouraging that in the last three annual reports of the Department of National Health and Welfare, the minister has reported a decrease in the number of druggists convicted for the illegal sale of drugs without prescriptions. But it is discouraging that there are druggists who disregard their legal and moral responsibilities. I understand that after conviction a druggist is brought before a disciplinary committee of his provincial college of pharmacists, but no step is taken unless a druggist is convicted on a charge brought by the crown. We know of no public announcement of the suspension of licence or other reprimand by this committee. In the meantime, this practice continues and has recently resulted in the death of a Toronto university student. This matter was recently brought up at the annual meeting of our association. While consumers involved cannot be exempted for part of the blame in this matter, since no consumer should attempt to buy ethical drugs without prescription, we feel that the policy of pharmacists in controlling this practice deserves investigation by this committee.

Need for Education of Consumers

It might have been expected that after the thalidomide tragedy consumers would be fully aware of the potential dangers of drugs and would have accepted the principle 'If it's not food, it's poison'. While it appears that this tragedy did make many people wary of taking pills and other drugs without medical advice, the above-mentioned death and the report of the poison control centres indicate strongly that many people are not fully aware of this danger. The latest return of the poison control centres (1961) reports the treatment of 14,452 poisonings of which 8,847 were due to drugs. The breakdown, as stated in the report is as follows:

Aspirin and aspirin compounds	3,471
Sedatives and tranquillizers	1,509
Laxatives, digestive and Genito-urinary system drugs	956
Other internal drugs and medication	1,467
Drug products for external use	1,444

The most disturbing statistic is that for the first group, and it is particularly disturbing since 2,590 of these cases were of children of four years of age and under.

These statistics indicate the need for more education of the public regarding the dangers of drugs. Through our branches across Canada and through our magazine *Canadian Consumer*, our association carries on an active campaign in this regard, as does the consumer division of the food and drug directorate. But this work does not appear to be reaching enough people. We consider that steps should be taken to begin education in the schools on the use and potential dangers of drugs. We also maintain that the advertising of drugs, especially on TV, should be more strictly controlled so that adults and children are not given the impression that it is safe to take any drug for any ailment

without regard to the directions of the manufacturers or the advice of a physician. We also maintain that warnings on the labels of drugs should be printed more prominently and always in contrasting colour.

It may well be that the ease with which many drugs can be bought today in selfservice stores and supermarkets may be a factor influencing consumers to regard drugs with insufficient respect. While we appreciate the convenience of this service, we consider that the number of drugs made available for sale in this manner should be more strictly limited.

In conclusion our association wishes to draw the attention of the committee to one further matter. At the present time a great deal of publicity is being given to the use of certain drugs as cures for cancer. We are concerned about the publicity given to these completely unproven and possibly dangerous cancer cures, and can we have assurance that the promoters of these drugs are required to meet all the requirements of the food and drug regulations? This is an assurance we must have.

In this regard I would like to add that this is a matter of great concern in the United States, as I am sure you gentlemen are aware. So much so that the American Medical Association and the food and drug administration have called two national conferences on medical quackery. I have here the proceedings of the second national congress on medical quackery to which the commissioner of the food and drug administration, Mr. Larrick, invited me to attend in Washington during the past year. They are very concerned about the amount of medical quackery in the United States, and, of course, how this appeals to people, especially people who are facing perhaps possible death. One of the things that they mentioned particularly are these charlatans who are introducing cancer cures. We are very concerned, for example, at the moment, that there are, as you know, before the courts these drug trials regarding the drug laetrile which was banned in California. The drug was brought up to Canada and now Canada is being used as a distributing and, I also think, a manufacturing place. Since it is before the courts perhaps it is not politic to discuss it, but this is a matter with which we are very concerned.

The CHAIRMAN: Are there any questions that you would like to ask Mrs. Plumptre?

Mr. MACKASEY: Mr. Chairman, I think that everyone has questions which are probably very similar questions. I would like to congratulate Mrs. Plumptre on the very concise and factual report she has presented. I see the association has pretty well confined itself to the topic at hand, namely, the safety factor. I am sure she has strong views on cost.

Mrs. PLUMPTRE: We have very strong views on cost, I can assure you, but we wish to leave that for another hearing.

Mr. MACKASEY: I appreciate that and I will co-operate as much as possible and keep my questions to safety. I am sure the Chairman will rap me if I stray, as I often do.

I have taken the liberty, at two o'clock this morning, to underline a few points here. On page two of your brief you pay a tribute to our pharmaceutical manufacturers and you emphasize something which I think most witnesses have emphasized. You go on to say, at the bottom of page one:

> . . . if it has been manufactured under procedures with careful quality control, so that its quality does not vary and meets the requirements of the formula in all respects. The responsibility for this type of safety must lie with the manufacturer. But to make sure that all drugs on the market are neither harmful nor fraudulently represented, government regulation is also needed.

You also say that:

> Consumers are fortunate in Canada in that both parties responsible for this safety—the Canadian pharmaceutical manufacturers and the food and drug directorate which administers the government controls—accept and carry out their responsibilities and ensure us a supply of safe drugs.

In these two general statements, in so far as the manufacturers are concerned, did you mean to add the word "association"?

Mrs. PLUMPTRE: I did not mean to add the word "association". Certainly it is rather general, but for the most part the manufacturers in Canada do try to be responsible for this safety.

Mr. MACKASEY: Why I stress this point, Mrs. Plumptre, is that after what prodding I have been able to do of Dr. Morrell and other witnesses I have come to the conclusion that of the 485 manufacturers and distributors—and Dr. Morrell admitted being able to inspect the premises of only a hundred odd firms—about 300 are left with no source of inspection. This is why I take exception perhaps to your generalization that Canadian pharmaceutical manufacturers in general are living up to the standards of safety. I would not want to take it upon myself to say that the 300 people who have not been inspected, or are not subject to inspection annually owing to the shortage of personnel in the directorate, are necessarily maintaining the type of control which I think is in the best interest of the public.

Mrs. PLUMPTRE: This is a justified criticism of my statement. When I refer to pharmaceutical manufacturers later I introduced the word "reliable". There is a distinction between "reliable" and "unreliable". I want to be careful not to give the impression that we were out to damn Canadian pharmaceutical manufacturers generally because I think we have a number of very good, reliable firms, and I think the association itself is trying to do a good job in giving us safe drugs. On the other hand, there are two points, here. First of all, I know that Dr. Morrell has said that they could inspect only 180 of those manufacturers this year. You will see that in one of the quotations I gave I say that one year they did 410 inspections. After all, this is Dr. Morrell's field, not mine, but I would think that the new legislation demands much more careful inspection, and therefore each inspection takes longer. That is why they have done only 180 inspections this year. In addition to this, I might say that just yesterday morning I saw a newspaper clipping where Dr. Morrell is reported as having said that in the future they are going to prosecute manufacturers who do not produce drugs that meet their standards in all respects. Quite frankly, I could not say that I know there has been an unsafe drug on the market because I have not seen myself any actual prosecution of a drug because it was unsafe, but I certainly agree with you, and I say later in the brief that obviously there are—as Dr. Morrell also said in one of the annual reports—some manufacturers whose manufacturing processes do not reach the optimum.

Mr. MACKASEY: Mrs. Plumptre, regardless of price—and I want to keep away from it—Dr. Morrell said, in talking about drugs, that if he were prescribing drugs he is sure he would tend to prescribe from companies which he knows. Do you agree with Dr. Morrell's statement?

Mrs. PLUMPTRE: I think it is probably so. I am sure doctors tend to use some drugs more than others and they get to know the reactions of those drugs on their patients and therefore they gain confidence in those drugs. On the other hand, you are getting very near the area of price here and perhaps it is difficult to distinguish, but I would like to think that the time would come when we would have enough inspections and sufficient control

of drugs in this country so that a doctor would not just prescribe a drug on the basis of the brand only. In other words, I hope that he would have perhaps more knowledge of the economic side and he would be able to, with a certain certainty and assurance, prescribe a drug which may not bear a brand name but would be reliable and perhaps less costly to his patients.

Mr. MACKASEY: To go on with this question, would you not agree that until such time as Dr. Morrell has at his disposal an adequate staff to guarantee that all manufacturers, regardless of the brand name, are inspected regularly, or that there be some form of regulation that would guarantee that all manufacturers live up to the standard of safety, we are almost pathetically dependent on those firms that we know are doing an adequate job of maintaining a certain level of safety?

Mrs. PLUMPTRE: To a certain extent I would go along with this. On the other hand, I do think there are some drugs on the market now which are not necessarily brand names and which are quite reliable. From time to time we have members writing in with various experiences. We had an experience here in Ottawa of a patient requiring cortisone. She was paying a large amount for it. We are on to price now but allow me a certain deviation. She was paying $30 per prescription, and it was a very expensive drug. She needed to take it regularly. It was suggested that she ask her doctor to prescribe this drug without using the brand name. She had found out from a friend who was having the same trouble. He did this. He said, "Yes, I will prescribe this, using the generic name", and he did so. She was then able to get the drug at a cost of $8. The reaction and the result were the same. I know it is easy to generalize in this field, but it is unfortunate if you do generalize.

Mr. MACKASEY: As the bottom of page two you say:

> We, therefore, ask that legislation be introduced which will require the registration of all drugs.

This has been brought up periodically. Could you comment on that? You say, "all drugs, both domestic and imported, which are sold on the Canadian market".

Mrs. PLUMPTRE: I might say that this is a matter which I did discuss with Dr. Morrell because I wanted to be sure I was correct on this point. For example, I might think that my grandmother had a wonderful cure for something or other, and therefore I go to my garage and make it. I can put it on the market and sell it until the food and drug directorate catches up with me. This may happen in two years, or maybe in 10 years if I get away with it. This is absolutely wrong. I am not even quite sure that this does not perhaps relate to what is happening with the laetrile drug. It has been prohibited in California and now I assume it is made here. Whether it is being sold in Canada I do not know—we are not discussing that now. The present legislation does not give us the right protection.

Mr. FRANCIS: There is a great variation in regional practice, is there not? In some parts of the country there is a tradition of a generation ago of home cures and prescriptions, and the use of self-medication dies very hard. In the urban centres where consumers are brought to a much higher standard of expectation of drugs, they are better informed in terms of modern medication. However, it would be very hard to try to prohibit in a blanket way practices which have been going on for generations in some parts of Canada.

Mrs. PLUMPTRE: But I do think this is something we have to aim at. We had an example of this about 18 months ago when a woman wrote in and said she had used a preparation on her small son. It was one of these preparations which you spray on a cut. He had a very strong reaction to this. Usually, if

there is anything in regard to health, we take it straight down to the food and drug directorate because they have facilities for checking. This was a preparation on the market which was not registered. This is the kind of thing which we would like to see stopped.

Mr. MACKASEY: In other words, reading your brief thoroughly as I have done several times, you keep coming back to one fact. I want to emphasize it because you make this point better than I. The whole brief is dependent on one factor, that is on Dr. Morrell having adequate staff to put the regulations into effect.

Mrs. PLUMPTRE: I could not agree more.

Mr. MACKASEY: All the recommendations in the world do not mean a thing unless Dr. Morrell is supplied with money and personnel.

Mr. PLUMPTRE: You are absolutely right. This is something with which we have been concerned. In 1960 we made our first representation, and then the following year they added the regulations regarding goofballs. That is also the year in which they brought in the regulations about meat from dead animals. Both of these things meant a tremendous amount of extra work. They had 86 inspectors to do all the work on the imported drugs, the food, cosmetics, and so on. It is ridiculous, and yet the public was not disturbed about this until the thalidomide tragedy brought to the attention of the public the fact that the directorate does not only need inspectors but also analysts and laboratory staff as well.

Mr. MACKASEY: I have one last question, at least for the moment. There has been a lot of concern expressed here by Dr. Morrell and by other people pertaining to drugs and raw materials coming in from certain parts of Europe. Have you people made any research into this field or have you any strong opinions on the subject?

Mrs. PLUMPTRE: This is quite beyond our field of research. When we were preparing the brief we gave before the restrictive trade practices commission, we were a little disturbed that there was evidence that the medical profession had given indications that all drugs coming from overseas were unreliable. I just do not think it is true. We were able to point this out. It had been pointed out in the material prepared by the combines investigation branch. We just do not think that is true because, as you know, many discoveries of drugs have been made in foreign countries.

Mr. MACKASEY: It is true it is too great a generalization to say that all our own manufacturers are living up to the standards of safety. If they were, we would not need Dr. Morrell very much.

Mrs. PLUMPTRE: Exactly.

Mr. WHELAN: Mr. Chairman, Mr. Mackasey has pretty well covered my line of questioning, and as one who, as Mr. Francis mentioned, comes from the hinterlands, I see some of these questions of mine were already asked.

Mr. ROXBURGH: Nice going.

Mr. WHELAN: The first question I would have is: How do the countries in Europe compare with Canada as regards inspectors?

Mrs. PLUMPTRE: This is outside our field of research.

Mr. WHELAN: Did you base your conclusion that Dr. Morrell's staff should be increased on the conditions in Canada or did you conduct a study on how many inspectors per thousand people other countries have?

Mrs. PLUMPTRE: We have not discovered that at all. We want to make sure that drugs available to Canadians are safe and since we feel that Canadian drugs should be inspected, therefore drugs coming in from overseas should also be inspected. We know they do spot checks on the drugs coming in. All of us

would probably agree that it is desirable to increase this amount of inspection. I have some general information about some of the practices overseas, but it is outside my field of research to be able to know what people in other countries are doing.

As Dr. Morrell said in his presentation to this committee when I was here one day, they do want to have inspectors to send overseas but the inspectors must be qualified and trained. We would like to see them do that too. We are not prepared to accept the statements and standards of other countries without our own inspections, nor are other countries prepared to accept ours.

Mr. WHELAN: In your brief, Mrs. Plumptre, you point out that some druggists are acting improperly or illegally with prescriptions and drugs. When this becomes evident to your organization do they ask to have these people prosecuted? Does your organization take any such action?

Mrs. PLUMPTRE: It is very seldom that we come across this but, as a matter of fact, I came across one just this week. It is sometimes very hard for us; one does not want to tittle-tattle because sometimes people do things with the best intentions. I do think we should go after the consumers, however. I think this is quite serious. I think, as the reports of the Minister of National Health and Welfare point out, the number of druggists who will do this seems to be decreasing. On the other hand, one of my friends gave me a bottle that she had been using for an ailment and I saw clearly on the label that it said that it was available by prescription only. I asked her where she had got it and she said she had got it because the doctor of a friend of hers in Montreal had recommended it to her friend and she, having the same ailment as her friend, went to the druggist here in town and asked him for it, and he gave it to her. The consumer was at fault for asking the druggist, but the druggist was even more at fault in giving it to her because he has a professional status and he should adhere to professional principles. It has not done any harm, but look what happened to the student in Toronto. If this student had not died, would we ever have caught up with this man?

Mr. WHELAN: In your brief you mentioned education in the schools. Do you not think that the average person is well aware of the dangers? Do you not think that the problems are caused more by neglect than lack of education?

Mrs. PLUMPTRE: No, I am sorry but I could not agree with you that they are aware. If they were aware, why would mothers leave ASA. tablets lying around? Why would 2,500 children have been rushed to hospital this year? We have talked to paediatricians about this. The paediatricians say it is absolutely amazing that, when children have taken 12 or 20 ASA tablets their parents have telephoned and said "Do you think we should do anything about this?" They seldom have an idea of the danger of these things.

Mr. WHELAN: Do you believe that the average young mother or father today who has prescriptions in the house is not fully aware of the dangers of the drugs and does not realize that they are dangerous in the first place although they have obtained them on prescription? Do you not think they realize and yet leave them around just through carelessnes? Certainly we cannot expect the children to know the dangers but I would think at least 90 per cent of the adults are aware of the potential hazards that the drugs constitute, but they are just neglectful about putting them in a proper place.

Mrs. PLUMPTRE: I do not know that you can say what is the "average person"; but I do think people are not just carefess about it I think people tend to be more careful with prescription drugs because they are something that people get from their doctors. As far as ordinary drugs are concerned,

drugs obtained from the store, I do not think people are aware of the dangers; if they were they would not be so careless in leaving them around.

Mr. WHELAN: With regard to some of the other drugs, drugs such as thalidomide. I remember very well in our own family's case that the doctor would not give this drug to my wife because he was not sure of it.

Mrs. PLUMPTRE: Then you were very fortunate.

Mr. WHELAN: Do you not think it is true in a great many cases that people associated with the medical profession want to be sure before they will allow the use of this drug?

Mrs. PLUMPTRE: I was not criticizing the medical profession although I think we all know that a number of these cases of thalidomide damage came from doctors using samples. Whose fault it was is outside our discussion at the moment. I am talking now about the general public in their own homes.

Quite frankly, I think a lot of the advertising today does not really impress upon people the need for care in handling drugs. I think this is often the result of not having given the matter enough thought. I can give you an example. You will probably all have seen during the last few years an advertisement carried by an aspirin company, an advertisement which ends up by saying "Don't forget we have special aspirins for your children", and then they would hold up the bottle—"the bottle with the saety cap'". De stested this cap. I started by giving it to a three year old and said "I'll give you a quarter if you can get the top off." It was empty, I might say. We had used the bottle a few times in our tests and we had taken off the cap, perhaps a dozen times. I had tightened it as tightly as I could and this child took it off in 20 seconds. She just used her teeth and took it off in no time at all. The bottle was not safe. We reported this in our magazine and we sent the magazine to the company concerned. Nothing happened. Soon after that I was asked to address the advertising and sales executive club in Montreal and I was talking about misleading advertising. I used this as an example of misleading the public by saying something was safe. It happened that one man who may have had the account for that company was at the conference and he took me up on this. I said "Look, we have tested it; we know it is not safe." The next week or so after, when I happened to see the advertisement again the last part of it had been taken off. I think they just had not realized the possible effect of the advertisement; but that is not good enough, is it?

I have brought some photographs with me this morning because I thought the committee might be interested to see this bottle. There was an article in the *Globe and Mail* about a safety bottle that was being patented for drugs and the man who did it has given me these photographs. I do not know whether any of the members would care to see them. This bottle would not necessarily be used as a container in which the drugs would be sold but rather as something for people to have in the house to which they could transfer the drugs they buy. I have the prototype here with me this morning. It appears to be an ordinary bottle but it has a false top. The effective opening is at the bottom and it screws the wrong way. Once the bottom has been taken off, once the bottle is open, it cannot stand up; it is weighted. Therefore when it is open one cannot keep liquid in it so one would tend either to replace the bottom or, if one was called away to the telephone for example, to take it away with one. I think this is the kind of thing that should be encouraged, so we do get more safety features on the market that parents perhaps can use.

Mr. WHELAN: I still say that the vast majority of these children who get hold of the drugs get them because of carelessness in the home. No matter how safe we try to make these things we will find that the children—even the children from the rural areas!—are quite capable of finding ways and means

of getting into nearly everything. I know how easily it is done from watching my own children and seeing how they become so ingenious at climbing up into cupboards, for example.

Mr. PLUMPTRE: There is no doubt about that at all.

Mr. WHELAN: That is why I say that the education—

Mrs. PLUMPTRE: It is very important.

Mr. WHELAN:—is important, starting in the schools.

Mrs. PLUMPTRE: I could not agree more. On the other hand, as one of my friends said to me the other day, she was surprised when she went into her daughter's home, where there are three little children under the age of four, and found them saying, "Mummy, I have a pain, can I have a candy aspirin. I want an aspirin." This is a result of advertising, and this is bad. They do have these special candy flavoured aspirins on the market, and our association has been asking for them to be taken off the market because children regard them as candies, and this is very unfortunate.

The CHAIRMAN: Do you have any further questions, Mr. Whelan?

Mr. WHELAN: No.

The CHAIRMAN: Dr. Rynard.

Mr. RYNARD: Most of the things in which I was interested have been asked, but I am wondering whether there is not a general indication from which we can learn when we see so many of the children having managed to get hold of these pills. I think we have to look a little in retrospect here and realize that from the age of five to 35 accidents are the great killers of people in Canada. I think there is a trend in this and an indication that this is possibly the dangerous age.

Then I was also wondering with regard to this drug business, if one cannot sell anything until it is tested, why we go to all this trouble. If one cannot sell a product until it is tested here and sent in here, I think it would be very simple to say that you cannot sell something and then it is tested, and when you have nobody selling a product that is dangerous.

I was very struck by the statement that about one in eight of the pills was a kidney pill. I would like to look at those statistics.

Another point which struck me was that if you wish to have the druggist prepare a prescription for a lot of the drugs that at the moment you can pick up across the counter or off the shelf, then immediately you will be increasing the cost to the people right across the board. My experience covering a good number of years in clinics is that druggists are very, very ethical when there is a doubt in their minds about a prescription or drug that people can use.

I think we have to keep in mind the facts about phenacetin. In Australia and in some other countries one cannot buy phenacetin because it has been proven that some people have died from it. I believe they had seven deaths reported in a couple of years. I think we have to look at this in retrospect when we are considering all these matters because I am sure that most druggists would be very glad to fill a prescription because they get a prescription fee. They have to have that, and that is only right and proper. It is only right that the man who handles those drugs and keeps them for the benefit of everyone in the community should have a fee, probably a dollar, for keeping it and making up a prescription, no matter how big or small it is. I do not want to go into costs, but we have to bear those in mind.

Mrs. Plumptre has given us an excellent paper, but there are always two sides to every story, and I think we should take a good long look at the other side when we are considering this. I want to congratulate Mrs. Plumptre on her paper.

Mrs. PLUMPTRE: Thank you. May I answer that, Mr. Chairman?

The fact that drugs come on the market and are registered and tested certainly means, we hope, that they are safe in that they do meet the formula and that they are therefore safe for use for the particular illness for which they have been evolved, but this does not mean that they are safe in the hands of people using them without direction or of people who may have picked them up—children, for example, who do not know how to use them.

We do not ask that all drugs be put under prescription, not by any means. We know in some cases—I think it is true in Prince Edward Island—that one cannot buy aspirin without prescription. We are not asking for all drugs to be put under prescription, but no matter how much care is taken in testing drugs and requiring prescriptions, one also has to have education of the public in handling them.

With regard to such things as phenacetin, as you know some products have had phenacetin withdrawn from their formulae because of the Australian experience. All these things have to be taken into consideration. However, what we are really saying is that we want to be sure that drugs on the market are well made and can be used by doctors for the prescriptions they want. We also want the public to be made to realize that these drugs, no matter whether prescription or not, must be treated with care.

Mr. RYNARD: I appreciate the explanation, which has been very well given. Any drug can poison. I have seen aspirin prescribed in huge doses; such huge doses that I have been frightened every time I have seen it prescribed for rheumatic fever. We have to keep in mind that no drug is safe, and the pharmaceutical profession is doing a good job in their profession in comparison with other groups. If we do see that drugs are proper drugs to use and we have instructions published on the label, that is as far as we can go. Of course, people have to read and write.

Mrs. PLUMPTRE: Yes. Unfortunately, people do not seem to read much these days. This is a matter that has come up. For example, there is a regulation with regard to aspirin which requires a cautionary statement on the bottles. But how many people read this?

The CHAIRMAN: I think Mr. Mitchell has a question. As far as the safety bottle is concerned, I do not think that the pharmacists can get it apart!

Mr. RYNARD: Just one comment, Mr. Chairman. I agree with Mrs. Plumptre; she is quite right in saying that. If you go out and drive a motor car and do not pay attention to the signs, where will you end up?

Mr. MITCHELL: I would like to ask Mrs. Plumptre a question in regard to the submission, in which she uses the word "drug" in many cases. What is your definition, Mrs. Plumptre, of the word "drug"?

Mrs. PLUMPTRE: I would think of a drug as something that had to be used in times of illness. I am sure there is an official definition, but I certainly do not know it. That would be my own personal interpretation.

Mr. MITCHELL: The difficulty is that there does not seem to be a definition.

Mrs. PLUMPTRE: Perhaps Dr. Morrell can answer that.

Mr. MITCHELL: No, Dr. Morrell cannot answer it either.

Mr. MORRELL: Yes, I can.

The CHAIRMAN: A drug as defined in the act?

Mr. MORRELL: That is the one upon which we act and I think it is a very good definition for our purposes. I think Mr. Mitchell knows that definition.

Mr. MITCHELL: Yes, I do, but at the same time many of the licensing bodies in the provinces do not consider the word drug in that light.

Mr. MORRELL: They do not use the same definition.

Mr. MITCHELL: That is why I asked Mrs. Plumptre. There is a discrepancy. Naturally, we know that morphine is a drug or narcotic, but then you mentioned ASA. Is that a drug or is it not?

Mrs. PLUMPTRE: Oh, yes, definitely.

Mr. MITCHELL: That is just where the difficulty comes in.

Mrs. PLUMPTRE: Do you not call that a drug?

Mr. MITCHELL: Not definitely, no. A drug defined definitely as a drug by the licensing body in any province cannot be sold in a supermarket. Do you see what I mean?

Mrs. PLUMPTRE: Yes, I see what you mean. However, as far as the public is concerned I think they tend to regard anything one needs when one has any kind of ailment as a drug, but I realize they may not be right legally.

Mr. MITCHELL: You mentioned the death of the student from the University of Toronto. Has it been definitely established that it was obtained illegally? I presume it was a barbiturate.

Mrs. PLUMPTRE: The jury has not yet brought down its actual verdict, I understand, but the statement here is that Mr. Bodkin, the pharmacist or druggist, said that the student had bought the drugs from him without a prescription by claiming he was a medical student. However, it does not mean that he is entitled to have the drug because he is a medical student if it is on prescription.

Mr. MITCHELL: Some have that licence.

Mrs. PLUMPTRE: Apparently this is for the court to decide.

Mr. MITCHELL: I know it has been peddled illegally but I wonder whether it was obtained illegally.

In your brief you mention quackery. I presume you mean by that medical quackery.

Mrs. PLUMPTRE: Yes.

Mr. MITCHELL: That would be the responsibility of the disciplinary committee of the Canadian Medical Association.

Mrs. PLUMPTRE: Yes, and I assume it comes under the food and drug directorate. A medical device can be a quackery device and it would come under the food and drug directorate then.

Mr. MITCHELL: I wonder if I could ask Dr. Morrell about that. Dr. Morrell, Mrs. Plumptre says that medical quackery can be policed by the Canadian Medical Association but that other things can be policed by your department, things such as "a medical device", whatever that may be. Is that correct?

Mr. MORRELL: Yes. We have a definition of a device in the act and it prohibits the sale of a device that is false, fraudulent, or injurious. We can go back to the old "Abraham's box" days. The Abraham's box was an electrical device. This device gave certain readings from samples of blood and then the person's disease or abnormality was diagnosed from that. This is quackery. There is no scientific or medical basis whatver for this type of diagnosis. We have come across a few of these in Canada and we have prosecuted.

Years ago a device was sold in Montreal which was just a metal cylinder and had a wire coming from one end and a wire from the other end. The wires were put round one's leg and one's arm, and one went to bed with it; and they had a book, "A new theory of disease". This device was called an oxydonor. It was of no use but it was recommended for a lot of things. I gave a lecture at McGill and one of the professors of mediicne said that he had come across this in his practice, that one of his patients with tuberculosis was relying on it to cure his tuberculosis. The patient got into a very bad state and

finally went to the doctor, but he was pretty far gone by then. The doctor blamed the confidence this man had put into the device for delaying proper diagnosis and treatment.

Of course, apart from the fraud angle where money is extracted from people for fees, there is the danger that they have something wrong with them and that they are not receiving adequate or proper treatment because they are relying upon such devices.

Mr. SLOGAN: May I ask Dr. Morrell a question? Inasmuch as it occurs, in addition to food and drugs you inspect gadgets and control them?

Mr. MORRELL: We have done very little work on gadgets. We have not the staff to do it. We did work on an anaesthetic gas machine used by dentists some years ago. There were some deaths from anaesthetics in dental offices and we looked at them and found that the dials on the machine were far from accurate and did not show the mixture correctly. We had a man working on them for about a year as a result of which the design was changed, and when we tested them at a later date we found they were accurate enough for the purpose for which they were used. This is a device. I am sure we could do something about hearing aids if we needed to; they would be a medical device. However, we have done nothing on any of them.

Mr. SLOGAN: Have you ever been called in to make an investigation in regard to faith healers?

Mr. MORRELL: Yes, we have had several as a matter of fact. There was one chap out in the west who sold handkerchiefs; he had prayed over these and then sold them. These handkerchiefs were good for this, that and the other. There were bracelets that were good, and necklaces that were good to prevent or treat goitre. We have had a lot of these odds and ends over the years and we have secured convictions.

Mr. MITCHELL: And teething necklaces are still on the market.

On page five of your brief, Mrs. Plumptre, you make the assertion that disciplinary action is taken against a pharmacist only after conviction in the courts, let us say.

Mrs. PLUMPTRE: This is the information given to me by the registrar of the Ontario College of Pharmacists.

Mr. MITCHELL: Well, I differ from that statement. I think every provincial licensing body in Canada has a disciplinary committee which, through its inspectors, is inspecting retail outlets of pharmacists at all times. Many—but I hope not too many—have had their diplomas lifted by the disciplinary committee of a graduating or licensing body long before the case reached the courts, and it probably never would reach the courts. I can mention reasons for this as being sloppy business quarters, sloppy business activities, alcoholism and so on in the store, which never reaches the court.

Mrs. PLUMPTRE: I was not referring to that kind of thing; that is a different matter. I was referring only to the fact that there are some druggists—and I do not want to give the impression that I am referring to all druggists—who issue drugs without prescriptions. The point made by the registrar was that they do not take any action in regard to this particular point of issuing drugs without prescription until a conviction has been brought by the courts.

Mr. MITCHELL: I am just as anxious as you or as anyone else about this and we are doing our best to police our association at all times, but it is absolutely incorrect to say that no action is taken.

May I ask for Mrs. Plumptre's personal opinion of a prescription prescribed by her doctor for her own use? Would you prefer a brand name preparation or a so-called generic preparation?

Mrs. PLUMPTRE: I think I have given my impression on this before. Actually, I suppose every patient takes his doctor's advice. I am in the position that if my doctor ordered me a prescription which cost $50 and I was ill, I could afford to pay it. However, I do know from my work with welfare associations that they have been very concerned that a lot of their people do not get their prescriptions filled because they cost too much. I know that doctors are too busy and just do not have the information—and how can they?—that there may be an equally good drug on the market which it would be in the economic interests of his patient to prescribe. He knows one or two drugs and he chooses which he prefers. I, as a patient, naturally accept my doctor's advice, but I would like to think we would come to a point where a doctor would have more information on the economic value as well as medical value and that he would take this into consideration where necessary.

Mr. MITCHELL: In your brief you praise the efficiency and quality control of the pharmaceutical manufacturers.

Mrs. PLUMPTRE: The reliable ones.

Mr. MITCHELL: The leading ones.

Mrs. PLUMPTRE: Yes.

Mr. MITCHELL: The doctor has full access to their statements of efficiency of their product, whereas a generic manufacturer has not that connection with the doctor; he does not have detailed literature to the point that he can go in to see the doctor and show the efficiency of the product against a so-called qualified and reliable manufacturer. If he is taking that as a criterion, then he may be taking a chance on the efficiency of a prescription that calls for generic drugs.

Mrs. PLUMPTRE: That may be so. I am not in a position to judge. We would like to feel we could get to the position at which we would know that the drugs which did not have brand names were reliable.

Mr. MITCHELL: I would like to quote a columnist in one of the papers. A pharmacist was given a prescription for an antibiotic for one of his family. He was asked about the value of the generic drug in the prescription, and he said "I don't want any of that generic stuff; give me a brand name." It depends upon whose ox is being gored, shall I say as to whose product they will take.

Lastly, commenting on the safety of the safety bottle here, I had occasion to have a safety control cap bottle which I thought was very efficient from someone who brought it into my pharmacy and asked me if I would forward it to the poison control centre in Windsor, to the particular person involved. He in turn has forwarded it to a manufacturer. It may reach the market and it may not. It is actually an extension arrangement and a child could not open it. A person would have to have not pliers but more likely a screw driver to open it.

Mrs. PLUMPTRE: Yes, I understand there are a number of people working on this. I understand at the last safety council annual conference there was a cap produced which is likely to be efficient. There is only one thing I would like to say; you know, if you give a child something with a cap, it will work at it and work at it and work at it until it gets it off. I have not seen this one and it may be that they can develop this to be safe. There are some very persistent little children, however, and if they are left alone with things they can usually get them open.

Mr. MITCHELL: Any child would need a machine shop to get this open.

Mr. FRANCIS: The answer surely is merely to keep these under lock key.

Mr. SLOGAN: It seems to me that Mr. Francis' suggestion is the most expected and efficient way of controlling this, that is to have a locker or a cup-

board or something under lock and key. Knowing children, I know that any safety device that will completely frustrate an adult can be opened by a child.

What I want to tell you is that the more witnesses we have before this committee, the more I become convinced that a lot of the fears in the public are unfounded, and that there is a tremendous amount of good work being done by the government and by the manufacturers and so forth. However, my big complaint all along is that this information is not getting down to the level where it can be utilized and made a benefit to the consumer, and that is the level of the individual medical practitioner and the individual pharmacist. I would like to read to you from the royal commission on health services.

On page 36 it says that they were told by the pharmacists association that pharmacists will not risk supplying generic drugs unless convinced of their purity and potency. The Canadian Pharamaceutical Association told the health services commission that they felt that the degree of quality control was not sufficient. On page 368 of this report they quote Dr. Morrell as indicating that in respect of the laboratory tests in 1960, 30 per cent of pharmaceutical samples examined were unsatisfactory. For example, there might be a variation in potency, but within tolerable limits. Dr. Morrell tells me that this might be a variation of five to 10 per cent. It is still quite acceptable. He went on to say that only five percent were objectionable to the point where they had to be withdrawn. It should be of course borne in mind that drug inspectors examine mainly those drugs which they have reason to suspect. So perhaps there is a much higher percentage which would be in the over-all market, because I understand that this would represent perhaps 10 per cent of the drugs on the market as a whole.

I think your suggestion regarding labelling is very important, and also the suggestion of the medical association regarding a body that would set specifications. It may be, just as this example showed, that the 30 per cent were not perfect but they were certainly acceptable. There would have to be some range of acceptance, but at least if there was a specification on the label which said that this met certain specifications, then the individual pharmacist would know that it is within this tolerable limit and he would have more confidence in making out the prescription.

There again I think it boils down to the fact that all manufacturers in Canada would have to be licensed, and that there would have to be more inspections. However, I do not believe they would have to go to the extent of inspecting every batch. What are the views of the consumers association regarding the setting up of a body such as this which would set up specifications? It would then be up to the food and drug directorate to carry them out. Would you be agreeable to seeing such specifications on the label so as to give each medical practitioner the assurance that this drug met the standards specified?

Mrs. PLUMPTRE: What do you mean by specifications? Do you mean a certain potency? Is this not already in the formula? Does it not have to be done already?

Mr. SLOGAN: It has, to a certain extent, but I think the matter of licensing is perhaps the most important thing because there might be drugs on the market which are not known and which appear on the market before the food and drug directorate can get at them. I think therefore the first step would be licensing, the second step would be more frequent inspections, and the third step would be something on the label that would indicate on the local level that it is satisfactory. I think then that the benefits of all this work would get down to the consumer.

Mrs. PLUMPTRE: This would be very helpful. I think certainly that if you had all the drugs registered there would be an opportunity to require, when they make this registration, that the drugs meet certain specifications.

Mr. MACKASEY: I have only one comment on the definition which Mrs. Plumptre gave on drugs. I have been trying to convince my wife for years that the hot rye I take for my grippe is medicine. I want to have some authority for saying that it is a medicine that I have been taking.

Mr. MACALUSO: I have been putting off any questions because as a member of the consumers' association I hate to ask my own president any questions. Be that as it may, Mrs. Plumptre, in the brief you suggest registration of all drugs, domestic and imported, on the Canadian market. When this committee was questioning Dr. Morrell, the matter of registration of manufacturers and distributors was brought up, and also registration of drugs. I think you would agree with the committee and myself that registration is really a matter of licensing which is a provincial matter.

Mrs. PLUMPTRE: Is this a provincial matter? I know there is some overlapping here but I would like to see this on a national basis.

Mr. MACALUSO: So would I.

Mr. MITCHELL: There is no licensing at the present time.

Mr. MACALUSO: Licensing itself is a matter of provincial jurisdiction. I am just commenting on this, that when the Ontario committee held its hearings on drugs I believe the association did present a brief.

Mrs. PLUMPTRE: Probably the provincial association did.

Mr. MACALUSO: Was the matter of registration brought before them?

Mrs. PLUMPTRE: I do not recall. I just do not know. I do not know what my provincial people said. I cannot remember at this moment; I will have to check it.

Mr. MACALUSO: You mentioned it also in the *Canadian Consumer* booklet that is distributed by the association. Could you, for the edification of some members of the committee, tell us what type of tests the association itself carries out on a drug or on a product that appears on the market.

Mrs. PLUMPTRE: The only drugs we have tested have been the A.S.A. tablets, and the A.S.A. compounds. These were done by qualified pharmacists. These were done professionally, and we paid to have them done.

Mr. MACALUSO: By pharmacists?

Mrs. PLUMPTRE: By pharmacologists, that is scientists working in a laboratory with a degree in pharmacology.

Mr. MACALUSO: I realize that at the present time in the United States you cannot get the 222 tablets without a prescription, whereas you can buy them right from the shelf of any drugstore in Canada.

Mr. MITCHELL: Up to an eighth of a grain of codeine.

Mr. MACALUSO: But anything with codeine cannot be purchased in the United States without a prescription, whereas it can here. Has the association conducted any tests on the dangers of, say, 222 being sold from the shelf?

Mrs. PLUMPTRE: No. We did not test for dangers. We did read some literature and quite a number of articles and we used this in the article we prepared on the A.P.C. and other compounds, drawing people's attention to it. We came out with the recommendation that you should not buy these compounds at all unless your physician orders them, that these are things you should use on the advice of your physician.

Mr. MACALUSO: To move on to the matter of labelling and education of consumers, which is referred to on page five of the brief, the problem here is a difficult one as we have found in dealing with our investigation of the labelling of pesticides. We found it is difficult to educate even an adult. You can have a label five feet high and they are not going to read it; they are only interested

in the product. That applies even to T.V. and to newspaper advertisements. What type of programming or education of the public would the association recommend?

Mrs. PLUMPTRE: I realize this is a tremendous problem and a number of people do not read labels; but we are making progress in this area. We have to keep hammering away at it. I am really encouraged by the growing number of letters that come into us from people having read labels on foodstuffs, on pesticides and on household products. I think they are becoming aware that in this day and age when they no longer have the personal advice in shopping that they used to get, not only in food stores and drugstores, they therefore have to take more care themselves. The only thing to do is to keep on hammering away at this. We do need to start talking about these things to children, boys and girls of high school age, to tell them that they have to be prepared to make their own decisions in so many fields of life and they have to read so as to get the knowledge to make these decisions. I would like to see in the advertisements for drugs, even the simplest drugs, more warning given on the care in the handling of these things, more warnings that they are not safe. You cannot just treat them as you would treat an ordinary drink or lozenge or candy. I think that while I agree with you that at least people do not read as we would like them to read, we have to keep on hammering away. I am encouraged that people are beginning to read labels more.

Mr. MACALUSO: You glossed over in your brief the matter of patent medicines or patent drugs. Has the association conducted any research into the matter of limiting the sale of patent drugs sold from a chain store or from a so-called patent medicine store that has no pharmacologist?

Mrs. PLUMPTRE: Perhaps this should be limited. I did read the evidence given by Dr. Turnbull on this point. He is more competent to deal with this than I. He mentioned there were certain bromide preparations which you could buy at a supermarket, and he considered this unwise. We would certainly go along with this opinion. You can get too many drugs too easily. It is very nice and convenient to pick these up while you are shopping, but I feel this should not be allowed to go on without some supervision.

Mr. MACKASEY: Recently in the province of Quebec an effort was made to limit the sale of this type of product through the drugstores. Unfortunately, it was defeated. The pharmacologist tried very hard to present this thing quite objectively, that our chain stores should stop selling cough medicines, and so on. Unfortunately, it was defeated. The problem, to my mind, emphasized the fact that we have probably ten different regulations, which makes Dr. Morrell's life pretty hectic, that is trying to stay within the regulations in each and every province.

Mrs. PLUMPTRE: It is very difficult to control because people want to have things available conveniently. On the other hand, it tends to make them regard these products with less respect.

Mr. MACALUSO: May I say that I agree with the submission made by Mrs. Plumptre that there should be registration involving both imported and domestic drugs. Dr. Morrell discussed this, and this is a most difficult problem, in regard to drugs made in a garage. As I stated, Dr. Morrell was at the committee meeting when I stated that I know personally of drugs that have come into this country from the West Indies or Jamaica which I do not think the food and drug directorate have knowledge of and of which it would be impossible

to get knowledge. They might have passed the customs somehow. This is a very important problem and I for one think that this committee should think very seriously of this problem in its deliberations.

The CHAIRMAN: Did you want to say something, Dr. Morrell?

Dr. C. A. MORRELL (*Director, Food and Drug Directorate*): I did, but I forgot.

The CHAIRMAN: Gentlemen, we will have Mr. Curran, the legal adviser to the Department of National Health and Welfare, appear before this committee on this matter, both provincial and federal licensing. As has been pointed out before, there is federal licensing dealing with biological products at the present time.

Mr. MACALUSO: Licensing itself per se comes under provincial jurisdiction, and you have to watch that.

The CHAIRMAN: This is done federally.

Mr. MITCHELL: I want to ask another question. In your concluding paragraphs, Mrs. Plumptre, on page seven, you use the words "drugs as cures for cancer" and you say that a great deal of publicity has been given to these drugs as cures. What kind of publicity do you mean?

Mrs. PLUMPTRE: Publicity in the press.

Mr. MITCHELL: What kind of publicity in the press?

Mrs. PLUMPTRE: Let us take Anablast. There was a great deal of publicity when this man came over from France. Quite frankly there was not enough publicity given to the fact that this drug was actually condemned in France. The French Health Ministry had declared this drug worthless and had forbidden its use in France. We did not see much publicity on that point. We saw a great deal of publicity on the fact that this man was coming over and was going to give it to this boy. We cannot interfere with what a doctor gives to his patient—that is not the point. If I am suffering from leukemia, and I see this, I will think this wonderful and I will want to try to get this. This may be very harmful and discouraging to a great number of people.

Mr. MITCHELL: To look at the other side of the picture, there are a great many clinical reports which are publicized by very eminent physicians who are working on a cure for cancer, which I think is good publicity.

Mrs. PLUMPTRE: Do these get into the daily press?

Mr. MITCHELL: Yes, indeed.

Mrs. PLUMPTRE: If it is publicity which puts the thing into perspective, then it is fine, but I feel at the moment this, and the other trial going on at the moment, and the way that this is brought to the people, is very misleading and very dangerous.

Mr. MITCHELL: Probably in your presentation here you could use the phrase "at the present time a great deal of bad publicity is being given".

Mrs. PLUMPTRE: I will go along with that.

Mr. MITCHELL: I think Dr. Harley will agree with me and Dr. Rynard would also if he were here. We get reports in the newspapers of new tests being carried out by eminent physicians, not only on cancer, and of other breakthroughs which may lead to an eventual cure for this or that disease. Those are also publicized.

Mrs. PLUMPTRE: That is a slightly different field from absolute quackery. The thing I am discussing is the case of laetrile the manufacture of which was forbidden in California.

Mr. MITCHELL: I realize that.

Mrs. PLUMPTRE: I am prepared to say it is "bad publicity".

Mr. MITCHELL: That is what I am getting at.

The CHAIRMAN: Are there any other questions, gentlemen? If there are no other questions, on behalf of the committee I would like to thank Mrs. Plumptre for coming and presenting her brief today. We appreciate your interest in our committee's work very much and we thank you for coming here.

The meeting is adjourned until Friday at 9:30.

HOUSE OF COMMONS

Second Session—Twenty-Sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 9

FRIDAY, JUNE 26, 1964

WITNESS:

Dr. Robert Imrie, M.D., in charge of the Poison Control Centre, Hospital for Sick Children, Toronto (Ontario).

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21033—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Casselman (Mrs.)
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jorgenson
Macaluso
Mackasey
Marcoux
Nesbitt
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

FRIDAY, June 26, 1964.
(14)

The Special Committee on Food and Drugs met this day at 10.05 a.m., the Chairman, Dr. Harry C. Harley, presiding.

Members present: Messrs. Côté (*Longueuil*), Enns, Francis, Harley, Horner (*Jasper-Edson*), Roxburgh, Slogan, Whelan, Willoughby (9).

In attendance: Dr. R. Imrie, M.D., Paediatrician in charge of the Poison Control Centre at the Hospital for Sick Children, Toronto (Ont.).

The Chairman announced that Dr. Theodore Sourkes of Montreal has been invited to appear before the Committee on Friday, July 3rd.

On motion of Mr. Willoughby, seconded by Mr. Whelan,

Resolved (*unanimously*),—That this Committee pay reasonable living and travelling expenses incurred by Dr. Theodore Sourkes, Assistant Professor of Biochemistry, Department of Psychiatry, Allan Memorial Institute, Montreal, by reason of his appearance before this Committee, and that a per diem allowance be made to him.

The Chairman introduced Dr. Imrie.

The witness gave a general outline of the operation and functions of the Poison Control centres. He had circulated among the members the forms to be filled at the Centre in each case of poisoning, and the cards of different colours filed for ready information about the contents of toxic substances and treatment thereof.

Dr. Imrie was questioned particularly on the main hazards and causes of poisoning of children, and on related matters.

The questioning being concluded, the Chairman thanked Dr. Imrie for his most interesting information.

At 11.00 a.m. the Committee adjourned to 9.30 a.m. Friday, July 3, to hear Dr. Sourkes.

Gabrielle Savard,
Clerk of the Committee.

21033—1½

EVIDENCE

FRIDAY, June 26, 1964

The CHAIRMAN: Gentlemen, we now have a quorum. Next Friday, July 3, we will have before the committee Dr. Theodore Sourkes, Assistant Professor of Biochemistry, Department of Psychiatry, Allan Memorial Institute, Montreal. I would like to have from the committee the usual resolution to pay for his living and travelling expenses.

Mr. WILLOUGHBY: I move that Dr. Sourkes receive his living and travelling expenses.

Mr. WHELAN: I second it.

The CHAIRMAN: Gentlemen, I would like to introduce to you Dr. Robert Imrie, paediatrician in charge of the poison control centre at the Hospital for Sick Children in Toronto. I think it was in 1957 that the first Poison Control Centre was opened in Toronto, and Dr. Imrie has been in charge of the program since that time. The best thing to do would be to turn the meeting over to Dr. Imrie. He has a few general remarks to make about the Poison Control Centre, and then the meeting will be open for questioning.

Dr. ROBERT IMRIE: (*Director, Poison Control Centre, Hospital for Sick Children, Toronto*): Mr. Chairman, it is certainly my pleasure to have the opportunity to sell my wares! It pleases me that we have a group of individuals from across the dominion who are interested in the problem of drugs. I, as a paediatrician, and specifically director of the poison control centre at the Hospital for Sick Children, am keenly interested in this whole problem because of the number of accidents which do occur, and unfortunately the number of deaths that do occur in this age group. As the Chairman has said, the poison control program was organized by the food and drug directorate late in 1956 because of the tremendous numbers of children coming into the emergency units in the hospitals who had consumed considerable quantities of tablets and various household preparations of one type or another. The poison control program was therefore set up and it was thought wise to place the poison control centres in the emergency departments in the hospital.

As you examine the statistics over the years you see that the biggest percentage of these accidents do occur in the large metropolitan areas. They therefore set up these poison control centres primarily as a place where patients could be taken and treated, and where information on the various drugs and the various household products, could be organized and be readily available. At the beginning there was very little information on who was at risk, was it an older child, was it a younger child, were they boys or girls, and what were the hazardous substances they took, where they were, what were the original containers. In 1956 little was known of the epidemiology of accidental chemical poisoning. The food and drug directorate devised a form that was easy to tick off and would provide good statistics easily. The first one was this report of the poisoning form. These are found in the various poison control centres throughout the dominion of Canada. The form gives the name of the patient, the address of the patient, the name of the hospital or the physician's office where the child was taken, the date it came in, the birth date, the sex. It is interesting that there is a preponderance of male children

involved in these accidents. It gives the type of product, whether it is insecticide, fuel oil or bleach; it states whether it was an accident or an overdose and the trade name of the product. This has proved very satisfactory because it was easy for the residents or for the physicians to complete and send to Ottawa, and statistics were then made from these particular sheets.

There were so many cases coming in and going home the next day that we devised another form "follow-up of the poison" case. This brought a lot of interest because it provided an opportunity to see thousands of cases in a year.

Much has been written in recent months about the safety of drugs, and much has been written about the testing of drugs. The pharmaceutical companies do a tremendous amount of testing, but all this testing has been done on adults, and really very little information is available on children. These "follow-up of poison" forms have proved excellent because many reactions of children to drugs have differed from the reaction of adults. We were able to get a considerable amount of information along this line because what we thought might happen to a child did not happen. The day after every child comes in my secretary phones to find out how the child is, and if anything has occurred in the interim period. If the child is admitted to the hospital you have the opportunity to examine him during that period of time, but this follow-up is a good idea and it gives us the opportunity to talk with the mother in an attempt to prevent this accident from recurring.

As far as the poison control centre at the Hospital for Sick Children is concerned, if we recognize the neighbourhood of the mother as being of a low socio-economic area, then we contact the public health nurses. They will then go in and talk to the parents within 12 or 24 hours after the accident, which is a great help because this accident is fresh in the parents' minds and you can do an excellent bit of public health teaching in this regard at that time. Therefore, those two forms, the report and the follow-up of poisoning, have given us a considerable amount of information.

As I mentioned before the poison control program was set up primarily because someone would come into the emergency unit and would bring a bottle on which all that was writen was "Zymophos". You had no idea that it contained glycerophosphates, alcohol and strychnine. The other day we had another one—Asceptine, which contained methyl salicylate.

So, with the co-operation of the patent medicine division these cards were printed and they were sent around to the various poison control centres. The government thought it handy to put on these cards the name of the product, such as asceptine and the fact that it contains methyl salicylate, boracic acid and alcohol. Originally there were 3,000 cards printed and these relieved a lot of apprehension associated with chemical poisoning and this has proved a very simple and effective method. These $2\frac{1}{4} \times 3\frac{1}{4}$ filing cards have proven very simple yet effective in listing the names of all the potent medicine, and many household products, and the substances they contain.

They thought it would be wise to put these on different coloured cards, primarily for ease of identification. The holes that you see in the bottom of the cards are for the card file wheel. We file them alphabetically just as they are listed in any dictionary. The white cards are for insecticides, rodenticides and pesticides. As you know, these are very hazardous and if a child gets any quantity of these we want to know about it more rapidly. They are on white cards and they are easily picked up. The green cards list suggested treatments for a particular product. If the child has taken perborates or bromates of sodium and potassium the card gives the best known method of treatment. These cards were sent around to the various poison control centres in the Dominion of Canada. As I say, they are very simple and they certainly give the information one needs to know about the various products.

The United States also have a system of cards which they send out. Their cards happen to be a little more comprehensive than ours, and that is all right but it is unnecessary really because there is a tremendous amount of repetition.

One can try as hard as one might, but no one can keep up to date with the number of products that come on the market every day. It has been conservatively estimated that there are 750,000 household products on the market, and hazardous household products come out at the rate of 800 to 1,000 a month. With the present mass methods of communication we can expect that this major public health problem will be with us for some time to come. When we become accustomed to one particular product used in the home, another comes along. This is why we have to be kept up to date. There are many books that list many thousands of products than are able to be listed on these cards.

When the child comes to the hospital he comes to the emergency unit, and quite often the mother will bring a container or a tablet that the child has taken or will tell us what the child has taken. The necessary information is obtained rapidly and the child goes into another room, which is affectionately known as "ye olde pump room", where the gastric lavage is done to empty the stomach of the substance which the child has ingested.

We do various tests. Sometimes if we know the child has taken aspirin we will prick the child's little finger to obtain some blood and measure the salicylate level of the child's blood. Sometimes we test the urine for various substances. This is all done in the emergency department. If we are worried about the child in any way or if the child has taken an unknown quantity of a relatively serious preparation, that child comes into hospital. When we are satisfied the child is well we send him on his way.

That is the general outline of the poison control centre, which functions primarily to treat these cases, but it also functions to do research work on various problems and to find out better treatments, and, most important, to disseminate as much information as possible to the lay and professional public on the ever present hazard of accidental chemical poisoning. These accidents can and do occur in every room in every house in the community.

The CHAIRMAN: May I ask a question? I am sure of the answer myself but it may be useful to the members. This poison control centre functions 24 hours a day, seven days a week?

Mr. IMRIE: Yes, it does. It operates 24 hours a day. We are changing the set-up, however, because currently I have a secretary there only between nine and five. While she is there it is quite effective but when she is not it is a little less effective because then the work falls to the residents on call. Recently the province of Ontario's department of health has become interested in manning the centre from eight in the morning until midnight, which will give us that much more accurate coverage.

Mr. ROXBURGH: Dr. Imrie, you have partly answered my question but I was going to ask you whether you have all the new drugs as they come out on the market. You have pointed out that they come out at the rate of 800 to 1,000 per month—new drugs or poisons or whatever it may be. Would it be practical or possible not to allow any new insecticide or drug which contains poison and could cause death to be put on the market until all facts are given to the control centres?

Mr. IMRIE: I have said that there are about 800 to 1,000 new products coming on the market every month. This includes drugs, insecticides, pesticides, cleaning solutions, sanitizing solutions, make-up, deodorants and everything that is present in your home. These come in under many aspects of government. They are now attempting to do this, I am sure, and under the poison control program we are being sent new cards; we are being kept up to date.

Mr. ROXBURGH: That is going a long way, granted, but is there any possibility of having a report sent in to the centres before any of these are allowed on the market? Surely that could be done; it could be sent to the centre in Ottawa and that would be sent on to you people. That is not in force at the present time, is it?

Mr. IMRIE: I would say it is to a considerable extent. I think the patent medicines department or the food and drug directorate are cognizant of the new products that come on the market.

Mr. ROXBURGH: But it has not yet been put into full force?

Mr. IMRIE: Not every product that comes out is sent to us. There must be a filtering process, the ones they think we should know about are sent to us.

Mr. ROXBURGH: It is only partially controlled?

Mr. IMRIE: Yes, I am sure it is only partially controlled at present.

Mr. ROXBURGH: It should be fully controlled.

Mr. IMRIE: Yes, I agree.

Mr. ROXBURGH: They have a control centre in the town where I happen to live. How is it brought about that it is that particular place instead of some other place where they have a centre? Is there a plan?

Mr. IMRIE: No, there is no plan or, rather, I should say there was no plan originally. However, accidents were occurring in other places in the province. It was really done in an haphazard way. If someone became interested they would apply to Ottawa directly saying that they wanted to set up a poison centre and they would ask the department to send cards; and then these people would begin a centre in their emergency wards.

In the last year or two the request for centres come through the department of health of each province. If you should say at Simcoe that you wanted to set up a poison control centre, the opportunity would be given to you, and the cards would be sent to you.

Mr. ROXBURGH: There has been nothing done in an organizational way provincially or otherwise.

Mr. IMRIE: Do you mean to limit the number?

Mr. ROXBURGH: Well, to see that the poison control centres are properly distributed.

Mr. IMRIE: I would have to say that in an organizational way, there has been no overall plan. But it so happens that it has been "effective" haphazard coverage. For example, I am thinking of the Children's Hospital at Halifax. This was one of the interests of the Canadian Paediatrics Society, which realized that chemical poisoning was a children's problem.

Mr. SLOGAN: How many are there across Canada?

Mr. IMRIE: Two hundred and twenty.

Mr. ROXBURGH: In the case of minor control centres, these are open 24 hours a day?

Mr. IMRIE: Yes, that is right.

Mr. ROXBURGH: Do they receive all the information that is necessary as fast as you do? I mean the information that we have been talking about.

Mr. IMRIE: Yes, to my knowledge it is sent to the poison control centres. They are all of the same status, and they all receive the same information.

Mr. ROXBURGH: Thank you.

Mr. IMRIE: I would like to stay on this subject. The reason I would like to stay on this subject is that we could have talked about the haphazard set-up. I think that is a good point. I cannot see any reason why there should be

a poison control centre at Simcoe. With the excellent communications available, I think it would be much better if there were one or two large information centres in our country. I think it will come about in time. Then they could be staffed adequately with all the information readily available, so that all you would have to do would be to phone from Simcoe to Ottawa, or to Montreal, and you would get your information in a hurry, and would know that it was the best information.

At Simcoe the Poison Control Centre might be taken over by a local practitioner who is not really interested in it. Or, it is left to the nurses. They get the cards, and the material is shoved into a corner, and it is not kept up to date.

We would like to see—and I think it is coming—one or two well organized and highly developed poison control centres where all this information is kept in much greater detail, and where you can find it.

For example, in New York city there is a tremendous poison control centre which is run by the department of health. This is just one. Then in Washington there is another big one. And there is another in San Francisco. So if anyone has a problem, he phones anyone of these three centres and they have up to date high class information available on a 24 hour basis. It would be impossible to do this at Simcoe.

Mr. ROXBURGH: That is what we really need.

Mr. IMRIE: Yes. I am sure.

Mr. WHELAN: One of the things I wanted to ask Dr. Imrie about has been partly covered in his answers to Mr. Roxburgh's questions. However, last night on the C.B.C. they interviewed a doctor from some place in the United States. I think he was speaking at some annual meeting at Vancouver, and he said that a doctor would have to spend nearly full time studying the new drugs that come out at the rate of 30 to 40 a year, and that it was hard for them to keep up with the information. He said—and maybe I should not use the word—that they are running a hazard in the use of some of these drugs because if they waited until all the information was available there might be undue suffering because the drugs were not being made available. That is the meaning I got out of the statement. Might I ask if that is the feeling of Canada in the matter?

Mr. IMRIE: I did not see the program you refer to, so I cannot say. But I think you must remember that you have to be very careful in what you do. You must remember that you have to crawl before you walk, and that you have to learn to walk before you run. In the development of drugs, if they are not tested effectively in as many different ways as possible, it becomes extremely hazardous. Therefore, we should be extremely careful. I think we have sufficient information on the subject to say that we will never have a thalidomide problem again. There may be 10, 15, 25 or 30 new drugs coming out in a year; but the problem there is quite different from that of new household products which children can get hold of. They come out at the rate of 1,000 a month in the North American continent.

In the case of new drugs, we should be more careful in the future than we have been in the past to make sure that they are properly tested. They are now tested on adults, but it is a little ticklish to test them on children. However, there are one or two rules of thumb you might follow.

An adult might swallow a pound of aspirin. But that adult may weigh 170 pounds, and if we say that he can take one pound of aspirin, and here is a child weighing only ten pounds, therefore we can safely give that child 1/17 of a pound of aspirin—this is utter nonsense. You have to know for sure how much the child can take. This is something which should be investigated, but it has not been done.

Or take the case of morphine. An adult may be suffering tremendous pain and you can give him $\frac{1}{8}$ or $\frac{1}{4}$ of a grain. On the other hand, we can use $\frac{1}{8}$ or $\frac{1}{4}$ grain on a child and not be alarmed, actually very safe because a child tolerates morphine, to this extent.

We have in the past tested drugs primarily on adults, and then worked downwards to say: If this can be good for a 150 pound man, therefore, $\frac{1}{6}$ of the amount should be all right to give to a 25 pound child. But that is not right. It is easy to test a new drug on a patient who is dying of cancer. You simply ask the patient for permission, and he will say very well. But how can you do this in the case of a five year old child?

But it has to be done in the future. Of course a parent might say: Would you like to test this and give it to the child? It is important that we test drugs on children which are to be used on children and not simply rely upon having tested those drugs on adults. We cannot say that if it is all right for an adult therefore it is all right for a child.

Mr. WHELAN: In the treatment at poison control centres, or at your own Sick Children's Hospital, what do you feel is the main reason that these children are poisoned and require treatment in the first place?

Mr. IMRIE: The main reason is ignorance on the part of the parents of the hazards involved with these every day products that are available. People may say, for instance: "Well, there is nothing the matter with headache tablets, or aspirin. If you can feed them to a child, they cannot be too bad." But they do not realize that to take one every four hours is fine, but to take a whole bottle is too much.

Or, for example, a member of the family may be sick. He may have to remain in bed. He may have a bottle of pills with instructions to take one every five hours or so. That bottle of pills may be left on a bedside table not too high off the floor, and within the reach of a child. A child may come in and take the pills, perhaps a whole bottle of them. That is not good.

Or, again, in a given household there may be a grandmother suffering from heart disease. The grandchildren come to see her over a week end. She may leave her heart tablets on a bedside table, which is a handy place to keep them, and she may not think that the three year old grandchild would eat them. However, he is of an age when he eats all the things he is not supposed to. If you give a child too much digitalis, he can die. These people do not realize that these are hazards, and that these drugs should not be left within the reach of children.

Mr. WHELAN: The Canadian Association of Consumers recommended that we teach safety in the use of drugs to our school children.

Mr. IMRIE: I think it would be much better to leave these medications alone. This is not a child problem. It is an adult problem, strictly. If you want to be sure, you must keep these preparations out of the reach of children.

Mr. WHELAN: I am of the same opinion. Now, one other thing: In the area in which I live we have a poison control centre at the Hôtel-Dieu hospital at Windsor.

Mr. IMRIE: Yes.

Mr. WHELAN: We are quite proud of it. I have the local telephone directory of my home town before me, and I notice that they have it right on the front page "Poison Control Centre", and it is plainly shown there for anyone who wants to use that service. How do you do this in Toronto?

Mr. IMRIE: The same way.

Mr. WHELAN: It is listed?

Mr. IMRIE: Yes. The telephone companies have co-operated in this. I would not be surprised if this is true throughout the whole of the dominion;

that is, that on the front page where they have the number of the hospital, the police, and the fire station, they also have the poison control centre. The Bell Telephone Company is listing the poison control centres on the first page.

Mr. WHELAN: In metropolitan Toronto your poison control centre is the only one?

Mr. IMRIE: Yes, the only one in operation.

Mr. ENNS: Did you say there are some products which are improperly labelled; that is, that they do not list the contents or the poisonous substance? Was I correct in hearing that?

Mr. IMRIE: Yes; I think you were. The way it was developed in 1957 was that a lot of things came into our Poison Control Centre and they did not have the ingredients listed on the outside. This is not so to the same extent today. Most of the products which you see do have the name of the substance.

Mr. ENNS: At earlier meetings of this committee we have been very concerned about labelling and the fact that labels should have the information. We have been wondering about making a recommendation concerning the style or method of labelling so that the information will be dramatically drawn to the attention of the consumer. Obviously, this has been done to some extent.

Mr. IMRIE: Yes. This was the problem when it first came in. So many of the containers did not have any information. It might say, for instance, roach powder on the outside, but it did not say that it contained fluorides or malathion; but now it does, and it is not as much of a problem now as it was—if you get the container; but someone may come in and say it was Black Leaf 40, but does not have the container, and then you look it up and find that it contains nicotine.

Mr. ENNS: You believe it would be better to have a few up to date centres rather than the smaller ones?

Mr. IMRIE: Yes. If you are interested in things, you are looking into them all the time and reading about them; in that way you become much better at it. I am sure that two or three well developed centres are much better. The present multi-centre organization here has spread "the gospel" in respect of chemical poisoning throughout the Dominion of Canada. In this way many people have become more interested in it and are talking about it. Now, however, I think we should go one step further and make it more highly organized.

Mr. ENNS: In respect of these cards which you have circulated, I take it that the first two mainly are for statistical control.

Mr. IMRIE: Yes. It helps us organize this. In the eastern part of Canada we find that fuel oil is a big problem because, apparently, a number of people cook with it. It does not happen in Ottawa or Toronto at all, but in some places this is happening and it is good to know what is happening and where.

Mr. ENNS: This type of information would allow you to tabulate the incidence of certain poisons and the fatalities resulting from the use of these. Generally, would you be able to say what is the biggest killer?

Mr. IMRIE: Without any question at all, the biggest killers are medicines. That is why the medical profession has to be interested in it. Directly or indirectly these commodities are in the house on our suggestion. Sixty per cent of all the cases we see are due to the ingestion of one type of medicine or another, like headache tablets, cough mixtures or pain relievers.

Mr. ENNS: Would these items head the list?

Mr. IMRIE: Yes. Sixty per cent of all the cases in our hospital, in the Winnipeg General or any hospital, are due to the ingestion of one type of medicine or another. Therefore, this could be all controlled if every home had a medicine cabinet and everything was stored in a locked medicine cabinet.

This would be a very effective method of reducing the hazard. The remaining 40 per cent is cleaning and polishing solutions, paint, cleaners, insecticides, pesticides, turpentine, etc., etc. If we could make sure that all the medicines in the house—which involve 60 per cent of the problem—were kept in a locked cupboard, I would be out of a job!

Mr. ENNS: Generally, how old would the children be who are involved?

Mr. IMRIE: Ninety per cent of them are children who are under five years of age; 90 per cent of the problem involves preschool children. You do have older children, but it is rare.

Mr. CÔTÉ (*Longueuil*): Most of them would be children who have not attained the reading age.

Mr. IMRIE: Yes. That is why the parents must see to it that these things are locked up.

Mr. CÔTÉ (*Longueuil*): Do you think that flavouring of pills, and so on, by these companies may have an effect?

Mr. IMRIE: Yes; this enhances the problem. You can clearly see this in the case of the headache tablets—aspirin.

Mr. CÔTÉ (*Longueuil*): Aspirin tastes very badly.

Mr. IMRIE: No. This is just namby-pamby nonsense. In 1934 or 1935, you would take a five grain acetylsalicylic acid tablet and cut it in half and give it to a child. Then people began to make the drugs taste better and colour them. They said, if we colour it or make it taste better it will be more palatable and the kids will go for it. Chocolate coated tablets were first, and then they said, we will work on the colouring of it. They chose pink, just the same as the red lights that you can see further away. Then they made them candy flavoured. They said, "Take your aspirin; it tastes just like candy". This is what we buy, and this is what the mothers will say: "Be a good little boy, take your tablets because they taste like candy". Then he sees a bottle and he will eat the whole bottle. In Great Britain they do not have any aspirin problems. There are very few in that regard because all their aspirins are white, five grain and of a chalky type.

About a year or so ago I received a letter from the professor of paediatrics in Glasgow asking what we do in respect of iron poisoning, and the treatment we use. He asked me to correspond. When I looked up our files in this regard I found we had nothing on the subject, and I could not understand what the problem was. I made some inquiries and found that overseas they use iron quite freely in their iron tablets, which are green and candy flavoured. It is rather obvious that the colour does make a difference, but you cannot blame the manufacturer in that regard.

I do not make any important suggestions in respect of this difficulty because we still must refer back to the basic problem. Parents are responsible for the welfare of their children. Tablets should be kept somewhere where children do not have access to them. However, the colour and taste of the tablets is rather important, because children will eat large quantities.

The taste of pills in itself is not a deterrent. Children will drink turpentine, for example, and there are people in this room who will eat pepperoni, think of that! We cannot hide under that guise. We cannot make the taste terrible and expect children not to eat tablets.

Mr. SLOGAN: Referring again to the matter of labelling, is it true at this time that the information appearing on labels must contain some warning in addition to the name of the ingredients?

Mr. IMRIE: I do not know.

Mr. SLOGAN: Does the information on labels contain a warning in respect of the contents as well as a list of the ingredients of the product?

Mr. IMRIE: A great number of drug stores and pharmaceutical organizations voluntarily suggest to potential consumers that the product should be kept out of the reach of children. I think that is a very advantageous practice. At one time poisonous products had a label showing a skull and crossbones, but once the use of that symbol became common no one paid attention to it. Now in common use is a label with the suggestion to potential consumers to keep the product out of the reach of children. At least users can see that warning and know there is some danger.

Mr. SLOGAN: Many household products are dangerous if taken internally, and I know this is true in respect of your example of hairwaving preparation. Do you feel something should be stated on the label to the effect that these preparations are dangerous if taken internally?

Mr. IMRIE: I think perhaps that should be stated on the label or a warning to keep the product out of the reach of children.

Mr. SLOGAN: Do you think that should be mandatory?

Mr. IMRIE: It could very easily be made mandatory, I am sure.

Mr. ROXBURGH: I certainly agree with that statement.

Mr. SLOGAN: I understand there are some 220 poison control centres in existence, and after looking at your cards, which are very fully distributed and no doubt filter down to the small communities, I have the feeling that some of the small rural hospitals receive them, but at times individuals may be brought into those hospitals when a doctor is not in attendance. I am wondering whether these cards should contain more information so that perhaps under those circumstances the nurse in attendance would have the benefit of that additional information?

Mr. IMRIE: A nurse would not treat a patient. She may assist the doctor in treating a patient but is not allowed to make a diagnosis or give treatment. A doctor always has to be in attendance before a patient can be treated. The nurse would not accept the responsibility of treating a patient.

The CHAIRMAN: I would think that is correct.

Mr. IMRIE: Treatment of a patient would be something beyond the ability of the nurse. The card which I have produced has been in my briefcase for some time. I am afraid it gives you a rather poor example, because in recent years there have been a great many more cards produced which include much more specific information.

Mr. SLOGAN: Would the cards you distribute indicate an antidote?

Mr. IMRIE: I am glad you mentioned that word because there is no such thing as an antidote. We hear many people referring to antidotes, and, with perhaps very few exceptions, there is no such thing as an antidote. If a patient suffering from morphine poisoning is admitted, that patient can be treated with a dose of nalorphine. People think of an antidote as something you can give a child, who has taken a poison, in a proportionate amount and counteract the effect. Each poisoned child must be treated on the basis of the particular symptoms shown by that child. The sooner we dispel this antidote idea the better.

Many people think that if a child takes a pound of aspirin all you have to do is give that child a pound of bicarbonate of soda and everything will be all right. Many people believe if a child takes two or three mouthsfull of turpentine you can give them two or three mouthsfull of gasoline to counteract the effect, but treatment does not follow that principle. There are no antidotes, each individual case must be treated in accordance with the symptoms shown the information appearing on labels under the general heading "antidote" are only suggested treatments.

The effects of potential poisoning vary considerably depending upon the individual. For instance, everyone in a family except the children may be going out for the evening, and the parents give the children a barbituate, such as seconal containing three quarters of a grain, so that the children will sleep, and the parents will then assume that the children will go to sleep but instead the chidren may be climbing the walls because the seconal does not have the normal effect, as a central nervous depressant, but has the effect of a central nervous stimulant. One cannot be sure of the effect of a tranquilizer because different individuals react in different ways. In any event there is no such thing as an antidote.

Perhaps I should qualify that statement by stating there are very few specific antidotes available today for the treatment of accidental poisoning. Each individual has to be treated in accordance with the symptoms developed.

Mr. SLOGAN: Would you agree nevertheless that there is some advantage to be gained by the inclusion of information of that type in directions printed on labels?

Mr. IMRIE: I would agree there is some advantage to be gained in that way, and the format in respect of labels used today is similar to what you suggest but the subject matter is more comprehensive.

Mr. CÔTÉ (*Longueuil*): Can you tell us how many children die per year as a result of accidental poisoning?

Mr. IMRIE: Approximately 300 Canadians die from poisoning each year, about 30 or 40 of which are children under five years of age.

Mr. CÔTÉ (*Longueuil*): Do those figures indicate that it is easier to treat children under five years of age than individuals over five years of age?

Mr. IMRIE: No. I am afraid those figures are rather confusing because they include such things as suicides. The figures relate to poisoning mortality and cannot be interpreted as relating to only accidental deaths.

Mr. CÔTÉ (*Longueuil*): You suggest 30 or 40 children die per year from accidental poisoning?

Mr. IMRIE: There are approximately 30 or 40 children under five years of age die per year as a result of the accidental ingestion of poisonous products.

Mr. CÔTÉ (*Longueuil*): You suggest there are 30 or 40 children under five years of age die per year as a result of poisoning. How many cases in all are involved? Do you know how many cases of poisoning are dealt with each year?

Mr. IMRIE: In 1963 there were 17,727 cases of accidental poisoning reported to the food and drug directorate. In order to arrive at any conclusion in this respect one would have to know how many cases occurred but were not reported. The officials in Simcoe may not report cases of poisoning to the food and drug directorate, for example.

An hon. MEMBER: That is perhaps a backward area.

An hon. MEMBER: It may be similar to Kamloops.

Mr. IMRIE: Did I hear someone mention Kamloops? Perhaps the officials there do not report cases of poisoning either. I am sorry to be stumbling in this regard but I understand there are approximately 300 Canadians killed per year of which 30 or 40 are children under five years of age.

Mr. ROXBURGH: Would you expect the number to be greater than 300 in the absence of control centres and the information made available through those centres to the treating physicians?

Mr. IMRIE: That is a very nice suggestion for those who work in this particular field but I do not think it is true. I think the major function of the poison control centres is to relieve the apprehension associated with the ingestion of one type of product or another, rather than to save lives, because

while there are some who ingest poisonous products there are relatively few who die as a result. Our mortality figures indicate that in 1957 we had one death; 1960, four deaths; 1961, three deaths; 1962, four deaths; and 1963, one death, all associated with the ingestion of one type of product or another. These figures are not absolutely accurate because some of those cases were transferred from one hospital to another. For example one case came from Newfoundland. The mortality rate has decreased. In 1963 we treated 1,554 cases of accidental poisoning with only one death.

Mr. ROXBURGH: The point I was getting at is that if we did not have these smaller poison control centres throughout the country with the information which is available to them and a case came in, say from my county, or any other place, death might be more apt to happen if this information was not available.

Mr. IMRIE: Yes, but if there was a case, say, in Norfolk county, the person would be taken to the emergency unit of the Simcoe General Hospital and cared for by the doctors who were in attendance there. I know when you are interested in something it is wise not to bend too far over backward in favour of yourself, but if this person was taken to the Simcoe General Hospital, as I say, treatment would be given there by the doctors in that area. But, I am sure we have this organized much better and we do get this information to the doctors in a hurry. But, these centres do have the effect of relieving a lot of apprehension. This is something similar to law enforcement. No matter how hard they try there is still a great number of traffic deaths on the highways and byways of this country. This also is true to an extent of us. But, as I say, we do relieve a tremendous amount of apprehension, which is good. I do know that we treat aspirin poisoning better now than before because we are conscious of it.

Mention was made of a meeting out west where Dr. Medovy was speaking. He said that they have many cases in their hospital where patients come in and are not known as poison cases when they come in and sometimes it takes one or two days before they find out. But, we do not experience that problem in Toronto because of our different set-up. The internes are sharp in regard to this chemical poisoning problem; they are thinking of it all the time, as a result of which a diagnosis can be made in a hurry and treatment given in a hurry. The same child may not die at the Winnipeg General Hospital but it may take them longer to ascertain what the trouble is. Another thing which is of importance is that ours is a closed hospital. We have only paediatricians on the staff, whereas at the Winnipeg General Hospital, although there is a paediatric ward, all the doctors in Winnipeg can admit through there. Another thing, we are interested only in children, whereas the others have patients of all ages.

The CHAIRMAN: Although I know the answer to the question I am about to put, perhaps it would be helpful to others. You have mentioned that 60 per cent of all poisoning is caused from medication. Could you tell us what is the medication which is more responsible for poisoning of children than any other?

Mr. IMRIE: One third of all the cases are due to the ingestion of acetylsalicylic acid, headache tablets, pain relievers, whatever you like to call them. However, one third of the cases are due to that. If we could keep these aspirins in a locked cupboard it would be fine. This is the kind of information we should attempt to disseminate amongst our population. We should endeavour to educate them in this aspect of it.

Mr. HORNER (*Jasper-Edson*): Do these poison control centres receive any assistance? Do they receive a grant from the federal government?

Mr. IMRIE: No, there is no financial assistance, to my knowledge. But, when we set this up in 1957 we did receive some aid from the food and drug directorate.

Mr. HORNER (*Jasper-Edson*): But, is there not a national health grant to the provinces which would cover this?

Mr. IMRIE: Although I am not sure, to my knowledge there is not. They supply the information but they do not supply the secretarial help or the card files or anything like that.

Mr. HORNER (*Jasper-Edson*): In Alberta they have quite a system in this respect. We have one in our hospital. However, the trouble we have had out there pertains to the same thing about which you have been speaking, lack of better information. There should be a better information centre at the top.

Mr. IMRIE: Yes, I agree with you.

Mr. HORNER (*Jasper-Edson*): There should be more information available particularly in respect of the newer drugs that are coming out and the newer combinations of drugs, and in this respect there is little or no information on the card files. The thing is they do not catch up fast enough.

Mr. IMRIE: That is correct.

Mr. HORNER (*Jasper-Edson*): The difficulty we have been having is that we phone the university hospital and if they cannot give us assistance where do we go from there? I agree with you when you say we do not need so much a poison control centre as we do a poison information centre in order that we may obtain information about some of the newer things. Of course, out there, chemicals connected with the agricultural industry are very important and on a good many occasions we find that we do not know people have been poisoned because they may have been poisoned accidentally by 2-4D or other such things which have come into use recently. I think an information centre would be much more essential.

Mr. IMRIE: I believe Alberta did it differently from anyone else; they sent these cards out to every hospital. Is that not the case?

Mr. HORNER (*Jasper-Edson*): Every hospital has a card file and a circular file with all the information there. Then there is a central clearing house at the University Hospital in Edmonton. The only trouble with the clearing house is that there is not sufficient information available and it is not staffed, if I may say so, with staff who are as interested as they may be.

Mr. IMRIE: I know the fellow in charge of it out there and I agree 100 per cent with you. He is a paediatric friend of mine. It is run differently out there. The cards are changed around and no one is specifically designated to be in charge. But, if there was a problem all you would have to do is pick up the telephone and phone Edmonton.

Mr. HORNER (*Jasper-Edson*): We usually do that anyway.

Mr. IMRIE: They have a good centre there. Also, you could phone Winnipeg. You see, you do not need that many centres.

The CHAIRMAN: If there are no further questions I would like to thank Dr. Imrie for coming here today. He has given us some very interesting information on poison control centres.

There will be no meeting on Tuesday. We will adjourn until one week from today.

HOUSE OF COMMONS

Second Session—Twenty-Sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 10

FRIDAY, JULY 3, 1964

WITNESS:

Dr. Theodore Sourkes, Ph.D., Associate Professor of Biochemistry, Department of Psychiatry, Allan Memorial Institute, Montreal, Quebec.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21098—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Casselman (Mrs.)
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jorgenson
Macaluso
Mackasey
Marcoux
Nesbitt
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

ORDER OF REFERENCE

THURSDAY, July 2, 1964.

Ordered,—That the Special Committee on Food and Drugs be empowered to go to Pearl River, New York State (U.S.A.), on Tuesday, July 7, 1964, to visit, at the invitation of Cyanamid of Canada Limited, the Lederle Research Laboratories of the American Cyanamid Company.

LEON-J. RAYMOND,
The Clerk of the House.

21098—1½

REPORT TO THE HOUSE

The Special Committee on Food and Drugs has the honour to present its

THIRD REPORT

The Committee recommends that it be empowered to go to Pearl River, New York State (U.S.A.), on Tuesday, July 7th, 1964, to visit, at the invitation of Cyanamid of Canada Limited, the Lederle Research Laboratories of the American Cyanamid Company.

Respectfully submitted,

HARRY C. HARLEY,
Chairman.

(This report was concurred in Thursday, July 2nd, 1964)

MINUTES OF PROCEEDINGS

FRIDAY, July 3, 1964
(15)

The Special Committee on Food and Drugs met this day at 10.00 a.m., the Chairman, Mr. Harry C. Harley, presiding.

Members present: Messrs. Côté (*Longueuil*), Harley, Mackasey, Marcoux, Mitchell, Orlikow, Rynard, Whelan, Willoughby (9).

In attendance: Dr. Theodore Sourkes, Ph.D., Associate Professor of Biochemistry, Department of Psychiatry, Allan Memorial Institute, Montreal, Que.

The Chairman introduced Dr. Sourkes who read a prepared brief. He was questioned thereon.

The questioning concluded, the Chairman mentioned the visit to Pear River N.Y. and informed the Members that a letter will be sent by the Clerk of the Committee today, giving more information about this trip.

It was agreed that the Chairman ask the Cyanamid of Canada to present their brief on Thursday, July 9th instead of Friday the 10th, and that the Friday meetings be rescheduled to Thursday.

The Chairman expressed the appreciation of the Committee to Dr. Sourkes for his appearance, and for supplying information on the biochemical approach to the question of the safety of drugs.

At 10.30 a.m. the Committee adjourned.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

FRIDAY, July 3, 1964.

The CHAIRMAN: Gentlemen, as everybody realizes, the house meets today at 10.30. We have with us this morning Dr. T. L. Sourkes, from Montreal. I think, under the circumstances, we should go ahead with the meeting.

Might I just say that the steering committee have scheduled meetings up to July 17, but no meetings after that. I think that is probably a very realistic attitude.

Mr. MACKASEY: Mr. Chairman, if there are any more meetings already scheduled for Friday morning, perhaps we might reschedule them.

The CHAIRMAN: I was thinking of rescheduling the meeting set down for Friday, July 10, when we shall have a brief from Cyanamid of Canada Limited. I was thinking of rescheduling this meeting for Thursday, and I shall try to get the other two Friday meetings put down for Thursdays.

The witness this morning, as I have said, is Dr. Sourkes. I would like to correct a small error in the notice card. Dr. Sourkes is not a medical doctor, but rather he is a doctor of philosophy in biochemistry. He is associate professor of biochemistry of the department of psychiatry of the Allan Memorial Institute, Montreal. He is also a member of the ad hoc committee on parnate that we have been hearing so much about. Without further words I now call upon Dr. Sourkes.

Mr. T. L. SOURKES, PH.D. (*Associate Professor of Biochemistry, Department of Psychiatry, Allan Memorial Institute, Montreal, Quebec*): Mr. Chairman and members of the committee: I would like to read a brief statement to indicate my views:

> It is by this time commonplace to remark upon the great changes that have been brought about in the mental illness field by the advent of the psychopharmacological agents: the tranquilizers and anti-depressant drugs, in particular. Many people who might otherwise have had to go to hospital have, with the help of these drugs, avoided a hospital stay, and others have had their hospitalization shortened and made more effective than was possible, say, fifteen years ago. The introduction of these new drugs has been attended with negative aspects, and I am speaking here of the side effects or frankly toxic reactions that have appeared from time to time with this or that drug. The use of a particular drug for a particular patient always involves the judgment of the physician; his judgment is based upon the known actions of the drug and the patient's condition. My phrase "the known actions of the drug" implies a great deal about the scientific and clinical work that has gone into developing the drug and guaranteeing that it has a maximum of efficacy and safety for the patient.
>
> I think that the best way to present my views on this subject is to deal with the example of a specific group of drugs—the amine-oxidase inhibitors. These are used in the treatment of mental depression. They are called amine-oxidase inhibitors because they inhibit or stop the action of an enzyme (amine-oxidase) that is very much involved in the metabolism of brain, nerve, heart and other organs. Some of the drugs act more on one organ than another so that you find some being used in

the treatment of mental depression, and at least one of them for high blood pressure. Many substances that are formed in the body and used in regulating its functions are normally broken down and made inactive by this enzyme, once they have finished their work. On the basis of a great deal of scientific research in many laboratories it appears that the beneficial effects to the depressed patient are actually related to the reduced activity of amine-oxidase that is a consequence of taking these drugs.

However, certain drugs, like adrenaline, are transformed in the body by amine-oxidase, and if the effect of this enzyme is reduced because the patient has been placed under the influence of an anti-depressant substance of the type we are discussing, then the action of the second administered drug (adrenaline, etc.) will be prolonged or accentuated. Certain drugs used in cold remedies may also produce unanticipated effects. Not long ago a number of reports appeared describing headache and other effects, even death, when certain foods, particularly aged cheeses, were consumed by patients receiving amine-oxidase inhibitor drugs. Eventually this was traced to a substance that is formed during the cheese-aging process and that is normally broken down in the body quite rapidly by amine-oxidase.

This group of anti-depressant drugs have other biochemical effects: they slow down or prevent the transformation of certain other drugs, as well as alcohol. Unpleasant effects may result from these combinations.

I have recounted the above material to indicate the growing role of biochemistry in the field of drug action and drug safety. In the past the chemist and the pharmacologist, among the basic scientists, were the most involved in the initial stages of discovery of new drugs. But in the last fifteen years we have seen an increasing number of drugs appear that have distinct biochemical effects, and it is likely that this type of drug will become more and more common in the future, that is, drugs developed on the basis of their biochemical actions. I think that the pharmaceutical manufacturing companies should be encouraged to obtain as much information as possible on their drugs—metabolic transformation, influence on biochemical processes of the body, and interaction with other drugs that might be used simultaneously. Information of this type should be included in its preclinical submission to the food and drug directorate (Section C.08.005 of the Food and Drugs Act) to support its clinical use, and the food and drug directorate should expect to receive such information. I understand that the directorate is increasing the size of its laboratories and number of its personnel. The biochemical section is already expanding there. This is to be welcomed. However, the directorate may have scientific questions which can best be studied outside its laboratories, questions that may have to do with general or specific problems of drug toxicity, prediction of the pharmacological actions or of side effects in passing from the experimental animal to man, and so on. In this case there should be available a budget for extramural research, to be carried out by contract between the directorate and university departments, schools of pharmacy, specialized research institutes, or commercial consulting laboratories.

There has been considerable discussion in the past few years among clinicians, scientists, and the lay public about the risks involved in the use of new drugs. Unfortunately, no drug is without side effects, although in many cases there are not at all serious. Some individuals, for reasons of their genetic make-up, may have an adverse reaction to an otherwise safe drug. Others may show a reaction to such a drug for unknown

reasons (idiosyncracy). Under the present regulations a new drug goes through the stages of preclinical submission, clinical tests, and finally distribution for sale. It is widely recognized that this last stage, when the drug actually reaches the market, is also a stage in the testing, because the use of the drug on a much wider scale, with a large variety of patients in regard to age, severity of illness, dietary and life habits and so on, often reveals undesirable effects that were not apparent before. It may take one to two years or more from the time a new drug is introduced until this information is published, and even more time elapses before the reports are evaluated by experts inside the food and drug directorate and outside. It might be worth placing greater emphasis on the "provisional safety" of the drug during this period. In order to expedite the collation of information about adverse reactions, a network of reporting centres is needed. These centres would be located at teaching hospitals, provincial hospitals, and others, and would require the cooperation of the medical profession and of the medical schools, in addition. The assistance of the medical associations as well as of the basic medical sciences societies, such as those making up the Canadian Federation of Biological Societies, should be solicited. The hospitals concerned would establish a drug reaction committee, one of whose members would be the reporter. He would receive remuneration in proportion to the amount of time spent in collecting information, interviewing, examining and preparing reports. The committees should have direct contact with the food and drug directorate and with one another through bulletins. The directorate, with other organizations, should sponsor conferences on the techniques of collecting, interpreting and reporting appropriate information.

This takes care of only half the problem. The other half has to do with clinical testing of drugs and evaluation of their efficacy. The present types of clinical testing of new drugs are quite variable in quality: some are very good and others not. It is often difficult, because of inadequate reports, to determine from the literature what the precise indications are for the use of a particular drug, and whether it has particular advantages over similar drugs or other treatments. There is, thus, an imperative need for adequately controlled clinical studies. The food and drug directorate can do much in fostering such studies and ought to be provided with a special budget for the purposes of conducting such trials, either on its own or by contract. Such studies can be conducted by other groups with specialized interests, such as the D.V.A. hospitals or the mental hospitals. I am aware of the fact that some collaborative studies are already under way in these hospitals, but centralization of the efforts is desirable. Some of the drug companies are paying more attention now than before to the design of clinical tests.

Finally, I should like to state my concern that decisions about particular drugs be based solely upon scientific and medical considerations.

The CHAIRMAN: Thank you very much, Dr. Sourkes.

Gentlemen, are there any questions?

Mr. MACKASEY: I do have some questions, but I would rather let someone more learned have the floor.

Mr. RAYNARD: Mr. Chairman, I think there is a great deal of useful information which has been brought out here; but on your point in respect of centralization, do you not think you might have carried it a little further and said we need a world organization? After all, we have only 19 million people in Canada. Do you not think we must go a little further?

Mr. SOURKES: I am fully in agreement with that. The only reservation is that the Food and Drugs Act pertains to specific Canadian conditions and has developed here historically. It is remarkable that the regulations in the United States and in England, for example, are different. I think the World Health Organization has begun to discuss this question of safety of drugs. Certainly, however, a world wide network reporting adverse reactions would get the information very, very quickly and protect the public from unanticipated effects of drugs.

Mr. RYNARD: Another point I would like to bring up is that we do not want to get compartments too small. In other words, we do not want to get a drug shut in a compartment and say this is the disease and this is the way you use it. I think this has been proven very well recently. In any event, it came up the other day where people were on drugs, such as rauwolfia, serpasil and apresoline, for low blood pressure. They felt it was dangerous; they could not get their pressure up. I was quite amazed two weeks ago to learn that this idea was for the birds and we can go right ahead now, because the blood pressure had nothing to do with the situation and it can be handled satisfactorily.

This is exactly what I meant by compartmentizing or mentalizing things into too small an area. Someone did enough work in respect of the situation to which I referred to prove it wrong even though it was accepted as gospel for a long period of time.

Mr. SOURKES: I think the problem also involves a matter of awareness. The public and the medical profession are much more aware of possible inherent dangers in respect of drugs, but I think we need a mechanism for getting the information distributed quickly. There are reports in respect of these drugs published as well as letters to the editor appearing in the British journals for some period of time, but a letter here and a letter there does not carry much weight unless there is an organization to discuss the information and assess it.

Mr. WILLOUGHBY: I should like to ask a question supplementary to that asked by Dr. Rynard. Do you imply here by your centralization suggestion that this is in respect of a specific drug, or specific subjects relative to diseases? In other words, I understand from the medical research council there is a certain supervision of the research work being carried on in different parts of the country along certain lines to avoid duplication, but I presume you are referring to a specific drug; is that right?

Mr. SOURKES: No, I was thinking in terms of trials that were carried out a number of years ago, I believe in the United States, and possibly here, that were collaborative trials in respect of the chemical treatment of tuberculosis, for example. Many veterans administrative hospitals in the United States collaborated in this effort on a more or less common design, although each hospital had perhaps a different type of patient or different population of patients. Centralization came from the fact that they collaborated. They all had one steering committee that would collate the material, call conferences and carry on discussions. This is where centralization came in. As far as my experience is concerned, when the food and drug directorate considers there is some question of safety or efficacy in respect of a group of drugs it might be interested in sponsoring a trial of that group of drugs.

Many of the trials that have been carried on in respect of drugs may be very good in themselves, but too often there is a failure to compare the new drug with the old established drugs or treatments which means that we may end up with a new drug but not know whether it is better, worse or less effective than the old drug. This is the type of thing of which I have been thinking.

Mr. WILLOUGHBY: Do you think this function should be handled by the Medical Research Council or are you satisfied it is being handled adequately now?

Mr. SOURKES: I do not think the Medical Research Council has any jurisdiction over testing of drugs. There are grants to investigators who, in the course of their research work, would be studying this or that drug, but these grants are not aimed at the testing of drugs, and I think this is where the food and drug directorate has a special role. That is why I have suggested the extramural budget for the food and drug directorate.

Mr. WILLOUGHBY: Obviously there is a medical research relationship between the study of new drugs and the treatment of certain diseases.

Mr. SOURKES: I agree with that statement and have stated somewhere in this brief that the clinical testing should involve the co-operation of the teaching hospitals, for example, where a great deal of medical research is carried out. I do not think they should be excluded, but the difficulty is that testing of drugs is not held in very high esteem by the medical profession. It is considered to be a rather routine type of work. I think it is very necessary and I would not like to see my medical colleagues have more work foisted on them than they can do simply in respect of testing drugs; but if the work of testing drugs on a carefully designed, scientifically designed, statistically designed basis, comparing one drug with another, one treatment with another, were carried on as part of a collaborative effort, I think the quality of the work would increase and they would be more inclined to go into this type of work as another aspect of their research.

Mr. MACKASEY: Dr. Sourkes, you have made some reference in your brief to the pharmaceutical people changing their style of clinical testing. Would you care to elaborate on that statement?

Mr. SOURKES: I cannot give you very satisfactory details in that regard, but I know a number of firms over the past few years have been employing statisticians concerned with design of experiment, which is the technical term, and the method of controlling the tremendous number of variables that are involved in trials on the human population. This situation is very much to be welcomed. As you know, the drug company itself does not do the trial testing of a drug but collaborates with somebody in a hospital or in practice. However, some of the more forward looking companies will lend the services of their statisticians to the clinician who is going to be testing the drug so the statistician can help him design a more satisfactory assay. It is to the advantage of the public and to the advantage of the company to have accurate scientific information in respect of the value of their drugs.

Mr. WILLOUGHBY: Do you find generally that drug companies are sufficiently interested in safety to take these steps on a voluntary basis rather than a compulsory basis at the direction of the food and drug directorate?

Mr. SOURKES: I think that the changes that have been taking place generally have been through gentle persuasion. It became apparent with the thalidomide story that more measures had to be taken. Many of the drug companies now have good biochemical sections—they always have had strong pharmacological sections—and they are now beginning to put more effort into this problem of biochemical interactions which is different from past experience with pharmacological interactions where a drug may be too active in a place in the body where you do not want it to be. They are now doing this.

Mr. MACKASEY: You also emphasized in your remarks that in the final analysis the possibility exists that every drug acts differently on every individual. I presume this is certainly something that cannot be brought out

by pre-testing before a drug is put on the market. Are you then suggesting that the individual cases must be compiled and held with some recognized authority?

Mr. SOURKES: May I explain. I used the term "differences" because of genetic makeup. There are two aspects of this. In other words, every individual reacts differently, and this is where the statistical design of experiment is necessary to rule out population variation.

There is another type where an individual, because of his genetics, actually may be missing a biochemical step or an enzyme in the body. There is a drug which is used for the relaxation of muscles, for example, which is short lasting in action. This action is terminated rapidly by an enzyme in the serum used for operations.

One individual out of 2,000 is relaxed and may be completely immobilized for a very long time, a matter of hours. This is unanticipated and it is because his serum does not have the enzyme that terminates the action of that drug. This is what I was specifically referring to. That is a type that we cannot do very much about except recognize it and tell the patient not to let anyone use that drug on him in the future. The same applies in respect of idiosyncrasies; some people have violent reactions to a drug which is due to an unexplained cause. In this case the patient merely has to be told he must ask his physician not to give him this or that drug in the future.

The CHAIRMAN: Have you a question, Mr. Orlikow?

Mr. ORLIKOW: Mr. Chairman, I have several questions along the line of more centralization. I got the reverse impression, that you were suggesting, possibly under the food and drug administration, that there be a good deal more testing in teaching hospitals, universities and by drug companies but that some agency, probably the food and drug administration, either do the collating or arrange for centralization, using the information that comes in so that we will end up with more complete information. Is that what you have in mind?

Mr. SOURKES: May I explain my remarks. First of all, so far as safety of drugs is concerned, the Food and Drug Directorate is presumably doing work along these lines. I know they are. But, they may not be able to handle all questions or they may find there is an expert outside the food and drug directorate who could do it. In the event of this happening, I think they should have the necessary money to go to this man and ask him to undertake a certain piece of research for them. This is feasible so far as clinical testing of drugs is concerned. Unfortunately, the medical profession itself and the association does not have any mechanism for this and someone must take the lead. I think the Food and Drug Directorate is the logical one to take the lead in sponsoring conferences and urging clinicians to undertake the testing of new drugs on a scientific basis. This is the degree of centralization to which I am referring. I think it would help a great deal if the Food and Drug Directorate brought together people from the medical profession, the scientific profession, hospitals and government to discuss this question.

Mr. ORLIKOW: I have one other question. The last thing you said in your formal presentation was that you thought that the decision in respect of drugs should be based only on medical considerations.

Mr. SOURKES: Medical and scientific consideration.

Mr. ORLIKOW: Would you expand on that. What other considerations do you feel have existed?

Mr. SOURKES: Well, I think that Dr. Rynard brought this up in a way. We have a variety of regulations in countries that have centrally the same level of development of medical science and drug industry and the fact that a decision in one country immediately becomes public knowledge may oblige people in

Canada to change their minds or to take action which they might not have planned to do. I think this came up in the case of the parnate question in the United States. I do not know the intimate details there but I think that the day after the food and drug administration in the United States ordered parnate withdrawn it was removed from the open market in Canada. Now, I think that the question of the safety of parnate or other amine-oxidase inhibitors or any other drug can be assessed best by a scientific and medical committee without taking into consideration what other people have been saying about it.

Mr. ORLIKOW: Who removed it in Canada?

Mr. SOURKES: The company.

Mr. ORLIKOW: The company itself?

Mr. SOURKES: Yes.

Mr. ORLIKOW: Surely that is a voluntary thing and there is not much that anyone can do about that.

Mr. SOURKES: I think there were discussions about it and the company, in the face of public pressure, decided to withdraw it until the question of its safety and the safety of any amine-oxidase inhibitors could be assessed.

Mr. MACKASEY: In all fairness to the Food and Drug Directorate, the question of the parnate situation has been brought up in parliament. The company probably anticipated the action of the food and drug directorate and wisely co-operated and withdrew the drug voluntarily in co-operation with the directorate.

One thing that strikes me is that listening not only to you but many witnesses through the weeks I find the activities, the expansion, the necessity for research into the safety of drugs in Canada developing so rapidly, that it is well beyond the physical development of the food and drug directorate. Despite the fact we have put more money and more people at their disposal it seems that in comparison with the almost spectacular growth of the drug industry and the necessity of safety on the lines you mentioned today and on the lines other people mentioned, the food and drug directorate is falling hopelessly behind. This is no reflection on Dr. Morrell who impresses me greatly and on the dedicated people out there. There is certainly a lack of adequate facilities for their staff which does nothing to attract people of high calibre in biochemistry. There is certainly no overabundance of people trained in this field. What they need is a decent salary, adequate manpower and money. I am amazed they can do what they are doing, but it does not solve the problem. We have to face the facts and re-evaluate the role we expect of the food and drug directorate. Perhaps there is going to be an offshoot of the food and drug directorate which could take care of liaison among all the voluntary groups. The responsible groups could get together and help to solve these problems on a voluntary basis or on a humanitarian basis, perhaps. I cannot possibly see how the food and drug directorate can keep up with all the recommendations, which are all by themselves necessary and important, when Dr. Morrell tells us here he has over 400 manufacturers and distributors to police perhaps once a year and he can cover only 180 of them in one year. That would leave the implication that it would take him three years to make the rounds of the present industry. You wonder how he can possibly get to do the other things which obviously must be done.

Mr. SOURKES: I think that because of this very situation and the possibility that everyone who is concerned with medical science and clinical medicine in Canada could ultimately be involved in this 24 hours a day, it is all the more important to have a start made at assessing the problems of drug safety and

drug efficacy. Again I think that the Food and Drug Directorate, in collaboration with the Canadian Medical Association, the specialty organizations and the scientific organizations, could take a lead in this. It would certainly allow for discussion of the immediate problems on their own merits, and would, I hope, allay any fears on the part of the public that this matter is not being taken care of adequately.

The CHAIRMAN: Are there any other questions, gentlemen?

Mr. ORLIKOW: I just wonder whether you think, Dr. Sourkes—and we all agree it is unlikely that the food and drug directorate could get the staff to do all the work itself—that discussions with the teaching hospitals and universities and their research organizations could be helpful in working out new patterns so that the work could be done in these institutions on behalf of the food and drug directorate much more than has been done until now.

Mr. SOURKES: I think that there could be an expansion of this type of work. You must recognize, of course, that scientists generally do not like to be directed in their research. On the other hand, if they voluntarily recognize the importance of a problem presented to them by, let us say, a national agency such as the food and drug directorate or a national conference on this question, they may be all the more impelled to undertake it. But I think it is simply a matter of calling experts and interested parties in the field to a conference which would probably reveal that there is a great deal more information available; it just has to be collected and put into the proper boxes.

The CHAIRMAN: Are there any other questions, gentlemen?

The clerk of the committee is sending all the members a letter about our trip on Tuesday. I might just briefly mention to you now that we are to leave Ottawa at seven o'clock, departing Uplands airport at eight o'clock. There is no facility on board the aircraft for breakfast; only coffee will be served. We will arrive in the United States at 9.30. United States authorities have been notified of our trip and they will have some immigration and customs people there to go through the formalities. On our return trip we will leave the airport there at eight o'clock and arrive back in Ottawa at 9.30 p.m.

If anyone would like transportation to the airport will he please mention it to me or to the clerk of the committee. We should leave the south entrance of the West Block on Wellington street not later than seven o'clock. I will be there with my car, and I think the clerk of the committee will also be there. We leave here not later than seven o'clock and board the aircraft at 7.45.

As I mentioned earlier, we will try to arrange from now on to have the meetings which have been set for Fridays switched to Thursdays in the hope that we will have the advantage of the attendance of more members.

If there are no other questions, I would like to thank Dr. Sourkes for coming before us this morning. We appreciate his coming up from Montreal to give us the biochemical approach to the question of drug safety.

The meeting is adjourned, gentlemen.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 11

THURSDAY, JULY 9, 1964

WITNESSES:

Mr. S. R. Stovel, President, Mr. N. J. McDonald, Assistant to President; and Mr. J. A. Bertrand, Manager, Medical Products Department, all of Cyanamid of Canada Limited, Montreal; also Dr. J. T. Litchfield, Director of Research, Dr. J. D. Gallagher, Director of Medical Research, and Dr. H. D. Piersma, Director of Quality Control, all of the Lederle Laboratories Division, American Cyanamid Company, Pearl River, N.Y.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21100—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Gauthier	Orlikow
Asselin (*Richmond-Wolfe*)	Jones (Mrs.)	Prud'homme
Basford	Horner (*Jasper-Edson*)	Roxburgh
Casselman (Mrs.)	Howe (*Hamilton South*)	Rynard
Côté (*Longueuil*)	Jorgenson	Slogan
Enns	Macaluso	Whelan
Francis	Mackasey	Willoughby—24
	Marcoux	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

Note: Mrs. Jones replaced Mr. Nesbitt on Tuesday, July 7.

CORRIGENDA (English copy only)

Issue No. 7—Friday, June 19, 1964
In the Minutes of Proceedings and Evidence—

Page 185, Line 8, should read:
"....I recall at the time *Dr. Banting* had decided not to...."

Issue No. 10—Friday, July 3, 1964.
In the Minutes of Proceedings and Evidence—

Page 288, the 2nd paragraph should read:

"Mr. Rynard: Another point I would like to bring up is that we do not want to get compartments too small. In other words, we do not want to get a drug shut in a compartment and say this is the disease and this is the way you use it. I think this has been proven very well recently. In any event, it came up the other day where people were on drugs, such as rauwolfia, serpasil and apre soline, for *high* blood pressure. They felt it was dangerous *in cases requiring anaesthesia;* they could not get their pressure up. I was quite amazed two weeks ago to learn that this idea was for the birds and we can go right ahead now, because the blood pressure *drugs* had nothing to do with the situation and it can be handled satisfactorily."

ORDER OF REFERENCE

TUESDAY, July 7, 1964

Ordered,—That the name of Mrs. Jones be substituted for that of Mr. Nesbitt on the Special Committee on Food and Drugs.

LÉON-J. RAYMOND,
The Clerk of the House.

21100—1½

TUESDAY, July 7, 1964

VISIT TO LEDERLE RESEARCH LABORATORIES PEARL RIVER, N.Y.

The Special Committee on Food and Drugs proceeded this day at 7.45 a.m. by private airplane to Pearl River, New York, at the invitation of Cyanamid of Canada Limited. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Gauthier, Harley, Mackasey, Mitchell, Prud'homme, Whelan and Willoughby (8).

In attendance: Messrs. S. R. Stovel, President, N. J. McDonald, Assistant to President, and J. A. Bertrand, Manager, Medical Products Department, all of Cyanamid of Canada Limited, Montreal.

The Committee was received at the Lederle Research Laboratories by officials of the Lederle Laboratories Division of American Cyanamid, and heard a welcoming talk by Mr. R. P. Parker, the President. (Copy of this talk is reproduced in the evidence of the meeting of July 9).

The members visited three research laboratory areas concerned with the discovery of new drugs and the demonstration of their safety and effectiveness in animals; they were briefed on each subject.

Following a luncheon break, the members heard talks by Drs. Litchfield, Piersma and Gallagher. (Dr. Litchfield's remarks are included in the Evidence of July 9).

During the afternoon the Committee was conducted on visits to actual production areas where drugs are being formulated, tableted, encapsulated and packaged. They also saw the pharmaceutical and quality control laboratories.

After the visit, the Members were driven by automobile to Wayne, N.J., where they were entertained at a buffet supper by Dr. W. G. Malcolm, the Chairman of the Board, and the Directors of Cyanamid Company.

At 8.15 p.m. the Committee returned to Teterboro Airport by automobile and boarded the airplane to return to Ottawa.

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

THURSDAY, July 9, 1964.
(16)

The Special Committee on Food and Drugs met today at 9.40 a.m. The Chairman, Dr. Harry C. Harley, presided.

Members present: Mrs. Jones and Messrs. Armstrong, Harley, Mackasey, Mitchell, Prud'homme, Rynard, Whelan, Willoughby (9).

In attendance: Representing Cyanamid of Canada, Ltd.: Messrs. S. R. Stovel, President; N. J. McDonald, Assistant to President; J. A. Bertrand, Manager, Medical Products Department, all of Montreal. *From Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York State, U.S.A.:* Dr. J. T. Litchfield, Director of Research; Dr. J. D. Gallagher, Director of Medical Research; Dr. H. D. Piersma, Director of Quality Control.

The Chairman welcomed Dr. Jones, who has just been appointed to the Committee. He introduced the representatives of Cyanamid of Canada Limited.

The Committee agreed to take the submission as read.

Mr. McDonald made a brief statement and introduced those in attendance.

Mr. Stovel made a few general comments in relation to Cyanamid of Canada and the American Cyanamid Company.

The witnesses were questioned on different topics of the brief, more particularly on research, testing, quality control, relationship of generic name prescribing to drug quality.

During the questioning of Dr. Litchfield, Dr. Willoughby moved, seconded by Mr. Prud'homme,

Resolved,—That the comments made by Dr. Litchfield and others during the visit of Lederle Research Laboratories at Pearl River, N.Y. on July 7th, by the Committee, be included in the record of today's proceedings.

To illustrate the presentation, Mr. Bertrand produced an example of a submission to the Food and Drug Directorate of Canada in respect of a new drug.

At the conclusion of the questioning, the Chairman announced that the last two hearings before summer recess will be held next week.

Dr. Rynard complimented the witnesses for having ably represented both sides of the story.

On behalf of the Committee, the Chairman expressed thanks to Cyanamid of Canada for having made these witnesses available to the Committee, and to Drs. Litchfield, Gallagher and Piersma for having come from Pearl River to appear before the Committee.

He also expressed his gratitude to Mr. Stovel and his associates for their assistance, also for their hospitality and their effort in arranging the interesting visit to the Lederle Research Laboratories at Pearl River, N.Y.

At 11.20 a.m. the Committee adjourned to 9.30 a.m. Tuesday, July 14.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

THURSDAY, July 9, 1964.

The CHAIRMAN: Gentlemen, we have a quorum. I would first like to welcome a new member of our committee, Dr. Jones. I am sorry that her appointment did not come through a few days earlier so that she could have taken our trip to Pearl River. I am sure she would have enjoyed it as much as we did.

We have with us this morning the representatives of Cyanamid of Canada Limited who have presented a brief which is now before you. What we have tried to do is to lay down an agenda. We will first ask Mr. McDonald to say a few words, and then the president of the company will speak. I have written down the general headings of the brief and I thought we might discuss them under those headings. I will ask Mr. Norman McDonald, the executive assistant to the president of the company, to make a few general remarks.

Before I ask Mr. McDonald to speak I would like to have the agreement of the committee that the brief presented today appear at the beginning of today's proceedings.

Agreed.

(The brief of Cyanamid of Canada Limited follows:)

Cyanamid of Canada Limited is a subsidiary of American Cyanamid Company, Wayne, New Jersey, which operates an international organization engaged primarily in the development, manufacture and marketing in most countries of the free world of a wide range of chemical and pharmaceutical products. It is worth noting that the worldwide Cyanamid organization stems from its first plant built in 1907 at Niagara Falls, Ontario.

American Cyanamid occupies a prominent position in the pharmaceutical industry as a result of its manufacturing operations in 15 countries of the world, and through the operations of its Lederle laboratories division at Pearl River, N.Y., (hereinafter for convenience referred to as "Lederle"), which is one of the world's major research centers for the discovery and development of pharmaceutical products.

In this country, Cyanamid of Canada, through its medical products department, manufactures pharmaceuticals by the most advanced methods under the strictest possible systems of quality control. These pharmaceuticals are ethical drug products in the true sense of the term; that is, they are sold only by pharmacists on the prescription or recommendation of a physician. They are identified by the Lederle label.

While Cyanamid of Canada carries on a major drug manufacturing operation in this country, the company depends on Lederle for most of its research. Because of the tremendous capital investment required to establish a research center such as Lederle has developed, the quality of the professional and technical personnel located there, and the high operating costs involved, it is understandable why this research center is relied on to serve all of the American Cyanamid companies which manufacture and market Lederle pharmaceuticals. Cyanamid of Canada underwrites a share of the operating costs of the Lederle research programs.

This close association today of Cyanamid of Canada and Lederle laboratories recalls that since 1917, before it became a part of American Cyanamid, Lederle Antitoxin Laboratories had a Canadian office in Ottawa.

Lederle has consistently played a prominent role in the field of public health in Canada and the United States. As the name implies, Lederle Antitoxin Laboratories had as its main business biological and bacterial products. It had the reputation in North America of being the foremost in its line of antitoxins, vaccines, toxoids and sera. In 1917 and 1918, when the influenza epidemic was raging in Canada and the United States, Lederle influenza-combined vaccine and pneumococcus-combined vaccine were supplied to emergency hospitals. In 1927, during the severe typhoid epidemic in Montreal, Lederle supplied large amounts of typhoid-combined vaccine to the Montreal City Board of Health.

The business of the Lederle Antitoxin Laboratories was purchased by American Cyanamid in 1930. Today, Lederle pharmaceutical products are marketed in this country by the medical product department of Cyanamid of Canada.

Lederle products marketed in Canada include broad spectrum antibiotics such a Declomycin demethylchlortetracycline, Achromycin tetracycline and Auremycin chlortetracycline—and steroids such as Aristocort triamcinolone, biologicals, hematinics, vitamin preparations, diuretics, and many other pharmaceutical specialities. The Lederle product line includes over 90 individual products in over 200 individual package forms.

Over 60 per cent of Lederle sales volume in Canada is represented by products entirely manufactured in Canada using Canadian raw materials. For example, the above tetracyclines are the only ones which are produced completely in Canada.

While there are eight Cyanamid of Canada manufacturing plants in Canada at the present time producing a wide range of chemical and other products for health, home, agricultural and industrial purposes, only two of these plants are engaged in manufacturing pharmaceuticals. Cyanamid of Canada has invested approximately $3.5 million in pharmaceutical manufacturing facilities and currently employs about 200 people in its ethical drug manufacturing operations.

The executive offices of Cyanamid of Canada are in Montreal, and the principal manufacturing and production center of pharmaceuticals, in operation since 1952, is in the town of Mount Royal, Quebec. Cyanamid of Canada is a member of the Canadian Pharmaceutical Manufacturers Association.

Because the medical products department of Cyanamid of Canada Limited is, in effect, a duplication of the manufacturing, quality control marketing and administration procedures of Lederle, the major distinction between the two is research. In effect, the research facilities of Cyanamid of Canada exist at Pearl River as a part of Lederle's operations in this sphere.

Therefore, Cyanamid of Canada believes it proper that it should, in outlining safety procedures, describe the research and other operations which it has available to it, and on which it depends, at Lederle.

Lederle Research

Lederle's objectives in research and development are progress in the diagnosis, prevention control and cure of disease and the alleviation of symptoms of disease.

There are three major research concepts:

Basic Research—involves looking for new scientific knowledge without a specific, practical view in mind.

Applied Research—covers investigation and experiments in which a practical or commercial end is more or less in sight.

Development—is the long period in which a scientific discovery or concept is translated into an actual product or process.

Lederle has a professional staff of 1,000 scientists and technicians (25 per cent of the total Pearl River staff).

The scientific community is organized into five sections: biochemical research, experimental therapeutics research (animal testing), viral and rickettsial research (virus vaccines, the search for compounds effective against viruses, diagnostic antigens), organic chemical research (steroids), and mechanical research and development (equipment, methods).

Since 1939 Lederle has spent a quarter of a billion dollars in research.

The Financial Risks of Research

Lederle spent $16 million and 16 years in the development of an oral vaccine that would guard against all three types of polio. When the United States licensed production of the Sabin strains of oral polio vaccine, the investment had to be written off as a private enterprise loss. Yet the public benefit was there because Lederle's experience was there to qualify it as a licensed producer of Sabine vaccine and developer of the trivalent form of vaccine.

The research costs for the broad-spectrum antibiotics produced by Lederle totaled almost $12.6 million, while their development costs have surpassed $9.2 million.

Since 1939 Lederle has spent more than $10 million in search of anticancer agents, but the problem is so complex that research seems to indicate that one chemical or one method of therapy will not solve the problem. At present, more than 5,000 different chemicals are tested annually for possible antitumor activity.

The development phase of research is continuous; there is no point which can be considered final. In the highly competitive drug industry, leadership in product development is not less important than product discovery—in some cases more so. And product development work often requires more people, more processes and more time than product discovery.

For each new important product that reaches the pharmacy, it is estimated that almost $5 million is spent on the research and development of it.

For example, Lederle carried out a six year research and development program on Aristocort triamcinolone before marketing this product for the treatment of arthritic patients. The first broad spectrum antibiotic, Aureomycin chlortetracycline, was under investigation for four years prior to its introduction to the medical profession. Lederle's newest antibiotic, Declomycin demethylchlortetracycline, required a six year research and development program prior to introduction.

Lederle's research is concerned with most aspects of infectious diseases—bacterial, parasitic, fungus and virus-caused; also nutrition, cardiovascular-renal ailments, mental health, endocrinology; and relationship of the viruses, steroids, and antibiotics to cancer. About 50 per cent of Lederle's research time and money are devoted to areas which are not directly related to any product.

Achievements

Research has some of the features of a lottery, or gambling, because research is buying a chance that a worth-while product or process will be descovered within the time limits dictated by the amount of money available for the research project. The risk in pharmaceutical research is so high that one cannot borrow money to finance it—research must be supported by profits. However, research cannot always be judged in the light of immediate commercial results, for research which produces no product may also be considered a success. It represents a valuable contribution to the general level of scientific knowledge.

Some examples of achievements in recent years by other drug companies engaged in this type of research are: Discovery and development of vitamins, the sulfa drugs, antibiotics, steroids, diuretics, tranquilizers; development of a technique of mass-producing penicillin; tissue culture research which led to the development of antiviral vaccines; better drugs for treatment of anemia, tuberculosis, cancer.

Some of Lederle's accomplishments as the result of its research activities are: Development of sulfadiazine, discovery and synthesis of folic acid (essential in human nutrition) which made possible the development of several compounds that have proved to be weapons against leukemia and other forms of cancer; discovery and development of the broad-spectrum antibiotics, Aureomycin, Achromycin, Declomycin; the first non-mercurial diuretic, Diamox acetazolamide and Orimune polio vaccine, the first live oral trivalent polio vaccine.

Cyanamid of Canada's research conducted in Canada has produced Temposil calcium carbimide, a pharmaceutical used in the treatment of chronic alcoholism. The extensive clinical trials preceding its introduction in early 1959 were carried out principally in Canada under the guidance of Dr. J. K. W. Ferguson, chairman of the medical advisory board of the alcoholism research foundation, Toronto. This chemotherapeutic innovation is produced entirely in Canada by Cyanamid of Canada Limited, and is being marketed in some 67 countries throughout the world.

When these accomplishments are measured in terms of their effects—longer life span, control of many diseases, decline in mental illness, et al, it is apparent that the research programs of the drug industry are one of the greatest guarantees in the world of good health.

Clinical Research

To test new drugs, the pharmaceutical industry long ago evolved, first of necessity and only later by law, a system of clinical testing. In fact, the industry has set most of the quality and control standards there are.

Any new drug, that is newly licensed, has probably been tested from three to five years on animals and humans. Lederle's Declomycin for instance, a broad-spectrum antibiotic widely used in the treatment of many bacterial infections such as pneumonia, went on the market after two years of human testing preceded by two years of animal testing, preceded by the years of research in the field of antibiotics generally.

This long course of development is necessarily expensive. For example, after three years of preliminary work on Aristocort triamcinolone, a cortisone-type drug used to treat rheumatoid arthritis, it was decided that the drug merited clinical trial. It was estimated that one kilo, or 2.2 pounds of Aristocort would be needed to obtain useful information. The cost of producing this first batch, to be used only for further study, was one million dollars.

However, even with all this expensive and extensive testing, conducted as a matter of course, we can never be sure that any drug, even aspirin, is completely safe when used on humans. The aberrant side-effect may show up only after years of use in millions of patients. The increasing occurrence of penicillin sensitivity is a prime example.

Cyanamid of Canada is one of several major Canadian pharmaceutical manufacturing companies supporting financially the Canadian Foundation for the Advancement of Therapeutics. This foundation was formed early in 1964 for the purpose of encouraging the study and development of the science of Therapeutics under the chairmanship of Dr. F. S. Brien of the University of Western Ontario, and the vice-chairmanship of Dr. Jacques Genest, head of the Clinical Research Department of the Hotel-Dieu Hospital in Montreal.

Significance of Animal Testing

The use of experimental animals in research and development of drugs rests on a firm basis. The commonly used laboratory animals have physiological and biochemical systems very similar to man. In many cases, diseases can be produced in these animals which closely resemble a similar disease in man. In consequence, the laboratory animal is a substitute for a human being in the testing of new substances whose properties are unknown. Without knowledge of the hazards which a new agent might possess, one could not consider the first administration to a human. In the search for new drugs, many thousands of chemicals may be examined; this is possible if we use laboratory animals but clearly impossible to consider for humans. Even though most of these will be found inactive, a few will be found extremely toxic and hazardous.

It must be noted, however, that one species cannot be expected to give results which are the same with another species. If this were not so, we could not tell the two species apart. Consequently, studies of drugs in animals are going (1) to give some information which has no relevance to man, (2) to give some information which applies directly to man, and (3) to fail to disclose information which will only be discovered by studies in man.

Frequently, a drug will produce an effect in a laboratory animal which can later be correlated by hindsight with a different effect in man. For example, a deficiency of a particular vitamin in man may be manifested in a fashion entirely different from the same deficiency in a laboratory animal. It follows, therefore, that there have been and will continue to be important drug actions discovered in man rather than in the laboratory. An important example is the effectiveness of cortisone in relieving arthritis in man. No such action is exactly demonstrable in laboratory animals.

We depend most importantly on studies in animals to guide us in deciding how to safely use a new drug in man for the first time. For this purpose we set out to expose several species of laboratory animals to excessive doses of the drug at first as single and then as multiple doses. It is our clear objective to establish in laboratory animals the nature and extent of harm which the drug may produce, which organs and tissues are affected, what doses are safe and which are not. With the full knowledge that some of our findings will be inapplicable and that no matter how careful we are, we will not disclose all of the toxic potential of a new drug, we will bring to the clinical investigator the best possible information on the risks that may be involved.

When we use this approach, almost every new drug has a toxic level in the laboratory and we can evaluate this with reference to the level that is effective. It is important to realize that drugs which have serious toxic potential may nevertheless be of great value in man. A good example of this is the drug methotrexate. In laboratory animals this has some anticancer activity, but like most folic acid antagonists it is very toxic. In addition, it is a potent teratogenic agent. If we were to have hidden our heads in the sand and denied this compound a clinical trial or, even worse, to have decided that it should never be given to women before they reach menopause because it might have harmed their unborn children, we would never have discovered that this drug can cure choriocarcinoma, a cancer which is otherwise fatal in about one year.

One must therefore conclude that in the last analysis, the safety of a drug a welcoming talk by Mr. R. P. Parker, the President. (Copy of this talk is Studies in animals can only lead the way.

To Test in Humans or Not to Test

At the end of animal testing, after statistically analysing all the data from hundreds of blood liver, kidney and other biological or histopathological studies, weighing species differences, balancing off good against bad effects,

and extrapolating data and dosages by gram weight or centimetric surface area from mice to men, the momentous decision must be made whether the drug is safe enough to test in a man. This decision can only be made by a trained and experienced doctor.

Some idea of the extent to which our industry must go to discover a new drug may be obtained from this fact: in one recent year the United States pharmaceutical industry examined 114,000 new compounds. Only 1,900 of these were considered safe and active enough to test in humans, only 40 survived to be marketed.

In pharmaceutical research, the safe usage as a drug of any chemical discovery requires sound research into all of the possible risks involved. The discovery of a compound is only the beginning. Before a new compound becomes a safe, effective medical product, much research must be done: animal research to discover the compound's safe and toxic dosage levels; its effect on animal organs and tissues; and probable therapeutic value; chemical research to insure its stability and purity; pharmaceutical research to determine the best form for the drug and to assure its purity, potency and stability in each dosage form; and clinical research to discover its actual therapeutic value in man.

On the average, only one of 2,500 compounds tested and evaluated can hurdle this course of applied and developmental research. Yet the costs of research on all of these compounds must come from that one success.

How Clinical Trials are Conducted

Clinical testing on humans is approached in three phases. In the first phase a small group might be fed the drug, starting with the minutest doses and gradually stepping up, to test and observe closely man's tolerance to it. During this phase, extensive tests on the subject including liver, kidney and blood studies are conducted to determine the effects of the new drug on the human body. If all went well, then the drug would be tested on another small group to find out whether it has the desired pharmacological effect. A large percentage of new compounds are eliminated in this stage, despite all promising animal indications, as being too toxic or inactive in humans.

If a drug is satisfactory so far, but is designed for some chronic disease, it must go back into animal testing for a period of six months to a year or more to explore the long-term effects of taking the drug.

Meanwhile, in larger and larger test groups, the drug that passes muster moves on to the second phase on patients, for whom it is designed, for the final stage of human testing, which also has two phases. In the first, the drug is experimentally given to a limited, controlled number of patients in hospitals, clinics or other institutions, where effects can be closely watched and studied.

In the third and final phase, large experimental amounts of the drug are distributed to specialists and physicians who have agreed to perform judicious tests on patients to discover, if possible, the aberrant effect or side-effect that usually shows up only after a drug has been administered to a large sample of the population.

During this phase, it is the Lederle policy to ask physicians known to deal most often with the diseases the drug is intended to treat, to test its drug and to supply these physicians with adequate forms and instructions for reporting results.

Clinical Investigations

For clinical human testing, a pharmaceutical house generally must go outside its own laboratories to find medical specialists who are attached to institutions and willing to take on the job as part of their research. When Lederle decides that a drug is ready for clinical testing, it is their policy to ask the men

most highly regarded as authorities in the field of medicine to which the drug relates, to do the clinical testing. Two of the clinical researchers who test Lederle's antibiotics are good examples.

One, Dr. Maxwell Finland, is probably the world's leading authority on antibiotics. He is employed, not by Lederle, but by Harvard University and the Boston City Hospital. He is the author of some 400 papers on infectious diseases. His advice is sought by many cities, states and other institutions and by such organizations as the New England Heart Association, the Armed Forces Epidemiological Board and the National Academy of Sciences.

Dr. Harry F. Dowling is another example. He is head of the department of medicine at the University of Illinois Medical College and supervises the treatment of many thousands of patients annually. He has held numerous public appointments and worked closely with the national institutes of health and the armed forces.

Much has been said about the shortage of adequate clinical investigation facilities in Canada, particularly with respect to trained investigators and to the required equipment. Cyanamid of Canada, through its support of the Canadian Foundation for the Advancement of Therapeutics, together with a number of other major pharmaceutical firms, and its medical education program is striving to assist in the development of new and improvement of existing facilities. Through the years, Lederle has endeavoured, wherever and whenever possible, to have clinical testing of its research results carried out in Canada. To cite a few representative examples:

Kynex Sulfamethoxypridiazine

Dr. Harry Medovy,
Professor of Pediatrics,
University of Manitoba.

Antibiotics

Dr. K. J. R. Wightman,
Professor of Medicine,
University of Toronto.

Temposil Calcium Carbimide

Dr. Gordon Bell,
Alcoholism Research Foundation,
Toronto.

Cancer Chemotherapeutics

Dr. Jean Marie Delage,
St. Sacrament Hospital,
Quebec City.

Aristocort Triamcinolone

Dr. Hans Selye,
Institute of Medicine,
University of Montreal.

Dr. Bram Rose,
University Clinic,
Royal Victoria Hospital,
Montreal.

Dr. Jacques Genest,
Director, Clinical Research,
Hotel Dieu Hospital,
Montreal.

Lederle Aid to Medical Education

Lederle, and almost all leading pharmaceutical houses, regularly give substantial grants to research institutions, medical schools and universities and individuals for medical study, particularly in the field of research.

Lederle Medical Faculty Awards have contributed to the support of 161 full-time faculty members of 66 medical schools in the United States and Canada for periods of one to three years. Since its inception ten years ago, Lederle Medical Faculty Awards totalling $127,624 have been awarded to the following Canadian medical schools:

	No. of Awards
University of Western Ontario	1
Laval University	2
University of Saskatchewan	2
McGill University	2
Queens University	1
University of British Columbia	1
Total Awards:	9

These Lederle Medical Faculty Awards are made to assist able men and women who aspire to full-time academic careers in the preclinical and certain clinical departments of medical schools. The program provides financial aid for the support of individuals who have demonstrated their capacity both as teachers and investigators in the disciplines of anatomy, biochemistry, biophysics, genetics, microbiology, pathology, pharmacology and physiology in order to encourage them to remain in these disciplines. These awards are administered by an independent committee composed of professors representing various preclinical and clinical sciences drawn from various medical schools from application submitted to the committee through the office of the dean of the medical school.

Cyanamid of Canada, through its medical products department, also makes available two medical student research fellowships of $650 each to undergraduate students in each of twelve major schools of medicine in Canada. This contribution of over $15,000 annually enables such students, who are selected by the university, to work on university sponsored research projects in the summer months.

These and similar contributions expand the medical profession's knowledge of drugs and therapy, and thus benefit the public, the medical profession, and the pharmaceutical industry, although Cyanamid of Canada gains no specific benefits therefrom.

Quality Manufacture and Quality Control

Grave responsibilities are imposed on a pharmaceutical and biological business which is dedicated to the advancement of medical knowledge, the discovery of products for the conquest of human disease, and their supply to the medical profession.

The Cyanamid organization conducts such a business and accepts these responsibilities as an implicit condition of its endeavour.

Possibly the most important responsibility is in the area of quality manufacture and quality control. This is the *sine qua non* of the research oriented pharmaceutical company.

Every medical product identified by the Lederle label must be as near perfect as possible. The Cyanamid organization has accepted the burden of this responsibility. Where the health of people is concerned nothing less is acceptable.

Certainly, manufacturers in every kind of industry want to turn out the best products possible, but with most kinds of products if something does go wrong or if someone does make a mistake, there is usually a service department to help rectify the error or replace a faulty part.

The pharmaceutical industry does not get an opportunity to correct mistakes with a service department. An error can cost lives. The Cyanamid organization stakes its reputation and existence on every package of every product on which it places the Lederle label. It is for this reason that the Cyanamid organization must manufacture according to the highest quality standards possible, and, then on top impose the most rigid quality control assays.

Although the governments of Canada and the United States have established minimum standards for testing drug products, the self-regulation imposed by Lederle usually goes beyond these basic standards. Most of the government tests, incidentally, have been devised by the reputable drug firms themselves. But, the governments simply cannot test all drugs.

In Canada, the regulations governing a new drug require that a manufacturer obtain clearance from the Food and Drug Directorate before clinical trials may be initiated. The Food and Drug Directorate also passes on the effectiveness and safety of a new drug before it is marketed in Canada. It issues approval for marketing if the drug is shown to be safe and effective for use under the conditions recommended in its labeling. This is the result of long, painstaking compilation of research and clinical data provided, again, by the originator of the drug. Also included in a new drug application submitted to the Food and Drug Directorate are the manufacturer's procedures for the manufacture, control, identification, and assay of the drug.

While the maintenance of these minimum standards is inherent in permission to market a drug, the Directorate cannot possibly check the quality of every lot of every drug. Thus, in the interest of the public and their reputations, the vital check on the quality of drugs has to be by the pharmaceutical companies themselves.

Once a drug is introduced to the medical profession, and is established as a useful one, it may be included in one of the official compendia or books of standards, such as the United States Pharmacopeia or the British Pharmacopeia.

These official standards indicate the quality level below which no official product may fall in order to be acceptable. In general, regulatory agencies can condemn only those drugs falling below the established minimum, but cannot indicate which are excellent, good, or fair.

Lederle products are tested far beyond minimum standards established by government agencies responsible for public safety. In Canada, Cyanamid of Canada conducts the same number of tests on its antibiotics during production as Lederle at Pearl River where 34 more tests are performed than required by the United States government. This figure itself can be very misleading since not the number of tests, but the extent of testing and the effort in both manpower and money involved are more important. This comprehensive checking program protects the public and the Lederle reputation in both countries.

In the manufacturing processes carried out at Cyanamid of Canada's plant in the town of Mount Royal, there are 79 full-time employees. Of these, seven are engaged in quality control activities: five of this group are university graduates, and two are occupied in clerical non-technical capacities.

As you can see, this commitment to quality imposes specific economic responsibilities. The establishment of strict manufacturing standards and procedures, and the quality control procedures necessary to check large quantities of drugs, therefore, must be reflected in the price of the pharmaceutical product. Further, the reliable pharmaceutical house places its sense of responsibility to patients and physicians and scientific objectivity above economic considera-

tions. This philosophy, plus the mechanism for implementing it, means that the drugs sold by that firm must bear these costs. There is no short cut to quality.

Naturally, the manufacturer who competes primarily on the basis of price is concerned only with not violating official minimum standards and requirements. Frequently, he does not go beyond that and usually cuts corners in a variety of ways to keep his costs low enough to underprice his competitors. Thus, by not performing all of the essential tests, he introduces the element of chance into the pharmaceutical equation. Herein lies the major danger in the use of "cheaper" pharmaceuticals.

Drug manufacturers who compete primarily on the basis of price often ignore or dismiss as being unimportant the key phases of the drug producing process of pharmaceutical development, quality manufacture and quality control. But these processes, while extremely costly, cannot be dismissed as "frosting on the cake". They are precise scientific disciplines and are inextricably linked with the research process.

Frequently, entirely new tests have to be developed for each drug. A detailed knowledge of the interactions of the bulk chemical and the vast number of ingredients employed in formulations must be known under a variety of changing physical conditions. Improper particle size, poor selection of vehicles, inattention to stability and compatability under a wide variety of changing circumstances, and lack of knowledge about disintegration times and degradation products are just some of the factors that have rendered drugs inactive or frankly dangerous.

No one assumes that all manufacturers have an equal investment in research competency and facility. It is equally foolhardy to assume that all manufacturers have equal sophistication in these important disciplines.

The Lederle Quality Control section is divided into eight departments, each one responsible for a separate category of testing. The Product Security Department constantly checks products, inspects manufacturing and packaging operations and obtains samples for testing.

Two other departments carry out tests on vaccines for viral or bacterial contamination and test antitoxins and toxoids. Microbiological assays on antibiotics and vitamins are the responsibility of another group. A separate group of chemists and technicians handle chemical tests on raw, semi-finished and finished material. There is also an Analytical Development and Specifications Department containing chemists and biologists whose job it is to develop new tests and write specifications for them. The two additional departments do no laboratory work, but handle administration and general services for the rest of the group.

An important part of Lederle's quality control activities centres around animal testing. For instance, well over one hundred thousand animals are used in Lederle's quality control procedures each year to help assure the identity, purity, safety and potency of all products.

The testing of a product, particularly a vaccine, is a truly significant part of the production process. For instance, it takes us just a couple of weeks to actually produce a batch of smallpox vaccine, but the "curing" and testing period has lasted as long as two years.

An important consideration in the marketing of any product at Lederle is "how should it be tested". Long before a product can be placed on the shelves of pharmacies, members of the product development section's job is to formulate the new product in many forms for stability and other characteristics of the product as well as the convenience of the physician and the patient. Thus, a new product may appear as a capsule, tablet, ointment, syrup, injectable suspension, and so on.

The task of the quality control group is to determine whether the active ingredient in the product will be stable throughout normal shelf-life. Therefore, tests must be set up to answer all such questions.

Specific tests are set up to check the drug at every stage of production. From raw materials, through intermediate stages, to the final product, literally hundreds of tests are run to assure a perfect product. This is particularly apparent with some of Lederle's vitamin products where as many as twenty or more individual ingredients must be blended in precise amounts into one capsule. Tests are conducted all along the line to determine that each ingredient is present in exact measure. And when the product is packaged and labelled, the whole batch is placed in quarantine until quality control completes its final testing and releases it for general distribution.

Quality control does not stop at the plant gate. Every batch of drugs marketed by the medical products department of Cyanamid of Canada has a lot number which is used to keep track of its distribution. The quality control group could determine the whereabouts of every shipped vial, bottle, or tube distributed by this company and, if necessary, can recall any drug should a question arise.

As a further test, Lederle and Cyanamid of Canada retain several samples out of every batch of medicine manufactured. In this way it is possible, periodically, over the years, to run spot checks to determine not only its potency, but also whether it loses flavour, colour, and so on while sitting on the pharmacies' shelves in different parts of the country under different climates.

These methods for testing are constantly being revised, and increased in number as Lederle and Cyanamid of Canada learn of different things to test for.

It is not unusual to find that testing a product is more expensive than its manufacturing costs. Lederle's live, oral Poliovirus Vaccine is an example of a product in which the testing costs far exceed the costs of manufacture. A substantial staff of chemists and biologists, spends all its efforts in devising new test methods for new products or improved test methods for other products.

Because of these precise control and testing procedures, Lederle has been able to produce a line of medicinal products over the past 50 years on which the physician and his patient can depend. By following the same procedures, Cyanamid of Canada has maintained in this country the high quality reputation of the Lederle pharmaceuticals manufactured at Montreal and Niagara Falls, Ontario.

The Relationship of Generic Name Prescribing to Drug Quality

Most of the proponents of the practice of prescribing by generic names make assertions that to follow this practice is a method of drastically reducing the cost of medicines. Seldom do they relate generic prescribing to drug quality. We are aware and agree with the committee's expressed desire to consider separately the questions of drug safety and effectiveness and the costs of drugs. However, we feel that the myth of "generic equivalency" must be considered both in relation to cost but equally, if not more importantly, in relation to the quality of drugs.

What is a "generic equivalent"? If "equivalent" is interpreted to mean "equal to" or "identical with", the term "generic equivalent" is deceptive and misleading. It implies that products of two different companies, each product containing an equal amount of active ingredient, are identical in their chemical composition and therapeutic action. It carries the hazardous implication that all manufacturers exercise the same amount of skill, care, testing, and technical "know-how"; employ identical equipment and trained staffs in identical factory environments; and that each of many materials necessary for drug formulation (the tablet, capsule or form that the patient actually uses) is identical.

There is in fact no assurance that formulations which contain identical amounts of an active ingredient are actually identical, either in total chemical

composition or in therapeutic value. Thus there is no such thing as an invariable "generic equivalent" of a formulated pharmaceutical product.

If such is the case, then certainly there should be convincing evidence that generic-name drugs are not equivalent to each other. Is there any such evidence? There most certainly is. Many examples of such differences have been reported in the literature. A few may be cited to show the subtle and sometimes hazardous range of differences:

Drug	Findings in Brief
Amphetamine preparations	Eight 15 mg. commercial products were evaluated. Physiologically available quantities of the drug ranged from 5 mg. ($\frac{1}{3}$ of stated dose) absorbed over an extended period, to 15 mg., (full amount) absorbed at once.(1)
Dicumarol tablets	Larger tablets of the usual dose produced by the same manufacturer did not yield the same therapeutic response in patients. Only the quantity of the supposedly inert base was increased to make the tablets larger.(2)
Ophthalmic preparations	Ten were examined. Contamination tests indicated that some were preserved with such slow-acting preservatives that continued use after accidental contamination could lead to serious eye infections.(3)
p-aminosalicylic acid	Granules of drug with various coatings, used in treatment of tuberculosis, Shellac-coated granules in usual dose gave, when the granules aged, blood levels less than levels considered therapeutically effective.(4)
Phenoxymethyl penicillin tablets	Tablets meeting U.S.P. standards can vary widely in efficiency.(5)
Vitamins	Contaminated with estrogens due to lack of proper cleaning of manufacturing equipment. Gynecomastia was found in children taking the capsules.(6)

Perhaps the most dramatic evidence of the myth of generic equivalency and its relation to safety is contained in a letter published by a prominent Windsor, Ontario physician in January 12, 1963 issue of the Canadian Medical Association Journal. This communication describes the difficulties encountered by a diabetic patient, serious enough to require hospitalization, when a "generic equivalent" was substituted for a brand-name product which had controlled

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(1) Shenoy, K. G., Chapman, D. G., and Campbell, J. A. "Sustained Release in Pelleted Preparations as Judged by Urinary Excertion and Vitro Methods", Drug Standards, 27, 77, 1959.

(2) Lozinski, E., Canad. Med. Assoc. J., 83, 177, 1960.

(3) Dale, J. K., Nook, M. A. and Barbiers, A. R. "Effectiveness of Preservatives in Commercial Ophthalmic Preparations" J. Amer. Pharm. Assoc., Pract. Phcy. Ed., 20, 32, 1959.

(4) Tarmowski, Acta Tuberculosea Scand., 34, 76, 1957.

(5) Juncher et al, Antibiotic Medicine and Clinical Therapy, 4, 497, 1957.

(6) Hertz, R. "Accidental Ingestion of Estrogens by Children" Pediatrics, 21:203, 1958.

the patient's condition for the previous 11 months. The physician concluded by writing:

> This case, which has been a traumatic experience for the patient and myself, of course, does not necessarily indicate all or even the majority of unbranded drugs as being suspect. However, since diabetes is one of the few areas of therapeutics where failure of response to a drug can be observed clinically and measured objectively, I consider this instance most significant and revealing. It makes one wonder how many product failures occur in other circumstances where results are less obvious or dramatic.

Patient conditions make generic prescribing hazardous. A physician prescribing for a diabetic will avoid preparations containing sugar. He can do this by selecting a brand-name dosage form known to be sugar-free. This is difficult to do on a generic basis, because a so-called "generic equivalent" may differ only in that it has a sugar base. It is important that no drug containing a sodium salt be given to a heart patient on a restricted sodium diet. Brand specifications may be important to ensure that preparations do not contain any contraindicated materials.

Generic prescribing can be unsafe when prescription refills are involved. Patients must often take medication over a long period, requiring refills of prescriptions. There is no assurance that the same manufacturer's drug will be supplied each time, either by the same or different pharmacies, if the prescriptions by products of different manufacturers, varying slighly or significantly from uniformity, might lead to variations in therapeutic response which could mislead the physician in treatment of his patient. There is no such problem when a brand name drug is prescribed. With a brand name drug, exactly the same medication of identical composition is dispensed on each renewal.

The Relationship of Patients to Drug Safety and Effectiveness

Just as those who follow the will-of-the-wisp of generic equivalency almost always relate it not to drug quality but to drug costs, those who propose the destruction of pharmaceutical patents argue in terms of drug costs, and wholly or almost completely ignore the vital relationship of drug quality with the patent system. Certainly there is need to talk of patents and prices, and we again agree with the committee's decision to postpone this discussion until the primary question of drug quality has been fully discussed. Thus we in this submission will speak only of patents as they relate to drug safety and drug effectiveness.

How can we say that drug patents and the patent system in general have and are making a significant contribution to drug safety and effectiveness?

The foregoing pages describe in detail the costly, slow and careful scientific processes involved in pharmaceutical research, product development and quality control in manufacturing and distribution. We have seen how the Lederle research program has resulted in major accomplishments in the medical field—new products and new and improved processes for manufacturing and testing both old and new products. Without this kind of continuing research by those research oriented pharmaceutical companies, this kind of progress would have never been made. The incentive value of the patent system in drug development is confirmed by the fact that nearly all important new compounds introduced since 1939 were discovered in the United States, the United Kingdom, Germany or Switzerland, all countries with patent laws many years old. There is simply no question about the incentive value of patents. In Italy, where Mussolini abolished pharmaceutical process patents, there have been no important advances in the field.

Advances in the field of drug safety and effectiveness require a research program. Such programs require a tremendous investment in money and technical manpower. Without patents to safeguard such investments, Cyanamid and all the other companies engaged in research would be forced to abandon all of their promising research projects.

Only if the world community can conclude that here and now—on July 10, 1964—it has reached the absolute zenith in its quest for new and safer drugs—only then can it with a clear conscience say that pharmaceutical patents are an obsolete commodity.

We at Cyanamid of Canada firmly believe that pharmaceutical patents are as important today as they were twenty-five years ago, probably more so. We are proud of our achievements in the pharmaceutical field and proud of the reputation enjoyed in the medical community by the Lederle name.

Mr. N. J. McDONALD (*Executive Assistant to the President, Cyanamid of Canada Limited*): Cyanamid of Canada Limited is pleased to assist this committee again, and I would like to introduce our president, Mr. Stovel of Montreal, and the manager of our medical products department, Mr. John A. Bertrand of Montreal, and the three specialists who have come to help us today—from the right, Dr. H. D. Piersma, director of quality control of the Lederle Laboratories Division of American Cyanamid Company of Pearl River, New York; Dr. Litchfield, director of research and Dr. Gallagher, director of medical research.

Mr. S. R. STOVEL (*President, Cyanamid of Canada Limited*): I thought it might be helpful if I made a few general comments. You may become confused this morning hearing about both Lederle and Cyanamid, and it might be worth while to straighten it out right from the outset. The American Cyanamid Company is the United States owned chemical company with broad interests in many fields. Lederle is Cyanamid's ethical drug division. In the drug field Cyanamid operates through Lederle a truly international enterprise with activities carried out on a world wide basis. In this country Cyanamid of Canada is a wholly owned subsidiary of the parent chemical company. Cyanamid of Canada also operates in many diversified fields here in this country. We operate a medical products department which handles all Lederle products, and in fact manufactures most of them in this country.

The second point—perhaps I might touch on this—is that we are and have been for many years an active member of the Canadian Pharmaceutical Manufacturing Association. We support the general recommendation contained in the brief that was recently submitted by that association. We volunteered to testify before your committee, feeling it would be helpful for you to know the specific situation as it applies to one of the larger ethical drug firms. We felt that our long background in Canada and our diversified business experience permit us to present a broad and balanced picture of the problems concerning the safety of drugs.

Finally, we have with us today three eminently qualified professional witnesses. You may wonder that we have not brought in our team our Canadian medical director. We would like you to realize that we consider a high calibre Canadian medical director as an essential part of our drug activities. Unfortunately, the man who filled this job for us for many years recently passed away. For the moment we are left without a replacement, and we must lean on Dr. Gallagher and his associates for assistance. However, we would like to point out that we have a Canadian physician with exceptionally high qualifications who will join us later this summer.

I think those are all the comments I wish to make at the present time.

The CHAIRMAN: Thank you, Mr. McDonald and Mr. Stovel.

In the brief itself there are several divisions. I thought it would probably be best to put questions in the same order in which they are presented in the brief. In the first part of the brief there are some introductory remarks. Starting on page four is the beginning of the discussion on research. I wondered if we could confine our questioning at the beginning to the province of research. I am not sure whether Dr. Litchfield or Dr. Gallagher wish to make a brief statement at this time on research or whether they just wish the committee to ask them any questions they have in mind.

Mr. MACKASEY: I have a few questions for Dr. Gallagher which I would like to ask him. They might be embarrassing. When we visited Cyanamid I was impressed in general with the plant, with the number of built-in safety factors, and so on which have been dealt with in your brief. It was emphasized to me during our trip how the company had full access to all these safety measures that are used in the United States plants. Nevertheless, I felt a little resentful when I learned that all the diversified aspects of research are done in the United States. I was wondering why you people cannot establish clinical structures in Canada and help develop the research facilities in Canada of which we would not be ashamed. There has been a lot of loose talk, as well as factual talk, that we are losing a lot of our research people to the United States. I can see why. I admit that the facilities in Cyanamid of Canada are certainly conducive to safety in testing; nevertheless, in some of the other plants I visited in Canada, I found testing going on here for the North American market, not only the Canadian market. Have you any plans in the future to spend a few dollars on this?

Mr. STOVEL: The matter of research in Canada is certainly one of real concern to us, and we do a lot of it. We have taken the position that we would be shortsighted if we attempted to duplicate research that is already being done elsewhere on a scale which we could not achieve and the associated sciences that are required to get together fully integrated teams. I think in this field you all know that the sums being spent on research are well beyond us. We have taken the position in Canada that we are increasingly going to do research that has the potentials that are inherent in Canada. We have an active research program going on in organic chemicals which are potential building blocks for the drug industry as well as other chemical industries. We feel that would be our best contribution to research in Canada.

Mr. MACKASEY: After my visit to your plant and my visit to other firms I have come to the conclusion that the physical structures are almost symbolic of the whole system of testing. You need manpower and data, and you certainly have both in the United States plant. Nevertheless, I feel I would like to see Cyanamid get into the research field in Canada, not necessarily for products of the past, but that they should do some research of future products.

Mr. STOVEL: We are doing it. We have an active program on that.

Mr. MACKASEY: When you say you are doing it, are you doing it through the medium of people such as Dr. Genest, or have you your own counterpart?

Mr. STOVEL: We have our own group which is highly weighted toward the medical field rather than the drug field. We do not do in Canada the type of drug research you saw the other day.

Mr. MACKASEY: Do you contemplate doing that type of work in Canada?

Mr. STOVEL: We do not contemplate doing that type of work in Canada as we feel such an effort would be merely duplicating, in a less able way, what is being done. There are fields in respect of which we think we have the ability to capitalize either on our export possibilities or raw materials, or a particular manufacturing situation. This is the direction in which we are putting our research dollars.

Mr. MACKASEY: Do you initiate any testing here in those fields, other than the pharmaceutical field, in respect of which the parent company takes advantage in a kind of reverse procedure to that followed in the pharmaceutical field?

Mr. STOVEL: Yes.

Mr. MACKASEY: I understand your research is centred in the United States because it is perhaps good business, and logical, not to duplicate that research in Canada. Nevertheless, I should like to see something of this kind initiated in Canada. I realize that Cyanamid of Canada Limited and other firms are supporting men like Dr. Genest through grants, but I should like to see some of the pharmaceutical firms initiate some research here in Canada involving the establishment of physical buildings, creating work for technicians and labourers, if I may use that expression.

Mr. STOVEL: I feel this is needed in Canada, but our contribution can be made in a better way by tapping the potentialities that are uniquely ours, and I do not believe this involves the drug research field, where one unit is relatively similar to another.

Mr. MACKASEY: Thank you very much.

Mr. WILLOUGHBY: Mr. Chairman, perhaps we could hear from the other representatives and then ask them questions in respect of their remarks. I am not criticizing the questions which have already been asked because I think they are pertinent.

The CHAIRMAN: Do you have a question, Mr. Whelan?

Mr. WHELAN: In how many countries in the world do you sell you drugs?

Dr. J. D. GALLAGHER (*Director of Medical Research, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N.Y., U.S.A.*): The drugs are sold world wide. They are sold virtually everywhere except in areas behind the iron curtain.

Mr. WHELAN: Your main research facilities at Pearl River are your research facilities in respect of drugs sold world wide?

Dr. GALLAGHER: That is correct, sir.

Mr. MACKASEY: Mr. Chairman, I would appreciate very much Mr. Stovel, or one of the other representatives, elaborating on his information in respect of clinical research.

The CHAIRMAN: Have you research in respect of human beings in mind?

Mr. MACKASEY: Yes.

The CHAIRMAN: Perhaps we could hold that discussion in abeyance for a few minutes. I think this subject is touched upon later in the brief and we might deal with it when we reach that stage of our considerations.

Do you wish to say anything about medical research or research in general?

Dr. J. T. LITCHFIELD (*Director of Research, Lederle Laboratories Division, American Cyanamid Co., Pearl River, N.Y., U.S.A.*): Those of you who were able to come to Pearl River, of course, saw the extent to which we are engaged in research in the broadest possible sense in the medical field. I tried to bring out in the remarks I made then the fact that this is a world wide effort, and we are doing research in respect of diseases unique to other parts of the world. We do not pretend that we can cover the entire research field, but I can name very important diseases in respect of which we have not touched at all. For example we have no research program in respect of antimalarials because we believe there are adequate antimalarials available. We try to achieve breakthroughs where breakthroughs are needed. A very important part of our research effort is engaged in protecting the drugs we already have developed and placed on the market. These are always subject to a risk or threat for competitive or other reasons, so we continue to do research in this regard.

I believe the comments which I made at the luncheon have been made a part of the record; is that correct? I gave a copy of those remarks to Miss Savard.

The CHAIRMAN: They have not actually been made part of the record because the committee did not officially make a record of its proceedings on that date. They will be summarized and made part of the record. If it is your desire to make those remarks again now they will appear in the record, or the committee has the power, if it wishes, to have your remarks made part of today's record. Is it the wish of the members of this committee to do so?

Mr. WILLOUGHBY: I move that we make the record of Dr. Litchfield's remarks, which is available, part of the official record of today.

The CHAIRMAN: Do we also have a record of the remarks made by Dr. Gallagher and Dr. Piersma?

Dr. GALLAGHER: My remarks were strictly extemporaneous but if it is your wish I can readily commit them to paper and transmit them to you. If that is your wish I will be glad to do so.

The CHAIRMAN: Perhaps we could ask Dr. Willoughby to extend his motion to include your remarks.

Mr. WILLOUGHBY: I certainly would include the remarks made by the other gentlemen. I was dealing with the present speaker but I am prepared to extend my motion to cover your suggestion.

Mr. PRUD'HOMME: I second the motion.

The CHAIRMAN: Is that agreable to the members of this committee?

Some hon. MEMBERS: Agreed.

The CHAIRMAN: We will make sure that these remarks are made part of the record today.

(The following is the welcoming talk of Mr. R. P. Parker, President of Lederle Research Laboratories):

It is my privilege to welcome your Committee to our Laboratories here at Pear River today, and doubly so because you are from Canada. You see, my wife was Canadian born and came from Hamilton, Ontario. My brother, earlier, attended your Medical School at McGill University, and my second son, now, is attending this fine school.

Lederle Laboratories at Pearl River was established in 1906 as a continuation of the Lederle Antitoxin Laboratories, earlier founded in New York City. Its business remained essentially that of developer and manufacturer of essential biological products until, in 1939, the president of American Cyanamid Company directed Lederle to embark upon as extensive a research program as possible, consonant with good business practice, to solve the problems of human disease. He stated that such a program was a great risk, but that, if just one medical problem could be solved, the public would be well served and Lederle would prosper. How Lederle contributed in its research role, and grew, is now history; and I believe the brief submitted to your Committee by Cyanamid of Canada details much of it.

My purpose in citing the above mission charged to Lederle by our president is to emphasize that our efforts are directed to the solution of human disease problems; not just United States disease problems; not Canadian—but disease problems which affect mankind in all parts of this earth. We at Lederle are, in reality, an international research-oriented laboratory, and we work in collaboration with scientists and physicians all over the world.

During your brief visit here today, we have planned your program with the objective in mind of clarifying and differentiating the ethical drug manufacturer's operations as they bear on—

(1) *research* which is directed to the discovery of new drug entities, and the laboratory and clinical research methods followed to demonstrate their safety and effectiveness, first in laboratory animals and, subsequently, in the human.

(2) *Development* and *production* directed to the establishment of the highest possible standards and most exacting procedures to manufacture "quality" drugs. By "quality" drugs, I mean those that uniformly meet the highest standards of purity, potency, stability and performance. By "quality" drugs, I also mean "safe" drugs, in the sense that your Committee has referred to them in previous testimony.

You will immediately note that I have used the word "safety" in two different ways:

(*a*) Safety, in the first sense, is the securing of the desired main effect of the new drug in patients relative to the undesired side or toxic effects. Said in different words—"Is the new drug safe relative to its effectiveness?"

(*b*) Safety, in the second sense, is the production of "quality" drugs which uniformly and reliably meet the highest possible standards.

It seems to me that it is highly important that your Committee understand this differentiation, for such understanding will clarify the research, development and production responsibilities of the drug manufacturer; and will serve to emphasize that these responsibilities are shared with a federal regulatory agency such as the United States or Canadian Food and Drug Directorate.

Neither party can act unilaterally and arbitrarily if the public interest is to be *best* served. The manufacturer who discovers the new drug in the first instance must—

(1) Develop the safety and effectiveness data in the laboratory, and then in the human.

(2) Develop the product standards, manufacturing procedures and control tests.

(3) Compile in detail all information relating to use of the drug; the indications, contraindications, dosages, administration, side effects, and precautions for its labeling, package circulars and brochures.

And the Food and Drug Directorate must study, disapprove or approve each and all of the above details. Once the details are approved, no further change, even though it be an improved standard, or test, or use, may be made in the product, or its manufacture, or its labeling or promotional claims, without prior study and approval by the FDD. So, you can see how this is a shared responsibility. Through our own Quality Control, for our own interest, we audit all of our own standards and procedures. And then, in the public interest, there is the audit of the FDD.

Our program here today will be in two parts. This morning, you will visit three research laboratory areas concerned with the discovery of new drugs and the demonstration of their safety and effectiveness in animals. You will briefly hear about the functions in each, and then have the opportunity to see for yourself.

At lunch, Dr. J. T. Litchfield, M.D., our Director of Research, will briefly review for you what you saw in the morning and correlate the research effort of the laboratories which you visited.

Also, at lunch, Dr. J. D. Gallagher, M.D., our Director of Medical Research, will speak to you about the procedures which he and many physicians follow to prove the safety and effectiveness of our drug discoveries in humans. He will emphasize the planning and evaluation of clinical programs which must be designed to produce the information required to answer the questions "Are the risks of this new drug low enough relative to the good it can do?" (its effectiveness)

Before starting on the afternoon tour, Dr. H. D. Piersma, our Director of Quality Control, will speak to you briefly on the other operational aspect of our business to which I have referred—"How do you build quality or reliability or safety into the manufacture of a new drug?" And—"What is the relationship of quality control to this important series of operations?"

Following this, you will visit some actual production areas where drugs are being formulated, tableted, encapsulated and packaged. You will also see the pharmaceutical laboratories where the procedures and standards for accomplishing such production of "quality" drugs are devised.

And, lastly, you will visit our Quality Control Laboratories which oversee every step of our operations to ensure that we, as human beings, make no mistakes—or, if such should happen, that we would be certain to catch them. And, to see that we, as manufacturers, accept the responsibility of continually looking to improve our procedures, raise our standards, and never sacrifice our quality.

I do hope sincerely, that, by the end of the day, you will have found your time to have been fruitfully spent. Doubtless, you will have generated many unanswered questions. And so, the gentlemen who will speak to you at lunch will join with you for supper at Wayne. They also will be present to respond to your questions at Ottawa this coming Thursday.

Talk given to Canadian Parliamentary Committee
July 7, 1964
by J. T. Litchfield, Jr., M.D.,
Director of Research, Lederle Research Laboratories

It has been a privilege for us to have you visit our research laboratories and to see our work at firsthand. We have tried this morning to show you how we go about the incredibly difficult task of finding a new and useful drug. Because the odds are so heavily weighted against us, we must research many fields simultaneously in order that our chance of finding a new product may be enhanced. For example, we tested in animals more than 15,000 compounds before we found one which was active against a virus infection and that compound was not useful.

Our effort is based on teams of chemists and biologists who work together, study and follow the literature, develop test methods, test and make new compounds. We gamble that sooner or later an active substance will be found or synthesized. When this happens, a well coordinated effort is undertaken to synthesize related chemical compounds, test them, check toxicity, build-up knowledge and move towards the point where we feel we have attained the safest and most effective compound as best we can judge under laboratory conditions. On the average, this seems to take about 3 years, but this has ranged from about 1 year to "never as yet". That is, there are some of our research areas in which we have yet to make a strike.

This is a very complex effort. It is not limited to research on disease conditions which affect the North American continent. Our research is on a

worldwide basis. For example, this morning you passed by a laboratory devoted to studies of a disease which occurs in 3 South American countries and nowhere else in the world.

Besides being complex, this research is very costly. We will spend about 16 million dollars this year in these laboratories in our efforts to improve medical care. Since there are about 1,000 employees involved in this research effort, you can easily see that our costs are about $16,000/man/year. However, if you consider that about one-half of our research employees are professionals —i.e. have a college degree, then our costs per professional man or woman are almost $32,000 per year. Today you saw certain efforts we make to keep the costs of research as low as possible. We automate analyses, for example. We plan to install a centralized weighing operation to serve all screening problems. Our systems of reporting research findings are being adapted to computers so that clerical effort can be maintained at its present level while our research output expands. If we can find the means for replacing a man by a machine, we do so immediately but then we put the man to work on a problem which we had not been able to attack due to shortage of manpower. The result is that we expand our research efforts without materially expanding our costs.

I have said a good deal about costs for the reason that we live with them day in and day out. These costs inevitably have to have an effect on drug prices and so you can understand why we are so conscious of them. You might wonder in this situation what motivates the research individual in our employ. Is he working for us purely for monetary gain or are there other important factors? I am convinced that most of our talented research men and women have chosen their profession and their position with us because of their ideals. They know that if they can help in the development of just one life-saving drug, their contribution will bring a benefit to mankind which is immeasurable.

I would not want you to have the feelng that our research is a machine-like operation devoid of human judgments and values. Our research programs and discoveries are under the constant surveillance of our Research Committee. We know from long experience that studies in laboratory animals cannot be anything but an imperfect substitute for studies in man. The reason for this is a very simple one. Man is a separate and distinct species. As a result, he reacts differently than laboratory animals in many cases. This is why the monitoring of our research by the Research Committee is so important. It would be all too easy to make rules concerning results in laboratory animals and substitute these for human judgment. Instead, the Research Committee consisting mainly of our Research Directors and representatives from our Medical Research areas must evaluate the evidence from the laboratory and decide (1) whether or not a potential new entity appears to be efficacious, and (2) if so, can it be tested safely for the first time in man. Later, if the drug is found effective in man, the additional evidence from the laboratory and clinic will have to be re-evaluated to decide whether the new entity can be used safely and effectively on a large scale.

The Research Committee consists of about half M.D.'s and the remainder Ph.D's in various sciences. In the early decisions of this Committee relating to a new drug, those close to the laboratory carry heavy weight while as the new drug is developed, those concerned with the clinical aspects must assume greater responsibility. Dr. James Gallagher of our Medical Research Section will speak to you next on the problems of getting a new drug from the laboratory into the clinic under safe conditions at every stage."

The CHAIRMAN: Do you have any further remarks to make Dr. Litchfield?

Dr. LITCHFIELD: For the benefit of those members who were not at Pearl River I should like to mention a few of the guidepoints which indicate the scope of our drug research. For example, we have about 1,000 people engaged in this effort, about half of them having professional degrees. This research effort costs about $16 million per year or $16,000 per employee engaged in research or, if we put this in terms of professional people, almost $32,000 per man per year. I do not know offhand the actual number of square feet we have devoted to the research laboratories there but it is, as I recall, something of the order of three or four hundred thousand square feet. We try to have these laboratories equipped in the most advanced fashion possible and as up to date as possible. I mentioned, for example the very great extent to which we automate our efforts, not to cut down the number of personnel, but to use our people most effectively by relieving them of things that can be done by machine.

I think those are all the remarks I should like to make at this time.

Mr. MACKASEY: While we are referring to research efforts, and I realize you have a great number of departments operating because of the vastness of the area, could someone indicate the progress being made by the obvious amount of research in respect of cancer being carried out? I realize you are making a genuine and sincere effort to do a public service in this way. I understand that one particular drug has been undergoing testing almost continuously since 1949 involving what I imagine is a staggering cost. Could someone give us some indication of the progress you are making in this regard?

Dr. LITCHFIELD: We have invested almost $10 million in this field and have really not recouped any significant amount. This program started well over 15 years ago and has been supported always from the top of the company on down as a public service effort. About ten years ago it evolved, in a rather new and dramatic fashion, into a special system of testing which permitted us to get the largest number of compounds tested with the animals and funds available.

This was the result of a new method which was developed during the war known as sequential analysis. It was developed really as a quality control test to allow you to accept or reject a material with the fewest possible number of tests. We learned how to apply this to our cancer testing on animals. I think we almost multiplied by five the number of compounds we were able to test by adopting this program. This program was subsequently adopted with very minor changes by the National Institute of Health in their cancer therapy screening program. They came to Lederle to see how we did the testing and then went back and adopted this just as we were doing it, using slightly different animal tumours than the ones we had selected. I think that without exception, in the last 10 years at least, we had one compound going into clinical trial about every two years. The funds which we devoted to this are by no means tremendous. The animal testing part runs to around $150,000 to $175,000 a year. The chemical effort that backs this program costs about $100,000 a year. On top of that comes the costs of clinical testing of any compound that we develop. Out of this program came three drugs which we sell—one is known as T.E.M., another one is known as Thio-Tepa, and a third one is Methotrexate. Recently we had Aminopterin which we took off the market because sales were very limited, and methotrexate is a better and safer agent. We have one drug in clinical trial now. We have still another one which is extremely interesting from the standpoint of what it would do on laboratory animals, and we hope, by the end of this year, it will be in trial. I would say this had been a very successful research project and one which we have really put our hearts into over the years, and we will continue to do so.

Dr. GALLAGHER: I would add to that, to emphasize what Dr. Litchfield said, that our financial returns over this period had been completely negligible, but this in no way has influenced the direction of the program. In fact, this goes back to some of the original instructions which were given by our early presidents to the people who run Lederle Laboratories, namely if you addressed yourselves vigorously and honestly to research and to curing diseases to serve mankind, inevitably you must prosper. If you set out only to prosper, then you abuse your inherent responsibilities in this business and inevitably you will fail. This example of what Dr. Litchfield has just said is illustrative of this principle. When we embark on a research program, our immediate returns in no way upset the orientation of this program because to do research in a true and sincere fashion you really start not knowing what will come from it. You cannot say, "I will buy so many pounds of research and get so many pounds of results". This does not happen. Anyone who has instituted a research program does not know what will be achieved from this research. Throughout the years, all the people I have been privileged to work with have always felt that good medicine is good business.

Mr. MITCHELL: May I ask Dr. Litchfield a question? In your cancer research have you any access to funds that have been publicly raised for that purpose?

Dr. LITCHFIELD: No. We have never taken one cent of funds from the federal government for this research. We were under great pressure to accept such funds four or five years ago when cancer chemotherapy in the national service centre was set up. There was a tremendous amount of money which they did not know where to place and they put great pressure on us to let them finance our program. Our management listened to them very carefully, we looked into it exhaustively, and the Cyanamid company as well as Lederle made the decision that they could afford to support this research and that we would not accept any government funds.

Mr. MITCHELL: Have you any idea where that money goes? Is there any other outside individual clinical research or are there any pharmaceutical manufacturers you know of who do work on cancer research and who do take some of this money?

Dr. LITCHFIELD: Some pharmaceutical companies have taken funds and have set up special laboratories to do nothing other than test antibiotics to see whether they have anti-cancer activities in animals. There has been one company that took grants to make compounds on request for the cancer chemotherapy centre.

I do not really think I can give you a complete story of how many companies accepted this money. However, I would like to bring out one thing. There is a very real problem with patents, which is perhaps beyond the scope of the discussion. If one takes federal funds, then the government requires all sorts of patent rights that it would not otherwise require, merely because that money was made available. They would also, quite properly, want to come in and examine your books and look into your accounting methods to make certain that the money they gave you was spent wisely. This is an unattractive feature.

Mr. MITCHELL: Are these organizations which solicit donations, say for the heart fund or for the cancer fund not government agencies?

Dr. LITCHFIELD: Oh, no.

Mr. MITCHELL: Where does that money go?

Dr. LITCHFIELD: It goes to support individual investigators.

Mr. MITCHELL: You would not be handicapped if you accepted some of that money, if it were offered?

Dr. LITCHFIELD: We would not be handicapped but I do not think they would offer it.

Mr. MITCHELL: Where do they put their money? Would it be in university research?

Dr. LITCHFIELD: Yes, university research and institutions such as the Sloan-Kettering Institute.

Mr. MITCHELL: I think we are all solicited about once a year to give money to these programs and I have often wondered how that money is administered. I still do not know.

Mrs. JONES: I would like to ask a question concerning the nature of the liaison that goes on between those conducting research in universities and people in the laboratories, the exchange between them and the progress they make.

Dr. GALLAGHER: I suppose Dr. Litchfield could speak to this. There is a very intimate relationship between many of the people who work for us in one research capacity or another. They are, of course, university trained, they belong to all of the same professional societies to which university workers belong. Our own internal policies are extremely liberal from the point of view of meetings between these people, and of course the greatest point of contact and exchange of information on research comes from research publications. In order to attract and hold good people in a research capacity you would have to be cognizant and fully aware of the needs that they have. We therefore have liberal travel policies regarding attendance at these meetings. We present our work, and this work is criticized by the university research workers. We exchange information of various types. I do not know whether that answers your question fully.

Mrs. JONES: Is this on an informal basis or is this a formally set up type of communication?

Dr. GALLAGHER: The mechanism for doing this is fully formalized, but when you come down to the actual exchange of individual pieces of information, this follows exactly the same pattern that exists between university workers exchanging information from one university to another.

Mr. WILLOUGHBY: I presume that clinical work is carried on in the university centres?

Dr. GALLAGHER: Yes, in a large part. I should like to underscore one point that I made previously. We do not predetermine necessarily that this work will go on in this state, or in this country, or in this province. What we are always looking for is an individual who has scientific competence and training in the given field in which we are doing this clinical work. Secondly, we are looking for an individual who has the interest, and thirdly for an individual who has the facilities to do this. Therefore, our approach to this is not confined to anyone, it is world wide. We will go wherever we find a person who has those three qualifications.

Dr. RYNARD: What I have to ask was very well covered except for this one point. The speaker was saying that they were carrying out cancer research on their own. They did not get grants from the national research council. I do not know whether it was made clear or not that there was a sifting out of all the information across the United States that would indicate whether experiments were being duplicated in various organizations or firms that might be carrying this out.

Dr. LITCHFIELD: I want to be sure I understand your question.

Dr. RYNARD: Does the national research council know the experiments which you are carrying out?

Dr. LITCHFIELD: No, they do not know this except to the extent that we publish them.

Dr. RYNARD: The point I am trying to make is that there may be duplication of the experiments you may be working on at Lederle in some other organizations or institutions.

Dr. LITCHFIELD: This could be possible if they happened to have the same compound for testing and happened to test it against the same kind of tumour. It would be largely a coincidence. I do not really feel that there is any tremendous duplication of effort. Our program is really geared to deal with the fact that about only one in every 300 to 500 compounds will have any activity at all. Consequently, you must test these hundreds of compounds in order to find the rare one that has some activity. Most of your testing is completely negative. There is no way to report this because there is no publication of which I am aware that is interested in publishing a fact that hundreds and hundreds of compounds were not active. They are very much interested in getting a paper on something that is active, but not on something that is inactive.

Dr. RYNARD: Probably you would not want to disclose what you are researching on.

Dr. LITCHFIELD: This is, to a certain extent, true because a compound that is not active in any particular test may turn out to be very active in another test. I could give you very many examples of this. One of the more interesting ones is of a chemist in our Stamford laboratories, in Stamford, Connecticut, who made a compound which he was certain was going to be an excellent additive for a battery. It would prolong the life of a battery and prevent it from running down as fast, and it would make it recharge faster. He made this compound, but it was found to be completely worthless. It was put into our compound collection, and in due course it was tested against tuberculosis in mice. It was found to have a very interesting activity. We then made a large number of compounds related to this structure, and in the course of this we found one which was substantially more active and substantially less toxic than the original compound. This has been in clinical trial for almost a year and a half. We found that over and over again a compound which is made for one purpose will have some entirely different useful properties. This is why we have a proprietary interest in this large collection of compounds, a collection of some 50,000 to 60,000 compounds. We are sifting through this collection constantly, trying to find those which are useful.

Dr. RYNARD: Perhaps we could continue speaking about this for a while. Would you agree with this then that if research became a national research effort then it would destroy all the incentive to get out and dig into all those various drugs which you test, and therefore we would have less and less new drugs for the benefit of mankind no matter how much money there would be at the top. Is this right?

Dr LITCHFIELD: The incentive is a terribly important factor.

Dr RYNARD: I think it should be stressed because I do not think many people realize the fact that once you put money into a central body you are slowing down research across the country. Am I right in making this statement?

Dr LITCHFIELD: I am biased on this.

Dr RYNARD: Is this point not true in Russia? This is important when we are dealing with research, particularly with research that does not take government funds.

Dr GALLAGHER: I feel it is quite correct I would say, to add to this statement, that one of the reasons why we never take government funds is, going

back to what I said before, that when we start a program we commit ourselves to this program; we are the sole source of the funds and we have the responsibility for them. We stand or fall on this. If you take an outside subsidy for your program, inherently you lose the direction of your program because they can change the allocation of the funds when you are right in midstream, and your program collapses about you. Therefore, we have found that this is one of the supporting reasons why we have elected to pursue this independently, and why we have elected to take this risk, so as to enable us to manage our own program and bring it to a point of completion which we think necessary and logical. Without the incentive, we could not do it.

Mr. MACKASEY: I would like to say a word there. I am not a doctor or a pharmacist, I am just one of the happy masses who buy your products on your recommendation. I have come to this conclusion—and this is my first year in the food and drug committee—not only after visiting your plant but also after my visit to Ayerst, McKenna and Frosst, that thank God under our democratic system at least the initiative is left to the drug firms. I have no illusion as to what their basic motivation is, that is to make a good dollar for the shareholders. I say, thank God we have them and that they are motivated by a desire to make a profit in doing this type of research. I shudder to think what would happen to us otherwise. I base this thinking on a little bit of reading that I have done on the type of development in new drugs. For instance, in the iron curtain countries, in Russia in particular, they do not have that motivation and therefore the incentive dies. It is left up to the government to do all the research. I see more and more as our meetings progress that if we had to depend entirely on the food and drug directorate for safety and also for prompt research we would be in an awful mess. I do not know how it is in the United States but I think the time has come for people to realize this. I am also amazed at the apologetic nature of the drug industry.

Dr GALLAGHER: I think you are quite right. I should also like to speak to the point you mentioned with respect to the Russians. I think they found that since no one was clearly responsible for his activities, they could not get any results, and no matter how many inspectors they put in a Russian plant they could never be sure. What is worse, they could not find out what was wrong. In our own view we have found no substitute for making a man responsible for his actions and being willing to support his actions.

Mr. MCDONALD: Maybe Dr. Piersma would like to comment on this.

Dr. H. D. PIERSMA (*Director of Quality Control, Lederle Research Laboratories*): While it is true that economics play a great part in stimulating research in private industry, I for one would like to say that it is not the only drive. There are many dedicated people in commercial organizations who have gone beyond the need for more than three meals a day or more than one roof to sleep under, or one bed to sleep in. Money will buy just so much. I must say that I have spent the major part of my life in Pearl River at Lederle and I have met the finest people in the world in this organization. It has not always been the dollar that motivated people—there was much beyond that.

Mr. MITCHELL: May I ask a question? Do you feel there is any danger in a national health plan which would result in a slowing up of research?

Mr. J. A. BERTRAND (*Manager, Medical Products Department, Cyanamid of Canada Limited*): I am not a researcher myself but I would echo what Dr. Litchfield, Dr. Gallagher and Dr. Piersma have said that any time you centralize funds you almost automatically slow up research.

Mr. MITCHELL: When I asked that question I was thinking that maybe there was some reluctance on the part of a government agency which feel that

it could not pay for the higher priced drugs, particularly in the antibiotics field. Personally, I am fearful of it myself but I hope I am wrong. It is a very common subject these days, particularly in Canada. I am wondering if this would not limit this research which is helping us along so much.

Mr. BERTRAND: I have to share your fears, Mr. Mitchell.

Dr. RYNARD: I think it has been fairly well proven that in those countries that have a health plan if you are over-prescribing what they feel is more than the average number of expensive drugs you have to report to a central body and justify your actions and therefore you always have a hammer over your head. This has been proved in countries that have national health plans.

The CHAIRMAN: Are there any other questions on research?

Dr. WILLOUGHBY: I have a question to ask on research. What are the methods used in the United States to check these fly-by-night organizations that are turning out pharmaceuticals at cut rate prices? What method is used to check the quality of the products they are developing? Is there a way of curtailing inferior drugs supplied under generic names which would not be competitive to a high quality drug?

Dr. GALLAGHER: Efforts are being made in the United States to do this. However, my own private opinion is that the amount that you can achieve by this has a very practical limitation. I do not think one can ever regulate it to the point where you are no longer dependent on the confidence and the integrity of the manufacturer. For example, the bureau of standards has not been able to protect the housewife from the dishonest butcher putting his heavy thumb on the scale. Unless you control production completely it is not possible to do it. I do not think you can ever be one thousand per cent sure that every batch of every product that is produced by every manufacturer does meet minimum standards. I think you can make tremendous efforts in this direction and I think and these serve as a deterrent. Here again the way to build a sound, constructive and reliable pharmaceutical industry does not depend on helping the manufacturer to fall down on his own responsibility and rely on someone else to check his quality. To have a strong industry you have to fix the responsibility where it belongs, that is with the manufacturer himself.

To summarize my answer to that question, I think that the steps that have been taken in the United States have gone a long way towards providing the greatest measure of assurance that it is practical to supply, but if one ever has a real doubt about a fringe operator or the reliability of the operator, it is almost impossible to control that operation 100 per cent of the time. As you have learned, I think, when Dr. Morrell was here, he took you through the various steps that must be involved in completing inspection, and these steps are staggering, they are vast in number. For example, there is nothing to stop a fringe operator—assuming for the moment that there is such a thing as a fringe operator—from getting around the law if he chooses to do it, that is from omitting the simple act of sterilizing the machine between fills of one drug or another. If this is not done you run the real risk of contamination. Inspection cannot be done every day of the year. I went through a mental exercise to try to get some estimate of the enormity of the job of checking every batch of drugs produced in the United States. I do not pretend to know how many drugs are released in the United States but I recall one survey made simply based on 50 companies. I think that these companies had something in the neighbourhood of 33,417 products. If you are worried about the quality of independent products, you have to consider the dosage of every product, and I do not know how many batches a year are made of these 33,417 products. A very conservative estimate was made which concluded that if each company made something like 10 batches, you would have to address yourself to the problem of checking or testing 335,000 batches. From this point of view the enormity of the problem

is staggering. You then think, "What do I need to do this?" For a company such as ours at Pearl River, where we may have something in the order of 200 dosage forms, we use 100,000 animals a year for testing procedures. I am giving you these facts to illustrate the point I am trying to make that there is a practical limitation to the extent you can check.

Mr. WILLOUGHBY: I understand that it involves a tremendous number of tests but I presume the food and drug administration in the United States does try to maintain a minimum standard in the products that are being sold.

Dr. GALLAGHER: In every way. They are doing a tremendously effective job within the limitation of what any agency can do even with the full support of the industry in that country. They are doing an excellent job in so far as any job can go.

The CHAIRMAN: Are there any other questions on this aspect? If not, perhaps we can move on to the next general heading on the brief on page 10, starting with testing. Are there any questions on animal testing between pages 10 and 13? Perhaps it would be best to combine the whole section of testing in respect of animals and humans.

Mr. MACKASEY: I did ask a question in relation to this subject earlier during our meeting. It was quite logical, of course, that during our visit we could not dig into all the questions in respect of testing on humans, but I presume the system is pretty well the same in the United States and in Canada, in that testing work is farmed out to dedicated researchers such as Dr. Genest and others who are listed on page 17 of your brief. Perhaps Dr. Gallagher could elaborate a little in respect of that aspect.

Dr. GALLAGHER: Are you referring to the actual method we use in testing?

Mr. MACKASEY: Yes.

Dr. GALLAGHER: How far back would you like me to go?

Mr. MACKASEY: I do not want you to go too far back. Knowing your name is Gallagher and that the Irish usually talk too much I will not ask you to go back too far.

Mrs. JONES: Are you Irish?

Mr. MACKASEY: Yes, or I would not have made that remark.

Dr. GALLAGHER: It is indeed a small world and I am completely at your service in this regard. To answer your question as briefly as possible I will refer to what are actually six steps.

Firstly, what is it that makes us decide to test something? What do we do before we test on a human, and what do we do later? What makes us decide whether to test or not to test? We very carefully examine all the animal evidence that exists.

The animal studies are done essentially in two parts. These studies are designed to indicate whether or not a drug has some suggestion of useful activity in man. Will it be useful against a given disease area? Of course when you look at these questions you look at many factors. How good is the activity? At what doseage does it occur? Are there other agents which are just as good for this kind of thing? Then you address yourself to the animal toxicity without ever going to man, and this is a tremendous factor. One thing you have to do and one principle on which you have always to rest, going as far back as Hippocrates, is that you must do no harm if it is at all possible. We have to look at animal toxicity. We are interested in trying to determine first of all if there is a toxicity produced and, if so, what kind of toxicity. At what doseage level is the toxicity produced? Is this toxicity specific or is it disseminated throughout the whole body? If it is disseminated throughout the whole body it is obviously a more serious problem. There are a whole series of factors which I have abbreviated for the sake of saving time.

Then you start this balancing process which is a big factor in respect of all human testing. As I have said before, this balancing process extends right down into the individual doctor's office everytime he sees a patient. You might ask what is the balancing process. It is a balancing of the good that you may do against the harm that you may do. In order to proceed from one step to another you must always have that favourable balance. You must always feel you can do much good and that your chances of doing harm are completely minimized. Then at this particular point you are ready to start, and this is, as I have said to you previously, really a confrontation with the unknown. Animal studies are extremely important. You must have them, and it would be unconscionable not to have them. They are however very limited in manner because you cannot safely relate the results that have occurred in animals to man. There is no way of doing this. One of our most urgent problems in research today involves finding ways of doing this kind of thing.

At this particular point we ask ourselves such questions as: Who is going to give the drug? I think this is more immediately related to your original question, who is going to take the drug and where is the giver going to give it to the taker? Is the drug going to be given in a closed hospital community? Is it going to be given in an outpatient situation or is it going to be given in a prison?

Then we sit down and have a free and open discussion with prominent clinical investigators in this field. I repeat what I said earlier, we go anywhere where we find a man of competence and training, a man with the interest and a man with the physical facilities to do the job. We give him freely all the information we have developed. He sees this for himself. Then together we work out a plan.

At this point in connection with safety to the patient I should state that we do not put a pill in a person until we make a submission to the regulatory agencies, the feed and drug directorate in Canada and the food and drug administration in Washington. Before we even put one human being to any element of risk we have filed all of the animal work and everything that we have done on investigation with the regulatory agency. We file with that agency information in respect of what we plan to do in man, including the name of the fellow who is going to do the work so that they have some idea whether the men we are going to have do the testing are qualified or not.

From this point we go into the three phases of testing in man. This is an oversimplification but I think it holds true.

Again this whole procedure has to be punctuated with the words caution, caution, caution, precision. Everything you do you go about first in a series of ever widening circles, cautiously calling upon all your human experience.

In the first place in going to man you are involved with just a very few people; a limited number of human beings and just a couple of investigators. You start with a very low dose. You may find out a suggested dose from animal testing and you take only a fraction of this dose. At this first stage it is very limited. You find out whether the drug is active or inert, at what dose it is active, and a few more characteristics of the drug. When you find this out you stop and you go through this balancing again to determine the possible benefits to the patients compared to the risk that may be involved. You decide whether it is safe to go on.

You then go to the next phase which involves a few more people, perhaps up to 100 in this situation, and a few more investigators. In this particular situation your objectives are, perhaps, to confirm what you have seen on the first trial and to extend your knowledge.

Once you get this information again you stop. You stop and make this balance again. You weigh this information and decide if it is safe to go on a step further to the so called phase three in respect of which I have said

before that it is tremendously important because it gives you a preview of what might happen when this drug gets out into general use. This is another quality step in an attempt to minimize your risk to life. As I have said before, automobile manufacturers and aircraft manufacturers have an extensive testing system, but before they release anything for general use they spend months and years seeing how that plane or car will react under ordinary conditions of human useage.

From the point of view of safety in this phase three, what we have been talking about up to this time is what happens when you bring about a meeting of the drug and the ordinary person. What you are concerned about is what is going to happen when you bring about a meeting of the drug and a person who is not ordinary but who is unaverage. He may be unaverage by virtue of the fact that he is allergic to the drug or the environment in which he takes the drug. These people are extremely rare. If any of us around here tried to predict which of us would be sensitive to a drug we would be unsuccessful. There is no way of looking at individuals and telling which are sensitive and which are not sensitive.

We need a large number of people to get at this particular thing, and you proceed with it in this way. When you get your information back you go through your final balancing process trying to determine whether or not the good that you have done outweighs the potential risk. It is the old benefits to risk assessment. Then you make a decision, in a company like ours, whether or not this whole thing is worth while. If it is not worth while you drop it and you never go back to the regulatory agency. If it is good you file with the regulatory agencies. You do not use those agencies to make your decisions for you. You do not even file unless you think you have got a worth while substance. If you do not think it is worth while you do not file at all.

Does that essentially answer your question, Mr. Mackasey?

Mr. MACKASEY: Yes. Thank you very much.

Mr. MCDONALD: Mr. Bertrand has a submission which I am not suggesting you read, but which you might like to see to have some indication of what a submission to the Food and Drug Directorate is like.

Mr. J. A. BERTRAND: I think Mr. Mackasey could read this before lunch.

Mr. MACKASEY: Is that submission in respect of one product?

Mr. BERTRAND: Yes. They are not all that large, of course.

Mr. MACKASEY: Is this an actual submission?

Mr. BERTRAND: This is an example of a submission made perhaps a year and a half ago to the Food and Drug Directorate here in Canada in respect of an antihypertensive drug which we are now marketing.

Dr. GALLAGHER: Some of these submissions are much larger than that.

Mr. MACKASEY: I may be out of order in asking this question, Mr. Chairman, but our last witness, Dr. Sourkes is reported at page 288 of the Minutes of Proceedings and Evidence of Friday, July 3, 1964 as having said in answer to a question:

> It is remarkable that the regulations in the United States and in England, for example, are different.

He was talking about comparative safety regulations in Canada and the United States. This is an amazing situation in view of the fact that you work almost internationally between Canada and the United States in respect of research and you explained this situation existed because of facilities, yet you are working under two sets of safety regulations. Perhaps I could pin somebody down to say which set of regulations are preferable to Canadians rather than to the company.

Dr. GALLAGHER: From a practical standpoint I think that statement, applied to every product issued to the market, by and large does not take into consideration the fact that the standards are quite international. We have the international pharmacopoeia; we have the British pharmacopoeia and we have the United States pharmacopoeia. These are all edited and published with close collaboration between the editors of those compendia. Certainly if any toxic substance is recognized the scientists of every country in the world will take advantage of this sort of information and avoid the inclusion of those things in drug products. I think from a practical standpoint there is uniformity of standards among countries.

Mr. MACKASEY: Perhaps the answer to my next question is obvious but I must ask the question anyway. Is there any difference in quality of products which, as far as we are concerned, appear to be the same, or is there any lessening of the safety factor of a product being sold under one type of regulations as compared to that sold under another type of regulations? I am referring to a product being sold in Canada and in the United States under different regulations.

Dr. LITCHFIELD: Let me answer that question. I am sure Dr. Piersma will support me in my answer. The reason I can answer so firmly is because it has been a firm and absolute policy statement, as far as Lederle products are concerned, that there is one world wide standard of quality irrespective of whether there is or is not a regulatory body in a country. This policy has been developed all the way from the chairman of the board of Cyanamid down through the Lederle company.

Mr. MACKASEY: Thank you.

Dr. GALLAGHER: Perhaps I may comment on your question regarding the previous testimony, Mr. Mackasey. The situation in England is very different from that in Canada and the United States. Canada and the United States are very close in respect of the manner in which drugs are regulated. In England they really have no regulations whatever, but they now have what is known as the Dunlop committee to which drug manufacturers submit essentially this same kind of information for evaluation. There is no regulatory structure. There is an important point which one should always keep in mind, and that is that you cannot legislate safety.

Mr. MACKASEY: You made reference to that fact at page 23 of your brief, I believe, and I intended to ask you to elaborate in that regard.

Dr. RYNARD: I should like to ask a supplementary question in respect of England having no regulatory body. We have a regulatory body in Canada and there is a regulatory body in the United States, and it is my understanding that the United States is now going to release parnate, or you have made a recommendation that it be released, is that right?

Dr. LITCHFIELD: Are you referring to parnate?

Dr. RYNARD: Yes.

Dr. LITCHFIELD: That is marketed by a different company so I do not know that I can speak about this with complete accuracy. I understand it is back on the U.S. market again under revised labelling.

Dr. RYNARD: It is back on the market again in the United States, is that right?

Dr. LITCHFIELD: It is back on the market in the United States.

Dr. RYNARD: That is right, but I do not think it is back on the market in Canada.

Dr. LITCHFIELD: I can only give you my personal opinion, that this drug should never have been removed from the market in the first place.

Dr. RYNARD: Do you suggest it should not have been removed from the market?

Dr. LITCHFIELD: I think they should merely have revised the labelling, which is all they have done.

Dr. RYNARD: I should like to make perfectly clear the fact that the officials in England did leave the drug on the market and were right in their stand.

Dr. LITCHFIELD: It is difficult to say whether someone is right or wrong in this respect.

Dr. RYNARD: It is easy to say something with hind sight, but it has been proven that we were wrong in our stand on this continent and the officials in England left the drug on the market and were right in their attitude. Perhaps we were a little bit overcautious, but this drug has proven to be very useful and I am quite pleased it is being placed back on the market.

The CHAIRMAN: Are there any other questions relating to testing generally?

Mr. MACKASEY: I should like to ask another question. I think I saw on a bulletin board at the Cyanamid laboratories a statement to the effect that Cyanamid carries out 34 tests over and above the minimum number. Inidentally I think this also applies to Ayerst and Frosst of Canada. I wanted to put that statement on the record because I think it is important that people know that drug companies do make tests over and above the minimum required. This fact supports your suggestion that we cannot legislate safety. Your company has gone beyond the minimum standards and I think it is important to know that there are firms in existence which just live up to the minimum requirements and as a result, I imagine, produce their products a little bit cheaper.

Dr. GALLAGHER: Your statement makes a point that frankly is a favourite of mine and in my mind is one of the principal distinctions between a company which sells only generically and a company like ours. This point has to do with what I call on-going surveillance. We have a policy in our organization which involves two things. We constantly address ourselves to an attempt to improve a product once it is released. We have this tremendous on-going program of product improvement.

Secondly, a company such as ours scrutinizes in great detail any kind of complaint that comes in, no matter how trivial, and acts on the complaint. What I mean by acting on it is that we may have to fall back on the very research facilities which developed the product in the first place. I can give you one or two casual examples of how we deal with these in our company, and this makes a distinction, I believe, between minimum standards and what the physician is thinking about or talking about when he is using perhaps the vague word "quality".

At one time we released an antibiotic substance. This drug met the minimum standards and exceeded them, but as part of the on-going program, trying to improve this product, we were involved in an investigation in terms of mechanism of absorption of a drug. How could we change this and how could we improve it? In the course of doing this we found an inert excipient. Something that had been regarded as being inert by everybody in the industry for years had the capacity of suppressing the absorption of this substance. The curious thing here,—and this is why in our organization with the on-going surveillance program, was might find this and somebody else would not,—a generic company would be satisfied to let it ride because the drug met minimum standards, but by further removing this substance we were able to increase considerably the quality of the product.

The CHAIRMAN: If there are no other questions in respect of this page perhaps we might now move to a consideration of page 18 and 19 under the

heading "aid to medical education". Are there any questions in respect of this portion of the brief? Perhaps I might just say in passing that I do not see the University of Toronto listed here.

Mr. MITCHELL: The University of Toronto has won many awards.

The CHAIRMAN: If there are no questions in respect of this part of the brief perhaps we can move to a consideration of the major portion of the brief appearing from pages 19 to 27, in respect of quality control.

Mr. MACKASEY: Mr. Chairman, I think the answers which have been given to or questions pretty well cover this subject. I should like to think that quality control is synonymous with safety control. I think Dr. Gallagher and the other gentlemen here have pretty well emphasized the safety aspect.

Dr. GALLAGHER: There is only one word I should like to add and that is, it is not only the things you do in developing quality which are important, but the way in which you go about doing them.

Mr. MACKASEY: One suggestion appearing on page 23 intrigued me, and that is the suggestion that there is not shortcut to quality. Perhaps you could elaborate somewhat in this regard?

Dr. PIERSMA: Yes. In a sense the use of the phrase "quality control",—and I am thinking of control particularly,—is a bit unfortunate because it does suggest that the organization responsible for quality control actually places quality into a product. On Tuesday after the luncheon I intended to point out that a quality control organization audits—perhaps I should not use that word—the work of the production group and constantly stimulates the production group, by one method or another, to remain quality conscious. We do not have a magic wand in quality control that we can wave over a bottle of drugs, or a number of drugs, and raise a low quality product to a high quality product. High quality must be built in by the manufacturing people. We do participate in the formation of specifications for each drug product we manufacture to the extent we originate specifications for a product, and have a strong voice in determining the specification for a product.

In this regard it is rather interesting to recognize what a fluid situation one has relative to the specifications for products. One is constantly trying to tighten and improve specifications for drug products. Quality control people dig their heels in and resist mightly any lowering of specification standards. Of course during a national emergency, such as a war, you have to make concessions but other than for that reason we do not make concessions.

Let us bear in mind also that every industry contributing to the supply of the raw material or packaging supplies is constantly making improvements, and to compete you have got to know what these improvements are and tighten up your specifications accordingly. Sometimes the specification writers get a bit too enthusiastic about tightening up specifications, and as an example I should like to cite the oral polio vaccine.

As you know, when oral polio vaccine is manufactured the organization is expected to put out a live virus product containing one or more of the three types of polio virus. The attenuated polio virus in that product must be guaranteed to be free from any other adventitious agent. There are many viruses we do not recognize today because we do not know them. We do not know how to test for them. We do not know their existence. Possibly in 1974, ten years from now, we will know of certain viral agents that we can test and recognize, but we cannot in 1964 write specifications for a product that will be available in 1974. In 1964 we cannot expect to manufacture and sell a product with 1954 specifications. The specifications group is constantly moving forward, making changes here and making changes there. This is where a great deal of fun comes in and where there is always great challenge.

Dr. GALLAGHER: Perhaps I could add to that statement, and I promise you this will only involve one sentence. I think I make the distinction in respect of quality control in this way. No company should take the position that its quality control department is so good that it rejects 75 per cent of its batches. It should not have to reject one. Quality should have been built in way back here and if you are only catching these at the end there is something wrong. You are really not doing quality manufacturing.

The CHAIRMAN: Are there any other questions in respect of this subject? As Mr. Mackasey has said, we covered quality control pretty well as we moved along.

Perhaps we can now move on to a consideration of that part of the brief beginning at page 27 dealing with the relationship of generic name prescribing to drug quality, but we should remember that we are only dealing here with generics in respect of the safety of drugs and not in respect of the cost and price.

Mr. BERTRAND: Basically we feel that we should point out that it is vital to relate this practice or theory, if you want to call it a theory, to the question of safety rather than as usually happens, specifically to price and cost. We felt that the relationship to safety was the most important of the two relationships.

The CHAIRMAN: Are there any questions in respect of generics?

Mr. MACKASEY: Mr. Chairman, I was out of the room for a minute or two and do not know the section with which we are dealing.

The CHAIRMAN: We are dealing with the section beginning at page 27, the relationship of generic name prescribing to drug quality.

Mr. MACKASEY: My first question is rather blunt. I am wondering whether the Cyanamid company produces the same drug under two different names to be sold at various prices. Is a drug sold under one name at one price in the United States and under another name at a different price in Canada? Would Lederle sell a product at one price and another company such as Ajax sell it under another name at a different price? There is a prevalent feeling among members of the public, right or wrong, that you can go into one drugstore and purchase a Lederle product under a brand name for $4, for example, and go down the street to the next drugstore and purchase the same product under a generic name for $3. I am not referring to cost particularly, but I wonder whether that situation does exist, and whether this has some relationship to the safety factor.

Mr. BERTRAND: No, Mr. Mackasey. Having read the transcripts I know this question was referred to earlier but I do not think the situation was thoroughly understood.

From the point of view of the Lederle product we never, never, market a product under a brand name and then market the same product under the generic name. That just does not happen with Lederle, and as far as I know it does not happen with any other ethical pharmaceutical manufacturing concern. We would consider such a practice to be unethical.

Mr. MACKASEY: This question was asked two weeks ago of the representatives of the Pharmaceutical Association. Perhaps the spokesman at the time did not understand the question but it will appear in the record that he stated this situation was possible but that his particular firm did not do it. I am asking the representatives of every firm who appear before us whether they follow this practice. That is the only means I have of obtaining that information.

In respect of the generic side of the question I might suggest you have some excellent examples of the dangers involved in switching from brand names

to generic names. I feel convinced about this situation because no less an authority than Dr. Morrell took the stand that he would not buy a product under the generic name in preference to the same product under the brand name even though there may be a difference in price. Since the brief will be made part of the record I do not think I should go any further into the subject, but I do think everyone should have the opportunity of reading this portion of your brief.

Mr. McDONALD: Would you care to make some comment Dr. Litchfield?

Dr. LITCHFIELD: I could perhaps comment, although I may tend to confuse the matter. Lederle does sell some products under the generic name and other products under a trademark name. We have no brand name for methotrexate.

Dr. GALLAGHER: One or the other, not both.

Mr. BERTRAND: Your question was whether we sold the same product under the brand name and under the generic name.

Mr. MACKASEY: When we come to the price question, we will get into it a little more exhaustively. I am interested in the safety factor, and I think we have been pretty successful in divorcing the two aspects, but the implication has come up constantly from people representing your industry that if we prescribed generic names more frequently the cost of the drugs would be smaller. I would agree with that, provided it does not automatically mean some relaxation in safety.

Dr. GALLAGHER: I must amplify what Dr. Litchfield said. In those instances where we might have a generic name instead of a brand name, this does not come about by preference. It may come about by virtue of the fact that we may spend 10 years investigating a drug. During this period the generic name has become so well known that countless doctors all over the world use the most commonly known name. However, we guard that product just as jealously and just as zealously as we do anything with a brand name. So that, unless circumstances interfere, we use the brand name by choice, but we do not use both.

The CHAIRMAN: Are there any other questions on this section?

Dr. RYNARD: The point then is that it is possible that in most cases the generic drug is all right. However, the other point is that in most diseases that must be regarded as serious a doctor would not use a generic product solely from the standpoint of its safety.

Mr. BERTRAND: Perhaps I might sum it up by saying that it is the integrity and the reputation of the manufacturer that is important, and not the name.

Dr. LITCHFIELD: I would just like to say one more thing. There is a publication of the U.S. Food and Drug Administration which comes out each month in which they list various products that they have seized and the reason for the seizure. I wonder if the Canadian Food and Drug Directorate does not also have such a listing? The United States publication is very interesting from the standpoint of this generic question.

Dr. WILLOUGHBY: The suggestion which Dr. Litchfield made is an extremely interesting one and very important. Are those publications available and can they be received by communicating with Washington?

Dr. LITCHFIELD: Yes. We can look it up and make it available to you.

Dr. WILLOUGHBY: Can those publications be received on request?

Dr. LITCHFIED: That is right.

Dr. WILLOUGHBY: I would think it would be worth while to get this United States publication by the Food and Drug Administration.

Mr. BERTRAND: I think you will find that Dr. Morrell is familiar with this and you might address your inquiry to him.

The CHAIRMAN: We could ask the clerk of the committee to write directly, as we have done with other literature, to the food and drug administration in Washington.

Dr. WILLOUGHBY: I think it would be an excellent idea.

The CHAIRMAN: Are there any other questions?

Mr. MACKASEY: I have one other question. It arises out of previous testimony. It relates to the contact man. I do feel that too much is left to the contact man when he sells his wares to the doctor or to the dentist. It seems to me, judging from the previous testimony, that too much stress is laid on his ability to transmit the side effects to the busy doctor or dentist in the short time at his disposal. I am wondering whether Cyanamid do have some other means of communication to supplement the contact man's information. I am going to suggest, later on, that the side effects portion of any literature should, if possible, be printed in red or in some other colour than the rest of the submission, in order that the side effects be emphasized to the busy doctor who could then easily be made aware of them. Does Cyanamid use some other method?

Mr. BERTRAND: I would like to answer that question and then I would like to have any additional comments made. This whole problem of medical communication is exceedingly difficult. There are a whole series of ways in which we communicate information to the medical profession and to the pharmacists. None of these are perfect. I do not think there is any system of communication whereby you can say that this could never be improved upon. Obviously if we could improve upon it, we would like to do so, but it is a difficult problem. You have such things as a new product announcement. When a firm such as Lederle,—and there are other ethical manufacturers who do this,—introduce a product, they communicate with the medical profession giving the doctors a full disclosure of the product, what it is, what we know about it, what the side effects are, and what the contraindications are, in what form it is available, the package styles, and so on. That kind of information is sent to the medical profession. Everything that is sent to the medical profession is also sent to the pharmacists and to the hospitals across the country. The Canadian Pharmaceutical Association happened to pick this one out as a tribute to the work we did in notifying pharmacists of the development.

Mr. MITCHELL: You mean plus automatic shipments?

Mr. BERTRAND: Right. The trade journal advertising comes into play in the sense that the information is communicated through the trade journal advertisements. There are direct mail brochures and there is a whole program to handle inquiries received from the medical profession and from the pharmacists concerning products. There is a medical advisory service about which perhaps Dr. Gallagher will speak later. There is of course the detail man. It is his job to communicate with the medical profession. The point I want to make is that this communication through the detail man is not by any means the only source of information to the medical profession. The detail man talks to a physician about a product. He will also generally bring to the physician something in writing which obviously cannot completely outline everything we know, but he also brings a file card which summarizes what the product is, what is the recommended usage, in what form it is available, what are the side effects and the contraindications. The detail man is only part of the total communication program.

Mr. MACKASEY: What portion of the physical area of the detail man's literature would be devoted to the side effects?

Mr. BERTRAND: That would depend on the importance of the side effects. Sometimes they are given a great deal of prominence.

Dr. GALLAGHER: I would say first of all that I think the most valid and basic document which contains everything, good and bad, about the drug is what we call the package circular which is worked out by a series of discussions and negotiations between the manufacturer, the food and drug directorate in Canada, and the food and drug administration in Washington. This comes about as a result of the appraisal of all the information. This then is your official document. The detail man is told that he cannot deviate from what is contained in that document. Our detail men are instructed along the following lines. This has all the approved indications for the drug, the contradictions for the drug, and things of that sort, as well as historical information that is pertinent and relevant. This is the basic document. Even those of us who choose to discuss the drug cannot deviate from the approved language without getting the approval of the food and drug directorate. Our detail men and our salesmen are schooled in this. You cannot in any way deviate or make a claim that is not approved. The detail men's essential function, in calling on the doctor the first time, is to bring the product to his attention and to leave with him certain things that he can read and peruse for himself, so as to acquaint him with the product and acquaint him with the means of making up his own mind, because in the final analysis it is the doctor who selects the agent that he is going to use, based on his own experience. You cannot fool a doctor. Anyone in this business who attempts to is foolish and will not be in business long. To reinforce this situation we have at Lederle in one of my departments a staff of 20 people among whom are four full time physicians. Our salesmen are instructed that when they are talking to the doctor they are not there to practise medicine. If the doctor has additional questions he is put in contact with our medical advisory department. He can do this seven days a week, 24 hours a day. As an illustration of what goes on, last year this department with four physicians answered 10,000 direct medical inquiries for detailed information. There were an additional 12,000 people, doctors, nurses and paramedical people who wrote to us for general information without asking specifically whether or not a drug was useful in this or that situation. In order to supplement what is done, this medical advisory department writes in great detail such brochures as I have here. This is entitled, "Cancer control through chemotherapy". This gives you all the historical background of certain agents. Let me also say that our physicians are there to give good medical service. People call us wanting to know about a drug which is not ours and we put them in touch with other companies or other sources of information. If they ask us about medical problems not related to our own products, they are given this information as a free professional exchange. There is nothing of a sales nature about this. We found this to be the most effective and efficient way of attempting to bring our products to the attention of the doctors and to reinforce the information. In addition to this procedure, when anything develops as a result of this survey I talked about, we spontaneously address a personal communication to every doctor in whatever area this is pertinent, either in the United States, or in Canada, bringing to their immediate attention these new and recent developments that had occurred. We do not even wait for it to be disseminated throughout the organization. Does that answer your question?

Mr. MACKASEY: I can see one or two flaws. You say the detail men are instructed not to go beyond the information. What happens to the detail man who conveniently eliminates some of this information and does not mention the side effects of a drug? For instance, Dr. Slogan who is a very respected member of this committee gave us a very pertinent example of a product he bought on the recommendation of a detail man and then found out, months later, that it had an adverse effect on teeth. He was not informed about the side effects of the drug he acquired. Nevertheless, he was using the drug for

a month or two before he became aware of the side effects. He put the blame on the detail man's presentation of the product.

Mr. BERTRAND: I think this comes down to this question, that the ethical companies, ourselves included, do all they can to train the detail men to the best possible degree. You can train some of them better than you can others. Some are veterans and have been in the business 20 years, but some are bound to be new. The other day at Pearl River you heard about the sales program that is in force there. We do not depend on them for the training of our people in Canada although we use parts of it. We have our own sales training program, both departmental and corporate, for knowledge of products. I do not think you could expect us, or any other company, to guarantee every call on a physician that is made. Sometimes these calls last only one or two minutes. We cannot guarantee that every detail man will remember every piece of information that we had given him about a product. I would say that in time a doctor who was being called on by a detail man who continuously withheld information about the adverse effects of any particular product would soon lose confidence in the company which this detail man represents. It is therefore to our advantage to do the best possible job in training these detail men.

Dr. RYNARD: Mr. Chairman, I think that all this boils down to the conscience of a doctor. I do not think that any doctor is going to be fooled by a detail man coming in and telling him the qualities of a drug. If he is prescribing this for the first time, he is going to check himself or else he will not use the product. If he wants any further information on it, all he has to do is check his own pharmacopoeia. What it comes down to is the conscience of the doctor. I found the detail men to be excellent on the whole. They will try to tell you all the things they can. Sometimes it is the doctor's fault if he does not get the information He can be in a hurry and will want to push the detail man out of his office, or he might be busy with something else. No doctor is going to use a product without checking the literature and without checking, if necessary, his pharmacopoeia.

Mrs. JONES: I feel that detail men are most helpful on the whole, and it has been both my experience and that of my colleagues that one of the first questions we tend to ask is what are the side effects and what can be injurious about a new product. There is then a great deal of discussion which goes on after the visit of the detail man among the medical people themselves.

Dr. WILLOUGHBY: I can certainly confirm that. I think that all of us in the medical profession must recognize that these detail men are trying to do a good job. They usually represent ethical companies trying to do a good job. The shortcomings are not so much on the part of the detail man as on the part of the medical man in not making a further study of the literature that is available when using a new drug.

Mr. MACKASEY: I like to hear medical men criticizing medical men—it is sweet music to my ears.

The CHAIRMAN: In Dr. Slogan's absence I should tell the gentlemen who are with us today that Dr. Slogan is a dentist and he was somewhat disturbed that on the literature on tetracycline it was not mentioned to him that this would stain teeth. This was his complaint.

Dr. RYNARD: Tea will do the same.

The CHAIRMAN: Are there any other questions, gentlemen? If there are no other questions, I would like to bring to the attention of the committee that next week we will be having our two last witnesses. On Tuesday we will have the Proprietary Association of Canada appearing before us. I understand they are the Patent and Proprietary Medicine Association of Canada and they are here to speak particularly to the question of safety of drugs.

On Thursday, although I have not been able to get in touch with him, we hope to have Mr. Curran. Mr. Curran, as you remember, is the legal adviser to the Department of National Health and Welfare. That will conclude the meetings which have been arranged.

It was the feeling of the steering committee that the committee should recess until the call of the chair some time early in the fall. We will then conclude with our witnesses on safety of drugs so that we can have a report ready before the house prorogues, probably at the end of the year.

Dr. RYNARD: I would like to compliment those gentlemen who have come here and who have represented both sides of the story so well and so ably.

The CHAIRMAN: I was just going to conclude the meeting by thanking Cyanamid of Canada Limited for making these people available to us. I would especially like to thank Drs. Litchfield, Gallagher and Piersma for coming up from Pearl River, and I thank Mr. Stovel and his associates for arranging all this, and I also thank them for their hospitality and their effort in letting us see their facilities in our trip to Pearl River.

The meeting is adjourned until Tuesday at 9:30 a.m.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 12

TUESDAY, JULY 14, 1964

WITNESS:

Mr. F. C. Buckley, of Toronto, member of the Board of Directors of The Proprietary Association of Canada.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21102—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

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Jorgenson
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Marcoux
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, July 14, 1964.
(17)

The Special Committee on Food and Drugs met this day at 9:35 a.m. The Chairman, Mr. Harry C. Harley, presided.

Members present: Mrs. Jones and Messrs. Armstrong, Côté (*Longueuil*), Francis, Harley, Mitchell, Prud'homme, Roxburgh, Slogan, Whelan and Willoughby—11.

In attendance: Mr. F. C. Buckley, of Toronto, member of the Board of Directors of The Proprietary Association of Canada.

The Chairman introduced Mr. Buckley to the Committee.

The witness read the brief of the Association into the record.

He was questioned thereon, more particularly on stability tests, advertising and marketing techniques, and labelling.

Mr. Prud'homme expressed the wish that this Committee will enjoy the facilities for recording the evidence adduced in French when it reconvenes after the summer recess.

The Chairman outlined the program for the future meetings on *safety of drugs*; it was agreed to invite a manufacturer of generic drugs to present a brief or appear before the Committee to give an opinion on this aspect of the Committee's study.

The Chairman thanked Mr. Buckley for his appearance and at 10:30 a.m. the Committee adjourned to 9:30 a.m. Thursday, July 16, to hear Mr. Curran, Q.C., Legal Adviser of the Department of National Health and Welfare.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

TUESDAY, July 14, 1964.

The CHAIRMAN: Gentlemen, there is a quorum.

The witness this morning is a representative of The Proprietary Association of Canada. His name is Mr. Buckley, and he is a member of the board of directors of that association.

I think the best way to proceed would be to have Mr. Buckley read the brief, which is a fairly short one, unless the members of the committee wish otherwise.

Some hon. MEMBERS: Agreed.

The CHAIRMAN: Would you proceed with the reading of your brief, Mr. Buckley.

Mr. F. C. BUCKLEY (*Member of the Board of Directors, The Proprietary Association of Canada*):

The Proprietary Association of Canada appreciates having the opportunity of presenting to the Special Committee on Food and Drugs of The House of Commons the views of The Proprietary Association on the safety of medicines that are registered under the Proprietary or Patent Medicine Act.

The Proprietary Association of Canada is one of the oldest established trade associations in Canada having been founded in 1896, and its membership comprises those companies who produce an estimated 90 per cent of the volume of products registered under the Proprietary or Patent Medicine Act. While it does not represent all manufacturers of such products, the association is generally recognized as the spokesman for the industry. The association and its committees have been pleased to work with the Food and Drug Directorate of the Department of National Health and Welfare in connection with such matters as sampling regulations, manufacturing regulations, new drug regulations, advertising matters, and so on. In addition to this, individuals belonging to member companies have represented the association on various government committees such as, the Drug Advisory committee, and the committee on Drug Standards of the Canadian Government Specifications Board.

Before examining further and safety of proprietary medicines we should like to comment briefly on the principle of self-medication because it is generally accepted that the layman uses proprietary medicines for self-medication of simple ailments. Self-medication is a privilege which man has enjoyed from time immemorial and a man with a headache or a woman with a constipated child cannot afford, in either time or money, to consult a doctor for these everyday illnesses. They know from experience the nature of their problem and from experience how to treat it. Nor has the medical practitioner the time available to diagnose and prescribe for these hundreds of cases of minor illness occurring daily. It is only because a wide variety of mild, not serious, conditions are treated by the patients themselves, on the basis of experience and common sense, and by using established, safe, efficacious proprietary medicines that this portion of the total public health care requirements are met. If the principle of self-medication were not accepted, it would throw an added burden on the medical profession which would mean that much time would be used in taking care of inconsequential illnesses, and thus diminish the time

that would be available for intensive treatment of those conditions which need the highest levels of skill and attention for the best therapeutic results.

If the principle of self-medication is accepted, it follows that the safety of proprietary medicines is of fundamental importance to the users of same. Thus the requirements for safety in proprietary medicines is considerably greater than, and in some respects maybe different from, those which are acceptable for many pharmaceutical specialties. This is because a proprietary medicine is used by lay people who are not as able as physicians to judge all the conditions surrounding the condition requiring treatment. The disorders which may properly be treated by home medications are, in general, the more minor conditions which can be readily recognized by the person himself and can be treated or ameliorated by proprietary medicines, the safety of which is high. Only a very low order of risk, from the safety standpoint, can be tolerated in proprietaries because the conditions treated are sufficiently mild that no substantial risk, of a side effect from the medication, is therapeutically justifiable.

In Canada we are fortunate in having, with respect to most proprietary medicines, some built in safety factors that result from a law which is unique to Canada—The Proprietary or Patent Medicine Act. This act is the result of the findings of a Canadian parliamentary committee established in 1907. These findings were submitted as a bill to Parliament in the session of 1907-1908, and the bill received royal assent in 1908. Since that time, and with amendments thereto, The Proprietary or Patent Medicine Act has provided safeguards to the Canadian public with respect to medicines registered according to its provisions. An examination of the act will point out the safety features but, naturally, absolute assurance of safety can never be provided. The act provides that an manufacturer, desiring to register a medicine under the Proprietary or Patent Medicine Act, must submit with his application a quantitative formula and a statement of claims that he proposes to make on labels and packaging materials. These are examined by the staff of the food and drug directorate for approval before a certificate of registration is granted. The act also provides for the appointment of an advisory board whose composition includes the chief dominion analyst, the deans of two colleges of pharmacy, and two medical men one of whom is a pharmacologist. The advisory board has various powers including the right to establish dosage level of schedule drugs contained in medicines registered under the act, the limitation of alcohol content and the possible addition of new drugs to the schedule. In addition to this, the medicines registered under the Proprietary or Patent Medicine Act, must also meet the requirements of the Food and Drugs Act. Because of the requirement for presubmission under the Proprietary or Patent Medicine Act, medicines registered under this act are subject to greater scrutiny before marketing by the food and drug directorate than are pharmaceutical specialties, with the exception of those classified as new drugs, that are marketed under the Food and Drugs Act. Thus, the requirement of the Proprietary or Patent Medicine Act of registration of a product prior to marketing is a unique feature of this act and provides an inherent built-in safety factor that is not present in the Food and Drugs Act.

In spite of this certain queries have been raised about the safety of medicines registered under the Proprietary or Patent Medicine Act in three general areas:—

a. The secret formula section of the act.
b. The advertising claims made for proprietary medicines.
c. The channels of distribution of proprietary medicines to the consumer.

We would like to comment on each of these.

We feel that the concern over the secret formula provision of the act is exaggerated. It is a requirement of the Act that the scheduled drugs be disclosed and this is a safety factor in itself. However, the complete formula is not secret in the true sense because it is declared at the time of registration and retained by the department in Ottawa. No manufacturer may change the formulation of a medicine registered under the Proprietary or Patent Medicine Act without once again applying for a certificate of registration, so that the current file of registrations is a permanent record of all medicines registered under the act that are available to the Canadian public. However, the association agrees that the elimination of the alleged secrecy requirement is desirable and went on record to this effect two years ago with the food and drug directorate. It should be realized that many of these same medicines are sold in other countries with the full formula disclosed. The Proprietary Association also recognizes the need for these formulae to be known to the various poison control centres throughout the country and, at the request of the food and drug directorate a few years ago, circularized its members and obtained approval for the distribution of these formulae to the poison control centres.

In the matter of advertising of proprietary medicines, we have three areas of concern expressed:—

1. The fact that advertising promotes the unnecessary use of dangerous drugs.
2. That advertising induces the uninitiated consumer to take more and more medication on a self-medication basis.
3. That advertising is causing the consumer to create a disrespect for medicines and the dangers of medication.

We are concerned here only with advertising for proprietary medicines that appears in the recognized media.

In the first instance, drugs which have been deemed to be dangerous are not permitted to be included in the formulations that are accepted for registration under the Proprietary or Patent Medicine Act. It would appear then, from the point of view of safety of proprietary medicines, that the first concern is not relevant.

In the second instance, with the exception of that fractional percentage of the population who would continue to take medication anyway, advertising would only be detrimental to the well-being of the consumer if, by encouraging self-medication it hindered or delayed unnecessarily the action of the consumer in consulting his physician. The assumption was made earlier that the consumer has a sufficient degree of intelligence to distinguish between serious conditions and those which he recognizes can be relieved by self-medication. If this is true no amount of advertising will induce the consumer to use medicines which he feels he does not need, nor will he indulge in self-medication when conditions indicate that he requires professional attention.

In the last instance, we can find no information that supports this contention. We are not aware of the fact that the Canadian consumer is gradually creating a disrespect, or even unawareness, of the potential dangers of medication. You can readily understand that, if this opinion were prevalent, members of this association would be greatly concerned and well informed of such a trend.

It appears to us that much of the concern over advertising stems from erroneous conclusions on the degree of controls of advertising claims. The food and drugs act specifically prohibits false and misleading statements with respect to all drugs including those medicines registered under the Proprietary or Patent Medicine Act. This applies not only to label claims but to all types

of advertising. The food and drug directorate maintains a close scrutiny of all advertising and, in addition, acts for the Board of Broadcast Governors in reviewing broadcast continuity for all drugs, which must be approved prior to use in accordance with the terms of the Broadcasting Act. There is a further control with respect to broadcast continuity in that the Canadian Broadcasting Corporation also has its own commercial acceptance department to approve continuities used on the corporation's stations. A further control, as far as the advertising of proprietary medicines is concerned, lies with the right to halt the sale of any proprietary medicine if advertising claims are false, misleading or exaggerated according to section 8, paragraph 1, subsection F of the Proprietary or Patent Medicine Act. We, therefore, submit that existing controls over advertising of proprietary medicines are consistent with our previously stated safety requirements for proprietary medicines and that this advertising is not a danger factor in the public health of Canada.

The third area of concern with the safety of medicines registered under the Proprietary or Patent Medicine Act seems to be related to the channels of distribution by which these medicines reach the consumer. The distribution of drugs is a provincial matter and provincial legislation provides that all drugs, with certain exceptions, shall be sold to the consuming public by licensed pharmacists. One exemption granted by all provincial pharmacy acts is for medicines registered under the Proprietary or Patent Medicine Act. These exemptions are a recognition of the historical fact that this class of medicine was sold by general merchants before the advent of the drug store and before the writing of the provincial pharmacy acts. Pharmacy acts came into being after the middle of the last century and the exemption written into them was a recognition of an existing fact. The legislatures intended simply to recognize this fact and to exclude certain fully compounded and prepackaged articles from restrictions of the newly born pharmacy acts.

If these exemptions were valid almost 100 years ago, they are even more so today. The quality of medicines registered under the Proprietary or Patent Medicine Act today is infinitely superior to those of 100 years ago. As pointed out above, the requirements for registration contain certain built-in safety factors. In addition to this the manufacturer of proprietary medicines is required to meet the regulations of the Food and Drugs Act with respect to manufacturing in the same way as is the manufacturer of pharmaceutical specialties. The result of this is that a properly packaged medicine registered under the Proprietary or Patent Medicine Act rarely requires the pharmacist to inject his professional knowledge into the sale of such a medicine. By law the manufacturer is required to provide adequate directions for use and dosage schedules on the label and in the package. He also puts on any warning statements which prudence would suggest and which regularly authorities think desirable, to warn the prospective user of this medicine against any special limitations surrounding its administration. It would be a rare occasion indeed when the pharmacist could or would add in any way to the information provided in this comprehensive labelling and package insert information. Thus it would appear that the distribution of medicines registered under the Proprietary or Patent Medicine Act, in stores other than licensed pharmacies, does not constitute a health hazard to the Canadian public. The safety of the product is built in to it by the scrutiny of its formulation prior to marketing, and by the information carried on the package and this stays with the product in the household medicine cabinet until such time as it is used.

The Proprietary Association of Canada, therefore, contends that medicines registered under the Proprietary or Patent Medicine Act presently being used by the Canadian public, as part of the total national health care picture, are safe and play a beneficial role in the total health care of the Nation.

The CHAIRMAN: Thank you very much, Mr. Buckley. Are there any questions? Well, Dr. Willoughby.

Mr. WILLOUGHBY: Mr. Chairman, I congratulate the witness on what I consider to be a most excellent brief. Any points I shall bring up are those which I think we should consider more thoroughly in regard to some of these things. I recognize the fact that this started originally away back in the early days when pharmacists were not available. At the same time I feel there are some things in regard to the indiscriminate sale of some of these products which might be better with a little closer supervision. I know it can not be completely effective, but I think we should watch some points more closely.

One of the points of criticism I have is in regard to some of these medications which we are told have no efficacy. They are pretty much placebos, and they have no potency. On the other hand, there are some of them which if used in large amounts are toxic. It is true that the label says not to take them in those amounts, but they are toxic. I am thinking of such things as certain nasal drops which are irritating and which definitely can cause aggravated conditions. I just question whether or not there is anything further that can be done in that way, and I bring the point up for discussion as to whether or not we can do anything more.

I would like to ask if there is any way to check the stability of these substances before they are marketed? Is the formula actually adhered to?

Mr. BUCKLEY: Well, Dr. Willoughby, I think you will find that most of the major companies involved in the business have quality control operations within their plants and that stability tests are a normal part of their operations Stability tests are established because the industry is concerned too that the consumer receive in his or her hands a product which it is conceded is properly labelled. I am not aware of how frequently the department with its inspectors pull packages from the shelves and make test checks on them. But from our own experience we keep back samples of all products. We are required to do so under the law for three years, but we do it for five years. We keep back samples of production on which to perform stability tests. We keep back samples of production to determine whether they meet our stability requirements, and are built according to our process and formulation. So that there is a check conducted in this way. Most manufacturers I think go through this same type of process in various forms in one way or another.

I can give you one example of our own. The department picked up a bottle of our product where the quantity was not right. It turned out after investigation and going back through it that the cap people supplied us with the wrong type of liner for the cap, with the result that we had evaporation of the product in the container. We eventually pulled back that part of the pack. This type of thing happens from time to time because the departmental inspectors are continually picking up products at various places throughout the country, having them analysed, and making requests of the manufacturers, if there is anything out of line.

Mr. WILLOUGHBY: You say there is control over the advertising of these things. It appears to me after watching some of the advertising done, especially on television, that it is pretty exaggerated at times.

Mr. BUCKLEY: Are you speaking of Canadian television or of American television? Let us get the differential.

Mr. WILLOUGHBY: I am speaking of Canadian television.

Mr. BUCKLEY: Well, if you think it is exaggerated, we would have to disagree with you because, for instance, when you prepare a television commercial, before you can use it, you prepare a story board. Then the commission which deals with the food and drug part examines it, and anything that is

exaggerated is taken out. Then it has to be submitted through the channels of the B.B.G. The food and drug department gets it first, because they act on their behalf. They scrutinize the material, and if there are any faults or misleading things in it, either from the point of view of visual production or from the point of view of the spoken word, they are deleted.

After that is completed and it comes back to the B.B.G., they examine it in the area of good taste, when any offensive words are eliminated. Then it goes back when it is referred to the commercial acceptance department of the C.B.C. which evamines it from the point of view of both vocal as well as visual approval; and when it goes through the process of the food and drug department, they have their medical advisory staff examine it. They have their normal people who would scrutinize the continuity, and this applies to radio as well as to television.

There is pre-examination of printed advertising. It is a requirement, not of the Broadcasting Act, but under the Food and Drugs Act, that such advertising must not contain any false or misleading statements. If the advertiser makes any such statement, they are stricken out. The advertiser may then argue the point if he pleases.

Mr. WILLOUGHBY: Is it a pharmaceutical committee or a commercial committee which supervises the advertising?

Mr. BUCKLEY: It is actually done by a division in the food and drug directorate, under Mr. Soucy, who is chief of the proprietary or patent medicine division, and who is a graduate pharmacist. He is the supervisor of that group. They have many inspectors who review food and drug continuity for the department, to ensure that it meets the requirements of the Broadcasting Act.

Mr. SLOGAN: How much of this advertising originates in the United States, as far as your production is concerned?

Mr. BUCKLEY: Creatively for a great many of the companies that are part of large national corporations much of their creative thinking is done in the United States. However a lot of it is done here. For a company like ourselves—we are a Canadian company—a lot of our material originates here in Canada.

Mr. SLOGAN: Would there not be a lot of material on Canadian television which originates in the United States?

Mr. BUCKLEY: No. If you go back to the battle of the A. & B., when the analgesic manufacturers in the United States attempted to move that material into Canada, it was never permitted for use here. It had to be redone, because according to our requirements we are not permitted to use comparative statements. For example, we cannot say something is better or is faster here in Canada. These words may be permissible in the United States because they do not have the requirement there for pre-submission of copy that we have in Canada. Under the United States law you can go ahead and prepare your advertising, whereupon it is up to the F.T.C. or the F.F.D.A. to take you to court to prove that you are wrong. Under United States law one goes ahead and prepares one's advertising, and then it is up to F.D.F. or F.D.A. to take you to court to prove that you are wrong and to cut out your advertising. Here in Canada we have to submit it for approval before we can use it.

Mr. SLOGAN: Are patent medicines different from soaps?

Mr. BUCKLEY: There are no requirements for soaps. This is a requirement under the Broadcasting Act which is specifically directed toward drugs advertised in the broadcast medium.

Mr. SLOGAN: Do you feel that advertising does induce people to use more proprietary drugs than they should be using perhaps?

Mr. BUCKLEY: We do not think so. We have done some consumer research in the area to assess validity—and any research is only as valid as the sample—and we have found that one cannot, for instance, induce a consumer to buy

a bottle of cough medicine of my particular brand if a consumer has a bottle of some other brand already on the shelf or has part of a bottle of my brand still on the shelf. With the exception perhaps of general analgesics, in which case people usually think at some time they will use them and therefore there may be an extra bottle of A.S.A. or if I may usurp Mr. Tilston's trade mark—aspirin tablets—generally speaking people will not buy an excessive amount of medication. Most average consumers are reasonably intelligent and they know the requirements of their household, and purchase accordingly as necessary.

Mrs. JONES: I would like to ask the witness why the full formula is not disclosed.

Mr. BUCKLEY: Because it is a requirement of the Proprietary or Patent Medicine Act that it be not disclosed. I have my own interpretation of the act and I have argued with the legal people in the justice department that even under the terms of this act the formula could be disclosed. This is my own opinion, not that of the association. It is a question of interpretation of section 2 (1) (d) of the act. As I say, this is my own interpretation.

There is certainly no advantage to be gained by us as manufacturers in not disclosing the formula because—and let us be honest—any reasonably intelligent person can take any proprietary or any other type of medicine off the shelf and have it analysed and find out the contents. All the people in the world can take Eno's fruit salts and tell you what is in them; but not one person can tell you how to put those ingredients together and people have been trying to figure that out for years and years.

Mrs. JONES: I have not seen the package for T.R.C.'s recently but I know that in the past certain patients have divulged that they were taking this drug and they thought there was some sort of magic with it. Some time ago the advertisement was combined with a radio program that was of a religious nature, so their faith in this medicine was further supported. I grant that some of these people can obtain some help from this type of drug, but it can also amass an organic condition that can be very serious. I think there is some danger here.

Mr. BUCKLEY: I think that is true, and I think that is why you will find the claims that are permitted for this type of medicine, both by way of labelling and advertising, are extremely limited. In regard to the other factor, one is getting into the area of psychosomatic medicine, and this is something entirely different.

Mrs. JONES: It is not just a question of the intelligence of the person who buys the product; it is a question of knowledge, and they have not this knowledge. I think this is a difficult field.

Mr. BUCKLEY: Some of the directors of the association and Dr. Morrell and his colleagues at food and drug had a meeting two years ago dealing with the question of this secrecy clause in the act. We all agree that there was no need for it and we all agreed that it should be changed. A change is quite acceptable to us in the industry; we realize the validity in removing it. I think an attempt is being made to work out an adequate and good definition to fit into this act, and this may cause something of a problem.

Mr. MITCHELL: The block, then, with regard to changing this provision is in the department? It is not with the patent medicine people?

Mr. BUCKLEY: I think everyone wants to do it. I am speaking now strictly off the top of my hat: I guess any time any department wants to change an act or to change some legislation they have to go to justice, and justice probably has to point out to them that if they change the particular thing they

are asking to change, then something else must be changed, or that they cannot change it. I think there is some problem in the legal terminology in this particular act. However, that is only my own opinion.

Mr. MITCHELL: As you say, your association agreed two years ago that this be done, so recommendations from this committee could force the hand of persons who would make this workable.

Mr. BUCKLEY: I would assume so.

Mr. MITCHELL: In other words, it is a government agency and not the patent medicine people who are preventing this being done?

Mr. BUCKLEY: I do not like the use of the word "preventing", Mr. Mitchell. I think we are all trying to do it. We have stated our position; we feel it should be done. They have stated their position; they feel it should be done. I think what they are trying to do is to figure out the means for the change. That is the problem. I do not think anyone disagrees that the elimination of this clause is desirable; I think that is totally agreed upon.

Mr. MITCHELL: It is a question I have asked of other witnesses and it has appeared that they have been in favour of such a course of action. I do not mean that the quantities of ingredients should be given, but the names of the ingredients are necessary.

I would like to ask a question for the benefit of the committee. Are you people included in the new regulations which prevent sampling as far as the physicians are concerned?

Mr. BUCKLEY: Yes, we prevent sampling period, very definitely.

Mr. CÔTÉ (*Longueuil*): Do you not think that too much emphasis in advertising is placed upon the taste of the drugs for children? If it is advertised as having a good taste and as being something that children like, then they seem to think it is candy or something and tend to use too much of it.

Mr. BUCKLEY: I could get into long arguments with you, sir. This is a marketing technique. Whether people feel it is acceptable or not acceptable is another question. One of the things we face here, because of the requirement for pre-submission of a great deal of our material, is that more and more, in spite of what you might think about advertising, the department is restricting the things we can say about our product. Therefore, it is a question of attempting to use those factors which one feels one can successfully use in the proper marketing of one's product. If taste is a factor in making a product acceptable to children, then I think people who are marketing the product feel this is a logical and legitimate method for advertising. Whether it is bad for the country or not I do not know.

Mr. CÔTÉ (*Longueuil*): Most of this advertising hits the children more than the adults.

Mr. BUCKLEY: I would like to make a comment on that. One thing we have definitely established—and this is something one of our competitors found out at great cost—is that one cannot advertise and successfully sell our products to children. One cannot influence children because it is the mother who makes the final decision in the household with regard to this type of product. One can influence children in buying Shredded Wheat or in buying shoes and one can influence children in certain other areas; but when it comes to the use of medicines in the household one cannot influence children. A direct appeal to children is not successful in this field; the appeal has to be made to the mothers.

Mr. CÔTÉ (*Longueuil*): I do not mean that children will buy those drugs; I do not think they will ask their mothers to buy them. What I mean is that if they see it advertised as tasting like candy, for example, they will take it when they see it.

I do not like to quote personal examples but I think it is pertinent to do so in this case. I never gave my children Castoria but one of my children went to my sister's house and saw a bottle that she had seen advertised as tasting very good—so she tasted it. They used to say on the advertisement that baby cries for Castoria, but she cried after Castoria! She drank almost the whole bottle.

Mrs. JONES: I wonder if the question of further care and labelling of, say, aspirin should be considered.

Mr. BUCKLEY: Dr. Jones, as you know, with respect to all salicylates there is a general statement in the act which makes it obligatory to inform people to keep this product out of the reach of the children. That is a requirement for the label. Then there are other cautionary things which appear. You can determine how many cautionary statements you want.

Mrs. JONES: Could it not be made more specific? A great many children come into emergency departments of hospitals having taken bottles of aspirin.

Mr. BUCKLEY: That is right, but do you not think that most of the children you get with salicylate poisoning are below the age at which they can read?

Mrs. JONES: But their parents can read.

Mr. BUCKLEY: This is parental responsibility.

Mrs. JONES: I am not talking about the children.

Mr. BUCKLEY: There is a regulation which is part of the act with regard to all salicylate products that cautionary statements should appear.

Mrs. JONES: It is perhaps of interest to note here too that the toddlers and young children who swallow aspirin in quantity are inclined to repeat the act, regardless of the uncomfortable experience through which they have gone.

Mr. FRANCIS: In your opinion, is the market for patent and proprietary drugs an expanding market? I have the impression that a generation ago there was a much larger market for this type of thing.

Mr. BUCKLEY: I would say you are quite correct; this again is a personal opinion. I would say that of the total drug sales the percentage of those now evolving from proprietary or patent medicines is less than it was 20 years ago. There is a tremendous development in pharmaceutical specialties and we have a tremendous number of what we call o.t.c., or over the counter, items which are continuing to grow. Of all the drug sales the proportion of the proprietary drugs on the market is less. I will not say that the total volume of business is less because it is not; one has a dynamic expanding market, so naturally one is going to get an increase. However I would say that the market for the proprietary goods would be shown on a graph as increasing but the market for the total drug industry would be shown as increasing steeply.

Mr. FRANCIS: There is a steadily expanding market for the proprietary and patent medicines?

Mr. BUCKLEY: For the good ones, yes, but there are those which come and go like all the rest.

Mr. MITCHELL: On page 4 you say that:

> We feel that the concern over the secret formula provision of the act is exaggerated. It is a requirement of the act that the scheduled drugs be disclosed, and this is a safety factor in itself.

It is my impression that no scheduled drugs can be contained in the preparation.

Mr. BUCKLEY: There is a schedule to the Proprietary or Patent Medicine Act.

Mr. MITCHELL: I am talking about schedule G drugs.

Mr. BUCKLEY: But there is a schedule in this act, the Proprietary or Patent Medicine Act, and any drugs in this must be shown on the label. Schedule G drugs are not permitted for inclusion. A certificate of registration will not be granted if a product contains schedule G drugs.

Mr. MITCHELL: May I ask a further question for the benefit of the committee?

Would you enlarge upon schedule G drugs and tell us roughly what are the main families?

Mr. BUCKLEY: There are a lot of phenobarbitones and there are the amphetamines—all those stimulant and depressive drugs are contained in schedule G under the Food and Drugs Act and are not permitted for registration under the Proprietary or Patent Medicine Act. If one submits a formula containing these drugs it is refused.

Mr. PRUD'HOMME: Mr. Buckley, is there any provision for bilingualism in respect of your claims? I know there is a provision in respect of advertising, which serves a very good purpose.

Mr. BUCKLEY: Do you mean under the act?

Mr. PRUD'HOMME: Yes.

Mr. BUCKLEY: Under the act itself, no.

Mr. PRUD'HOMME: What about the feelings of your association?

Mr. BUCKLEY: Well, most of the members of the association put all the information that is required under the act on their labels bilingually. I am referring to dosage, directions, claims and so on.

Mr. PRUD'HOMME: Well, that is very important.

Mr. BUCKLEY: Any scheduled items which have to be included there appear on the bilingual labelling. Some people use split labelling and some use the front and back. The mechanics of it depend on the nature of the information required. But, the basic information, dosage, directions, and so on, are all put on bilingually and, of course, the product identification.

The CHAIRMAN: Are there any other questions which anyone wishes to put to Mr. Buckley?

Mr. PRUD'HOMME: Mr. Chairman, if there are no other questions on this specific subject I have a point to make at this time.

If my understanding is correct, next Thursday is going to be the last meeting of this special committee for this part of the session.

The CHAIRMAN: Yes, that was the feeling of the steering committee.

Since you have brought the subject up, there are some other witnesses we wish to call.

We thought we should call a manufacturer of generic drugs. I think the committee would be very interested in doing this. I am going to ask representatives of one of the larger generic manufacturers to appear before the committee. However, this meeting will be at the call of the Chair.

Mr. PRUD'HOMME: But that probably might be after the recess.

The CHAIRMAN: That is quite possible.

Mr. PRUD'HOMME: My point is that in order to facilitate more the participation of those who are French speaking members of this committee—I have waited a little while to bring this up because I did not want to push it too quickly and make a noise all through parliament—I would ask, if possible, that when we meet again we will be furnished with the same facilities which other committees which are sitting at the moment are using.

The CHAIRMAN: Are you referring to an interpreter?

Mr. PRUD'HOMME: I have abstained most of the time from asking questions, and I know others have too, because it is sometimes very difficult for French-speaking members to participate. I am sure everyone will understand our problem.

I understood this morning that we are going back to the two party system in this country. This might be a reason things are going so smoothly.

I am not trying to make things difficult for you Mr. Chairman, but having known you for some time now, I hope you will do all in your power to obtain for this committee what the other committees have. Since a complete reorganization is undertaken, I would like the authorities to consider our side of the problem with regard to this special committee on food and drug. I am sure the members would appreciate it.

The CHAIRMAN: Mr. Prud'homme, at the beginning of our work in this committee we did have an interpreter. He was in attendance and never used, so we thought there was no point in having one. This is the reason an interpreter has not been present during our latter meetings.

As I said, we did have an interpreter in attendance at our earlier meetings but as there were no French-speaking members who actually required an interpreter we said that it would not be necessary to have one any longer.

Mr. PRUD'HOMME: That is all right in respect of the interpreter but I am referring to the taking down of the evidence adduced in French. The interpreter will not take the place of a reporter. The worst problem is not in respect of an interpreter. So far as I am concerned and so far as many other members are concerned, our problem concerns the recording of evidence given in French.

The interpreter might do his job well and we might not need him, but it is very important that we do have a record of what is said in French.

The CHAIRMAN: I think perhaps by the time the committee reconvenes or, at least, by the next session, there will be a recording apparatus to take notes. This facility is being tried out in another committee at the present time.

Mr. PRUD'HOMME: I know reorganization is taking place and that is the reason I personally have not pushed it. If it is going to be done, let it be done. I am not trying to be difficult about it.

The CHAIRMAN: Is there any other point anyone would like to discuss while we have general topics up for discussion? Is there any particular witness that anyone thinks we should call for a future meeting that we have neglected calling to date?

We still have a few clinicians to hear from. We hope one of the manufacturers of generic drugs will appear before the committee.

Mr. ROXBURGH: How many witnesses were you anticipating?

The CHAIRMAN: Probably not any more than between three and six.

Mr. ROXBURGH: Are there that many?

The CHAIRMAN: They probably will not appear before the summer recess.

Mr. ROXBURGH: I was just thinking that if there was just one we might as well go ahead and finish off this part of our hearings. But, if there are more than one, as you have indicated, that is a different situation.

Mr. FRANCIS: I think it might be a good idea if we had one or two French speaking witnesses.

Mr. PRUD'HOMME: If Mr. Mackasey was here this morning he might have asked to have Dr. Genest appear before us.

The CHAIRMAN: We all saw Dr. Genest down in Montreal and I am not sure if Mr. Mackasey would want him back. Dr. Genest gave us an excellent talk down there.

Mr. MITCHELL: You were speaking of inviting a manufacturer of generic drugs. I think you meant so-called generic drugs because I am sure you and I understand that all chemicals have a generic formula.

The CHAIRMAN: I should have said those people who put on the market products with names on a generic basis.

Mr. MITCHELL: Would that be advisable inasmuch as their big problem with the market is in respect of price?

The CHAIRMAN: Yes.

Mr. MITCHELL: And, the differential cost. Would it be advisable to nail these people down to quality control and safety and not allow them to go into the cost of drugs. Actually, that would be the next basis of our inquiry, and there is no doubt about the fact that the person that you would ask to appear would be expected to divulge the difference in the cost of a similar product under a trade name. I do not know whether it would be advisable to invite him back afterward.

The CHAIRMAN: I was going on the basis that we probably would invite them back afterward. We have done this with everyone else. During our hearings we have heard a great deal about generic drugs and the reasons why some people do not like to prescribe them. This has nothing to do with the cost but, rather, quality or quality control, and I think it would be fair to the manufacturers of generic drugs and those who market them on that basis that they should be given an opportunity to come back before the committee to give their side of the story in respect of only safety.

Mr. MITCHELL: Has anyone volunteered?

The CHAIRMAN: No. But, I am going to write one of the bigger companies and request that a representative appear before the committee. If they do not appear, that will be fine. But, in my opinion, they should have an opportunity to put their side of the story before the committee in respect of the question of safety only. Would the committee agree with that?

Some hon. MEMBERS: Agreed.

The CHAIRMAN: If there are no other questions, I would like to thank Mr. Buckley for coming to see us on behalf of the Proprietary Association of Canada. I think he has an airplane to catch in a short while.

We will adjourn until this Thursday morning when we will hear Mr. Curran, the legal adviser to the Department of National Health and Welfare.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 13

THURSDAY, JULY 16, 1964

WITNESS:

Mr. R. E. Curran, Q.C., Legal Adviser of the Department of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21184—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Gauthier	Orlikow
Asselin (*Richmond-Wolfe*)	Horner (*Jasper-Edson*)	Prud'homme
Basford	Howe (*Hamilton South*)	Roxburgh
Casselman (Mrs.)	Jones (Mrs.)	Rynard
Côté (*Longueuil*)	Jorgenson	Slogan
Enns	Macaluso	Whelan
Francis	Mackasey	Willoughby—24
	Marcoux	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

CORRIGENDUM (English copy only)

Issue No. 12—Tuesday, July 14, 1964

In the Minutes of Proceedings and Evidence—

Page 343, lines 30 and 31 should read:

(Mrs. Jones) ".....", but it can also *mask* an organic condition that can be very serious....."

MINUTES OF PROCEEDINGS

THURSDAY, July 16, 1964.
(18)

The Special Committee on Food and Drugs met at 9.40 a.m. this day, the Chairman, Mr. Harry C. Harley, presiding.

Members present: Mrs. Jones and Messrs. Enns, Harley, Mackasey, Marcoux, Mitchell, Roxburgh, Rynard, Slogan, Whelan, Willoughby (11).

In attendance: Mr. R. E. Curran, Q.C., Legal Adviser of the Department of National Health and Welfare.

The Chairman announced that he had, for the perusal of the members, the literature published by the Food and Drug Administration in Washington, which was mentioned at a previous meeting, namely:

1. Report of Import Detentions—June 19, 1964;
2. List of Seizures, Prosecutions, and Injunctions—Report No. 102—June 29, 1964;
3. FDA Report on Enforcement and Compliance—June 1964.

These publications could be supplied to the members on request.

The Chairman brought to the attention of the Committee an article of The Canadian Medical Association Journal of February 22, 1964 and entitled "The Case for Prescribing by Proper (Non-Proprietary) Name", by Dr. Russell A. Palmer, M.D. of Vancouver. After the members have read it, the Committee can decide whether Dr. Palmer should be asked to appear at a future meeting.

Mr. Curran was introduced. He read a prepared statement on the legal situation as it relates to the Food and Drugs Act in its present form, with regard to licensing of a drug manufacturer as a condition of his carrying on his business. He was questioned thereon.

On behalf of the Committee, the Chairman thanked Mr. Curran for his expression of opinion and the information supplied to the members.

Dr. Rynard congratulated him for giving a definite and frank statement.

At 11.15 a.m. the Committee adjourned to the call of the Chair.

Gabrielle Savard,
Clerk of the Committee.

21184—1½

EVIDENCE

THURSDAY, July 16, 1964.

The CHAIRMAN: Gentlemen, we now have a quorum present. I would just like to say, before we start today's meeting, that I have here some literature that was discussed at the previous meeting. Anyone who is interested, might have a look at it. These are the following publications: The report of import detentions, a list of seizures, prosecutions and injunctions, and the food and drug administration report on enforcement and compliance. Anyone who is interested in having a look at this, is free to do so. These copies belong to the Department of National Health and Welfare, and they would like them back. If any member thinks we should have copies for the committee, we can get them directly from Washington.

I wish to bring to the attention of the committee that there was an article in the Canadian Medical Association Journal "The Case for Prescribing by Proper (Non-Proprietary) Name" by Dr. Russell Palmer. He has sent it to me. I have not yet had a chance to read it. When I have a chance, I will read it, and then if any other member of the committee wishes to read it, he can do so. We can then decide whether we should ask Dr. Palmer to come down as a witness before the committee.

We have with us this morning Mr. Curran, legal adviser of the Department of National Health and Welfare. I think Mr. Curran has a prepared statement he would like to give us, and then the meeting will be open for questioning.

Mr. R. E. CURRAN (*Legal Adviser, Department of National Health and Welfare*): Mr. Chairman, members of the special committee, I thought it might be more convenient if I read from a prepared statement so as to get my views on the record as I prepared them, and after that I would be very glad to answer any questions which relate to the subject matter.

During the proceedings before this committee, the question of licensing drug manufacturers in Canada, and perhaps outside of Canada, has come up on a number of occasions and for a variety of purposes. I have been asked to appear today and to attempt to explain the legal position, both provincial and federal, in so far as it relates to licensing of a drug manufacturer as a condition of his carrying on his business.

I will direct my remarks to the legal situation as it relates to the Food and Drugs Act in its present form. Matters of provincial licensing will, I think, become self-apparent.

I should like also to make it clear that in commenting on licensing for various purposes, I am not dealing with the merits of each purpose or proposal that may be involved. It is perhaps unnecessary to point out that however desirable licensing may be and regardless of how many persons or companies would support it, a legal basis for it must exist.

There is one other observation that I would like to make before discussing the subject and this relates to the possibility of different opinions in the field of constitutional law as to what is or is not within the competence of the federal or a provincial government. The most eminent lawyers in the field may differ in their interpretation of complicated constitutional matters and it may well be that other lawyers will not agree with the views that I hold. I will, however, deal with the legal stiuation as I interpret it.

The Food and Drugs Act is designed as criminal law. Criminal law under the British North America Act is within the exclusive jurisdiction of the federal parliament. The jurisprudence that has been decided relating to the Food and Drugs Act has held it to be criminal law.

The purpose of the Food and Drugs Act as criminal law is broadly to protect the public health to the extent possible from hazards to health and to prevent fraud in the manufacture and distribution of foods, drugs, cosmetics and therapeutic devices.

I need not elaborate on the provisions which the Act and the regulations contain that are directed to the accomplishment of this purpose.

The licensing of a particular trade is, generally speaking, within the exclusive jurisdiction of the provinces.

To find a basis for federal licensing of the drug industry, under the Food and Drugs Act, it would be necessary, in my view, that licensing was so directly related to the protection of the public health in the prevention other than to make it an integral part of the purpose of the regulation. In other words, it would be necessary to show that there are such hazards associated with the manufacture and distribution of drugs, regardless of their kind or purpose, that cannot be controlled other than by the licensing of the manufacturer or, to illustrate further, that there are such evils inherent in the distribution of drugs as require their effective control through licensing.

I have used these two examples, which relate to health rather than fraud, deliberately, because they can be illustrated by licensing action that has already been taken under the authority of the Food and Drugs Act. I refer here to Section 12 of the act which provides authority in respect of biologicals which the Chairman specifically referred to during the proceedings on June 23, last. Even under the former act, regulations had provided for the licensing of biologicals to insure that the manufacturer had adequate facilities and competent staff to manufacture that class of drugs. The present act continues this in Section 12, with supporting regulations. This control was considered to be necessarily related to the purpose of the act because of the special hazards involved in the manufacture and use of this particular class of drug. The licence here is, therefore, directly related to the purpose of the legislation.

The other illustration relates to an evil which needed to be controlled. This is illustrated by that portion of the legislation which deals with controlled drugs, Part III of the Food and Drugs Act. There was evidence of an illicit traffic in goofballs, which was the popular name for what are now controlled drugs. Utilizing our experience in the field of narcotic control which posed comparable problems, it became apparent that a form of licensing was necessary to control or prevent the development of an illicit traffic in respect of these drugs. Incidentally, the Narcotic Control Act on which our controlled drug legislation was substantially based, contains provisions for licensing. These have been held to be valid as part of a criminal law enactment and necessary to control the evil for which the Act is designed.

I think this broadly sets out the basis on which authority to licence would need to be found under the Food and Drugs Act to be valid.

In the proceedings, various expressions or terms have been used in relation to licensing, such as registration and certification. It would seem from a reading of the proceedings that some of these have been for different purposes.

It will, I think, become apparent that there may be two forms or kinds of licensing that are being discussed. The first relates to licensing of particular substances or activities for the protection of the public health. This has already been provided for as I have explained. The second type of licensing which has been discussed, however, relates to authority for a general requirement that no

person shall engage in the business of a drug manufacturer or drug distributor, regardless of the nature or purpose of the drugs involved, unless he has first secured from the Food and Drug directorate a licence to permit him to do so. It is essentially in relation to this class of licence that legal difficulties arise. I should like to illustrate these difficulties in relation to the apparent differences of purpose as they have come out during the course of these proceedings.

The number of drug companies in Canada in relation to the difficulty of making frequent and satisfactory inspections has been discussed.[1]

I think Dr. Morrell referred to the fact that last year there were 160 odd inspections from, I think, a total of 485 drug companies. The point that was raised was the physical difficulty of making periodic inspections of such a large number of manufacturing firms. In this connection the question of licensing has been raised as being a solution. I express no opinion as to whether this would be so, but I think it becomes obvious that any form of licensing must surely involve careful inspection and, therefore, unless licences were to be granted on request, the physical difficulties inherent in our present system would not be overcome by a licensing requirement.

Another use for licensing seems to suggest some form of certification or guarantee to a physician or a pharmacist of the quality and safety of the drug which he is using or dispensing. I am not sure that it is made clear as to how this would result because licensing per se, even coupled with inspection, would do no more than show that a manufacturer at that time had a proper plant and perhaps a competent staff with which to carry on business. The quality of his product at any time would need to be tested regardless of licensing, to establish that it was in conformity with the requirements of the law. Licensing would not, therefore, guarantee the safety or quality of the product.

Another suggested use of licensing was that it would provide useful information to the food and drug administration as to who was in business and the names of the products that they were making. Some suggestion was also made that this would provide information as to the nature and constitution of the products that were on the market. In my view, it would be difficult to relate this information to the purpose of the act as to support licensing as a condition of carrying on business.

I think, however, a satisfactory result could be achieved by a regulatory requirement for returns to be made by drug manufacturers. The type of regulation that I have in mind would be one requiring a manufacturer to file regularly and from time to time, a return showing such information, including the products he manufactures and sells in Canada, as might reasonably be required for the purpose of administering the act. This requirement would be entirely separate from his right to carry on business and failure to file the return would not imperil his right to engage in business but would subject him to a penalty for failure to comply with a requirement of the law. I think that Section 24 of the act, which provides for regulations, might be construed so as to provide authority for this regulation. If, however, it is not within the present authority, then, of course, consideration would need to be given to the provision of specific authority for this purpose.

The question of licensing has also been raised in connection with the safety or quality of drugs sought to be imported into Canada, as well as raw materials used in drug manufacturing. It is, I think, unnecessary to say that the licensing of foreign dealers or manufacturers outside of Canada would have no enforcement value. The only effective control that can be exercised with respect to foreign goods is that which is established as a condition of the entry of such goods. Here, there are a variety of procedures that could legally be adopted.

I express no opinion, of course, as to the policy aspects of additional or other procedures, beyond saying that parliament could impose such restrictions with respect to imported goods as it deems fit. Relating this, however, to

licensing of Canadian manufacturers under the Food and Drugs Act, it is difficult to see how licencing per se would achieve safety in relation to the importation of drugs or raw materials from abroad.

In other words, it would still be necessary to subject drugs to individual testing. The licensing of a Canadian manufacturer would not of itself guarantee what can only be done by individual inspection and testing.

In case this has not been touched on already, Section 22 of the Customs Act contains provision respecting importation of goods which are controlled or regulated by or under any act of parliament. The food and drug regulations also make provision with respect to the entry of goods which, if sold in Canada, would be in violation of the act. The good housekeeping regulations, moreover, are designed to put a foreign manufacturer in the same position as a Canadian manufacturer as regards the conditions which he must meet to market his drugs in Canada. None of these, of course, relate to licensing but are nevertheless legal controls that are already in force.

To recapitulate, we have under the authority of the Food and Drugs Act engaged in a form of licensing where particular hazards are involved that present special need for this type of control. The kind of licensing which has up to the present time been developed under the Food and Drugs Act is limited to certain substances or activities in the trade. In my view, this is quite different from the licensing of a trade or industry unrelated to such activities or substances.

Presumably our present system could be substantially extended as public health might require. It must, however, always fall considerably short of anything such as a general licensing requirement as a condition to the carrying on of business as a drug manufacturer or distributor. To justify the latter, it would be necessary to show, in my view, that the protection of the public health and the prevention of fraud could not be accomplished unless all manufacturers or distributors of drugs were so licensed. I express no opinion, of course, as to whether this could be shown, but from what I have read of the proceedings, I am not of the opinion that it has been clearly shown. If this is to be considered, I respectfully point out that it would be necessary to have a very clear understanding of the purpose to be gained by licensing in order to relate it to the legal authority on which it must rest.

The suggestion was also made that if there was difficulty in finding a federal basis for licensing, this could perhaps be achieved through some transfer of legislative authority from the provinces to the federal government. From the legal point of view, exclusive authority to legislate, either in the federal government or in the provinces, cannot be delegated or transferred to the other. I do not express any opinion as to policy arrangements as they might be developed for the administration at the federal level of a provincial requirement. I would be glad to elaborate on that.

Mr. Chairman, I hope that my review of the legal position of licensing under the Food and Drugs Act for the various purposes which have been suggested, may be helpful to the committee in considering this aspect of the problem. I should be very glad to answer any questions that I can in relation to the legal aspects that are involved.

The CHAIRMAN: Thank you, Mr. Curran. Does the committee have any questions to ask Mr. Curran.

Mr. MACKASEY: Mr. Chairman, I was late in coming in, so I ask my question quite objectively. Was this brief available to the committee before today?

The CHAIRMAN: No.

Mr. MACKASEY: I must say—without casting any reflections on anybody, because legal aspects are something we cannot pick up just from listening to a speech—that there are an awful lot of points on which I should like some

clarification. If I had the brief a few days ago, I could have prepared them. I cannot presume to say what is in there and what is not in there because I am not a lawyer, and even if I were one—perhaps more so—I would like to look at the thing a little more carefully from the other side of the picture.

The CHAIRMAN: I think I should say that this is not really a so-called brief; it is an opinion which Mr. Curran has been working on. There is no reason why, at a later date in the fall, Mr. Curran could not come back. I am sure he would be agreeable to doing that after everyone has had a chance of going over today's proceedings. Perhaps before the preparation of the committee's report, Dr. Morrell and Mr. Curran could come back and answer questions.

Mr. MACKASEY: Mr. Curran has obviously read our proceedings and noted the number of times we have referred to licensing, not only the committee members but also the witnesses. However, we have never devoted an entire session to licensing—which I think we should do—to get the pros and cons of it. I sense from your remarks, Mr. Curran, that you take a dim view of the idea.

Mr. CURRAN: Perhaps I should not just give a categorical answer to that. I think that if the committee wanted to recommend licensing, it would also have to consider the question of the constitutional aspect. This is something which you cannot guarantee, and on which only the Supreme Court of Canada could give a final answer. Lawyers will always differ. In fact, what I am saying is that constitutional arguments are grist for the lawyer's mill rather than for the committee because you can always find lawyers to express different views on any given point, even though it may seem to be very clear.

You say I take a dim view of the authority to license. I want to make it clear that in expressing my view I am not saying that I think licensing is undesirable. I can see many cases where licensing would be most helpful.

Mr. MACKASEY: You did not bring them out.

Mr. CURRAN: In what way?

Mr. MACKASEY: I felt that all your statements were negative in so far as licensing was concerned. I am not criticizing your opinion. I did not hear anyone even recommend to the committee that licensing should be investigated further.

Mr. CURRAN: I thought that the positive suggestion which I made for a regulation or requirement which would require annual returns would be going in that direction.

Mr. MACKASEY: You qualified this by saying that this would not jeopardize the man's right to do his business, that he could perhaps be fined $500.

Mr. CURRAN: The amount of the fine is a matter for the courts.

Mr. MACKASEY: Why did you qualify it?

Mr. CURRAN: Because then it would be a licence. If you said that a man cannot carry on business until he has done that, whether you call it a return, a registration or anything else, it is still in effect licensing. If you say to a man, "You may not carry on business of a general character until you first hold a licence from the federal department", then you are establishing federal authority or control over his right to carry on business. This is where I think the difficulty arises. If you can relate licensing to a particular need related to the purpose of the legislation, then perhaps a legal basis can be found. However, it is necessary to relate it to the purpose of the legislation, which is to protect the public health.

Mr. MACKASEY: You lost me there in the legal aspect of it. As I have mentioned several times in the committee, I represent the masses who buy the products. I cannot quite reconcile your suggestion that they must make returns—obviously they must make returns on the safety factor—and your

qualification that if they do not make returns, it will jeopardize their right to stay in business. It seems to me that the two statemens are opposed.

Mr. CURRAN: Let me see if I can illustrate it. You may have a situation where a man fails to make a return and is subjected to a penalty. He is fined in respect of that violation. This however does not affect his general right to carry on business. However, if he continues that, then the court might very well impose such penalties as would virtually put him out of business. There are other weapons in the legislation which can be employed. You have the right of inspection if a man fails to make a return and you have reason to know that he is in business. You can take action under the authority of the act by seizure and other means which will virtually accomplish the same purpose. Therefore, the fact that he merely pays a penalty for failing to make a return does not affect the right of the government to examine what he is doing in the interests of public safety.

Mr. MACKASEY: According to your own statement, and the one made by Dr. Morrell, with the present facilities—which are a big improvement I understand over the facilities which were available a couple of years ago— they have only been able to visit a ratio of one of three plants. The fact that the firms are subject to inspection does not hold much water because there are not too many teeth in the regulations regarding inspection. We have not the facilities to inspect them all.

There is one question which I would like to ask you. Many witnesses from the drug companies have advocated licensing. Would you care to elaborate on why they would think it desirable?

Mr. CURRAN: No, frankly I would sooner not express any opinion on what may be the purpose of the drug manufacturers in suggesting a form of licensing. I think I should point out that the brief you had from the drug manufacturers was presented by an association representing 55 out of 485 manufacturers in Canada. I think I brought this out, that no matter how many people might support licensing, you still have to find a legal basis for it because otherwise you are always faced with the risk that a maverick will challenge the licensing authority. The majority of the trade would be happy to conform to a form of licensing but at any given moment one person can challenge that.

Mr. MACKASEY: We are not interested whether you can make the law tighter. We are interested whether the thing is desirable. There is one reason why I am interested in licensing. Before I came here I was alderman of a city where everybody, including the dogcatcher, had to be licensed. You must have some control over the physical aspects of a particular firm going into business. Let us take the candy store at the corner. You would make sure that it has proper toilet facilities and a fire exit; that they have a certain amount of space, sunshine and light. These are at least one of the good aspects of licensing. I cannot see why this should not also apply to the druggist. The inference I have been getting from many witnesses, who may have been painting a blacker picture than necessary, is that at present a person can literally form a drug company in his backyard, his garage or sub-basement, provided he can get his hands on the raw materials which he might get from Europe. When a man applies for licensing, his facilities, and a number of other physical aspects of the place, are subject to some type of inspection, and so are his quality control facilities.

Mr. CURRAN: I tried to point out that if inspection presents physical difficulties in relation to the number of inspectors that the department has and the number of companies that are involved, you would still have the same difficulty if you required licensing.

Mr. MACKASEY: We have to wait until we get around to it. At the present time we have to wait until the government gets around to deciding whether it is desirable or not desirable.

Mr. CURRAN: I think it is true, but I am only trying to point out my interpretation of the law. I do not want to discuss what may be the desirable thing to do.

Mr. MACKASEY: Whom do you think we should discuss it with. Who could give us this kind of advice on it? The legal department will not, so who could do it?

Mr. CURRAN: I have been asked to come and explain the situation on licensing. If the committee wishes to have a meeting devoted to what might be the desirable procedures that could be brought within the form of the law, that is a different matter. I was not asked to discuss that today. At a later date I would be very glad to see what we could do about that.

Mr. RYNARD: A recommendation could come out of this committee. If, in our final report we come to this conclusion, then this could be recommended.

Mr. CURAN: This is exactly the point I am making. I am trying to point out the position as I interpret it from the law, and I am also trying to warn the committee that any recommendation must be related to the real purpose of the law, which is to protect the public health. Within those two extremes the committee can make an appropriate recommendation which would then need to be given careful consideration at the policy level to see how it might be implemented.

Mr. MACKASEY: Could this committee recommend that the law be amended?

Mr. CURRAN: The committee can recommend anything that in its wisdom it wishes to.

Mr. MACKASEY: Then we are not confined to the law that presently exists?

The CHAIRMAN: Mr. Curran came here today to give us a legal opinion from the department on whether licensing could or could not be carried out under his interpretation of the law. What I think Mr. Curran is telling us is that there is no point in our doing any of this if the Supreme Court of Canada is going to throw it out and say, "You have no jurisdiction to license".

Mr. MACKASEY: I disagree with you. This is not the inference I got from Mr. Curran's remarks. After I have seen Mr. Curran's remarks on the record I will be able to analyse them more carefully.

The CHAIRMAN: Perhaps we should put this in the form of a question. From what he said I understood—perhaps incorrectly as you say—that what Mr. Curran is saying is that if, under the present regulations, the federal government licensed all manufacturers, unless you can prove it is for the safety of the people of Canada, then the supreme court could probably reject that and say, "You have no authority to license".

Mr. RYNARD: May I interrupt here? The point that Mr. Mackasey made is simply this, that it would be better to hold up licensing until they are sure. This is the only point involved in this question. All that has to be done is that this be put in our report. We have nothing to do with the supreme court or with any other court.

Mr. CURRAN: This is right.

Mr. WILLOUGHBY: Mr. Chairman, I think that when we get a chance to study this brief a little more carefully we will probably be able to come up with more suggestions. However, it seems to me that the question of licensing does not appear to be practical at the present time because of the number of firms that are involved, as well as the fact that there are provincial-federal complications arising from it, and also the fact that foreign firms have no

power over them. It comes down pretty much to a question of inspection rather than licensing. It might be a problem of increasing the inspection staff so as to improve inspection of all materials processed in Canada and of materials coming into the country. Am I correct in suggesting that this would be the answer rather than licensing?

Mr. CURRAN: That is right because even if you had the physical facilities for initial inspection to authorize a licence, you are still going to have to maintain continuous inspection not only of the plant but of the products which are on the market. This is a manpower problem rather than a legal problem, because if we had the manpower, then we could theoretically at least maintain a constant supervision over all plants in Canada and over the products which come from those plants so as to ensure the desirable quality of safety and potency. It is really a manpower problem, as you point out, so that even licensing will not avoid the need for constant inspection. You can license everybody, but it does not replace the need for inspection. By the same token, a person has a permit to drive a car but this does not avoid the need for constant police action to supervise the operation of that vehicle. The fact that a man needs a licence showing he has passed a test in driving does not guarantee he will not violate conditions under which his permit was issued. Our people are really in the nature of an enforcement agency. They have to maintain constant vigilance to the extent of their manpower facilities. I should not say this on behalf of the department but I think they are doing an excellent job with limited facilities. It becomes a matter of judgment on how far the government will go in extending those facilities. You have much the same problem in Ottawa where you have the present crime outbreak of petty thievery. The mayor is faced with the possibility of increasing the police force. It becomes a matter of judgment on how big you can make your police force so as to prevent an outbreak of crime. It is a matter of judgment on the extent to which the facilities of the food and drug directorate might be expanded to provide the necessary policing.

You then run into a difficult problem, the problem of imported drugs. Evidence has brought out various processes of manufacture where you might buy from a company, say in England, but you do not necessarily know that the drug was made by that company; the raw materials may have been brought from another country. Somebody brought up the illustration that a drug company in Italy, bearing the name of an Italian manufacturer, imported its raw materials from Bulgaria—I think that was the country mentioned. No inspection that we could carry out in Canada would of itself check all the sources of supply. It would be a very difficult thing. Our present law does a great deal. I have mentioned the Customs Act which gives the right to hold or detain at the port of entry goods which are covered by an Act of the parliament of Canada. Drugs are covered by the Food and Drugs Act. There is authority there to detain at the border any drugs which are brought in from outside of Canada.

This brings me back to the point that you made, physical manpower and the quality and quantity of inspection that would be necessary in every case to ensure that the drug conformed in all respects not only with the end result but with the manufacturing conditions which our law requires. Under the "good housekeeping" regulations Dr. Morrell is given authority to satisfy himself that the conditions of manufacture of a foreign drug are such as would have been required had the drug been manufactured in Canada. We are putting the foreign manufacturer on the same footing as the Canadian manufacturer in terms of the conditions that he must have to manufacture a drug. The physical aspect of doing that is of course a different problem. There you have manufacturers in Canada to whom you have ready access, but you do not have the same access to plants in other countries.

The question of sovereignty is also an important one because some countries might regard it as unwarranted interference with their sovereignty if Canada purported to send inspectors abroad, except on a voluntary basis. So you see there is a physical and a practical difficulty here in maintaining that kind of inspection, which I think the public expects to have and which I think they are entitled to have.

Mr. WILLOUGHBY: This is not a legal point but I presume you would agree that the way the public have to be protected in Canada is not a legal problem but a problem of inspection, and that no drug should be allowed to be sold in Canada until it has completely passed the food and drug department's inspection.

Mr. CURRAN: I would have some reservation in saying yes to that quickly because to give full effect to that it would mean that the food and drug directorate would have to make a physical examination of every drug before it could be brought to Canada.

Mr. WILLOUGHBY: They could accept authentic verification of the product.

Mr. CURRAN: I think they do that at the present time. Shipments coming in from unknown sources—that is a drug company of which we do not know much—are inspected. I think the department would naturally be more exacting in examining shipments from a company they knew little or nothing about. On the other hand, when you have a shipment from a well known agency about which we know a great deal there is less hesitation in accepting their products. There would be less hesitation in accepting a shipment from a reputable company that we knew all about than from one about which we know little or nothing. From a practical point of view you could afford to lete a great many products into the country from reputable sources while you would have less reason to do so from unknown sources.

Mr. WILLOUGHBY: That is what I meant when I suggested the food and drug directorate would not necessarily have to physically examine the material as long as they were satisfied, by evidence produced, that it was a safe product.

Mr. MITCHELL: I should like to ask you, Mr. Curran, if you feel that there is already provincial authority for licensing which would not fall into the category of federal intervention or interference. If that is correct, would it not be satisfactory if it were left to the provincial authority? Of course it would not be satisfactory if one province wanted to license and another one did not, but at the same time I think I gathered from your remarks that you do not think licensing under federal jurisdiction is a satisfactory answer.

Mr. CURRAN: Licensing under federal jurisdiction might be satisfactory, it might be desirable, so as to bring about a basis of uniformity. If you had licensing at the provincial level, it might be difficult to achieve the same uniformity.

There is a device, which I touched upon, which would need to be examined. I express no opinion on how practical it would be for provincial licensing to be administered at the federal level. That would result in some uniformity provided the basis of the licensing was uniform under provincial law. In other words, each province could require licensing, if they have not already done so. The difficulty here, of course, is getting uniformity of administration. I am not discounting the possibility of some administrative arrangement being developed which would result in that. This is something which was barely touched on during the proceedings, and I did no more than refer to it, but I have not developed it. This is obviously something that could be brought about. How practical it is, I do not know.

Mr. MITCHELL: What would be the difference between provincial legislation and federal legislation? Why should the federal authorities go the whole hog

and do away with provincial legislation? It seems to me it would be approximately the same thing if they were administering provincial legislation.

Mr. CURRAN: As I say, it may seem to you that there lies a distinction without much difference. However, the basis of the legislation is provincial, and we would only be acting as a sort of an agent of the province in attempting to administer the provincial legislation. To some extent this has been done in other areas. I do not say whether it could or could not be done here. This would take some working out. Certainly, to do this you would be going around your elbow to get to your thumb. We would need to give careful thought to the extent to which a federal license could be constitutionally valid. That is the starting point. We would have to see the extent to which you could have federal control before you got into the other more difficult area of ten different jurisdictions, in trying to reduce that to one of uniformity. I would certainly not quarrel with anyone who suggested the desirability of central control. I am only saying I think it has to be very carefully examined in relation to the problem which you are trying to solve so as to get a satisfactory legal basis for it. I am not saying it cannot be done. I am only pointing out that it is necessary to relate it wholly to the purpose for which the criminal law is in force. If you can relate it to that purpose, then I do not think you have any question on your right to have licensing as an ancillary adjunct to the federal purpose. However, it needs to be carefully examined in relation to that.

One of the things I did try to point out is that in the suggestions that have been made—and I was careful to illustrate all of these because so many of them are for different purposes—you use the word licensing in a very general way. If you analyse the evidence of individual witnesses in the context of their remarks, you will find that licensing may be suggested for a different purpose in each case. Some of them talked about a form of licensing, a certification of quality, potency and safety. Licensing per se will not achieve that. Licensing per se will only give you the satisfaction of knowing that the company had competent staff and competent facilities at a given time, but it will not provide any guarantee that the goods which they are turning out are at all times satisfactory.

Mr. MACKASEY: Can I interrupt you? Would you not say that the chances of a firm, which was judged competent at the beginning, remaining on that level are greater than the chance of a firm you do not get around to until they have been in business for three years and who never did have these housekeeping facilities?

Mr. CURRAN: That is right. I think you do, to some extent, achieve that in licensing.

There is another feature of licensing which was not touched upon, and that is the continuing desire of the manufacturer to maintain the validity of his licence by complying at all times with the requirements of the law. This is an incentive. I do not say it is not already here, but there is an additional incentive to a manufacturer to observe the law at all times if his right to do business were jeopardized by his disregard for the requirements. But then that raises another difficult question. I am digressing a bit here. Suppose you had a manufacturer whose licence was in continuous jeopardy because of the meticulous requirements of the law. You would always have an administrative problem if you found that his labelling was incorrect. Do you cancel his licence? Do you put him out of business because he is violating the law in a minor respect? This is a matter of judgment. This is a question that should be brought up by the manufacturers who say they like licensing, but if they were faced with the possibility that out of 90 products 85 were found to be 100 per cent and five products violated the law in some minor respect, would they feel that it was

proper to cancel their licence and put them out of business? These are questions one would have to worry about.

Mr. MACKASEY: Do you know of any law that does not have flexibility? You have a case of a man judged on Monday and sent to prison for six months and the same case appearing on Tuesday and receiving three years. It seems to me that the law is flexible.

Mr. CURRAN: The administration of law always requires judgment because many violations of law take place every day on which no action is taken. In one case a charge is laid and in another case a charge is not laid and the person is let off free. The same offence may be committed elsewhere with a different result. This is inevitable in any system of this kind.

Mr. WILLOUGHBY: There is one other question which I would like to clear up. You speak about the question of licensing being a provincial matter rather than a federal. Is that because food and drugs come under health rather than manufacture?

Mr. CURRAN: Not exactly. The British North America Act divides legislative responsibility between the federal parliament and the provinces. At the provincial level property and civil rights are provincial. When licensing of a trade or a profession involves the question of civil rights, it is a provincial matter. You, doctor, were not licensed by the federal government; you were licensed by your provincial licensing authority, because that is the licensing of a profession. By the same token, licensing of a trade is, generally speaking, a provincial matter. The same parallel can be drawn of a pharmacist who is not licensed by the federal government but by the province.

Mr. MITCHELL: So far.

Mr. CURRAN: You said it, I did not.

Mr. MITCHELL: There is a new bill now.

Mr. ENNS: During our discussion this morning there has been a continual reference made to the fact that licensing, if it is to be considered, must at all times have the basic aim of safety to the consumer in mind, or there must be an established need for licensing on this basis of safety to health. It would appear perhaps that there has not been a sufficient threat to the health and safety of the consumer under the present regulations. Is this one reason why licensing does not seem to be such a ready answer, or that there does not seem to be such a need for licensing?

Related to this comment is the question of how great is the number of offences that the food and drug directorate has had to deal with in a given period of a year or so? Can you comment on this? How many people are violating standards?

Mr. CURRAN: A great many of the problems that the food and drug directorate deal with will involve matters of labelling. These seldom get to the point where you have to take legal action. As a rule, we have been able to work in harmony with the firms concerned regarding the necessary modification of the labelling so as to bring them in conformity with the Act. If you have a recalcitrant individual who says, "I won't conform", then you have no alternative but to go to the court and let the court decide. Fortunately, we have not had a great many of those cases.

Mr. ENNS: Under what authority can such a manufacturer be taken to court if there is no licensing in control?

Mr. CURRAN: We set out in the Food and Drug Regulations a certain quality of labelling. I will give you an illustration. I am now talking about food. We have a provision which says that the main panel of the main label shall set out three basic features: Who makes it, what it is, and how much do I get. These

are pieces of information which we feel, and the law supports it, that the customer is entitled to have at a glance. Supposing you had an individual who said, "I don't like that law. I am going to have my kind of label. The dickens with what you put in your law". We would try, through persuasion, to get him to modify his label so as to meet the requirements of the law. If he does not, then we would lay a charge against him for violating that particular regulation. We have had a number of those cases. In the course of a year they do not amount to very many numerically. The ones that do occur are important. Occasionally we have cases of individuals who adulterate food. Let me give you an illustration again. You have cases involving the use of preservatives which are not permitted in hamburger, for instance. That is a good illustration. The manufacturer will use sulphur dioxide in order to prolong the healthy appearance of hamburger. We will prosecute him for selling hamburger which has been artificially made to look better than it is through the use of an unwarranted preservative. If a sausage manufacturer, for example, turns out a sausage which is mostly fat, we have a regulation which fixes the maximum constituent of fat in sausage. The same applies to bread crumbs. We permit, I think, four per cent of bread crumbs or filler as a binder in a sausage. If a manufacturer thinks he can make better sausage by putting in eight per cent bread crumbs, this may sound like a very minor violation of the law, but if you multiply it by the amount of sausage he manufactures it comes to a substantial amount. Four per cent is a small part of the total sausage. This becomes not a health matter but it is a fraud because you are paying 60 cents, or whatever it is, per pound, for bread crumbs. This becomes an economic cheat. I had a case some years ago. This was the exact point. The lawyer said he did not think the court was going to take a very serious view of this difference between four per cent of cereal in sausage being increased to seven per cent. I asked what the volume was. He checked and he said it is about 100,000 pounds per week. That amount multiplied by the difference in excess per centage means he is getting an extra profit on the sausage at the expense of the consumer. The magistrate agreed with that.

These are cases on which we take legal action. Fortunately, we do not have to take as much legal action in Canada as they do in the United States. We have developed a philosophy of education here. We prefer to deal directly with the individual on the basis of persuasion, whereas in other countries, such as in the United States, far more actions are taken through the food and drug administration, and they go to the courts much more often. I am not going to express an opinion on which is the best approach, beyond saying that ours has worked very well. We can almost count on the fingers of one hand the number of times we have had to take firms to court for offensive labelling in a given year. There are very few.

Mr. ENNS: May I interrupt at this point? From a consumer's position—relating food to drugs—if it is the kind of sausage that has just been described, the consumer comes to this kind of conclusion also and says he will not buy this brand, he will pick another one. This is the way of fighting back at that kind of manufacturer. However, if he is in need of medication of some sort, the consumer is not in a selective position where he can say, "I will choose this, rather than the other one". He has to take what has been prescribed, and perhaps this is already bottled for him when it is delivered from the pharmacy. There is a more serious danger here as a result of some malpractice or lack of conformity to standards.

Mr. CURRAN: There are two dangers in the point you made. One, of course, is the unscrupulous manufacturer who is deliberately negligent or who deliberately does not bother to supervise his product. The other is the innocent mistake which may occur in the course of a manufacture. The innocent mistake is less likely to occur (*a*) with a good manufacturer and (*b*) with good

regulatory control. Where the law is specific in its requirements—and I think ours is reasonably specific in its requirements—every person is presumed not only to know the law but to abide by it. I think this is perhaps the reason why we have had so few cases of serious and wilful violation. By and large the manufacturers are most meticulous in trying to observe the requirements of the law to turn out a good product. I think it goes without saying that a manufacturer is only in business for repeat sales. No manufacturer can survive on single sales. Therefore his own reputation, not only supported by the law, requires him to observe very great care in what he is turning out to the public. I think these points always have to be kept in mind when we talk about legal controls. There are ample controls in the present law. I do not know of very many weaknesses in the law which would permit a person to legally sell something which was bad or unsound. Our law is pretty careful in this respect.

We then come back to Dr. Rynard's point regarding the quality of inspection to ensure these standards are continuously being met by all manufacturers. As I said earlier, licensing by itself will not guarantee that this will not happen. There would only be one sword over the head of every manufacturer if you brought in licensing, and that is a risk to his licence. However, at the present time the manufacturer risks just as much because he can be taken to court and exposed for selling an unsound product. This is a threat which the law already imposes on everybody, that is the risk of being taken to court and exposed. No manufacturer wants to disagree unnecessarily with the food and drug directorate and be taken into court because some of the mud is always going to stick. This may be one of the reasons why we have had such harmonious relations, because nobdy wants to go to court. It is always a bad mark against a manufacturer to be a defendant in a case involving some kind of a hazard to health, or a fraud.

Mr. ENNS: I have one more question which is perhaps related to what Mr. Mackasey was saying. If someone thinks he has sufficient skill to produce some volume of manufacture in his own back yard, and this is obviously possible because it is a fact that there are manufacturers who are not known to the food and drug directorate, what happens? I am not asking whether it is a fact, but whether it is a possibility.

Mr. CURRAN: There is a theoretical possibility that a person may engage in the manufacture of a drug who does not have any skill or facilities of any kind. The law says you may not do that until you have the facilities and the skills. I would think it is a very theoretical possibility, although I do not have any information which would indicate there is any substantial amount of engagement in the drug trade by thoroughly inexperienced, unscrupulous or other types of people who should not be in the trade. If their business constituted any size, it would not be very long before this became known. I do not think there have been many secret activities of drugs being manufactured and sold without any brand name and without anybody knowing who manufactured them because quantitative distribution is a thing that every manufacturer is looking for, and so the possibility of a person commencing operations and carrying on for an extensive period of time without anyone knowing who he was is, frankly, remote. I do not say it could not hoppen, but it is remote. You have not only our own inspection staff, but you also have the police action of competitors. I think you have heard a great deal about the detail men who go around and look to see what is on the drugstore shelf. Mr. Mitchell would bear this out, I think. A pharmacist could not stock something for very long without the trade knowing about it, because the detail men do make periodic inspections to see what is on the market. This is a very competitive industry. I think the chances are very small for a product making its appearance and gaining any support without

everybody knowing what the product was and all about it. I think it is a very remote possibility.

Mr. SLOGAN: I have a question along the same line. I think it is a fact at the present time that a new manufacturer can have his drug certified without having his premises inspected.

Mr. CURRAN: I am not quite sure what you mean.

Mr. SLOGAN: I mean approved.

Mr. CURRAN: Are you talking about a new drug? Theoretically, this would be possible. However, practically speaking, it is not possible because, in the first place, our new drug regulations require a submission by the manufacturer which must set out a great deal of information which involves the quality of his facility. In other words, the submission which he makes to us must show the facilities that he has for manufacturing a drug and all about it before any notice of compliance is given. Therefore, no form of certification or so called approval would be given to a particular product until the department knew a great deal about not only the product but the conditions under which it is manufactured.

Mr. SLOGAN: My understanding was that a lifetime may elapse before our inspectors would go down and inspect the manufacturing process and the premises.

Mr. CURRAN: All I would say to that is that conceivably there could be, but you must distinguish between new products coming into the market and products already established. Let us deal with the new products for the moment.

Mr. SLOGAN: You mean a different category of product or a new product under a new brand?

Mr. CURRAN: Either one. This could be a new product put out by an established manufacturer, or it could be a new product put out by a new manufacturer. In either case the manufacturer has to file with the department a new drug submission which would show not only what the drug is and what it is intended to do but the facilities he has to manufacture the drug. If it is a brand new company of whom you have never heard, automatically an inspection would be made. If it is a company that is a well entrenched business, we do not need to make an initial inspection as fast as in the case of a new product.

Mr. SLOGAN: Supposing somebody is putting out another brand of aspirin. Would his premises be inspected before this product is approved?

Mr. CURRAN: I would say yes. If you had a manufacturer of a product who had not previously been in business producing a new drug, when his preclinical submission comes in we would automatically wish to know more about his conditions of manufacture, and an inspection would be made. This would be an automatic requirement before any notice of compliance would be given to him.

Mr. MACKASEY: I think you mentioned earlier that the Food and Drugs Act referred to facilities. Is there anything in the act saying that a building must be so many square feet, must have windows, doors, a laboratory, and so on?

Mr. CURRAN: It does not appear in the Act. It appears in the regulations which I have referred to as the "good housekeeping" regulations. We do not specify the number of square feet; we refer to the adequacy of the premises, the cleanliness, the migration of dust, the sterility of certain types of premises, and so forth. These are all quality requirements, and the manufacturer is required to meet these requirements as a condition of his right to turn out a product. I do not think it would be quite feasible to say that no plant should

have less than so many square feet because you have to have regard for the kind of drug manufactured. Some drugs require completely different types of facilities than others.

Mr. MACKASEY: Whether he has or has not these facilities, in the final analysis it depends on when he is being inspected.

Mr. CURRAN: That is right.

Mr. MACKASEY: I keep coming back to the fact that this is one of the requisites of licencing. We would then at least make sure that everybody starts out with the minimum standards that you say are necessary for safety. You mentioned such things as cleanliness, dust, the cleaning of machinery, and so forth. At least with licensing they would have to have these facilities which are outlined in your regulations. Under the present circumstances—to go back to the statistics which Dr. Morrell brought out and you repeated today—it is conceivable that a plant would operate for at least three years before your people came in and pointed out to them that they do not have the facilities which the regulations insist they should have.

Mr. CURRAN: What you are saying is a matter outside my responsibility. It is a judgment that would be exercised by the administration regarding the immediate inspection of a new plant. I think that if Dr. Morrell were here he would say that when we have information of a new manufacturer coming into business for the first time the inspection of his plant would be given priority.

Mr. MACKASEY: Is there anything in the regulations which says within what time an inspection should be made?

Mr. CURRAN: Not in the regulations but I am quite sure that in Dr. Morrel's administration you would find a standing directive that an inspection would be made of any new facility which comes into being for the first time.

Mr. MACKASEY: Is there a time limit in his directive?

Mr. CURRAN: Knowing the thoroughness with which he administers his responsibilities, an immediate inspection would be made of a new plant as soon as the information is received.

Mr. MACKASEY: Earlier in your remarks you mentioned the petty crime wave in Ottawa and the desirability of more police. You summed it up by saying it is a matter of judgment. In your judgment do you think Dr. Morrell is understaffed or overstaffed?

Mr. CURRAN: I am not sure it is a proper question for me to answer.

Mr. MACKASEY: You opened the door by your remarks.

Mr. CURRAN: At the risk of sticking my neck out a bit I would say that Dr. Morrell needs all the support he can get from the committee in terms of adding to his staff within what reasonable number the government would decide. I certainly feel that his problems would be much simplified if he had more staff of a competent character, although Dr. Morrell did point out that a considerable increase in his staff has been authorized. He has pointed out on more than one occasion the difficulty of getting competent people, and he spoke of the training of these people before they really become useful to his administration.

Mr. MACKASEY: I might say at this point that I was very favourably impressed with Dr. Morrell on the few visits he was here, and we are very fortunate in having him. My questions are not designed to embarrass him but to bring out the facts so as to give this committee an opportunity to come up with some recommendations.

Mr. CURRAN: I have no hesitation in echoing what Dr. Morrell has already said because he has gone on record as saying that he needs more staff, and

that even where staff is authorized it is not always an over night solution to get them because there are difficulties in attracting and holding competent people at the salaries which are paid. I express no opinion on salaries. The directorate has to compete with industry. Dr. Morrell did point out that in the case of pharmacists, they may earn as much as $6,500 in a drugstore, and the starting point is something like $5,000. There is a difficulty in attracting good people.

Mr. MITCHELL: Your figures are low, Mr. Curran.

Mr. CURRAN: That was what I read.

Mr. MITCHELL: From my experience your figures are low.

Mr. CURRAN: I thought that figure was low when I read it. There is a physical difficulty in attracting and holding the kind of people that Dr. Morrell would like to have associated with his administration.

Mr. ENNS: Mr. Chairman, would you, through the clerk, get the information, which Dr. Morrell obviously has, regarding whether or not there is something in his administrative instructions concerning a time limit within which a new plant should be inspected. That would help me to make up my opinion before the end of the session.

The CHAIRMAN: I think that the best idea would be for the committee to have Dr. Morrell come back as a witness before we prepare our report.

Mr. MACKASEY: Nevertheless, you could still get the information. Dr. Morrell may not be back for several months.

The CHAIRMAN: I will look after this.

Are there any other questions?

I wonder whether I might ask a question, Mr. Curran? To go back to the point that Mr. Mackasey brought up originally and which I mentioned earlier, you mentioned the following point: Suppose the federal government did decide that they would require the licensing of manufacturers and they brought this legislation in. They would first have to decide whether this was advisable. Who would make the final decision, would it be the Supreme Court of Canada the first time someone challenged the legislation?

Mr. CURRAN: It is a little more complicated than that. If the committee made a recommendation, it would then be a matter of government policy whether it will be adopted and whether the Act should be amended. That would be a matter of government policy. The point would then be submitted to the Department of Justice to draft the appropriate legislation in accordance with the recommendation of the government. It would then become law, and in the event of a challenge, it might be challenged, in the first instance, in a magistrate's court. From the magistrate's court it would find its way up to the higher courts. The only court of final adjudication would be the Supreme Court of Canada. I am not saying the Supreme Court would inevitably decide on these points. It might well be decided and accepted at a lower level. There is no guarantee that every point which is raised has to go as high as the Supreme Court of Canada. Very few cases get that high.

There is an interesting point here. A couple of years ago, you may recall, the Court of Appeal of Ontario held that a portion of the Highway Traffic Act of Ontario was ultra vires because it related to driving to common danger, which is covered by the Criminal Code. That never reached the Supreme Court. The same point arose in Manitoba in the last year. That case went to the Supreme Court, and the Supreme Court came to a different conclusion. I used that to illustrate the difficulty of a lawyer in saying categorically "This is good, this is not good", because I am sure that lawyers and judges of Ontario in deciding that particular point used their best judgment. Almost precisely the same point in another province came up to the Supreme Court of Canada, and

a different view was reached. This illustrates the difficulty that I have in being categorical on whether this can be done or cannot be done. I think it needs to be explored very carefully. I am not saying at this moment that it could not be done, far from it, but what the purpose of licensing is should be very thoroughly understood, and it should then be related to the purpose of the Food and Drugs Act.

Mr. SLOGAN: In what position then would the province be placed? Would they have to be consulted prior to that and would they have to give permission to the enforcement of this act?

Mr. CURRAN: The extent to which the government might consider it desirable to consult the provinces is a policy question. This would be a matter of government policy.

Mr. SLOAN: Would they have to consult the provinces?

Mr. CURRAN: No, the government does not have to consult the provinces on everything it does. There are certain areas where it is politically wise to consult them. They might or they might not decide this was such an area.

Mr. SLOGAN: Does not the area of licensing normally come under the provinces?

Mr. CURRAN: Normally, yes.

Mr. MACKASEY: If licensing was tied in with criminal law, would it not be a federal matter?

Mr. CURRAN: This is the part I am trying to make clear, that the purpose of the act is to prevent injury to the public health, or to prevent fraud. If you can relate the need for licensing to those purposes, then it certainly and necessarily is an ancillary to the criminal purpose. Let me illustrate. You have the Narcotics Control Act where the licensing authority requires that all dealings in narcotic drugs have to be pursuant to the licence. The courts have held that that is not a licensing act, or an act to licence a particular trade, but a criminal law with licensing as a necessary feature of controlling the evil for which the legislation was passed. The legislation is essentially passed to prevent the illicit traffic in narcotic drugs, and licensing has been held to be a necessary part of that control. Our controlled drug situation is very much the same where we have an evil to meet, and licensing of the trade became a necessary adjunct to suppressing the illicit traffic in "goofballs".

Mr. SLOGAN: In other words, this would just be an extension of the Act as it stands regarding narcotics?

Mr. CURRAN: It would be an extension of the Act, and it would be on parallel lines, but it would still need to be related to the purpose for which the Food and Drugs Act has been passed.

Mr. MARCOUX: I would like to make a brief comment. According to what we heard in this committee—or what I heard myself—we are faced with the problem of small companies selling drugs for a lower price than those sold by big companies. The big companies say that they have the facilities to scrutinize the purity and safety of the material, and that the small ones do not have those facilities. They say therefore that licensing would enable the government to know which companies manufacture those drugs. According to what we heard this morning, it is almost impossible for any company to bring out a new drug, or at least a new product on the market, without it being known to the food and drug directorate. You therefore do not see any advantage in licensing a company for the sole purpose of knowing that this company is in existence.

Mr. CURRAN: I am not sure whether you were present when I mentioned this, but I did indicate the possibility of a requirement in the law that manufacturer should make a return to the department. This may be interesting

because here is a recommendation which has been made and is under consideration, on the kind of information which should be given. It is as follows: The name of a product, the chemical names and chemical structure of the active ingredients, the dosage form and quantitative amount of the active ingredients, the class of drug, informational material used, dosage recommended and route of administration, the source of the drug and the name of the manufacturer or distributor. That is the type of information that might be required in this type of return. This would be the same type of information which a licensing requirement would involve.

Mr. MARCOUX: Is this not actually done?

Mr. CURRAN: Not as yet, but as I said this morning, if licensing was to provide information on who was in business and what they were making, I felt that this could be done under the authority of our Food and Drugs Act either in its present form or perhaps through some amendment which would give us the right to require this information to be furnished. If that is the purpose of licensing, then I think it could be done short of actual licensing.

Mr. MITCHELL: Mr. Chairman, when the witnesses from the pharmaceutical manufacturers were here I understood they did not object to licensing. As you mentioned, those were 55 companies which, I think you will also agree, were the leaders in the industry. They were very much in favour of a licensing arrangement. I can see that they would favour it because they feel that they have the necessary standards under that particular licensing and it would protect them from being tarred with the same brush as the manufacturer who might run afoul of the law. If this committee recommends that this licensing might be required, following the suggestion of the better manufacturers, I understand that you feel this licensing would be rather difficult to put into action. I am wondering how we as a committee would handle such a suggestion?

Mr. CURRAN: Do I understand your question, Mr. Mitchell as referring to the companies that were not included in the presentation of the substantial portion of the drug industry which have expressed themselves in favour of some form of licensing as a condition of carrying on business?

Mr. MITCHELL: No. My suggestion is that licensing would protect the members of the manufacturing firms who are members of the Canadian Pharmaceutical Manufacturers Association of whom roughly, 55 were here as against 400, as you mentioned. I know that these people who were asking for this licensing would certainly qualify as opposed to many others who would not.

Mr. CURRAN: I think probably that is right.

Mr. MITCHELL: My question was: If this committee recommends, following the manufacturers' recommendation, that licensing be administered, my impression is that you have drawn a red herring across the trail because it would be very difficult to do. That is what I am driving at.

Mr. CURRAN: I am not sure that I fully grasp the question. Are you suggesting that because 55 companies would have no difficulty in meeting the licensing requirements it is a red herring to say that there might be legal difficulty in making that a general requirement for all concerned?

Mr. MITCHELL: That is what I am driving at. As I understand it, your view is that licensing is either not necessary or it is not possible to properly administer it.

Mr. CURRAN: I would not like to say that I expressed a view that licensing is not desirable. I think perhaps it is desirable. However, I am not sure, from what I have read so far, that licensing as a general requirement would of itself provide a solution to the various problems that have emerged in the course of

this committee's proceedings. I think that you cannot avoid by licensing the continuous inspection which must go on, whether or not licensing is part of it. I do not think you can avoid that by initial licensing. All you would have done is to say that you are satisfied at a given moment that this manufacturer has the proper facilities and perhaps the competent staff to make the goods which he is going to make. However, you still have to maintain a constant supervision of what he makes. Licensing by itself would not guarantee that.

Mr. MACKASEY: I have not heard anyone on the committee say that licensing would eliminate policing. I have never heard that statement made either by a witness or a member of the committee. I would not like to create that impression because when a place is licensed we would automatically take it off the list of firms to be policed.

Mr. CURRAN: Perhaps I have misread some of the evidence that has been brought before the committee, but the expression "licensing" has been used as providing some automatic solution to some of the difficulties which have appeared.

Mr. MACKASEY: I would like to put myself on the record as saying that I realize licensing would have to be in conjunction with continuous policing which Dr. Morrell's department does. What I am saying is that it seems ridiculous in this day and age that a candy store down the street is licensed by the municipality and has to meet certain standards, while people concerned with our safety, the drug manufacturers, do not. Nobody, including yourself, has changed my opinion on that. To a layman this does not make sense.

Mr. RYNARD: I wonder if Mr. Curran would support the following statement, that if we had adequate staff then we could go along with the thesis that we ought to have inspection before licensing?

Mr. CURRAN: Oh, yes. I do not think that licensing without prior inspection would amount to anything.

Mr. RYNARD: I mean repeated inspections. This solves a problem which Mr. Mitchell had. He was asking in effect if this was not the right way to do it, that we have pharmaceutical firms of a high standard and the rest should therefore be inspected to bring them up to the standard. You have yourself stated that you have insufficient staff to do this. It therefore boils down to the point where you do agree with inspection together with licensing if you had adequate staff. Am I right in coming to that conclusion?

Mr. CURRAN: Yes. If a legal basis is established for licensing as a condition for commencing business, then it should be coupled with continued inspections giving a right to continue business, because there would not be any point in issuing a licence and forgetting about the licence holder. There is need for constant vigilance at all times. The degree of vigilance varies with the individual. Certain people would have to be inspected more frequently than others. This would be a matter of Dr. Morrell's judgment on which people needed constant inspection.

Mr. RYNARD: The tendency would be to raise the level right across the board.

Mr. CURRAN: Yes, in accordance with the present requirements for adequate premises, suitability of manufacture, and so forth. Everyone should meet those conditions right now because the law requires it. Licensing would only give you a base on which to commence, but you still have to couple that with constant vigilance to ensure that those conditions are maintained.

The CHAIRMAN: Are there any other questions? If not, we would like to thank Mr. Curran for coming before the committee to present his opinion on these matters and for answering the many questions.

I think that before the committee makes its report, as I mentioned earlier, it might be a good idea to have Dr. Morrell and Mr. Curran back here to answer any further questions that may come to the committee's attention after they have thoroughly studied the things that have been said today.

Mr. RYNARD: I would like to congratulate Mr. Curran on coming out with such a definite statement. He was very frank with us this morning, and most of us appreciate that.

Mr. CURRAN: I hope you all appreciate that I am expressing my own personal view based on some experience, and that I am not speaking for the government. I cannot speak for the government. I tried to be as non-evasive as I could in answering your questions.

Mr. MITCHELL: You started out by saying that these were your views but in many cases legal minds could disagree with you.

Mr. CURRAN: That is right. I mean that there has been some disagreement already expressed by one or two of the witnesses who suggested that perhaps the view of the federal lawyers was too narrow.

Mr. MITCHELL: Not in those words surely.

Mr. CURRAN: No, not in those words, but the implication was that they did not agree with the views that had been expressed.

The CHAIRMAN: The committee is adjourned until the call of the chair.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 14

FRIDAY, NOVEMBER 6, 1964

WITNESS:

Mr. L. L. Winter, President, Empire Laboratories Limited, Toronto.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21186—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Horner (*Jasper-Edson*)	Prud'homme
Asselin (*Richmond-Wolfe*)	Howe (*Hamilton South*)	Roxburgh
Basford	Jones (*Mrs.*)	Rynard
Côté (*Longueuil*)	Jorgenson	Slogan
Enns	Macaluso	Wadds (*Mrs.*)
Francis	Mackasey	Whelan
Gauthier	Marcoux	Willoughby—24
	Orlikow	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

CORRIGENDA (English copy only)

Issue No. 12—Tuesday, July 14, 1964

In the Minutes of Proceedings and Evidence—

Page 342, 3rd line should read:

. . . They scrutinize the material, and if there are any *false* or misleading *also*

1st line of second complete paragraph should read:

There is *no* pre-examination of printed advertising. . . .

Issue No. 13—Thursday, July 16, 1964

Page 352, the first sentence of the fifth paragraph should read:

To find a basis for federal licensing of the drug industry under the Food and Drugs Act, it would be necessary, in my view, that licensing was so directly related to the protection of the public health *and* the prevention *of fraud as* to make it an integral part of the purpose of the *legislation.*

MINUTES OF PROCEEDINGS

FRIDAY, November 6, 1964.
(19)

The Special Committee on Food and Drugs met at 9.35 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Mrs. Jones, and Messrs. Côté (*Longueuil*), Enns, Harley, Howe (*Hamilton South*), Mackasey, Marcoux, Orlikow, Prud'homme, Roxburgh, Rynard, Whelan and Willoughby.—(13)

In attendance: Mr. L. L. Winter, M.A., M.C.I.C., President, Empire Laboratories Limited, of Toronto.

At the opening of the meeting, the Committee attended to administrative matters, as follows:

According to the resolution passed on July 9, 1964, a paper prepared by Dr. Henry D. Piersma, Ph.D., Director, Quality Control, Lederle Laboratories, Pearl River, N.Y. and entitled "INTERESTING ASPECTS OF QUALITY CONTROL IN DRUG MANUFACTURE" is printed as an appendix to the proceedings of today. (*See Appendix "A"*).

On motion of Mrs. Jones, seconded by Mr. Marcoux,

Agreed,—That a Memorandum concerning the Safety of Drugs, from Dr. Ewen Cameron, Director of Allan Memorial Institute, Montreal, be printed as an appendix to this day's proceedings. (*See Appendix "B"*).

On motion of Mr. Côté, seconded by Mr. Enns,

Resolved,—That the Clerk of the Committee secure three copies of No. 4 Report of the Commission on Drug Safety for the use of the members of this Committee.

It was also agreed that a subcommittee comprised of the Chairman, Mr. Enns and Mr. Côté give a review of this report and the basic recommendations contained therein to the steering committee on agenda and procedure.

On motion of Mr. Willoughby, seconded by Mr. Prud'homme,

Resolved,—That this committee request Dr. Wightman to appear before it on Tuesday, November 10, and that reasonable travelling and living expenses as well as a per diem allowance be paid in connection with his appearance before the Committee.

It was agreed to postpone the meeting scheduled for Friday the 13th to Tuesday, November 17th.

The Chairman introduced the witness, Mr. Winter, who made a preliminary statement and was questioned at length.

At 11.15 a.m. the Committee adjourned to 9.30 a.m. Tuesday, November 10.

Gabrielle Savard,
Clerk of the Committee.

21186—1½

EVIDENCE

FRIDAY, November 6, 1964.

The CHAIRMAN: Gentlemen and lady, we have a quorum present and while we do not at the moment have our witness appearing before us this morning I think we should take this opportunity to go ahead with a lot of administrative detail which we can get cleared up perhaps before he comes.

First of all, the committee had previously invited Dr. Ewen Cameron, Director of the Allan Memorial Institute, to appear. He was unable to come because he was moving to the United States, and on July 3 the committee heard Dr. Sourkes from McGill in his place. However, Dr. Cameron has sent a six page memorandum concerning the safety of drugs, and he made certain recommendations in it. There are only a few copies available. I wonder if it is the wish of the committee that this memorandum be printed as an appendix to today's proceedings so that we will have it as evidence.

Mrs. JONES: I would so move.

Mr. MARCOUX: I will second it.

The CHAIRMAN: It is moved by Dr. Jones, seconded by Dr. Marcoux, that a memorandum concerning the safety of drugs from Dr. Ewen Cameron, Director, Allan Memorial Institute, McGill University, be printed as an appendix to this day's proceedings. It is agreed?

Motion agreed to.

Mr. Allmark, Assistant Director of Drugs of the Food and Drug Directorate, informed me that the commission on drug safety, which was founded by the Pharmaceutical Manufacturers' Association in the United States, issued a report a few weeks ago. During the time this commission was in operation, a number of publications were issued.

The clerk of the committee wrote to the Federation of American Societies for Experimental Biology in Washington, but was informed that no complimentary copies are available. The price for a copy of the report is $5. No one has as yet seen the report: it is not available through the Library of Parliament and we have no knowledge as to its contents other than that it deals with drug safety. If we wish to acquire one or two copies for our study, we will have to have a resolution of the committee.

Mr. CÔTÉ (*Longueuil*): I would so move.

The CHAIRMAN: How many copies would you suggest? Should we have three copies?

Mr. CÔTÉ (*Longueuil*): Three copies would be enough.

Mr. ENNS: Would it not be useful to set up a subcommittee or to assign someone to give a review of this report if we are not all going to have it, and probably we would not have time to read it? It would be very helpful to the committee if someone were to bring in a review of the basic recommendations in this book. Would this be an acceptable suggestion to the committee?

The CHAIRMAN: I think it is a very reasonable suggestion. Would someone undertake to make this study?

Mr. ENNS: I think the mover should undertake to do it.

Mr. MACKASEY: I move the Chairman study it.

Mr. HOWE (*Hamilton South*): I will second it.

The CHAIRMAN: Perhaps the committee would agree, if we are to have only three copies, that Mr. Côté, Mr. Enns and myself will each read one copy and then have a meeting of our subcommittee to decide whether this should be gone into further.

It is moved by Mr. Cote and seconded by Mr. Enns that the clerk of the committee secure three copies of this report. All those in agreement?

Agreed.

Gentlemen, when Dr. Wightman, Professor of Medicine of the Banting Institute, University of Toronto, appeared before the committee on June 2, he was representing the Canadian Medical Association. It was then suggested that he be called again at a later date as a separate witness. Dr. Wightman is ready to appear next Tuesday, November 10. I would like to have a resolution to pay for his usual expenses.

Mr. WILLOUGHBY: I will so move.

Mr. PRUD'HOMME: I second it.

The CHAIRMAN: It is moved by Dr. Willoughby and seconded by Mr. Prud'homme that this committee request Dr. Wightman to appear before them on Tuesday and that reasonable travelling and living expenses, as well as a per diem allowance be paid in connection with his appearance before the committee.

Motion agreed to.

There is one other matter that I would like to mention before we move on. Dr. Wightman will be here on Tuesday of next week. On Friday we have Dr. Showalter, who is an employee of the Department of Industry and chairman of the interdepartmental committee on pharmacy. I wondered if it was the feeling of the committee that we should sit next Friday, or should we put that meeting over until the following Tuesday? We are not sure what will happen in the house with Wednesday being a holiday.

Mr. PRUD'HOMME: Let us postpone the Friday meeting.

The CHAIRMAN: I am sure it would not make any difference to Dr. Showalter. It is then agreed that we will postpone the Friday meeting until the following Tuesday.

Will the committee excuse me for two minutes while I introduce myself to Mr. Winter?

I hope the committee will excuse me for being so rude. I had never met Mr. Winter before and I wanted to have a few words with him and to explain to him the procedure of the committee.

We have before us today Mr. L. L. Winter, President of the Empire Laboratories Ltd. in Toronto. By profession he is a biochemist. I think the best thing to do is to let Mr. Winter make whatever statement he wishes to make. He has not prepared a brief. The meeting will then be open for questions.

Mr. L. L. WINTER (*President, Empire Laboratories Ltd., Toronto*): As a preamble to the introduction of the topic of drug safety let me say that our business started out as a diagnostic medical laboratory many years ago. When I graduated from the university I opened a clinical laboratory, that is a dignostics laboratory, where we did blood studies, pregnancy tests, urinalysis, and so forth. Empire Laboratories is an outgrowth of that clinical laboratory. The question of the safety of drugs is of great concern to us because we manufacture and also distribute our own pharmaceuticals.

In line with manufacturing we are most concerned with ensuring that our drugs have the labelled potency and efficacy; in other words, that they do the job. If you go back a few years, perhaps four years, you will remember that there were a lot of news releases and news reports on the cost of drugs, whether certain cheap drugs were efficacious, whether they were quality products. The large pharmaceutical firms had a head start of many years of activity in producing drugs, and we knew that we had to overcome a barrier,

in other words we had to be accepted by the medical profession. If you are going out to purchase a drug with a brand name the price of which was decidedly lower, you would think you were getting an inferior product, an off-brand product. This might be true of certain pharmaceutical manufacturers in the world today, but with us at Empire it has always been a dedicated policy to produce quality. We have standards. There are official standards and there are also our house standards. It would be interesting if you could visit our operation, and indeed our door is open. If you gentlemen would like to see a generic operation operating, you are more than welcome to visit with us.

We have just expanded by adding 42,000 square feet of air conditioned premises. We have been in operation four and a half years. All our equipment is new. There is no magic to producing pharmaceutical products. All the equipment is fairly standardized, so are the testing procedures and the instrumentation. The only variable is the personnel. Of course, if you have an electric typewriter, it will not type a letter accurately unless the operator knows what he or she can do with the machine.

So too when we come down to safety. This point has a human element. We are all prone to mistakes. This is what we remember in our daily routine, the mistakes that we perhaps have not made, or could have made, or have made. I feel that qualifications of personnel have an important bearing on the manufacturing of pharmaceutical products. By equipment I mean facilities and premises which would induce good housekeeping procedures. You cannot make a kid glove out of a sows ear, neither can one manufacture quality pharmaceuticals in a loft.

I have not prepared a brief, but if you care to ask any questions I will answer them as best I can.

The CHAIRMAN: I was just going to tell Mr. Winter that for his benefit, as each member asks a question, I will write down his or her name.

Mrs. JONES: I would like to ask Mr. Winter a question. It has to do with the clinical studies that may be carried out on some of these drugs. Last June the Canadian Psychiatric Association met and was very much interested in the discussion of pigmentation which resulted from large dosages of chlorpromazine, not only pigmentation but liver damage. Subsequently there has been a report in the journal of the Canadian Medical Association in connection with deaths that have resulted from the use of this drug. I believe that our food and drug directorate are conducting studies on the clinical effects of this drug usage. Have you been asked to submit any clinical studies by your company on your brand of chlorpromazine?

Mr. WINTER: No, Dr. Jones, we have not, but if I might say this, chlorpromazine, although I am not an authority on the drug, is an accepted pharmaceutical product used in practice today. Once a drug has shown its clinical efficacy, the two factors remain, the side reactions and the stability of the drug. The drug is foreign to the body; it is not a compound that is naturally present in the body because it is an organic medically active substance. I would say that the human effect of the drug has been studied and these effects have been found to be helpful, and the drug became designated as being official; then if there are additional indications of possible or potential toxicity, then one has to take a calculated risk and either approve it or disapprove its introduction. A further study on the adverse reactions should then be undertaken to find out if there are reasons for withdrawing the drug. I do not think one can tell by its chemical structure if the drug is going to cause liver damage or pigmentation. I think it has to be tried. Perhaps a new drug will come along and take its place with less side effects.

Mrs. JONES: I would like to ask a further question.

Mr. WINTER: May I answer your question directly. It is common practice that if we hear of any adverse reaction on any drugs or products that we

distribute or manufacture, we of course keep close tab and notify the Directorate.

Mrs. JONES: Whom can the food and drug directorate turn to to get information on clinical studies, because these clinical studies have to be carried out?

Mr. WINTER: My thought is that there should be more disclosure by the industry. A doctor or scientist publishes a paper and it is read around the world. You get letters to the editor contradicting certain facets of its presentation. This is studied and then perhaps a conflict develops and additional scientific facts come out. We may find that that man did not do the control work properly or that it was a small set-up, the number of patients used were not adequate for the study. This has a bearing on safety of course. If there were a common denominator published by the industry saying "We have assessed it in Spain, in France, and in Germany, what do the clinicians say there?" then certainly Rhone-Poulenc or the discoverers of chlorpromazine in France would have access to the clinical work on the product. Instead the industry keeps its findings confidential.

Mrs. JONES: What you are saying then is that you as a company are taking no responsibility for the development of the drug in connection with the safety of the drug?

Mr. WINTER: It all hinges on various elements. For instance, a doctor in a hospital would rely on the pathologist of the hospital. If he made a faulty diagnosis the pathologist would be directly involved in the result. We as manufacturers want to do the proper thing, but if the powers that be establish the status of the drug, one has to produce it if the doctors want it.

Mrs. JONES: I am concerned with the clinical testing and the dissemination of information to doctors on side effects because, as you well know, doctors do not have time to write to individual companies in regard to the possible side effects and new aspects of new drugs or new aspects of drugs that have been in use for some time. It seems to me that some responsibility should be taken for the development and the clinical testing and dissemination of information to the medical profession.

Mr. WINTER: Unfortunately some of the pharmaceutical houses are in it purely for financial gain. I cite this because it has been shown that some of these clinical tests had been rigged, and in the United States today legal action is pending by the government over some statements made by certain doctors during clinical studies. In other words, they were paid a reward for work done that was not done. They did something that was wrong. This unfortunately might happen, could happen and did happen. It is just like running your home. We have certain house standards and certain rules.

Mrs. JONES: I have just a couple of questions more. I would like to ask Mr. Winter if he has a medical director in the company? Let us consider the following example: Suppose a druggist in filling a prescription supplied what is supposedly the same drug as one with a brand name but which has a different effect, and suppose an emergency ensues. Is there a medical director who is a physician in your company with whom the doctor can get in touch immediately?

Mr. WINTER: Do you mean a mislabelled drug?

Mrs. JONES: I am not referring to mislabelling but to a drug that may be chemically pure but which in its generic form has a different effect on the patient than a brand name drug.

Mr. WINTER: I do not believe you could tell the different effect.

Mrs. JONES: Dr. Frances Kelsey came up to the Canadian public health association meetings last year and at that time she referred to an instance

which had occurred in Canada where a generic name drug had been prescribed to a patient following a brand name prescription, and it had a totally different effect, with rather unfortunate results.

Mr. WINTER: But we in our clinical laboratories are drawing bloods every day. If a prothrombin activity is being done on a patient and in the process of a technician inserting a needle in the patient and that patient has a heart attack are you saying that it is because of the girl drawing out the blood? If you are saying that there is a different reaction between a person taking an officially named drug and a trade named drug you are making a mockery of the official compendium. As you know, many tests are made before it is established as an official drug. I do not think it is logical for anyone to assume there would be any difference in the chemical or biological activity.

Mrs. JONES: But, this has occurred.

Mr. WINTER: Yes. There have been statements made that the inert ingredients—that is, the factors that are holding the compound in its total form have different dissolution rates. If you are taking the dissolution factor into consideration, that is fine. But if it is up to B.P. and N.F. committees on standards, as we know it must be before release to the public, then that should be sufficient. One of the larger houses came into the limelight by persuading and brainwashing the physicians to the effect that the binder does not release the drug properly. This is not so; it may not release it identically in time with the brand name drug, but you should get the same effect clinically. The drug may not be instantaneous but from a clinical point of view your patient should get the same effect because of an established disintegration time for that drug dosage form. Do you not agree with that?

Mrs. JONES: You are using the word "should".

Mr. WINTER: But if it is up to B.P. or N.F. standards then it is a drug that has the required effect.

Mrs. JONES: But the fact is many physicians have said there is a difference.

Mr. WINTER: But they are physicians.

Mrs. JONES: Well, as physicians, they are interested in the effects.

Mr. WINTER: Yes. As physicians they see the effect, but clinicians have to be scientific and they say: this is the cause because of the variables.

Mrs. JONES: But, physicians must rely on the companies to help them out.

Mr. WINTER: But, there are so many variables.

Mrs. JONES: Yes, but we are concerned with the effects on our patients. If one gives a certain drug, and then uses another drug which has a different effect, and then comes back to the original drug, and there is a different effect again, I do not think this is proper.

Mr. WINTER: Would you say thyroid Parke Davis is a generic drug? If you wrote that on the prescription would you consider it as generic or brand?

Mrs. JONES: You go ahead.

Mr. WINTER: It does have a large brand name use. You have prescribed thyroid P.D.?

Mrs. JONES: I do not use that because it is not in my field. The fact is that the large therapeutical companies do have safety guarantees built in and this is what the physicians are concerned about. That is my point.

Mr. WINTER: I do agree with you that whether it is a brand name house or a small manufacturer with one tableting press there should be standards to govern all of them. I could mention the Cutter laboratories—if I might use names—who had the polio vaccine, which was contaminated. As you know, Cutter laboratories has international fame.

Mrs. JONES: But you are bringing up exceptions.

Mr. WINTER: No, I have the latest statistics in the United States. In the last two and a half years there were 243 drug recalls and these came from major houses. Twenty-eight per cent was concerned with low potencies or high potencies, 17 per cent had label mix-ups, and 13 per cent had contamination. So, potency and label mix-ups can happen to all firms.

Mrs. JONES: They can happen but I believe that those drug firms will take the responsibility for meeting these situations.

Mr. WINTER: Then, if you agree they will happen they can happen on a grand scale because all these large firms have enormous distributions, and when it happens it is very serious. Why does it happen?

Mrs. JONES: The point is it does happen, but they do have certain standards.

Mr. WINTER: I do not agree that the largeness of the house has anything to do with it. I believe it is the organization as such which makes the difference. From the Kefauver hearings we know that one of the anti-diabetic drug compounds in use today was introduced to the U.S.A. public by a large firm, and it was partially misrepresented by them. Why did they do it? It was because some business executive had to make a gain and he pushed the button to sell prematurely and the others just fell in line. This can happen in a large organization.

Mrs. JONES: It can happen anywhere but the point I am making is that the physician should have some protection.

Mr. WINTER: If you prescribe a brand name pharmaceutical and your patient can afford it then by all means perhaps you should do so, if you so desire.

Mrs. JONES: But, it is not the largeness of the house with which I am concerned; it is a question of taking the responsibility for clinical testing.

Mr. ORLIKOW: Mr. Chairman, if I could interject a question, which I think is pretty important, I would like to do so at this time.

If you like, I could use your firm, as an example, because you know precisely to whom you distribute your products. Could you tell me who buys your prescription drugs?

Mr. WINTER: The format of our operation from the manufacturing, testing and distribution point of view is identical with the larger houses. We have a wholesale policy which is perhaps more stringent than some of the larger trade name houses because some of the trade name houses have a locked market, and if they detail and brainwash the physicians with four coloured advertisements—I was going to say Madison avenue advertising techniques—they could do whatever they wanted to do because the doctor writes the trade name and the chain of reaction must take place. In other words, the pharmacists get it, the drug wholesaler does, and all the way down the line.

I want to tell the doctor who is present that it is not the amount of money or the largeness of the organization; whether it is a small well run hospital with one operating room and a good surgical staff, or a teaching hospital with many operating rooms, the house rules have to be there and rigid policy laid down. You will get the same effect in either hospital if the instrumentation is there.

Mrs. JONES: I think some companies have to take the responsibility for clinical testing and the spreading of information to the medical profession and, perhaps, all companies should do that. I will just leave it at that.

Mr. WINTER: In your medical profession you have certification; you will not allow a young graduate to enter the cardiovascular unit and begin to operate; you want him trained and certified. On our staff we have a Ph.D. although

we are very small, three pharmacists and some of the finest electronic testing equipment available.

Mrs. JONES: But you have no member of the medical profession.

Mr. WINTER: I was going to say we have the same format not only in the operation of our testing but also in respect of our insurance. We are insured with one of the largest firms here in Canada. They have seen fit to insure us, the same as they would a large brand name house. What difference does it make so long as we produce an officially named drug such as chlorpromazine in our own laboratories with the same orthodox equipment, the same tablet press which perhaps you would see in a large drug firm and with established enforced quality control procedures.

Mrs. JONES: My question is in respect of clinical testing and the responsibility for it.

Mr. WINTER: Are you talking about clinical testing for new drugs? We do not have a new drug.

Mrs. JONES: It is not a question of the newness of the drug.

Mr. WINTER: What do you mean by clinical testing?

Mr. RYNARD: I have a supplementary question.

The CHAIRMAN: I think Dr. Jones is referring to research.

Mrs. JONES: Well, research is part of it, surely.

Mr. WINTER: If you were—

Mr. RYNARD: You are talking about testing, and you are stating that your products are all right. But the fact remains that all the generic ones are not all right, because I believe the Ontario government bought generic drugs in this province, and their saving amounted to about $500,000; yet at the same time they had to set up a laboratory in order to check these drugs, when they found that several of them did not come up to scratch.

Mr. WINTER: That is right.

Mr. RYNARD: You probably know the figure; it cost about $7 million to build this laboratory.

Mr. WINTER: Yes.

Mr. RYNARD: And with the other costs added to it, it came to $12 million. I think the point that Dr. Jones is getting at is while your products may be all right—and we have not gone into that in enough detail—she states that some of them are not, and you admit that, yourself.

Mr. WINTER: Yes, I admit it. Some of the products from manufacturers both large and small may not be of labelled potency. But if the product has the labelled potency, it can be produced in a small or a large operation, the clinical effect should and will be there. You are talking about new clinical drugs. But if you only want pre-clinicals after they have been endorsed, then it is just like asking a man to try an examination after he has been certified in medicine. You are going to make a mockery of the U.S.P. and B.P. specifications. We cannot endorse a drug as being official. The written standards are there. It is essential, I feel, in Canada, as Dr. Rynard has suggested, that if a man manufactures a drug to a labelled potency, then we must be sure that it has the labelled potency, and that if he is doing it incorrectly, then he should be shown perhaps how to do it correctly.

Mr. RYNARD: But this may mean somebody's life.

Mr. WINTER: You will admit that not every operation is successful. We all have human frailties.

Mr. RYNARD: Yes, but we always strive to keep these human frailties down to a minimum.

Mr. WINTER: Suppose you have an electric typewriter. Would you be able to assure me that your letter would be error free, simply because you have this beautiful machine sitting there? Or would it not depend upon the operator? You will readily agree that money motivates people, and it usually does; and that one may through the process of elimination find a $60 a week clerk who could produce a letter error free, and at the same time you could readily find a $130 per week stenographer or typist who would do the same letter.

Mrs. JONES: That is not a parallel situation.

Mr. WINTER: Yes. The point is that we are all prone to error, and we must have proper standards and take proper precautions so that we may be error free. What about the large firms with their million dollar laboratories? You mentioned the Ontario government, but I mean the large firms. Do they ever have drug recalls?

Mr. RYNARD: Yes.

Mr. WINTER: Why?

Mr. RYNARD: Because medical testing was not adequate enough.

Mr. WINTER: It is not medical testing.

Mr. RYNARD: Yes, it is, and I could refer you to chloromycetin, which was called off the market after it was on for two years. It came back because the good was balanced with the possible harm that was done. But you are talking about a different thing, about drugs going out wholesale across this province which may not be doing the job which the doctor has prescribed at all; yet this may not be discovered for a long, long time. Nobody knows this better than you do. If a fellow goes into an operating room and is doing something and the results are different, the drug may not be what the doctor expects it to be at all. Surely there is a great difference here.

Mr. WINTER: If it is an official product, what does it mean? What does the United States pharmacopoeia, or the British pharmacopoeia, or the national formula mean? What do they mean to you?

Mr. RYNARD: It does not always mean that you are not doing a bit of borrowing there, because you can put all the drugs that you speak of into a compound, but it may not have the proper solubility, and the effects may not be there. Therefore, it does not do the job that the individual takes it for.

Mr. WINTER: Who endorses the pharmacopoeia?

Mr. RYNARD: What we are trying to get at is this. In generic work, are they producing these drugs as properly as it is possible to make them?

The CHAIRMAN: There are many questions. Everybody has a question, so let us proceed around the table and everybody may ask one question, because we only have until 11 o'clock this morning. I have a long list of people.

Mr. ORLIKOW: We could have started that procedure half an hour ago.

The CHAIRMAN: I did not realize it.

Mr. MACKASEY: I have listened very patiently, and I do not know if I can limit myself to one question, but I shall try to be as brief as possible. As you know, I am not a doctor, and I am rather happy about it, because while sitting here I have learned that some doctors have accepted money and have prostituted themselves in the United States. But apart from that, I still have a pretty high regard for doctors and their integrity. But I should like to propose a definition. Perhaps I might state it. What is the difference between a generic firm and a brand name firm. I presume a generic firm is one that has the ability to produce an equivalent drug in all respects, and to be able to market it at a cheaper price than the brand name firm. Am I basically right in that?

Mr. WINTER: Academically speaking.

Mr. MACKASEY: I am not very academic.

Mr. WINTER: A car always has four wheels. If you see a vehicle here with four wheels, without a name on it, you would say that it was generic.

Mr. MACKASEY: That is all right. I agree with you. But suppose someone goes out to purchase a washing machine. He may not particularly care what the name is, as long as it functions. He takes it home, and if it functions, all right; but if it does not, he sends it back and will purchase a brand name product. Do you agree?

Mr. WINTER: The man with a dedicated policy of producing a good washing machine must of course produce his first design.

Mr. MACKASEY: Would he put his name on it after that?

Mr. WINTER: No. But let us say he does put his name on it, and that he has produced his first machine against competition. It is a good machine, and he produces 12 of them. Would your wife buy one? It is a good machine. Ten years from now he may be listed as one of the largest producers.

Mr. MACKASEY: Empire obviously is a forerunner in the generic field, yet no doubt you push other products, not necessarily drugs that are Empire drugs.

Mr. WINTER: Yes, trade name products, and we have our own trade name to identify the manufacturer.

Mr. MACKASEY: Now, whether you realize it or not, you are leaving the generic field and entering the trade name field when you are selling "Empire".

Mr. WINTER: You have a concept of the word generic which is not correct.

Mr. MACKASEY: I say you are leaving the generic field and going into the brand name field, and you are pushing it on the strength of your operations and clinical testing. You tell doctors that Empire produces a product as good as "Frosst" or "Cynamid" or anybody else.

Mr. WINTER: It produces quality of the highest possible standards.

Mr. MACKASEY: You are no longer generic in the sense of the term as I understand generic.

Mr. WINTER: That is right. We even put an "E" on our tablets now.

Mr. MACKASEY: So you are no longer generic according to my definition. I am under a disadvantage in not being a druggist or a doctor. But are you aware of a case which took place in Montreal on October 21, 1964, in the superior court, *Smith, Kline & French Inter-American Corporation,* petitioner, versus *H. T. Cheifetz et al,* respondents?

Mr. WINTER: I believe it came under the heading of potency.

Mr. MACKASEY: Let me quote from the judgment in that case as follows:

> Uncontradicted evidence made before the court is to the effect that the capsules sold by respondent to Turner contained an inferior product and did not meet the standards of petitioner's product, especially as regards the percentage of the drugs release, which, according to said evidence, was not the same. By so selling an inferior product which in many ways resembles the product manufactured by petitioner, respondent may cause considerable damage to petitioner's reputation and may even cause harm to the public.

I think that sums up pretty well what I feel about the generic trade, not necessarily Empire. And I have something else, an extract from the Montreal *Gazette* for Saturday, December 1, 1962, a note under the heading of "Medicine and Science", by Dr. Herbert Lampert. My point is, because this drug was mentioned earlier by you—and you must forgive my pronunciation—it pertains to the drug which was used very early for the alleviation of diabetes.

The CHAIRMAN: You mean Tolbutamide.

Mr. MACKASEY: Yes, and it mentions three cases of Tolbutamide, as follows:

> In Windsor, Ontario, last month, a doctor rushed his patient to the hospital when his blood sugar went out of control. The druggist had substituted a generic tolbutamide for the brand the doctor wanted and the tablets failed to dissolve.
>
> In Fort Frances, Ontario, a police sergeant fortunately suspected illness, not alcohol, when a Sunday "drunk" was brought in. The suspect was taken to the hospital and diagnosed as in a diabetic coma. Again the culprit was tablets that failed to dissolve.

It goes on and cites the third case which concerns me even more because it was a drug released by the government.

> In spite of this there is a strong movement in Canada to legalize substitution and to arrange for more extensive government purchase of generic drugs—

Then there is the case where the same thing happened with a government issue. You mentioned a million dollar firm makes mistakes. How much more possible is it that a $50,000 firm is going to make a mistake? You might say no.

Mr. WINTER: I agree. One can only be governed by our own house and our own company.

Mr. MACKASEY: You are here and rightfully so; but by your own admission Empire does not fall into this?

Mr. WINTER: No. We put an "E" on the tablet to tell the doctor it is an open name drug without a trade name, and it has efficacy.

Mr. MACKASEY: How do you pick the product you sell?

Mr. WINTER: By demand.

Mr. MACKASEY: Demand from whom?

Mr. WINTER: What the doctor is writing, what he wants.

Mr. MACKASEY: What products have you developed which you are selling now?

Mr. WINTER: None.

Mr. MACKASEY: None at all?

Mr. WINTER: None.

Mr. MACKASEY: In other words, you simply take the demand that has been created by some other firm—

Mr. ORLIKOW: By the doctors.

Mr. MACKASEY: Come off it.

Mr. WINTER: We have three products under wraps now that are new in Canada, but they are not new in the universe. They may come from a large pharmaceutical firm in Sweden which firm has marketed it for a number of years, or it might come from a firm in Germany. They have clinical trials there. What we do is bring these to Canada and follow the same format as the large firms. We will carry on clinical trials in Canada. Your homo sapiens in Canada are the same as in Sweden or Germany and, if it is substantiated, I feel the government will give us permission to introduce these products and we will then market them in dosage forms.

Mr. MACKASEY: I do not intend to get into prices, but I might have to touch on this aspect for a moment.

Mr. WINTER: I would like you to linger on that point. You seem to frame your questions as if we are parasites with no research and no development.

Mr. MACKASEY: Have you any example of research done by the generic firms?

Mr. WINTER: Do research and pharmaceutical manufacturing go hand in hand?

Mr. MACKASEY: Do they not?

Mr. WINTER: Not necessarly. Some of the greatest universities have produced first class developments in chemistry.

Mr. MACKASEY: Are you suggesting we should take the research out of the drug houses and hand it over exclusively to the universities?

Mr. WINTER: No; but it is my frank opinion that the directors of these large firms are not basically interested in the introduction of new drugs for the salvation of humanity, but are interested in the financial statement.

Mr. MACKASEY: When you introduce one in the future, what will your motivation be? Will it be a legitimate profit, or will it be for humanitarian reasons?

Mr. WINTER: If you want an honest and truthful answer I would say humanitarian reasons.

Mr. MACKASEY: Empire is set up strictly for humanitarian reasons?

Mr. WINTER: Yes, with a dedicated policy.

Mr. MACKASEY: I am glad you can afford such high ideals.

Mr. WINTER: If we were going to bring out a new product now, it would be wonderful, if it were new in Canada, because it would be a major breakthrough for a small firm.

Mr. RYNARD: Do you do research work?

Mr. WINTER: Yes, we do.

Mr. RYNARD: On new products

Mr. WINTER: Yes, we do.

Mr. RYNARD: How many have you developed?

Mr. WINTER: We have three under wraps.

Mr. RYNARD: But you have not developed any to date?

Mr. WINTER: Doctor, you did not come by your clinical procedures alone, but you use them after education. Does it matter who develops it?

Mr. RYNARD: Surely this would kill research.

Mr. WINTER: I wonder. Fleming did it in dusty laboratories in England.

The CHAIRMAN: Gentlemen, I think we should give some other members of the committee an opportunity. Mr. Orlikow?

Mr. ORLIKOW: Where is your plant situated?

Mr. WINTER: 77 Florence Street.

Mr. ORLIKOW: In what city?

Mr. WINTER: In Toronto, and then we have 301 Lansdowne which we have just acquired.

Mr. ORLIKOW: To your knowledge how many teaching hospitals are there in Toronto?

Mr. WINTER: I do not know, exactly, but there would be the Toronto General and its affiliated hospitals—the East General and St. Michael's. I would say about three.

Mr. ORLIKOW: How many of the dispensaries of those teaching hospitals have purchased prescriptions from Empire?

Mr. WINTER: One of the largest teaching hospitals in Ontario is practically exclusively with Empire.

Mr. ORLIKOW: Which one is that?

The CHAIRMAN: Perhaps this is information the witness really would not like to give.

Mr. ORLIKOW: I do not know why we should not have it. I think this is important. Consistently through the hearings, and particularly by the drug companies, there has been the suggestion that the products sold under the name commonly referred to as generic drugs are inferior.

Mr. WINTER: I would rather not give the name, because it could become a public record. Let me say this; we know that the food and drug directorate are doing a good job. The inspectors can walk in unannounced and they are welcome. They pick up samples. We know that if the large pharmaceutical firms with which we are competing could pick up any of our products which are not up to standard, they would certainly let the authorities know about it, and indeed we would know about it. The drug inspectors come in—they are more than welcome—to assist us. We are updating all the time. Whether it is through a small hospital or a large one, we want to grow and make our place here in Canada because it is our country. You cannot develop a teaching standard or teaching staff in a small hospital, but you may have a nucleus and may have a dedicated policy, and with time it may develop into a teaching hospital. The Doctors Mayo years ago perhaps dreamed of a centre. They had good standards, and their techniques and their knowledge are sought now after many years.

Mr. RYNARD: The centre was started by one, the father, and the boys came up.

Mr. WINTER: Doctor, with that history, why are there the innuendos that we do not do research?

Mr. RYNARD: But you are using the other fellow's research.

Mr. ORLIKOW: I am not a doctor. I used to be a pharmacist, but unfortunately for me I am a large purchaser of prescription drugs, because I have had sickness in my family. For a moment I would like to come back to what I started on. You mentioned a large teaching hospital in Toronto.

Mr. WINTER: I said in Ontario.

Mr. ORLIKOW: You mentioned it does use your products?

Mr. WINTER: That is correct.

Mr. ORLIKOW: Am I right in assuming that teaching hospitals all across Canada use prescription drugs purchased from yourself or other companies which sell generics?

Mr. WINTER: I cannot answer that yes or no; I do not know.

Mr. ORLIKOW: Is it fair to assume that if they do they will check to make sure it is a reliable drug?

Mr. WINTER: I am sure.

Mr. ORLIKOW: I ask that question for a very simple reason. My wife has been going to the Royal Victoria hospital in Montreal. I do not know whether or not you sell to them. She has recently been getting a product which Dr. Jones will know very well, a product called meprobamate. She has been getting it at the dispensary there for half the price at which she could obtain it from any drug store across Canada. I hope the Royal Victoria is making sure that the company from whom they are buying it is producing a reliable drug.

Mr. RYNARD: Tax enters into that, of course.

Mr. ORLIKOW: I have checked and I have found that it is not the meprobamate which is produced by the company that first brought it into this country. I want to make sure that it is reliable.

The CHAIRMAN: It is a well known fact that any hospital drug is a great deal cheaper whether it is a trade name drug or a generic drug than it would be if one were to buy it normally over a counter in a drug store.

Mr. WILLOUGHBY: Mr. Chairman, the subject that I was going to ask about has been dealt with briefly, but I think it should be enlarged upon.

The question of these generic drugs and their acceptance has been to a large extent based on economic factors. There is no question that they are sold at a more reasonable price than some of the trade name drugs. However, trade name drugs are more expensive for various reasons, probably, one of which is the fact that a certain amount of research is charged up to them. I understand from some of the reliable trade name firms that as much as 8 per cent of their costs go into research, which of course adds up to a great deal.

Speaking about research, you brought up the subject of Mayo starting out as a small organization. I can tell you this much because I know the Mayo organization very well, a lot of their progress has been made through research and a lot of our pharmaceutical progress has been made through research. I do not therefore think that we can write off research as not being a factor which should be taken into consideration in this matter.

The point is, however, that hospitals and public health services do use the drugs because of the cost.

From what you say we can assume perhaps that so far as your firm is concerned the drugs your company is selling are checked carefully for potency and accuracy, but unfortunately a great many companies producing generic named drugs are fly-by-night companies, and their products do not come up to the required standards. Because of this lack of standardization it is necessary to recheck some of these firms. I understand the department of health say they were saving several thousand dollars a year by buying generic drugs, but they have had to establish a research department of their own to recheck these drugs and it will cost them from $6 million to $12 million to put up this organization to check the drugs. In those circumstances, by the time they get this organization set up the drugs will cost more than if they depended on the research and checking that is going on in the recognized companies. I would like to know just how money is going to be saved by the establishment of an organization to check on the drugs—though not the drugs of your company necessarily.

Mr. WINTER: Dr. Willoughby, I took exception to the word "Empire" being classified as generic and I would like to emphasize that the term "generic drug house" does not necessarily connote a fly-by-night drug house, although we know there may be such companies producing pharmaceuticals. We know there are companies producing tablets that will not disintegrate. They feel that if they have a press for the tablets and they pay a few dollars for it, it will work and that it does not matter very much about the weight variations, etc.; they feel it will produce good tablets if they just load it. But this is not so. They market these on a price proposition, the lowest price. Empire products are not the lowest priced products. When we sent details to the physicians of our products we tell them that they are not the lowest priced products.

We release no product for packaging that has not gone through rigorous quality control in our laboratory. It must be checked. It must conform not only to official standards, but to our own house standards. The standard on an antibiotic drug might be 85 per cent, and if the product reaches 86 per cent that is fine, but our standard is 102 per cent; and this is a fact. The drug will be rejected by us if it does not reach that mark because if a drug is produced by Empire it must have effect and it must compare with the highest standards.

If we cannot produce a drug with these high standards, we just will not produce it. We cannot afford it because our reputation is at stake. I say that our reputation is at stake because we put an "E" on some of our tablets, and this means Empire. It also means that the drug is efficacious, it has the potency that is required, and it has the highest quality.

Mr. WILLOUGHBY: As a group it would seem to me that the manufacturers who are not recognized as trade name manufacturers should have some discipline in their own group to see that these so-called fly-by-night companies do not under sell you, under rate you, and put a product on the market that reflects on the whole organization.

Mr. WINTER: Mr. Mackasey brought up the subject of the tolbutamide incident. This was not an Empire product. When this matter was published in the Montreal *Gazette* we sent a copy to every physician, along with an accompanying letter, saying that the product referred to in the *Gazette*, generic tolbutamide, as not working in Windsor, not dissolving and not efficacious, had no bearing on Empire's tolbutamide, that we had rigorous laboratory standards and control, proper personnel, and that it could not be taken that Empire's tolbutamide was at fault. We have high standards, just as high as the other houses.

If another man wants to bootleg or down grade his establishment, he is free to do so, perhaps, at the moment, and therefore I believe there should be some certification; no doubt it will come. In other words, there will be a common standard just as the pharmacoepia has a common standard for a drug, and a drug is not endorsed in the pharmacoepia, is not certified, until the pre-clinical work has been done to ensure its standard.

Mr. WILLOUGHBY: This all leads up to the fact that the government of Ontario has had to establish an organization or an institution to check these drugs, and it will cost them more for their drugs than if they were to buy from the original producers of the drugs.

Mr. WINTER: Dr. Willoughby, I believe it is saving. Not only do they check the trade name drugs but they check all drugs that come in. When the large houses tender for a hospital or a provincial or federal government contract they throw away their price lists and they tender on a price proposition, and they compete. It might be that a batch of tablets would come in from a trade name house and they would go through the same channels in the provincial government laboratory as tablets which were unbranded. This is only an added safety valve.

In other words, when one has one technician doing a blood smear does one have a check? Does one have the routine things checked by another technician and then by another one? No. You get the odd ball, perhaps, the odd mistake checked out, but there has to be a stop on checking.

Mr. WILLOUGHBY: It would be interesting to know how many of the brand name drugs have been turned down by this new laboratory service in Ontario.

Mr. HOWE (*Hamilton South*): Mr. Chairman, most of the questions I had intended to ask have already been answered, but I would like to say that as doctors I think we are probably prejudiced individuals, and maybe we are not the ones who should be questioning the witness on this subject.

As you say, Mr. Winter, there has been a certain amount of brainwashing, justified or otherwise. As practising physicians, we are interested in the cost of drugs to patients because the cost of drugs is one of the most prohibitive items in the proper treatment of patients. We feel in our practice that quite a large percentage of our prescriptions never reach the drug stores because of the cost.

Mr. WINTER: Then, of course, the patient will not get the effect of the treatment that is prescribed.

Mr. HOWE (*Hamilton South*): The patient comes back—or does not come back—and has not received the treatment.

We know that the generic firms—or your own firm—are simply remanufacturing the drugs at less cost than the firm that manufactured it originally. Therefore our knowledge of the drug comes from the firm who originally manufactured it, maintained its development, and puts expenses into constantly looking for new drugs. This must have an effect on the cost of the drug that you are buying now because they are developing the next drug.

Mr. WINTER: Should there not be a level-headed equilibrium about the cost of drugs? How could a generic house gain an entree and do it profitably if these other profits were not exorbitant? In other words, if the large houses which do the research, let us say, brought out a drug and priced it reasonably with an aim for a legitimate profit other than—and I will use the word again—an exorbitant profit, the other houses would find it more difficult to gain an entree. Why should an anti-arthritic drug be $21 for 100 tablets? You as a doctor treating a patient who is a $90 a week wage earner and has three or four children, may prescribe the drug, but he will not take it because he cannot afford to take it. He comes back to you and he says, "Oh, yes, doctor, I have taken it." You do not know whether the drug did not have a clinical response or whether the patient did not take it. That is the issue. The patient might tell you, "Oh, yes, doctor, I took it", but how could he afford to take it?

The same pharmaceutical house that sells the drug at $21 a hundred, would then tender at $16 a thousand for a provincial tender. It is imbalanced; it is not realistic. It is not right; something is wrong.

A man then takes the same equipment, the same testing facilities and organizes a pharmaceutical house with high standards but instead of the high profits and four-colour brochures, the embossed stationery, he produces a first class product and puts it out on the market at a reasonable price. Is there anything wrong with that?

Mr. HOWE (*Hamilton South*): No, but is he not manufacturing it on the strength of the research done by the company which maintains very costly research departments? We certainly do not want to get away from that.

Mr. WINTER: We agree. The whole idea was premised on the fact that it was unreasonable. Unreasonable is the word for $21 a hundred.

The CHAIRMAN: Gentlemen, I think you are getting into the question of costs here.

Mr. ORLIKOW: If company A develops a drug does it not obtain a patent?

Mr. WINTER: There are patents; and there are certain restrictions. There are certain legal aspects that have to be taken care of.

Mr. HOWE (*Hamilton South*): May I make a complimentary remark? I have known the Winter Laboratories—and I assume this is your firm—on Bloor Street for many years.

Mr. WINTER: Yes, we have just moved into the Colonnade; we have extended our services.

Mr. HOWE (*Hamilton South*): I have known the Winter Laboratories for many years, although I have just moved into Hamilton now. I knew that Winter Laboratories were most reliable and I always sent pregnancy tests from Hamilton and elsewhere to them. I knew the company and therefore I was not questioning the reliability of your company, I was questioning the cost of drugs.

Mr. WINTER: There is a lot of altruism in the Winter Laboratories. I come from a medical family, and I can assure you that there is a certain amount of

pride and genuine endeavour in our attitude other than merely a dollars and cents attitude. I know there are other producers who are in the business for gain primarily, and I know that there are hit and miss operations.

Mr. MACKASEY: You mean other generic companies?

Mr. WINTER: Yes. I feel we are doing a good job and that we have the proper facilities to do it.

Mr. WHELAN: I would like to ask a question of the witness. Your firm does make a profit, does it not?

Mr. WINTER: Yes.

Mr. WHELAN: It is getting close to Christmas and you did not appear to me to be Santa Claus!

Mr. WINTER: We are not a charity organization as such, Mr. Whelan; we are in the business for a legitimate profit.

Mr. WHELAN: We have visited many research facilities. One thing I am in favour of is more research in universities and like institutions rather than in this type of institution. Does your firm make contributions to that type of institution?

Mr. WINTER: Yes, we make a yearly contribution to the Association for the Advancement of Pharmacy. When we gave them the first cheque we could have had photographers there taking pictures of the president handing out a cheque to the recipient. Each year we have given a percentage of our profit. Today we have a Ph.D. on our staff and we have an organization that is doing research. Research as such does not have to be done in the large emporium that you think about. Fleming discovered penicillin on a dusty old shelf. The old shelf was perhaps worth only a small amount of money.

Mr. WHELAN: We did see research done under possibly the worst conditions in the Hotel Dieu in Montreal. I fully realize you do not have to have marble halls and everything else.

Mr. WINTER: No. I do not think, basically, that these larger pharmaceutical firms are endorsing expenditures of money for pure research; they are working to a goal of a marketable and profitable product. They may be able to secure patent rights, and then I think they get their economic gain in return. They are in the pharmaceutical business, but whether one would be in the garment industry or in the farming industry one would want to exploit it and nurture out as much as one could from the soil; and that is it. Some of them have done it—large ones—with a disregard for basic concepts of good work, and honesty and integrity.

Mr. WHELAN: You intimated there that a good farmer does not try just to take everything from the soil but that he tries to maintain it so that it will be here in good condition for many years. I feel some of the drug companies are the same, regardless of how large their research facilities may be; they are there actually to create as much good as they actually can.

Mr. WINTER: Well, if they are, when they charge an unreasonable amount —a most unreasonable amount—for medication, certainly the man who endorses this amount is not a good farmer.

Mr. ROXBURGH: Dr. Howe has asked the question that I had in mind and has been fairly well answered.

The only thing that has perturbed me is a statement by Dr. Willoughby—and there has been no correction made by you, Mr. Winter—with regard to the fly-by-night organizations. Is there not inspection, serious inspection, so that no such thing as a fly-by-night organization for the manufacture of drugs for people, for humanity, can exist? Do not tell me that it is possible in the Dominion of Canada to have fly-by-night organizations and that there is little

or no check, that they can go and do such things and produce such products without any check.

Mr. WINTER: The government officials are only human, after all. Certainly there are bootleggers somewhere in this country and there are suppliers of illicit drugs, dopes, narcotics. You cannot put your hands on them. You have to be realistic about this.

Mr. ROXBURGH: On a fairly large scale?

Mr. WINTER: There was one in Quebec; I read the news item but I had never heard of the firm before. The government officials know that we are on Florence street in Toronto and they know we are in the drug manufacturing business. They know we are trying to do a good job and produce a good product, and they can see that we are doing it.

Mr. ROXBURGH: I am not talking about narcotics but about drugs that I as an individual can go into a drug store and buy. They are put in the drug store and sold by the druggist. Is there no check by top inspection so that products produced by fly-by-night companies which do not come up to standard are not sold in drug stores? If these products are sold they are bootlegging. Is that going on today? Is that a fact?

Mr. WINTER: I did not say that there is no check. I think it would be superhuman and impossible to have an official agency check every product immediately. For example, turning to the medical profession again, clamps have been left in the bodies of patients and certainly they must have checked. But what can you do? Can you check and double check after you have finished the checking?

Mr. ROXBURGH: I would like just a yes or no answer to this question, Mr. Winter. There are bootleg companies bootlegging ordinary drugs and they are being sold to sources in the Dominion of Canada—I will spread it out by saying in the Dominion of Canada—today?

Mr. WINTER: I would not like to comment on that. I think the official agencies do a good job.

Mr. RYNARD: I would like to sum up briefly. I wonder what would be our position today if we had not had that profit motive that enabled companies to carry on research. Surely you have to admit that in carrying on this research some of the companies have lost millions of dollars. You will recall that chloromycetin cost Parke, Davis $5 million. They were $5 million behind the ball when they took it off the market. That was a very useful drug.

I am saying that probably your drugs are good but—following your line, and you have separated the sheep from the goats yourself—in Russia where they have not had the profit motive, how many new drugs have been developed in the last 40 years? Not one.

Mr. WINTER: Oh—hold it a moment. That perhaps is not correct. I have something here to show you.

Mr. RYNARD: You mean just recently they have copied drugs from us. They are using our polio vaccine which was developed in Illinois.

Mr. WINTER: There is one for malignant tumours mentioned in this volume. I do not know anything about it; I have only just looked at it.

Mr. RYNARD: You must admit that there has not been a new drug produced by them until recently.

Mr. WINTER: I visited behind the iron curtain in February of this year and I was amazed at the new work going on in Poland, for example.

Mr. RYNARD: What new drug have they produced?

Mr. WINTER: I wish I knew. I am trying to find out.

Mr. RYNARD: If we did not have laboratories which make profits we would not be able to do this research and produce these news drugs.

Mr. WINTER: But the profit should be legitimate profit.

Mr. RYNARD: Is a profit of 11 per cent legitimate?

Mr. WINTER: When you call on a sick person you do not ask for the money in the palm of your hand before you inject the penicillin, do you, doctor?

Mr. RYNARD: No, never.

Mr. MACKASEY: This has been a very interesting hour. Perhaps the witness will come back to give further evidence because this has been very enlightening.

I think Dr. Rynard made one of the points that I had in mind. You emphasized that when this tragedy occurred in 1962 you immediately, and rightly, notified all the doctors that it was not an Empire tolbutamide.

Mr. WINTER: Yes.

Mr. MACKASEY: Right there and then you emphasized the necessity for branding the product.

Mr. WINTER: Yes. That is correct.

Mr. MACKASEY: In other words, if you were to go to the drug store and ask for the product you would ask for it by name. If one were to go and ask for the product without emphasizing the brand name one might get an inferior product. This is very important.

Then you mentioned Fleming and penicillin. It took 14 years to get penicillin on the market. Had it been in the hands of a big firm, motivated by profit, it would not have remained on the shelf for that period of time.

Mr. WINTER: Well, Dr. Waxman brought out streptomycin. We have that today and it is a rather less profitable product.

Mr. MACKASEY: I do not want to hold you up and perhaps I am being rude in hurrying along. But, we are talking about the things you manufacture. What about the products you do not manufacture. Where do they come from?

Mr. WINTER: Do you mean the basic materials? Mr. Chairman, have we time to go on?

The CHAIRMAN: Yes, proceed. Mr. Mackasey is interested in what you are importing.

Mr. MACKASEY: You must be a distributor as well as a manufacturer.

Mr. WINTER: No. But, when you say "manufacturer" we do produce or manufacture the dosage forms.

Mr. MACKASEY: From where do you obtain your raw materials?

Mr. WINTER: They come from the United States, England, Sweden, Denmark, Italy, Poland and France.

Mr. MACKASEY: What control do you have over the incoming materials?

Mr. WINTER: All materials are checked in our control laboratory before processing. We do this for two reasons. One reason is the safety factor, of course, to find out if it is up to potency and so on, and the other is economical. We are purchasing these products on their potency factor and we have to check, just as the government does.

Mr. MACKASEY: You have been intimating all the way through—and correct me if I am wrong—that the reason you are able to undersell the better known drug houses is their exorbitant profit and, secondly, you have intimated they have many frills, such as coloured brochures and engraved letterheads.

Mr. WINTER: Yes, window dressing.

Mr. MACKASEY: But, would you say they are inefficient in their manufacture and that you can manufacture goods cheaper than they can?

Mr. WINTER: I did not say they were inefficient in their manufacture.

Mr. MACKASEY: Can you explain why you can produce a product cheaper than, say, Frosst?

Mr. WINTER: We buy the basic product from the world market.

Mr. MACKASEY: Yes, you buy the basic product from the world market.

Mr. WINTER: For instance, if you wanted whale oil where would you go and look for it? Where would you find it?

Mr. MACKASEY: As close to the origin as possible.

Mr. WINTER: Where would that be?

Mr. MACKASEY: I do not know.

Mr. WINTER: Whales.

Mr. MACKASEY: I am sure you just do not go out and pick up poppy seed, for instance.

Mr. WINTER: Exactly. These same basic drugs are manufactured only in a few places in the world and it is economical to buy them there because that is the centre in which they are made.

Mr. MACKASEY: Well, we know some Italian recently stole a patent from American Cyanamid. I noted that from the newspaper. Then, they will ship this back to the United States.

Mr. WINTER: And, there is an American firm that has been cited, and litigation is now going on in respect of someone in California who infringed Lederle's patent.

Mr. MACKASEY: You sell tetracycline?

Mr. WINTER: Yes.

Mr. MACKASEY: In both forms?

Mr. WINTER: In liquid and capsule.

Mr. MACKASEY: In injection form?

Mr. WINTER: No, we are not equipped.

Mr. MACKASEY: Then, you do not meet or cannot meet Dr. Greenberg's standard in respect of parenterals?

Mr. WINTER: No, we have never produced parenterals. Should we desire to do so we would meet Dr. Greenberg's standards.

Mr. MACKASEY: But in the meantime you cannot, and you say you do not produce it?

Mr. WINTER: We market it. We have another firm which has been certified by Dr. Greenberg produce it for us under our label.

Mr. MACKASEY: And do you sell it on the market cheaper than the other firms sell it?

Mr. WINTER: We could, yes.

Mr. MACKASEY: But, do you?

Mr. WINTER: They do not sell it.

Mr. MACKASEY: When you say you could that intimates to me you do not.

Mr. WINTER: Let us put it this way. The firm's policy from which we are buying our parenterals is similar to the firm that manufactures all the soft gelatin capsules here in Canada. One firm manufactures all the soft gelatin capsules whether it is a trade name, high priced, or whether it involves someone else's firm. Now, they do not compete with those. They sell it to us. They do not market a product themselves. And, the injectable material we buy is from a certified parenteral manufacturer.

Mr. MACKASEY: But do you put the word "Empire" or the letter "E" on your product?

Mr. WINTER: Yes.

Mr. MACKASEY: You brand it?

Mr. WINTER: If it is generic we only put "Empire". The active ingredient is not trade marked.

Mr. MACKASEY: But you do put something on your product that will distinguish it.

Mr. WINTER: But the product is liquid. Are you referring to the package?

Mr. MACKASEY: In general, you do put some identification on your products?

Mr. WINTER: Yes, because there are other competing firms.

Mr. MACKASEY: I think you have been an excellent witness for Empire.

Mr. WINTER: I have a bit of a summation here, if I may be permitted to give it at this time.

The CHAIRMAN: That will be fine, if you wish to proceed. I do not believe there are any other questions.

Mr. WINTER: After reading the reports and the transcript of the other people that have attended, in my own view I feel that certification—

The CHAIRMAN: You mean licensing?

Mr. WINTER: Yes, or certification, is necessary to make sure that proper pharmaceutical and manufacturing procedures are regulated here in Canada. We at Empire laboratories do our best, but how do we know our manufacturing procedures are the best. I think there should be a set pattern in respect of certification. If someone came in and said that this procedure could be modified with a better result, then I think that should be taken into consideration. For instance, if I visited a competitor's firm here or in any other part of the world I would like to walk in and tell them that I am coming in without my blinkers on, that I wanted to see and ask questions. And, if I saw a procedure or a test, or some bit of apparatus I would like to have information on it. In this way we would update our basic present day standards. But, if a neophyte wants to get into the production of pharmaceuticals and he has X dollars, which is enough to buy him three or four pharmaceutical bits of equipment, he is in a position to enter the business. He may not know the first thing about manufacturing and yet he could go ahead and bring in a pharmacist and start to manufacture. However, he really has not a basic set of house rules.

Now, if in certification specifications were laid down so that each pharmaceutical firm would then have a norm in respect of procedures everyone would benefit. In respect of clinical data, as the doctor said, we are always worried about time. As time develops we worry about the build-up of the drug in the person's body and whether or not there may be an adverse reaction. These things must be studied. I believe that legislation now is in progress—and I think it is good legislation—to make sure that the health and welfare of the people who are taking these organic compounds are closely watched. In respect of clinical data, specifications and products standards, there should be no ambiguity. If one manufacturer has a dissolution rate that he thinks is important enough to publicize and sends letters to every doctor in Canada, then it must be important enough for the pharmaceutical committee, which certifies these things, to look into.

Mr. MACKASEY: You said something to the effect that if this dissolution rate is so vitally important—

Mr. WINTER: If it is.

Mr. MACKASEY: —to the success of the particular drug, it should be emphasized throughout the industry.

Mr. WINTER: Yes.

Mr. MACKASEY: Suppose a druggist or doctor in Alberta substituted a brand product that has a known rate of dissolution, how would you distinguish that from a generic which does not?

Mr. WINTER: Well, let me put it this way. Suppose your mother was making an apple pie.

Mr. MACKASEY: She makes good apple pie.

Mr. WINTER: Yes, good apple pie. And, if a baker makes another apple pie—

Mr. MACKASEY: Which is not quite as good?

Mr. WINTER: Right. And by the time it hits your taste buds it takes a little longer for the crust to dissolve, but it does not have any effect on your taste buds.

Mr. MACKASEY: The only thing that will happen is that I will get a belly-ache from the wrong pie but if the same was true in the case of drugs I may be dead.

Mr. WINTER: I do not think the dissolution rate as publicized is all important.

Mr. MACKASEY: Do you deny what the *Gazette* printed in respect of these three cases concerning diabetes?

Mr. WINTER: Suppose, you wanted motor oil with a bright yellow colour and I gave you green but it was the same viscosity which is established by the society of automotive engineers, would you object to that?

Mr. MACKASEY: You tell me that the rate of dissolution is not important?

Mr. WINTER: There are standards of disintegration but I would not like to comment on it. I do not think it is important to the efficacy of a drug.

The CHAIRMAN: The House bell is now ringing, the meeting is adjourned.

APPENDIX "A"

INTERESTING ASPECTS OF QUALITY CONTROL IN DRUG MANUFACTURE

By Dr. Henry D. Piersma, Ph.D., Director, Quality Control, Lederle Laboratories, Pearl River, N.Y.

(Talk given to the Members of the Special Committee on Food and Drugs on July 7, 1964.)

In contrast to the first two speakers, Drs. Litchfield and Gallagher, who spoke to you about their activities in testing various compounds for safety in animals and man prior to the use of these compounds as drugs for distribution to the market, my talk will be concerned with the testing of drugs for safety, potency, identity, uniformity, and stability after the drug has been approved for commercial distribution. It is, indeed, a grave responsibility to conduct appropriate tests on each lot of each drug product and to release such lots to the market for use in man and/or animals.

The concept and implementation of organized quality control in the manufacture of drugs in this country go back to 1820, when a group of physicians met in Philadelphia to outline and adopt standards for drugs in common use. It is not difficult to imagine how chaotic the situation must have been when each physician or apothecary dispensed drugs without reference to standards of potency and purity. These physicians met in what we now recognize as the first United States Pharmacopeial Convention and imposed standards of drug potency and purity upon themselves for the public welfare. Thus, the work of these physicians in 1820 was the foundation on which the first edition of the U.S. Pharmacopeia was built. At this moment the draft of the seventeenth edition of the U.S. Pharmacopeia is being completed by the Director of Revisions, Dr. Lloyd C. Miller, with a committee of sixty experts giving him advice and recommendations. It is interesting to note that self-discipline and self-regulation preceded regulation by our federal government by some eighty-five years, since the Pure Food and Drug Act was not adopted until 1906.

After the establishment of the U.S. Pharmacopeia in 1820, and as the drug industry emerged from the corner store to the larger and more capable drug manufacturing organizations, the development of laboratories for quality control purposes was prompted by many factors. With very weak governmental control in most states, if any existed whatsoever, and with no federal control of drug manufacture between the years 1820 and 1906, it may be said that deception, quackery, and irresponsibility were commonly practiced in the drug field. However, there were a small number of responsible drug manufacturers who recognized the necessity to render a public service, to build reputable drug houses and to avoid legal action. One of our leading American drug houses, during our Civil War, produced quinine which was not extended or diluted with pulverized sugar, and built an enviable record for high quality drugs. Incidentally, the president of this company personally signed his own name on each label used in identifying each bottle of each drug product distributed by his company.

In more recent times, the Pharmaceutical Manufacturers Association, with headquarters in Washington, D.C., has extended membership privileges to only one hundred and forty of approximately twelve hundred drug manufacturers or distributors in this country. On May 3, 1961, the Board of Directors of this organization adopted a statement about the "General Principles of Quality

Control in the Drug Industry." In this statement, which covers all aspects of the quality control function in a drug manufacturing establishment, the opening sentence is significant. It reads: "Control of quality in the formulation, manufacture, and distribution of pharmaceutical, biological, and other medicinal products is the organized effort employed by a company to provide and maintain in the final product the desired features, properties and characteristics of identity, purity, uniformity, potency, and stability within established levels so that all merchandise shall meet professional requirements, legal standards, and also such additional standards as the management of a firm may adopt." This constitutes the first written statement made on the principles of quality control in the drug industry, and was made, incidentally, considerably earlier than the recent changes in federal drug regulations in the United States.

Here at the Lederle Laboratories, Division of American Cyanamid Company, we have over three hundred employees in our Quality Control organization, with over 50 per cent of these individuals holding professional degrees. We are divided into two main areas, one of which is concerned with the testing of biological products, and the other with pharmaceutical products. Naturally, there are groups within our organization serving both areas of testing. Our Quality Control organization is administratively independent of the production function, and no one in our organization participates in manufacturing operations as such. The Quality Control group only audits and checks the performance of the production organization, and this fact leads us to a prime principle in the manufacture and distribution of high quality drug products. Quality is built into a product by the control and use of high grade raw materials, strict and coordinated production operations, and established high standards in the finished product. Quality cannot be imparted by a Quality Control group; it must be manufactured into the product. We also wish to point out that the Quality Control function assumes responsibility for keeping manufacturing personnel keenly aware of their obligations, by means of demonstrations or discussions on the importance of maintaining high standards of responsibility and performance in all assignments. The cost of operating our present Quality Control organization runs between five and six million dollars per year.

Within our organization we have a Specifications group, which initiates, suggests or recommends the standards for purity, potency, and identity of each product manufactured. Other groups, such as production, purchasing or sales may also make recommendations affecting the specifications for products, and final approval of each specification represents a plant-wide unanimity of opinion. We also have an Analytical Development laboratory, composed of about fifty individuals, who spend all their time and effort in improving test methods. As an interesting point, while various drug manufacturers have patents and/or confidential methods for the manufacture of various products, there are few secrets in methods of testing. We encourage our scientists to publish in the literature any improvements made in test methods, and we exchange information on test methods rather freely amongst reliable competitors and government regulatory organizations. There are three biological assay departments and two pharmaceutical assay departments to handle the routine testing submitted each day. Finally, we have a Product Security department, which inspects and checks all manufacturing operations, and takes samples of all incoming raw materials, packaging supplies, and final products.

In summary, I would like to outline the major objectives in operating our Quality Control program here at the laboratories. First of all, we recognize that we are in a highly competitive business, and to stay in business, we must produce the best quality drugs available anywhere. In this connection, I would like to point out that the management of this company, either directly or indirectly, has never asked me, as Director of Quality Control, to release to the

market a lot of product I have considered unacceptable for market distribution. I think this is a fine attitude for the management of a drug house to assume, and I appreciate deeply the confidence placed in my judgment. Secondly, we wish to avoid legal action, and, accordingly, we try to do everything possible to protect ourselves by protecting our customers. Thirdly, we must meet the regulatory standards of federal, provincial or state and city governments, and/or the standards of official compendia, such as the United States Pharmacopeia, the British Pharmacopeia, and the International Pharmacopeia, all of which are officially recognized in Canada. Finally, here at Lederle we believe in progress and a better tomorrow.

Henry D. Piersma

APPENDIX "B"

MEMORANDUM

to the

SPECIAL COMMITTEE ON FOOD AND DRUGS
CONCERNING THE SAFETY OF DRUGS

From D. Ewen Cameron, M.D., Director, Allan Memorial Institute, McGill University

July 10, 1964.

1. Drugs, especially those which have been introduced since 1950, have done more to open the doors of mental hospitals than any other form of psychiatric therapy.

2. This has been accomplished by reason of the fact that these drugs are considerably more potent than any previously available to the psychiatrist. This carries with it, naturally, the other side of the coin, namely, that their use in a certain number of instances may carry hazards.

3. All reasonable precautions should be taken to offset these dangers, but if we allow these precautions to run to the absolute, we shall do more harm than good, since we shall deprive innumerable patients of the use of drugs whereby they might recover.

4. Psychiatry is particularly aware of this possibility since, throughout the 18th and 19th Centuries, believing in and being influenced by the beliefs common in the public of that time, hospital psychiatrists consistently set up administrative policies based upon the exceptional case. Hence if a small percentage of excited patients were apt, as they were, to be violent towards the personnel, then all excited patients should be kept in restraint, possibly in seclusion and, only too frequently, in stripped-down and locked rooms. Since depressed patients may commit suicide, then all depressed patients should be treated as potential suicidal risks. Hence in hospitals in which policy was based on the exceptional case, every depressed patient had his tie, his belt, his pyjama string, cords on his window blinds, removed. All depressed patients had their glasses, nail files, pencil sharpeners taken away. It is difficult nowadays to recreate the appalling depths of misery into which thousands and, indeed over years, millions of psychiatric patients were plunged by carrying this philosophy of legislating for the exceptional case to its logical conclusion. It may seem quite incredible to those not familiar with the field, but a woman commissioner of one of the states in the U.S. actually had a mental hospital designed with machine gun towers because of the possibility that violence among the patients might occur. Psychiatrists are therefore perhaps even more alarmed, and properly so, than almost any other category of medical men by the present public response to the availability of more powerful drugs and hence, occasionally, more hazardous drugs.

5. What alarms us most is the evidence that, once more, legislation on the basis of the exceptional case has become apparent as exemplified in the sweeping measures which have been taken by the Food and Drug Administration of the United States. These measures have already taken useful drugs out of operation and—a still more serious matter—they have quite clearly begun to bring about a slowing down of research, both in pharmaceutical houses and

in hospital and university laboratories, thus depriving us of further development of the very drugs which have begun to mean so much to so many psychiatric patients.

6. I should like to pass from these introductory statements to some practical recommendations. In doing so, may I emphasize the basic conviction which affects these recommendations. This conviction is that progress in any field entails risk and the public, fortunately for humanity, has accepted risk as the price of gain. Few surgical procedures, such as tonsillectomies, examinations under anaesthesia, cosmetic procedures or vein stripping are free of a percentage of fatality. These procedures are often purely elective, but the public accepts the risk. If we turn from Medicine to other fields, we must certainly anticipate that the new airplanes presently being designed to fly at Mach 2 and Mach 3 will be established at the price of a number of deaths. No high rise building goes up, no large bridge is built, without accident and death. In all these instances, naturally, safety regulations are built in, but they are not built in to the point where progress is stopped or gravely retarded.

7. The danger of the new drugs is grossly over-estimated. At the Allan Memorial Institute we were among the first to use the new tranquilizing drugs when they became available about 1953. The first conference on the North American Continent upon the use of Tofranil was held at the Institute. We have investigated the clinical use of almost all the MAO inhibitors as they appeared, some of which are still on the market; others have gone. Testing of new drugs has gone on continuously in the Allan Memorial Institute throughout the last decade and we are presently actively engaged in exploring the new anti-anxiety chemical agents and the most recent anti-psychotic drugs. For many years we have had a Section on Psychopharmacology set up in our Laboratory for Experimental Therapeutics. During this time we found a number of side effects such as jaundice, postural hypotension, skin rashes and, earlier on, there were one or two deaths, possibly although not certainly attributable to the drugs. Against this, however, must be placed the number of deaths from suicide which have been prevented, the enormous shortening of mental illness, the gains which cannot be measured in terms of human welfare and happiness.

8. The procedures which I should like to urge are that:

(*a*) all clinical testing should be carried out in approved hospital and university laboratories, rather than through distribution to general practitioners as was apt to be the case a few years ago. It should be emphasized that where clinical testing is carried out in suggested settings, it is frequently possible to find ways of setting up safeguards against potential hazards in a drug. The Allan Memorial Institute, for instance, was the first to suggest that where Largactil was used, a routine weekly alkaline phosphotase should be run to give adequate warning of impending liver involvement.

(b) A method of continuous reporting of adverse reactions should be set up and be required of all physicians, whether in hospital or in general practice, to whom new drugs are issued.

(c) Where a drug is found to be productive of undesirable side effects, it should not be immediately taken off the market but its use should be limited to certain research centres where the possibility of controlling the side effects could be explored, with a view to the possibility of its ultimate return to general use. An excellent example of this is one of the first and certainly one of the best of the MAO inhibitors, namely, Marsilid, which was taken off the market in

this country because of a number of reported fatalities. Now, many years later, we are not so sure that the fatalities were due to Marsilid or to virus hepatitis. In any case, in those areas where its use was continued, the fatalities using modified dosages are either extremely infrequent or do not occur at all.

(*d*) All possible measures should be taken to encourage further research by the drug companies, either within their own laboratories or in the research laboratories of the universities or the hospitals, to press forward with research for drugs to control human behaviour.

9. While animal experimentation is an essential step prior to the testing of drugs in the human subject, it should be remembered that:

(*a*) Animal testing which goes on for several years will not only overload the animal testing facilities of the pharmaceutical houses to the point where very few drugs can be tested, but it will also, through its costliness, still further reduce the number of drugs which the company can possibly test.

(*b*) The simple fact should be borne in mind that animal testing is only a partial substitute for clinical trials. There are adverse responses which may occur in the human subject which cannot possibly occur in the animal and, conversely, there are a number of drugs which are well tolerated by the human subject and not tolerated well by the animals ordinarily used in testing.

10. May I summarize my recommendations, then, as falling into three headings.

(*a*) The fostering of research by the drug companies in their own laboratories and in association with the laboratories of research hospitals and the universities.

(*b*) Clinical testing to be carried out in approved research hospitals and university teaching hospitals.

(*c*) The setting up of long continued systems for the reporting of adverse reactions.

(*d*) The avoidance, by all possible means, of excessive legislation based upon the exceptional case.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 15

TUESDAY, NOVEMBER 10, 1964

WITNESSES:

Dr. K. J. R. Wightman, Professor of Medicine, Banting Institute, University of Toronto; Dr. C. A. Morrell, Director of the Food and Drug Directorate, Department of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21188—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Horner (*Jasper-Edson*)	Prud'homme
Asselin (*Richmond-Wolfe*)	Howe (*Hamilton South*)	Roxburgh
Basford	Jones (Mrs.)	Rynard
Côté (*Longueuil*)	Jorgenson	Slogan
Enns	Macaluso	Wadds, (Mrs.)
Francis	Mackasey	Whelan
Gauthier	Marcoux	Willoughby—24
	Orlikow	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, November 10, 1964.
(20)

The Special Committee on Food and Drugs met at 10:05 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Asselin (*Richmond-Wolfe*), Enns, Harley, Roxburgh, Rynard, Whelan and Willoughby—8.

In attendance: Dr. K. J. R. Wightman, Professor of Medicine, Banting Institute, University of Toronto; and Mr. C. A. Morrell, Director, Food and Drug Directorate, Department of National Health and Welfare.

The Committee attended to procedural matters, and on motion of Mr. Asselin, seconded by Mr. Rynard,

Resolved,—That this Committee pay reasonable travelling and living expenses, as well as a per diem allowance, to Mr. L. L. Winter, President, Empire Laboratories Limited, by reason of his appearance before the Committee on November 6th.

The Committee agred to invite Dr. F. S. Brien of the University of Western Ontario, Chairman of the Special Committee on New Drugs appointed by the Royal College of Physicians and Surgeons of Canada at the request of the Minister of National Health and Welfare in 1962.

The Chairman introduced Dr. K. J. R. Wightman, Professor of Medicine, Banting Institute, University of Toronto, who had appeared before on behalf of the Canadian Medical Association.

Dr. Wightman was questioned on the evaluation of new drugs in hospitals, the use of generic drugs, the Parnate Committee, labelling, side effects of drugs, and related matters.

Dr. Morrell answered questions on tests being carried out on the potency of generic drugs.

The questioning concluded, the Chairman thanked the witnesses for appearing before the Committee, and at 11:00 a.m. the Committee adjourned to 9:30 a.m. Tuesday, November 17th.

Gabrielle Savard,
Clerk of the Committee.

21188—1½

EVIDENCE

TUESDAY, November 10, 1964.

The CHAIRMAN: Gentlemen, we now have a quorum. Before we start with our witness this morning you will recall that our witness last week was Mr. Winter, who came at our invitation. I would like a motion to pay for the expenses incurred by Mr. Winter.

Mr. ASSELIN (*Richmond-Wolfe*): I so move.

Mr. RYNARD: I second the motion.

Motion agreed to.

The CHAIRMAN: I would like to mention to the committee that one proposed witness is Dr. Brien, who was the chairman of the special committee on new drugs, appointed by the Royal College of Physicians and Surgeons, in 1962. This committee heard Dr. Brien at that time. I believe he appeared before us at one of the first meetings of the original committee. It was this committee's work that was responsible for bringing forward the new drug regulations which are now in use.

I thought it might be useful if the committee called Dr. Brien again in order to get some idea how, in his opinion, this has worked out. Would that be agreeable to the members of the committee?

Some hon. MEMBERS: Agreed.

The CHAIRMAN: Gentlemen, I would like to introduce once more our witness for this morning, Dr. K. J. R. Wightman. We have had Dr. Wightman before us before but at that time he appeared as a representative of the Canadian Medical Association. Today Dr. Wightman is here as an individual rather than representing the medical association. He is a professor of medicine at the Banting Institute, University of Toronto. As Dr. Wightman has been introduced to you before I will not bother going into his background again.

Dr. Wightman has not a presentation to make this morning. He came to answer any questions in respect of drug safety and relative matters, as well as their clinical application. So, gentlemen, the meeting is open for questions.

Perhaps I could open the questioning by asking Dr. Wightman to advise the committee how much work is done on new drugs; how many requests he receives to test new drugs, and how this testing is done at the hospital. Doctor, how do you go about evaluating a new drug?

Dr. K. J. R. WIGHTMAN (*Professor of Medicine, Banting Institute, University of Toronto*): Well, as you probably have been told already, there are various stages in drug evaluation. For example, we receive requests to do very intensive studies of brand new drugs, which really have not been studied very much at all before in human beings, in respect of a very small number of patients in a special unit of the hospital, which is called the clinical investigation unit, which is a sort of metabolic ward, especially set up where there is special control of diet, special collections of urine and stools as well as blood, and observations are made of one or two patients at a time. In this way one finds out all one can about what this new drug does to one person in as many ways as possible; in other words, you study what effect the drug has in respect of what it is supposed to do in terms of influencing the patient's psysiology and body chemistry, and so on; and at the same time you investigate all sorts of other things that it is doing which is either not anticipated or not

known at all in order to get some idea of what sort of side effects the drug is having—that is to say, the physiological effects, the effects on body function, apart from the ones you wanted to have. And, you finally want to assess what damage, if any, it is having on any part of the patient's body. That is the first action, and we have a fairly large number of requests for that sort of thing. It is the sort of thing which one cannot do in respect of a large number of drugs at any one time and, of course, the facilities you use for this are already being used to study basic processes of the body in respect of diseases. So, there is a limitation on the amount of this you can do.

Then we come to another stage, that of ascertaining whether or not the drug has a useful action and whether, as a result of these studies, it is worth while applying it to a larger number of patients with a given disease. We take the drug onto the ward and perhaps into the outpatients' department. We use this drug on a carefully selected group of patients who have the disease we want to study and who do not have too many other diseases or other things to complicate the issue. We apply it to a larger number of patients still under very close observation and supervision. Perhaps we have more requests and more facilities for doing that sort of thing. This is a little easier to arrange. The drugs they bring to us for this purpose often have had their preliminary studies done somewhere else, in Europe or the United States, and they are trying to amass this kind of information from as many centres as they can because, again, the number of patients you can study in this way in any one centre is limited.

Finally, there may be a request to do something that is quite broad, to set up a trial for a drug in respect of all the patients who have a certain disease, angina pectoris, for instance. These patients are divided into two groups, one of which you treat with the drug while the others are treated with another drug or some kind of blank medication with no action in it, and you compare these over a long period of time to see what the results are.

Mr. ROXBURGH: What method of selection do you use in respect of these patients?

Mr. WIGHTMAN: Are you referring to this last group I mentioned?

Mr. ROXBURGH: Yes.

Mr. WIGHTMAN: It is done at random. You have this group of, say, 100 patients with angina pectoris. And then we say we will pick those at random, either alternately or by drawing out of a deck of cards or something like that, who will be treated with a particular drug. Some will get the drug and others will not. The patient does not know which treatment he is getting and perhaps the doctors who are supervising do not know either.

Mr. ROXBURGH: It has nothing to do with the advanced stage of disease or anything of that kind?

Mr. WIGHTMAN: No. We try to avoid that.

Mr. WILLOUGHBY: Are these drugs usually submitted by the drug firms?

Mr. WIGHTMAN: Yes.

Mr. WILLOUGHBY: Or, are they chosen by you?

Mr. WIGHTMAN: The drug firms bring them to us and ask if we are interested, and we either say yes or no.

Mr. WILLOUGHBY: Have you any connection with the so-called generic firms?

Mr. WIGHTMAN: In terms of testing, no, not really; they are usually interested in drugs already tested. The only reason they are interested in them is that they are already in wide use.

Mr. WILLOUGHBY: You do not have any way of giving us an opinion in respect of the potency and toxicity of the generic drugs compared with the standard manufactured drugs?

Mr. WIGHTMAN: No. We have had instances where the generic drug had some defect in it, either in the way it was packaged, if you like—that is, in the way the capsule or tablet was made, or in the effectiveness of the drug in respect of what it was mixed with as an ingredient to hold it together. Things of this sort have occurred on occasions. But, we have had no broad experience because really we are not interested in testing these drugs when there is such a demand to test new ones. The drugs which are important to science and society really are the new ones.

Mr. RYNARD: I wonder if Dr. Wightman could tell the committee whether the teaching hospitals use generic drugs?

Mr. WIGHTMAN: They use some, and again I am not in a position to generalize. I will say my hospital has had a limited trial in this respect. In respect of a few drugs we have put out a tender, where we say we want so much of this drug with certain specifications, and companies make bids. As I say, this has been done with a few drugs. I myself have opposed this. But, it has been done in instances, and we then hire someone else, some other company or some other analytical firm to check the sample that is provided to us, and analyse it to see if it meets the specifications we laid down.

Mr. RYNARD: We did have a witness who stated that his drugs were all right, and he was a generic manufacturer. But, he went on to say that some of the others were horrible, and I am wondering how you differentiate between the generic drugs that are good and the generic drugs which are bad.

Mr. WIGHTMAN: Someone has to test them.

Mr. RYNARD: In other words, you then have the cost of testing added to that?

Mr. WIGHTMAN: Yes, and the point is that the tests which are normally carried out are clinical tests in the laboratory; but these are not often backed up with a physiological test. In other words, very often you do not give this new drug or new preparation, as it were, to a group of patients to make sure it is producing the same blood levels and the same effects in the body. This falls by the wayside, and this is what is important. This is where you get into trouble. The important thing is to write down specifications for such a work. You can say that you want the drug to be present in such an amount; you want the tablets to be in a certain way. It is necessary to lay down various positive things. But, there may be things you do not know about that you cannot lay down; there may be certain impurities present in this sample that you do not suspect and cannot designate, to begin with, and cannot test for it. So, you might find that some unsuspecting effect occurs because of this impurity no one looked for because they did not know what to look for.

Mr. ENNS: Is this type of testing required only in respect of materials or drugs supplied from the generic firms or do you need to check out the quality of the drug from any supplier?

Mr. WIGHTMAN: No, we do not feel we do because the suppliers are doing this themselves, and we know that. We know that they realize that their reputation depends on it. We feel, as someone said before, that quality has to be built in; it cannot be tested in. I think that is a good way of putting it.

Mr. ENNS: Is there an increasing occurence of faulty manufacture of drugs in terms of the volume which is supplied to your hospital, or do you find that this is not the case?

Mr. WIGHTMAN: It is not a problem. We are not buying large amounts of the generic kind of thing. But, the other thing that worries us is the breaking of patents. This is the thing we feel that is wrong. If a drug really is a drug whose sole legal, in this sense, source, should be one company, then we do not

like the idea of going and buying it from someone else who really has no right to make it.

Mr. ENNS: It always comes back to this question of registry, certification or licensing the manufacturer and perhaps this is not the only way of getting control over the manufacturer of pharmaceuticals. Do you feel perhaps this would aid in the standardization of manufactured pharmaceuticals?

Mr. WIGHTMAN: It would aid it; whether it would completely solve the problem would depend on the facilities in force. It is all very well to make legislation but you have to have ways and means of enforcing it to make sure that the laws are being obeyed. It is most important that the food and drug directorate should know who is making and marketing a drug, and no one should be able to do this without them knowing. They should not only know what is going on but they should be in a position to see how it is being done and enforce certain standards. The other aspect, of course, is that it still comes back to the profession. None of these drugs we are talking about can be sold or reach the market without the doctors ordering them, and this implies that the medical profession in general has the responsibility also to exert some discrimination and to inform itself about some of these things, so far as it can.

The CHAIRMAN: If I could ask a question. You have been a practicing clinician for some years. You were the chairman of the committee on parnate. Is there anything in the regulations of which you are aware that you think this committee should consider changing. Is there any way that the government can change the regulations to make your job easier or which would make the drug safer without actually causing any restrictions on your practice? In other words, would it be your wish to have these regulations changed in any way?

Mr. WIGHTMAN: In respect of the regulations, I have always felt that what really counts is the way the regulations are enforced. You can write regulations in very very broad terms or write them in extreme detail but what counts is the way they are put into effect. Offhand, I cannot think of any particular regulation that is bothering me nor can I think offhand of any enforcement policy that is bothering me at the moment. I think this is something that has to be kept under continuous review. I think that in writing regulations or enforcing them there is a tendency to oscillate between very strict and a little bit lenient according to what is happening in the community. I think the main thing about any regulation or enforcement policy is that it should be under continuous review and that it should be flexible.

The CHAIRMAN: I have another question which particularly refers to the parnate committee.

Mr. WIGHTMAN: If I could interrupt, may I say this was a committee on mono-amine inhibitors; it was not just the one drug that was considered by this committee.

The CHAIRMAN: In respect of that committee, I was wondering if there has been some criticism. As you know, it took a long time to set up the committee and get a report. I am wondering if you think this type of committee should be a permanent standing committee?

Mr. WIGHTMAN: I think this is an interesting example of what happens in committees. The members of that committee worked very hard. I am not speaking for myself but for the other members of the committee. They worked together very well. I think they all felt they learned a tremendous amount from the experience. But, I think it would have been quite possible to sit down the first day and to say: "What do you think we ought to do about these drugs?" And, I think we would have received practically the same answer as we got on the last day. But, on the other hand, the committee had to be in a position to justify certain things in its own mind before giving the department or the directorate the decision.

In other words, they had to marshall and examine the evidence and come to a conclusion about some things in respect of which no conclusion really can be made. The whole thing was rather astonishing to me. I am not quite sure why I was asked to be on that committee because, certainly, I am not interested in these particular drugs in a practical way. Perhaps it was because I am interested in the sort of broad generality of the problem. But, as I say, to me it was astonishing to find that there is still in foreign circles a very wide difference of opinion as to the real value of this family of drugs, their real place eventually in therapeutics and so on. There were some people who had used the particular drug in question a great deal and were very impressed by it, and there were others who said they never used it. These people said: "It does not matter to me what they do about this drug." This was a bit of an eye opener. Again, there was the question of comparing drug treatments with other kinds, like electro-convulsive therapy and so on.

It was obvious that this really had not been done in a scientific way and that no one has yet compared the value of these two treatments, their effectiveness, their risk and all these things in such a way that you could sit down and say: "Here is the evidence; it is obvious these drugs are suitable for use in 25 per cent of this group of patients, 50 per cent, 75 per cent or 100 per cent." So, we very soon ran into areas of what you might call ignorance, as a result of which it made it quite difficult to come to a rational decision on what we thought we could define, as it were, and of which we really could feel convinced about. We went through a very large mass of material. We read hundreds of articles about these drugs. We even had manuscripts of papers that had not been delivered, in order to bring us up to date. We talked to a great number of people about the drug and about their experience, and that is what took so much time. This is what happened with the special committee which was especially interested in a problem which dealt with a limited field with limited objectives.

We were asked to make a decision on one problem. When one notes how long that took and how much work that involved and so forth, and then when one contemplates what would happen if this were a standing committee, the pace at which they would have to work, the enthusiasm and energy to be expended and the time available for this sort of thing, one would think it might gradually dwindle, and might work slower and slower, if it were a standing committee, which had broader objectives. So, there may be a place for some kind of nucleus committee to help organize the special projects that come up. I think probably the best return or the best function might be to have a series of special committees about special problems because you could say to them: "This is your problem; get down and work at it as hard as you can because when you are finished you are through." Theoretically, this is the idea. There is a need for a study of the function of committees, as it were, in that sort of a sociological problem.

Mr. WILLOUGHBY: What I have to ask Dr. Wightman probably is not quite in order but in view of the fact that you are a witness in a special field may I put this to you. We did have a witness last week who represented generic drugs. I understand that the province of Ontario has instituted a laboratory for the investigation of drugs. This laboratory will carry on work to ascertain the purity and potency of these things. Is this laboratory being brought into being mostly because of the fact that the generic drugs are the ones that are being investigated? As you have said, you do not consider it necessary to check the potency of the standard drugs you are using because those companies which produce these have laboratories which conduct their own standardization tests. If this is so, it would seem to me the generic drugs would be the only ones which should have these tests. Is that your impression?

Mr. WIGHTMAN: I cannot answer that question. I really do not know what laboratory you are talking about. The Ontario Research Foundation has tested

some of the drugs in connection with our hospital because they have special facilities for doing this. Some of the other tests are done in private laboratories.

Mr. WILLOUGHBY: I understand the department of health in Ontario is putting up a large laboratory to test out these drugs in respect of their potency. Are you not familiar with this?

Mr. WIGHTMAN: I am afraid not.

The CHAIRMAN: Perhaps Dr. Morrell, who is sitting behind you, could answer your question.

Mr. WILLOUGHBY: I would be pleased if he could answer it.

Dr. C. A. MORRELL (*Director, Food and Drug Directorate, Department of National Health and Welfare*): I do not know that there is a laboratory in the attorney general's laboratory in the province of Ontario that is carrying out tests for the provincial department of health on drugs that they are ordering for the mental hospitals and maybe for other hospitals that are under the jurisdiction of the government. They do analyse samples from the batches that are submitted to the government, and if they do not meet certain specifications they are rejected.

Mr. ENNS: Could I follow up this question to Dr. Morrell? If the suppliers in all cases continue to be the recognized producers, we heard from the witness this morning that they feel that follow-up testing does not seem to be necessary. However, would the laboratory testing be necessary? I am wondering, if this is meant to cut down the cost of the drug whether the laboratory testing may offset it.

Dr. MORRELL: I am speaking here out of my field but I do feel that an arrangement was made to make sure that the drugs they did receive were up to the specifications, and they do send out tenders. Anybody can tender who wants to, so they are comparing so-called generic drugs with other types of drugs and they want to make sure that these drugs meet these specifications that are laid down.

Dr. WIGHTMAN: One of the things we find is that if for any reason we are dissatisfied with a batch of drugs we receive from a reputable firm, our first recourse is to go to the firm and say "Look, there is something wrong with these capsules or tablets". They take them all back and give us a new lot. In other words, there is no problem about losing money on this. This is one of the things that our pharmacists like about dealing with these firms because they stand behind their products. The other point is that if it comes to our notice that something strange is happening, our recourse is to complain to the food and drug directorate and say to them "Something is wrong here and would you look into this for us?" They answer specific complaints. It is only when you are trying to anticipate or obviate trouble that you do this pre-testing. You buy the material, you have it tested for yourself, and then you use it. When you feel that you are not sure this has already been done by the manufacturer, you go through this process.

The CHAIRMAN: Could I ask you a question? You mentioned that you have had some trouble with generic drugs. What sort of trouble did you have?

Dr. WIGHTMAN: There was one instance where a drug should have been in a sealed capsule because it would take up water and the powder in it would then solidify and would either become altered chemically or would not be absorbed completely. We found the capsules were deteriorating in the bottle. That is one example. I think there were other examples where they felt that they were not getting as good blood levels as they thought they should get. In a given dose there was something that was interfering with the absorption of the drug even though the test was indicating that the drug was there. However, it was not

getting into the person's bloodstream properly. These are the two examples I know of.

The CHAIRMAN: Then, as a result of that, you do not use generic drugs in your hospital without getting them tested independently?

Dr. WIGHTMAN: I think it was an experiment that was tried. We agreed to try it with a limited number of compounds. I cannot tell you how many were found faulty. Certainly there has been no further expansion of this experiment and I think they have given up some of the drugs that they did have originally.

Mr. WILLOUGHBY: In other words you have found that a fair percentage of the generic drugs have not met the standards?

Dr. WIGHTMAN: I can only say it has occurred; I cannot say that a fair percentage has not met the standards.

The CHAIRMAN: Could I ask a question on labelling? I think there has been some evidence here in the committee that it was felt by some people that every drug should have on its label the chemical name of the ingredient involved as well as the complete list of ingredients, particularly as it relates to patent medicines where sometimes all the ingredients are not listed and in case of an accident the doctor does not know what exactly he is dealing with. What is your feeling on labelling?

Dr. WIGHTMAN: It would be quite impossible to do so with some of the patent medicines because they may have ten or twelve ingredients. In other words, you would have to have them in very large bottles or indicate the ingredients in such fine type that you could not read it. I think there is very little justification in our present day and age for having secret remedies; in other words, patent medicines the contents of which are not known. The question of labelling all the ingredients seems to me to add complexities which are perhaps unnecessary because I think that one can usually anticipate which ingredients need to be specified and which ones are likely to produce harm in the case of an overdose. That is already provided for in the patent medicine act. There is a list there which specifies that certain ingredients can only be present in certain drugs in such and such amounts, and they must be designated. I think this part is fairly well looked after.

One of the recommendations of the M.A.O. Committee was that the bottle of medicine that the patient gets from the pharmacist or the box of tablets should have on it some indication of what he is getting, not necessarily the name of the drug but the fact that it contains an M.A.O. inhibitor, because nowadays patients move around so much and go from one doctor to another doctor so much that it is impossible to keep track of them. We found that there was a list of about 20 drugs which a patient should not take at the same time as one of the M.A.O. drugs. It is an astonishingly long list. It is obvious that if a new doctor prescribed a drug for a patient which did not go well with the other he is taking because he was ignorant of the fact that the patient was taking the other drug, then he was getting into trouble which could be prevented. The same thing is true in an emergency situation, if a patient in an accident was brought into the emergency department and was given a drug in the treatment of his accident which would make him ill because he was taking other drugs and no one knew about it. We felt that if the patient knew, and if the drugs that he had in his possession had some label on them which would indicate to the new doctor that was involved in the situation that the patient was taking it and therefore this contra-indicated the use of a certain list of other drugs, it would be very helpful. We had an example of this.

I do not know whether it would interest the committee to hear of the case of a man who was found slumped over the wheel of his car in the Toronto area. He was brought into the hospital and it was found that his blood pressure was exceedingly high. They found out fairly quickly that he was taking one of these

antidepressive drugs, the M.A.O. inhibitors, and that in addition he purchased a cold remedy at a drug store to treat the cold he was getting. These two preparations working together had caused this great rise in his blood pressure and had perhaps produced a small hemorrhage in his brain. All that they could get out of the man was that he had a terrible headache, so they gave him some Demerol, which was the wrong thing to do as it was contra-indicated in the presence of this M.A.O. inhibitor. His blood pressure immediately came down and practically disappeared and he went into shock. The next thing to do was to give him a drug such as adrenalin and his blood pressure then shot up. That also was wrong. A whole series of misadventures happened to this patient because of what you might call pharmacological incompatibility among this group of drugs, drugs that do not mix well, not in the bottle but in the patient. This aspect of labelling is terribly important with certain drugs because we are finding more and more combinations of drugs producing ill effects.

The CHAIRMAN: This brings up a question which I would like to ask if I may. I have always been horrified at one thing that happens in hospitals but I have never seen any ill effects. If a doctor orders medication, say, three times a day and he happens to order six different kinds of medication including an antibiotic, a sedative, a tranquilizer and a vitamin pill, so often these six medications at the nursing station are dumped into the basket and the patient has to take all six medications at the same time. I was wondering what your feelings are on this and if there has ever been any evidence of trouble from these drugs being in the stomach all at the same time.

Dr. WIGHTMAN: Yes, occasionally. There is a very interesting study going on in the John Hopkins Hospital where they have an IBM computer in their dispensary, and they are analysing very carefully what the doctors are ordering. I think the average number of drugs that the average patient gets in that hospital is something like 11, and there were some patients who got 30. This was a rather astonishing figure. I am not certain of the percentages but I think something like 5 per cent of the patients that were admitted to the hospital were admitted because of a drug reaction of one sort or another, and another much larger percentage of patients developed some sort of adverse reaction to the drugs while they were in hospital. The accurate results of this survey are available if you wish to have them. It has been suggested that in any 1,000 bed hospital, 50 beds at any time are occupied by patients suffering from drug reactions. This is not a small problem.

The CHAIRMAN: Are there any other questions from members of the committee?

Mr. ENNS: I cannot think of a question at present but the headlines on the British antibiotic come into my mind. However, I do not think it has been in use in Canada.

Dr. WIGHTMAN: It has been tested at the Sick Children's Hospital in Toronto for over a year or a year and a half. The man who is in charge of that testing, whose name is Fleming, came to me almost a year ago and asked me "How would you like to undertake a joint trial of this drug? We could appoint a fellow between us, the drug company could pay for it, and he would work in both hospitals so that we could study its effect on a broader range of persons, on both adults and children". I agreed to this and said it would be fine. Nothing happened. I then asked him what had gone wrong and he said there was a question of a certain toxic manifestation that had slowed things down. It was either a matter of the dosage being too high or else there was some impurity or something about the drug that they did not know about yet so that they were not quite ready to embark on a large scale trial. I suppose he then just forgot about it.

I think it is a very interesting drug not only as an answer to our prayers, as it were, but because it represents the first member of a new family of antibiotics. I think perhaps you are aware of the fact that penicillin has now been modified in such a way that there are thousands of penicillins. The number that is in use has been increased to I suppose eight or ten. These new ones have special attributes that make them useful in special situations. It is hoped that this new drug can also give rise to a family of antibiotics which also may have a very wide application, particularly in patients who are allergic to penicillin. This is one of the problems, to know what to give to a patient who is allergic to penicillin. Penicillin is still the most potent of the antibiotics against a particular list of bacteria. One can find substitutes for it but they are not as good in terms of rapid action.

The CHAIRMAN: Is this drug related to penicillin?

Dr. WIGHTMAN: It is related in a way but it is not related in the sense that its structure is comparable. It is both related and different, if you like. It is sufficiently different from penicillin in that a person who is allergic to penicillin is not allergic to this drug.

Mr. WILLOUGHBY: Has it any effect on penicillin-fast organisms?

Dr. WIGHTMAN: Yes. The penicillin-fast organisms in general are so because they produce an enzyme that destroys penicillin, and this enzyme does not have any effect on this new antibiotic. However, there is a list of enzymes that destroy the new one, so there is always a joker in the pack.

The CHAIRMAN: Are there any other questions, gentlemen?

I think the last time you were here, or in subsequent evidence, there was some question about committees being set up in hospitals where doctors could report the side effects or the bad effects of a drug, and this would be related to the food and drug directorate. Has this been done in your hospital?

Dr. WIGHTMAN: One man has been appointed to work in our hospital, and another hospital has set up a sort of pilot surveying. We have a pharmacy committee of course which is alerted to the problem of any toxicity, but we want this man to go looking for the 50 cases that we have and find out who they are and what they are suffering from so as to give us some idea of what the problem amounts to and what the particular danger spots are. So far we have not got to the point of establishing a committee in each of the teaching hospitals, but I think that if this man does this work successfully and if he arouses sufficient interest, and if he finds things that are startling enough, then the hospitals will do this of their own volition and try to feed material to him as quickly as possible.

I think the crux of the matter is to have this identified, codified and fed into some central place as quickly as possible. There are many reactions that patients have of which you cannot be quite sure. You want to know whether this was really a toxic reaction to the drug or something funny about the patient or something funny about his disease. If a whole list of people all across the country say there is something funny going on in regard to this drug, it is pretty certain that someone will find some evidence about which we can be sure, but if things happen in isolation, without anybody saying anything about it, it may take a long time for the gossip, so to speak, to get around. In the preliminary stage, when some unusual reaction happens with some new drug, it takes quite a lot of time to amass enough evidence to have something more than a suspicion. You do not like to report a suspicion in the literature or write an article and say "A funny thing happened on the way to the forum", but you want to have enough evidence when you have something to prove. In order to do this you must pool information, if you want it to happen soon. I think this is the aim of the measures that have been set on foot in this country.

The CHAIRMAN: Are there any other questions?

Mr. WILLOUGHBY: The audience may not have been very large but all this was very interesting.

The CHAIRMAN: Yes. I would like to thank Dr. Wightman for coming. The dwindling size of the committee was not really due to the fact that your testimony was not valuable and interesting but to the fact that there are too many committees competing for the same number of bodies. This presents a problem. I would like to give our thanks to you for coming here. You have answered a lot of questions brought up by other testimony, and we appreciate your visit very much.

Dr. WIGHTMAN: Thank you for asking me.

The CHAIRMAN: The meeting will be adjourned until one week from today.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 16

TUESDAY, NOVEMBER 17, 1964

WITNESS:

Dr. H. A. Showalter, Chairman of the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers, Distributors and Agents, Chemicals Branch, Department of Industry.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21266—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

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Macaluso
Mackasey
Marcoux
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Wadds (Mrs.)
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, November 17, 1964
(21)

The Special Committee on Food and Drugs met this day at 10 o'clock a.m. The Chairman, Mr. Harry C. Harley, presided.

Members present: Mrs. Jones and Messrs. Armstrong, Côté (*Longueuil*), Enns, Harley, Howe (*Hamilton South*), Mackasey, Mitchell, Roxburgh and Willoughby. (10)

In attendance: Dr. H. A. Showalter, Chairman of the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers, Distributors and Agents, Chemicals Branch, Department of Industry.

Before examining the witness, it was moved by Mr. Willoughby, seconded by Mr. Armstrong, and

Resolved,—That the Committee request Dr. F. S. Brien of Western University to appear before it on November 24, and that reasonable living and travelling expenses as well as a per diem allowance be paid in connection with his appearance before the Committee.

The Chairman introduced Dr. Showalter, and suggested that he read his presentation in respect of the drug procurement standard for Canadian government purchasing, copies of which had already been distributed to the members of the Committee.

Dr. Showalter then read the first part of the presentation, and on motion of Mr. Willoughby, seconded by Mr. Mackasey,

Agreed,—That the second part of his presentation, "The Canadian Government Specifications Board Standard on Manufacture, Control and Distribution of Drugs," be printed as an appendix to this day's proceedings. (*See Appendix "A"*)

Dr. Showalter was questioned.

It was agreed to recall Dr. Morrell to elicit more information on certain questions that pertain to the Food and Drug Directorate.

The Chairman thanked Dr. Showalter for the information supplied to the Committee, and at 10.55 a.m. the Committee adjourned to 9.30 a.m. Tuesday, November 24.

Gabrielle Savard,
Clerk of the Committee.

21266—1½

EVIDENCE

TUESDAY, November 17, 1964.

The CHAIRMAN: Lady and gentlemen, we now have a quorum. Before we start examining the witness today I would like to have a motion to pay for the expenses of Dr. Brien of London, who is to appear before the committee next Tuesday. Dr. Brien was chairman of the special committee on new drugs which was appointed by The Royal College of Physicians and Surgeons of Canada at the request of the Minister of National Health and Welfare in 1962. Some of this committee's recommendations were followed in respect of the recent changes, and the feeling of the committee was that we should have him back to discuss the changes that were made and to ascertain how these changes are working. Could I have such a motion?

Mr. WILLOUGHBY: I move that the committee request Dr. F. S. Brien of Western University to appear before it on November 24, and that reasonable living and travelling expenses as well as a per diem allowance be paid in connection with his appearance before the committee.

Mr. ARMSTRONG: I second the motion.

The CHAIRMAN: All those in agreement? Opposed?

Motion agreed to.

The CHAIRMAN: Mrs. Jones and gentlemen, we have with us this morning Dr. Showalter, who is with the chemicals branch of the Department of Industry.

Dr. Showalter has his Ph.D. in chemistry and he is here this morning really as chairman of the interdepartmental advisory board on standards for pharmaceutical manufacturers. I think most of you probably have received and read his three page presentation. But, as it is short I think it would be worthwhile to have him read it, and then I will open the meeting for any discussion.

Dr. H. A. SHOWALTER (*Chairman of the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers, Distributors and Agents, Chemicals Branch, Department of Industry*): As the Chairman has requested, I will read my presentation in respect of the drug procurement standard for Canadian government purchasing.

This is an outline of the history and function of standard 74-GP-1 which is used for selection of suppliers of pharmaceutical products to the government of Canada, and the body known as the interdepartmental pharmaceutical board which administers the standard. Copies of 74-GP-la have been furnished in both languages.

History—Pharmaceutical products have been required for use by various Canadian government departments for many years. The principal users have been national defence, veterans' affairs, and national health and welfare (including emergency health services). While purchasing methods have not been entirely standardized among the various departments, the general practice has been to invite tenders from interested Canadian firms and to accept the lowest tender whenever there was a choice. Descriptions of the items to be tendered have not been worked out co-operatively among the departments, but in national defence at least there is a full catalogue of product specifications against which supplied material is inspected as to quality.

There has been dissatisfaction for many years in these various departments with the general level of quality of delivered pharmaceutical supplies. Many

faults and deficiencies were found in the products when submitted for inspection, with resulting delays in delivery. Many of the suppliers seemed bent on providing no better quality than the minimum permissible under the terms of the contract. Quality of workmanship or what is known in the industry as "pharmaceutical elegance" was often lacking. After delivery there were many cases of poor storage life, and on some occasions shipments were found to be heterogeneous, that is, not entirely identical with inspection samples. The general effect of these factors was to make procurement slow and more expensive, and to undermine confidence in the governmental users.

The problem appeared to be two-fold. First, the practice of competitive bidding on price seems to have resulted in obtaining supplies mainly from the least competent or possibly the least scrupulous suppliers. Certain few firms of questioned performance were obtaining a large share of the business. Second, the task of preparing specifications which would be technically and legally complete was almost impossible. The reason for this is that technology has been changing so rapidly that there has been no agency of government or of any other body devoted to or capable of such a task.

It may be asked, why is inspection of products before delivery unable to ensure quality of pharmaceuticals? Of the several purchasing departments, only D.N.D. had its own inspection agency, and this was kept very busy at the task. Others depended upon the food and drug directorate, which was able to conduct tests only at infrequent intervals. Many of the supplying firms did not have adequate quality control of their own, and others in many cases have been known to ship unsatisfactory goods though it had been passed by their quality control. The inspector's job contains two principal difficulties, first that for many of the modern complex drugs, chemical analysis methods have not been developed, even by the makers, in time for this use. Secondly, stability information cannot be obtained by analysis, and must await longer storage. It is doubtful that these problems will ever be fully solved, and some means is needed to limit purchases to products of those firms which clearly maintain a good competent operation and a highly responsible attitude.

This was the state of the problem in February, 1960, when a group of national defence officials met to see what could be done. Their discussion included a proposal to establish qualified products lists for drugs, but this was believed to be prohibitive because of the large number of products and their rapid obsolescence in favour of new products. Some time after the D.N.D. meeting, a series of discussions was held with the other interested government departments, which resulted in an arrangement with the food and drug directorate. That agency agreed to help write a description of an acceptable standard of drug manufacturing operation, and to conduct an inspection of all interested manufacturers. The period from September, 1960, to December, 1963, was spent in the preparation of the Standard, notification of the entire Canadian pharmaceutical industry, and inspection of all firms which expressed an interest. During this same period, the Standard was subjected to several revisions. This effort coincided, as it happened, with the development of a new and very similar standard by the food and drug directorate for their own use, and this circumstance made it possible for that directorate to use its inspection operation for its own purposes as well as for the purpose of establishing a list of qualified suppliers to government.

Standard 74-GP-1 was issued through the good offices of the Canadian government specifications board, who established a committee for the purpose, comprised of representatives of the interested departments and of the interested industrial and trade associations. Of the latter, representatives were sent by the Canadian Pharmaceutical Manufacturers Association, the Canadian Proprietary Products Association, and the Canadian Pharmaceutical Association. The present

form of the Standard has, therefore, the general concurrence of those groups, though it should be noted that the Canadian Pharmaceutical Association has persistently argued that this Standard should apply not only to those who would supply government, but also to those who would supply the public.

If I might, I would like to slightly amend this statement. Last week I had a discussion with the manager of that association who informed me that this is not quite correct; that is, they would like to have access to our list of approved firms so that their members in their purchasing could select their suppliers in the same way the government does. I think that slightly changes the intent of that statement.

The food and drug directorate replied to this argument that present legislation gives them no authority to implement this suggestion; that is, to make it mandatory to all those who supply drugs to the public.

The position of the purchasing departments has been that whereas the public has free choice of all the brands and sources of drugs on dealers' shelves, government users have no choice but to use the products kept in government stores, and that these must be purchased by a process involving competitive tender.

After the inspection of drug firms was largely completed, it became obvious that there was a need for administration of the standard and the relations of government with the industry in respect to this newer approach to Government procurement. In January, 1963, a board was formed of representatives of the Departments of National Defence, Defence Production, National Health and Welfare, and Veterans' Affairs, and official approval was obtained shortly afterwards from those departments. The function of the board is to notify industry of the need to comply with the Standard in respect to government procurement, to request individual inspections by the food and drug directorate, to make decisions on inspection reports, to maintain a list of firms which are found to conform and distribute the list to the government agencies using it. The board also corresponds with the firms in connection with inspection, and from this general experience, it also makes recommendations from time to time to the Canadian government specifications board as to amendments to the Standard.

A summary of the results of the inspection operation is as follows:

Firms receiving first letter and follow-up letter, September, 1962	140
Firms inviting inspection	86
Firms replying "no interest"	19
Firms not responding	35
Present list of conforming firms	63

Current Situation—Since 30 June, 1964, the participating departments have been purchasing their pharmaceutical supplies only from firms listed as conforming with the Standard, with the exception that in certain cases commodities can only be obtained from non-conforming sources. As of this date reports indicate that these departments are entirely satisfied with the system and believe that it represents a substantial advance over the previous period. Of course it is possible for a firm which conforms with the Standard to produce unsatisfactory products. It is also true that some time must elapse before results can be judged. However, the board believes that the application of the Standard has had considerable effect on the industry. The first round of inspections disqualified all the inspected firms. Of these a very substantial number have now made significant and in some cases, costly improvements in their plant, equipment, and methods in an effort to comply. In some cases, projected new construction was altered for the purpose. The industry has generally become more

conscious of the need for these improvements, and of the obligation they undertake when they accept a government contract. There has been no contention that the Standard is inappropriate or unduly severe.

The board hopes to continue its activity as long as it is needed, but no longer. It is prepared to revise its methods and the Standard whenever suitable ways can be found to do so. It has one serious problem yet to solve, namely, that some pharmaceuticals and semi-finished materials are imported from foreign sources inspection of which to our Standard is difficult or impossible. Efforts to deal with this problem are now under consideration.

Thank you, Mr. Chairman and gentlemen.

The CHAIRMAN: Thank you very much, Dr. Showalter.

The second part of the presentation is the Canadian Government Specifications Board standard on Manufacture, Control and Distribution of Drugs. I think everyone has a copy. Is it the feeling of the committee that this should be printed in the Minutes of Proceedings and Evidence?

Mr. WILLOUGHBY: I so move.

Mr. MACKASEY: I second the motion.

Motion agreed to.

The CHAIRMAN: The meeting is open for questions, gentlemen.

Mr. ENNS: The initial reaction to reading this material is one of almost shock that such a condition should really be prevailing in an industry which is designed to safeguard the nation's health. The main purpose of pharmaceuticals is to improve our health. We have heard from the witness that competitive bidding tends to draw supplies from the less able producers. Towards the end of your statement you said that after the regulations were agreed on the first round of inspections disqualified all the inspected firms. The firms began to get worried, and obviously this has had a very salutary effect on the industry.

Is there any way of insuring that the other half of the producers will be brought in? In your table on page 3 you mention that 140 letters were sent and 63 are now conforming firms. Are the letters being followed up in an effort to bring in this big bulk of the industry which still is not conforming?

Mr. SHOWALTER: Mr. Chairman, the firms which are not on the list at the present time are energetically trying to conform. As they feel they are ready for the inspection they write to me and I arrange the inspection. This is going on currently and gradually an increase in the list is being accomplished.

Mr. ENNS: But these people still are supplying their products somewhere. Is the board concerned over the standards of these suppliers while they still are listed as not acceptable for membership and certification?

Mr. SHOWALTER: Mr. Chairman, I should explain that this effort is purely for government procurement. That is the purpose for which this was started. I would not object if the effort that has been put into this could be harnessed for other purposes but I, myself, at present cannot undertake to do so.

Mr. ENNS: But, it does not necessarily follow that the product is substandard; it is just that some features of their procedure do not meet the board's standard. I think, perhaps, I have contradicted myself in what I have said. But, you were not able to consider a certain manufacturer as conforming with the standard which the board has set out but yet they are supplying large quantities to the public. Does it not follow then that the board should have some concern about the product being turned out under these conditions?

Mr. SHOWALTER: Well, of course, it is not the board's business to consider that problem. But, speaking as an independent citizen, I think I would say that is a matter of concern.

Mr. ENNS: Well, I am speaking as a consumer myself because I am not a medical person. I am very concerned from this point of view.

The CHAIRMAN: Would you proceed, Mr. Mackasey.

Mr. MACKASEY: Further to Mr. Enns question and the reply given, I find the figures set forth on page 3 are quite revealing. Of the 86 firms inviting inspection only 63 of these are now suppliers: that is, 23 failed to meet the inspection. Was this inspection carried out by you or by the food and drug directorate?

Mr. SHOWALTER: By the food and drug directorate.

Mr. MACKASEY: Then, you are not the person to ask what the food and drug directorate did in respect of these other 23. Mr. Chairman, I would like inquiries made as to what happened to the 23 firms who were unable to meet the government's requirements.

The CHAIRMAN: Well, Mr. Showalter can only answer questions which deal with his own immediate department.

Mr. SHOWALTER: I have reports on all the firms which conformed and those which did not. I have in a confidential file the reasons they did not conform. I wonder if I could go a little farther and point out that in the standard of conformity is determined not by a sort of go, no go, principle, as with a gauge, but by a rating, and there are maximum ratings provided for each of the paragraphs or major divisions of the requirements. And you add up the score, if you are the inspector, and determine whether that score is according to this standard. A 90 per cent mark is required for a pass. This becomes a matter of judgment. It is not easy to be perfectly consistent in respect of the judgment made in this regard. They do their best but, in some cases a reinspection is necessary to bring the firm into conformity.

Mr. MACKASEY: I congratulate you and your department for having the initiative to do this and, obviously, it required a great deal of co-operation with the food and drug directorate. However, we are concerned with safety in general and not only so far as government departments are concerned. We are concerned that there were 23 firms which could not meet your standard when this report was made up.

Now, at the present time there may be more or there may be fewer which, conceivably could meet the standards of selling to the gullible public. But, this is one of our main concerns. As we have noted, the food and drug directorate rendered a decision with regard to an inspection of these 86 firms, of which only 63 could pass, and I would take a dim view of the food and drug directorate if they did not prohibit these other firms from selling to the general public. In my opinion, if they are not good enough to sell to the government they are not good enough to sell to the general public. I know this, to which I am making reference is not your role; it concerns the food and drug directorate. And, I am not saying these things by way of chastisement. But. Mr. Chairman, I would like to know what has happened to these 23 specific firms which could not pass the test for the government; whether they were permitted to carry on selling to the public or whether the food and drug directorate should not kill two birds with one stone.

Mr. MITCHELL: Would these firms be generic drug suppliers?

Mr. SHOWALTER: I think most of these firms supply both kinds of drugs, by generic names, which concerns the largest number of government purchases, and by brand names of their own.

Mr. MITCHELL: Does that apply to both accepted and rejected firms?

Mr. SHOWALTER: That applies to both rejected and accepted firms.

Mr. MITCHELL: I do not believe the accepted firms would have both generic and so-called trade names.

Mr. SHOWALTER: In answer to that I can say that when I was engaged in the inspection of drugs for the Department of National Defence a number of firms, both those on the list and those not on the list, were engaged in supplying to the department, drugs under generic names. Now, I cannot speak beyond that, but I do know that was true.

Mr. MITCHELL: It is correct that some of the drugs have a generic name but, in my opinion, many of these firms with which you would be dealing would be using their own trade names.

Mr. SHOWALTER: Well, generally speaking, the departmental purchasing is done by generic name. In cases where the department purchasing people—that is, those who determine what is to be bought—feel that they cannot accept any alternative but a certain brand product there is an arrangement in departmental purchasing for that branded product to be specified, with no substitution to be allowed, and this requires high level approval within the department. But, this is in respect of special cases. Normal purchasing is by generic name.

Mr. MACKASEY: Mr. Chairman, I am very anxious to get a report on what happened in respect of these 23 firms which could not pass the inspection and, secondly, a report on the other 54 which did not answer the letter. I would like to know when was the last time that their premises were inspected under a regular inspection by the food and drug directorate?

The CHAIRMAN: Mr. Mackasey, only the food and drug directorate officials could answer that question.

Mr. MACKASEY: But, could the committee get a report in this connection? Could Miss Savard, our clerk, obtain a report so that we would have this information available?

The CHAIRMAN: I am sure Dr. Morrell would return to this committee to answer any further questions in this regard.

Mr. MACKASEY: I move that Dr. Morrell be summoned back to explain precisely what has happened to these firms, if anything.

The CHAIRMAN: We are dealing here with two separate things.

Mr. WILLOUGHBY: Actually, I think Mr. Mackasey's questions relates to two matters: What happened to these particular firms and, what is more relevant, what has happened to the drugs which have not come up to standard. It would be of interest to know whether or not they have been disposed of or what has happened to them. Have you any information in this connection?

Mr. SHOWALTER: Are you referring to the products of these firms not on the list which supply the public market?

Mr. WILLOUGHBY: Yes. I am referring to those drugs which have not come up to standard.

Mr. SHOWALTER: In respect of purchases by the government, if they have been delivered they are returned to the sender.

Mr. WILLOUGHBY: But, so far as the public is concerned they are still available?

Mr. SHOWALTER: That is true.

Mr. WILLOUGHBY: I know you will not be able to answer this question in exact figures but are many of the so-called standard reputable firms' products found lacking in respect of coming up to the qualifications which you insist upon?

Mr. SHOWALTER: I can say that when I was in inspection work for national defence quite often the product of some highly reputable firm was found to be not in conformity with the purchase specifications.

Mr. WILLOUGHBY: As you know, a great many of these firms have their own research departments. Are you familiar with them?

Mr. SHOWALTER: The larger firms have very elaborate systems of quality control and most of them have fairly good research facilities.

Mr. WILLOUGHBY: Are these firms to which you have made reference included in that list, and do they have such facilities?

Mr. SHOWALTER: Yes.

Mr. ROXBURGH: Mr. Chairman, I have a supplementary question. In respect of drugs which the government is purchasing from these so-called qualified and high class firms is it possible that because these drugs are being purchased by the government certain firms would try to get away with the minimum requirements when the same product which was sold to the public would be of a higher standard.

Mr. SHOWALTER: From the experience I have had in this connection I think that that is the case.

Mr. MITCHELL: Would not the price govern it to an extent?

Mr. SHOWALTER: That is true. Government prices often are much lower than non-governmental prices.

Mr. MACKASEY: If I could sum up, it is your feeling that the standard of drugs in general delivered to the government is not quite as good because of the price factor; in other words, there is a direct relation between cost and quality?

Mr. SHOWALTER: Yes, I believe that to be so.

Mr. CÔTÉ (*Longueuil*): Mr. Chairman, I think my question has been answered. I just wanted to point out that out of the 86 firms, 63 were accepted and, from what you say, it would seem that these 63 firms that sold drugs to the government sold drugs that were lacking in quality or something of a similar nature. I think this is very abnormal and it gives us a great deal of concern. There is an opportunity provided to check up on what is sold to the government but what opportunity has the public to learn whether or not the product being sold by these same firms meets the same standards. I think this is a very serious matter and a shocking situation.

Mr. ENNS: I agree with Mr. Cote when he says that this is a very shocking situation, and it is bound to give us a great deal of concern.

Mr. CÔTÉ (*Longueuil*): The government has a certain department to check on the quality of the products that it buys but the public has no chance at all to make a similar check. Even the dactors who prescribe for their patients have not an opportunity to know what is being sold to the public. This is real shocking to us who have had the opportunity this morning of participating in this discussion. In view of the situation which has come to light I think we should delve deeper and deeper into these matters in view of the fact that all of us are desirous of obtaining security for the public through better control.

The CHAIRMAN: May I ask a question to clarify something which I am sure has been bothering all of us. In respect of the specifications set out and whether or not these firms meet such specifications, is that based on the product involved or on the manufacturing plant involved?

Mr. SHOWALTER: The answer to that is that it is both. This standard, 74-GP-1a, is a measure of the quality of the manufacturing operation and all its trimmings, such as quality control and so on. There is in the purchase contract a specification for the drug itself but, you will note, it is not a simple matter to take a product, detach it by itself, with no associated information, blind as it were, and put it in the laboratory and ensure that it is the product

you want. As I mentioned, there were some products we had to inspect when I was in charge of this inspection. Our inspection people were highly competent and we had good laboratory facilities. But, there were drugs which could not be analysed and, in consultation with the manufacturers, we could not always get satisfactory methods of analysis to ensure that the important ingredients in these drugs were precisely what we wanted.

Some of you are familiar with the makeup of drugs and, if you are, you know it is easier to put something together than to take it apart. And, as you know, the active principles in many drugs are only part of the makeup of them. If a drug is to be put into a tablet there are certain materials which are required in it in order to hold the tablet together, to provide stability, to prevent oxidization and to coat the tablets so they will not be assimilated in the stomach in some cases but only assimilated, say, in the intestines. All these things have to be removed in order to find the identity and purity of the principle that is active as one of a number of ingredients in it. Incidentally, all these ancillary materials necessary to the makeup of drugs are important. But, there is a problem of breaking it down and ascertaining the unfailing answer in respect of the integrity of the materials in it, which proves difficult in some cases. To do it repeatedly in respect of the number of samples required in the laboratory to ensure that delivered goods are satisfactory would involve a great deal of work. In many cases this work can be done but, in many others, it cannot be accomplished.

The CHAIRMAN: Dr. Showalter, I would like you to clarify one other point which I think is mixing up certain members of the committee. For instance, if I was a manufacturer and I wanted to submit a tender, and I was not on the tender list, would I not be correct in saying that I would have to apply, and then you people would inspect my plant before I actually tender? Am I not right in saying that you are interested first in inspecting the manufacturing process of the drug and if I cannot pass that test initially my drug is not even tested.

Mr. SHOWALTER: That is right, with certain exceptions. There are cases where the government requires supply of something which is not obtainable from a "qualified" or conforming source.

Mr. MACKASEY: Mr. Chairman, I think perhaps there is a little misconception around the table this morning and the reporters may get the wrong impression of what we are trying to bring out. Would you correct me if I am wrong in this connection. We do have a food and drug directorate which, in theory, does protect the public. But, as you know, its work is limited by the number of personnel. In my opinion, if parliament is going to do something to protect the public the first thing is to see that the food and drug directorate is enlarged by putting more financial resources at its disposal. Your standards, as outlined here, pertain to personnel requirements, sanitation, raw material tests, and so on. But, are your standards more stringent than what the food and drug directorate demands? For instance, you have one clause in here in respect of "quality control department". I think it has been said somewhere in here that in respect of raw materials coming from Europe someone should be sent to Europe to inspect these goods at the cost of the supplier.

Mr. SHOWALTER: Yes.

Mr. MACKASEY: And, Dr. Morrell, in his testimony, deplored the fact that at the present time the food and drug directorate do not have this facility to inspect these supplies at the source. Drugs coming into this country are subject only to spot checks. The customs people make certain reports to Dr. Morrell but he does not have the staff to control these things. You, at least, have the benefit of these drugs going through this inspection before purchasing. We all know that the food and drug directorate do a certain amount of checking but the only problem is there just is not enough of this type of control.

Another thing you mentioned and looked for, which is important, is the rate of dissolution of a drug. Last week we had a witness here who was in the business only for his devotion to humanity, and yet he told me that the dissolution factor so far as he is concerned is not important. I am wondering, if he sells to you, how he can reconcile the two things. It is right in here, if I could take a moment to look it up. Perhaps someone else would like to put a question while I am looking for this. But, this man did tell me that the rate of dissolution is not important.

Mr. HOWE: Dr. Showalter, are these names of the drug firms not available to the public?

Mr. SHOWALTER: No, not yet.

Mr. HOWE: If they are not should they not be for these reasons, first, for public protection and, secondly, as an incentive for the firms to reach a specific standard. Should not this be one criterion to be taken into consideration. In this way I am sure you would have more reliable firms and as a result of this people would know which firms are reliable

Mr. SHOWALTER: Well, Mr. Chairman, there are two answers to that question. If I speak as the chairman of the interdepartmental board, which was organized for government purchasing, the answer is that the Board* has no authority and has not seen fit to make any decision on this subject. If I speak independently of that I might say that is an important subject to be studied. But, I am not the person to undertake such a study.

Mr. HOWE: Well, the point is this. Are you protecting the drug firms or the public?

Mr. SHOWALTER: At the moment I am protecting government procurement. There are several government departments which buy drugs. This is an age of *caveat emptor*. Our operation is to see to it that our drug products are satisfactory. If we could do something which could be used more widely I would like to see it used, but I am not in a position to do this.

Mr. HOWE: Are not government employees part of the same public which should be protected?

Mr. SHOWALTER: I am sure that is true.

The CHAIRMAN: Dr. Showalter's point is that his position requires that he do a certain job and it is not his responsibility to go beyond that.

Mr. HOWE: I was not criticizing Dr. Showalter personally.

Mr. WILLOUGHBY: Could we expect co-operation from some other departments in respect of procuring a list of this type. I put this question because I think it is an excellent suggestion which Mr. Howe has brought forward, and I think that those firms which have reached that standard of quality would be glad to have their names on the list. Would the food and drug directorate be the department to suggest such a standardization form?

Mr. SHOWALTER: Yes, Mr. Chairman. This personally appeals to me. If this were to be done I would suggest an approach to the several departments involved in the formation of this board simultaneously, indicating that it might be your wish to use the list in this manner and would they please make it available. But, I should explain this board is a voluntary co-operative effort of the several departments, and each one is represented in parliament by its own minister, therefore, the board, as an individual entity, cannot act independently of the departments because as a board it has no direct responsibility to the public.

Mr. MITCHELL: But you are liable to run into the combines investigation branch when you publish a white list which represents a black list, or vice versa.

*The Interdepartmental Pharmaceutical Board.

The CHAIRMAN: Would you proceed, Mrs. Jones.

Mrs. JONES: Is any effort being made to check into the clinical testing of all the drugs that are procured in this way?

Mr. SHOWALTER: I am a little out of my province here. I believe you are speaking in respect of the acceptance for distribution to the public of new drugs?

Mrs. JONES: Well, I do not mean just new drugs; this includes drugs about which any question has arisen in regard to their usage over long periods of time. This situation has cropped up. Has there been any attention paid to this aspect of it?

Mr. SHOWALTER: Is your question in respect of specific products, generically speaking, or to the product of a company?

Mrs. JONES: I am really thinking of every product that is used. I know that the larger companies do take the responsibility for this and I am interested in knowing, as well as the chemical analysis of the drugs, and the standard of purity and potency, and so on, which tests have to be made, whether in respect of the effect these drugs have on people if any effort is being made to meet the need in this connection.

Mr. SHOWALTER: There is no effort in that connection in which I am involved.

The CHAIRMAN: Have you a question, Mr. Côté?

Mr. CÔTÉ (*Longueuil*): Mr. Chairman, I would just like to revert to the matter of the list in respect of these manufacturers. What troubles me is this. Even if we produce a list to show these people are acceptable they do not seem to be selling the best product to the government. It would appear that the product they have sold to the government was not in accordance with the qualities which the government wanted. I do not think it is fair to allow the other firms, which are unable to meet the qualities set down by the government in respect of the soldiers and veterans, to sell to the public at large, when they are unable to reach that standard or quality which we require. I do not see why the soldiers or veterans should have a product which is better controlled than a product sold to the public in general. Is there a reason for allowing them to sell to the public a product which they are not allowed to sell to the government for the men in the armed forces or the veterans?

Mr. MACKASEY: In all fairness to these firms which do not sell to the government, we cannot presume because they do not sell to the government they are not reputable firms. There may be several factors involved, volume for one thing, a very small operation, inability to compete with the price factor, and so on. But, I do think that we should point out that we are very much concerned with the safety of all Canadians. You have taken the initiative, for which you are to be congratulated, in protecting these people who receive their drugs through some governmental department. Now, in theory, as I understand it, the food and drug directorate is supposed to be doing the same type of work for the remainder of the population, but we all know in our hearts that the food and drug directorate is unable to do this because of a shortage of staff. Dr. Morrell's testimony was—and this was several months ago—that in taking the number of firms into consideration at the time and the number of inspections that his department was carrying out it took over three years—in fact, close to four years—to get back to the first firm to see if there had been any deterioration or improvement in their facility.

Mr. Chairman, I think we are operating on a wing and a prayer so far as the public is concerned and it is going to take some form of catastrophe or tragedy to shake us out of our complacency. I think we should provide the food and drug directorate with more money. As you know, we are all motivated

by a sense of safety and sooner or later our recommendation will have to be that Dr. Morrell bring his standards up to date because you, Dr. Showalter, seem to be much better organized. Perhaps this is because you have a narrower field in which to work.

Has anyone taken advantage of clause 16, which reads:

> Where all or part of the inspection must be carried out in a foreign country, the necessary living and travelling expenses related to such inspection shall be provided by the supplier.

Have you had occasion to send men to Europe?

Mr. SHOWALTER: No, to date this never has been implemented, to my knowledge, in respect of any Canadian supplier.

Mr. MACKASEY: It has been in effect only since February. (June 1964 is correct.)

Mr. SHOWALTER: Yes.

Mr. WILLOUGHBY: In respect of this list and the summary you have here of the firms which are conforming and so on, does that apply just to firms manufacturing in Canada or does it also apply to importing firms?

Mr. SHOWALTER: This is a point of some embarrassment. As I already admitted in the outline, our situation is not perfect. We have one or two little problems here. The picture is not completely painted, if you like. There are some firms that are on our list at present which are only distributors, but they are on the list because they have been able to assure us that their sources are sources that are approved. We have informed others until their sources can be approved they will not be eligible.

Mr. ROXBURGH: I have a supplementary question to that put by Mr. Mackasey in respect of clause 16. You made the statement that that clause has not been implemented in any way to date. Are all products now coming in from foreign countries inspected when they reach Canada before they are put into use through the manufacturing firms.

Mr. SHOWALTER: Mr. Chairman, I cannot answer that question. I think this would be a question for the food and drug directorate to answer. They do have a system in that connection.

Mr. CÔTÉ (*Longueuil*): I would like to revert to my previous comments. You said that for many years there has been dissatisfaction on the part of the government in respect of drugs they have purchased and that the general level of quality has been below that which you would be desirous of obtaining. If I may, I will read from the first page of your presentation:

> There has been dissatisfaction for many years in these various departments with the general level of quality of delivered pharmaceutical supplies. Many faults and deficiencies were found in the products when submitted for inspection, with resulting delays in delivery. Many of the suppliers seemed bent on providing no better quality than the minimum permissible under the terms of the contract. Quality of workmanship or what is known in the industry as "pharmaceutical elegance" was often lacking. After delivery there were many cases of poor storage life, and on some occasions shipments were found to be heterogeneous, that is, not entirely identical with inspection samples. The general effect of these factors was to make procurement slow and more expensive, and to undermine confidence in the governmental users.

These were qualified by the government and still did not meet the requirements of the government, and these products are on the market for the public where you have no opportunity at all to check.

Mr. SHOWALTER: I might add a point which may not have been brought out clearly; that is, that many of these associated products actually were not purchased by the government. They were submitted by the holder of the government contract and were rejected after inspection. A rejection, of course, very often involves a return of goods if they already have been shipped, a delay in procurement, or perhaps renegotiation of a contract, and many other things which are costly to a government. Therefore, even in the majority of the cases where the material is not actually used, still it has cost the government something to have that situation occur.

Mr. CÔTÉ (*Longueuil*): But they were not used on account of these defects in the product

Mr. SHOWALTER: Yes.

Mr. CÔTÉ (*Longueuil*): But still they were sold to the government and not used. When they are in the drugstore or anything like that they are not sent back to the factory; the public uses them.

Mr. MITCHELL: Not necessarily.

Mr. CÔTÉ (*Longueuil*): Why not?

Mr. MITCHELL: We have return privileges.

The CHAIRMAN: I am sure they would be taken off the shelf. There is one point which I wanted to bring to the attention of the committee. In these figures actually there are 54 firms who were never inspected because they said they have no interest in government tendering. They should be taken out of the total because they were not inspected in any way.

Mr. MACKASEY: They may have been inspected by the food and drug directorate under the normal inspection.

Mr. ENNS: This is an area which may not be relevant, but the brief at the bottom of page 2 states:

> —whereas the public has free choice of all the brands and sources of drugs on dealers' shelves, government users have no choice but to use the products kept in government stores—

Take the first part of that, does the public really have a free choice? Perhaps Mr. Mitchell may have an answer to this. How does any purchaser know when he goes to a drugstore that this is a quality drug, or how does he know where the pharmacist gets his drugs? There really is no choice to the public. We get a prescription from a physician, take it to a pharmacist, and have it filled; but we have no idea where these drugs are supplied from and whether it is a standard house or a substandard house.

Mr. MITCHELL: The prescribing physician knows who the manufacturer is and the druggist merely fills the prescription.

Mr. ENNS: When reference is made to the public's free choice, it is really the physician's free choice. The public is not knowledgeable in this area.

Mr. MITCHELL: Not at all.

Mr. MACKASEY: At the bottom of page 3 it says:

> It has one serious problem yet to solve, namely, that some pharmaceuticals and semi-finished materials are imported from foreign sources inspection of which to our standard is difficult or impossible. Efforts to deal with this problem are now under consideration.

Are these efforts still confidential or could you give us an outline of what you would like to see happen?

Mr. SHOWALTER: They are not confidential. What I would like to see happen, and what I think would have to happen, under the aegis of the food and

drug directorate, would be that an arrangement be made with the various countries, which are many of our sources, to set up similar standards. I am informed by the directorate that practically nothing has been accomplished in that direction. There are food and drug regulations in many countries, but this sort of thing, or something parallel to it, has not yet been accomplished. Here I am not speaking expertly.

Mr. MACKASEY: So, at the present moment you still are at the mercy of the quality of the goods bought outside the country, for instance from Poland. You still are pretty much at the mercy of the importer?

Mr. SHOWALTER: Not entirely, because there is a policy of preferred Canadian content in most departmental purchasing.

Mr. MACKASEY: Have you no facilities of your own for inspection other than making sure the supplier has all the facilities necessary?

Mr. SHOWALTER: There are government inspection facilities. For instance, the Department of National Defence, which probably is the largest buyer, has its facilities for inspection. This is distinct from inspection of the source and standard of manufacture.

Mr. MACKASEY: Would everything coming into the Department of National Defence pass through these tests?

Mr. SHOWALTER: Yes.

Mr. MACKASEY: What about other government bodies, or is the Department of National Defence overloaded with its own purchases?

Mr. SHOWALTER: The Department of National Defence more or less is looking after its own alone. It gets some requests from other departments, but the other departments largely use the food and drug directorate.

Mr. CÔTÉ (*Longueuil*): On page 3 you say that since June 3, 1964, the situation has changed very much and that you have started a lot of inspections. How many firms were inspected?

Mr. SHOWALTER: Eighty-six. May I explain that a little more. Without taking too long, perhaps a little more background would be helpful here. Several things were occurring during the period when this standard was first promulgated and when we began to have a list. A number of firms were improving their facilities and practices considerably, since they were frightened by this. As you know, quite a number of our firms are subsidiaries to firms centered abroad. It bothered them to have their principals learn they had failed to meet some standard, whatever that standard might be. This is a matter of prestige, if you like. So, they began to make improvements, even firms which never had an interest in government procurement. Some of them came to my office rather indignant to have their product discredited when it was considered they kept a perfect house.

Another thing is that the food and drug inspectors were maturing in their job. I think it is realized that the very best inspector must have experience in order to gain a sense of proportion and a good sense of interpretation. These are broad requirements; it is not easy to lay down in precise and measurable terms what you will accept and reject. It is not easy to have a standard which will exactly spell out what you mean when you say a reputable and conscientious firm. To say we have accomplished this is almost the same as saying the highway traffic act is a description of a perfect driver. I am convinced there are drivers on the road who violate the highway traffic act who may be pretty good drivers and some who never violate anything who are pretty poor drivers. It is not possible to make a standard which permits of an absolutely accurate interpretation. Therefore it took a round of inspections to accomplish these several things at once. First, it was very important to see

where the faults were, and even the best had some. Second, it was necessary to evolve a more proportionate and mature inspection method, and, further, a more realistic and practical standard. All these changes were going on at once.

The first standard was a sort of absolute which indicated, among other things, that you must have a certain number of facilities and a certain number of personnel. If for instance a firm had one less cubicle in the washroom than mentioned here, even if it might be perfect in other ways, it could not pass. That is why we have put it on the basis of a rating. You could lose on one and gain on another, and if you had a passing mark you were considered good. It was a principle of how well the firm adds up and meets a fairly good level.

All these changes occurred simultaneously. This is why all firms were rejected at first, and gradually on the second and third round we began to get a list. It was not any one person's fault, but rather the fault of a growing process.

Mr. CÔTÉ (*Longueuil*): I think in all fairness to the firms you should mention why they were disqualified. If you leave out a report like that, it is not fair to these firms. If they have been disqualified for such little things as having too few toilets for so many people, that has nothing to do with drugs, and I think it should appear in the report.

Mr. SHOWALTER: The reasons for their rejection were all explained to them.

Mr. MACKASEY: So they could improve the conditions?

Mr. SHOWALTER: Yes.

Mr. MACKASEY: It seems that this is another type of bureaucracy. Here we have a case of the government remedying a situation when it affects it personally. Everybody in Canada is entitled to the same type of protection that is being granted in this case to a privileged few. Obviously, what has happened is that the Canadian government is seeing that certain people under their direct control are being protected and you people thoughtfully and logically have set up certain standards which give a certain segment of the population some protection.

It seems to me that this is the kind of initiative which is needed under the food and drug directorate. We have excused their inefficiency on the ground that they are short staffed. Perhaps parliament is more or less bound to do something about it. You have taken the initiative to do something for the soldiers or veterans who use the drugs, but the rest of the population is left to the will of the pharmaceutical association which, in turn, is faced with the loopholes in the law which permit certain companies to bring in poor products from outside the country.

Dr. Morrell stands by helplessly because he is under financed and the industry is growing so rapidly that he cannot possibly keep up. A year ago he told us that he could only inspect so many and the chances now are that there is only an inspection in one out of every four years, because the industry is growing rapidly.

This shows us how inadequate the whole situation is. There is no reflection on Dr. Morrell, because he is a hard working man going well beyond his call of duty for the money he is making. However, his department is a disgrace to the country. The bulk of the Canadian people are living on a wing and a prayer when it comes to buying drugs.

Last week a witness said to me there are standards of disintegration but he would not like to comment on it and that he does not think it is important to the efficacy of a drug. You set up a standard of dissolution which is important and this witness gets up and tells us it is not important. Earlier when I asked him he referred to an apple pie, and I said that if you get a bad apple pie you

get a stomach ache, but if you get a bad drug, you probably are dead. We have heard of pills taken orally which did not dissolve. In all probability this man who denies that the dissolution rate is important probably is selling to the government.

The CHAIRMAN: Of course his pills would have to follow government specifications and inspection or they would not be purchased.

Mr. MACKASEY: If this man sincerely believes the rate of dissolution is not important, he hardly is going to enforce this type of standard with very much good will in his industry.

The CHAIRMAN: May I ask a question; once a firm has undergone inspection, is required to improve, and finally receives the approval as being all right for government tender, how long does this ruling hold fast? In other words, does he have to be inspected after he tenders on an item, or is it once a year, or once every two years? How often do you consider you will go back to make sure he is maintaining the standard? This brings up a question of staff again; how often can you get around to seeing these people?

Mr. SHOWALTER: We have no rule in that regard. We are in the very early stages of this thing. It began in June. The previous effort was in getting the groundwork ready and getting a list that was fair. We have not actually got to this yet. If a firm which has been off the list is on as of today, a notice to that effect is sent to the departments to add that firm to their list.

As the years go by and a given firm is still on the list, and no reason has been found to put him off the list, there is no rule, as yet, for determining that at the end of a year or two years he should be re-inspected. However, you will notice there is provision for disqualification on the basis of demerits. Here we have copied a little from the highway traffic act. We have demerits for any failure to deliver satisfactory goods. If the product fails to meet its specification, there is a scale of points to be taken off its rating. There is for instance a provision for a three point loss. If it originally had 92 points, is inspected, and has lost three points because of a failure or something, it is disqualified and off the list. Notice immediately is sent out. We have not yet come to the point of deciding that firms which have nothing against them at all should be re-inspected at any given interval.

Mr. MACKASEY: Physically it would be quite a problem.

Mr. SHOWALTER: We have had excellent co-operation from the food and drug directorate. They have done excellent work; they have tried their best. Sometimes they have been slow. I have tried to be understanding with them. When anything comes up relative to this list, I discuss it with them to see what we can do to avoid thrusting an overload on them, but naturally we press for inspection as soon as a firm indicates it is ready, or when something comes up which suggests it ought to be examined again.

Mr. MITCHELL: In other words, the food and drug inspection staff is doing a double duty in inspection; they are doing it for you and for the general public. Therefore, you are getting the same results as the general public because of this inspection. Therefore one inspection cannot be inferior or superior to the other if the same directorate is doing it.

Mr. SHOWALTER: Mr. Chairman, all I can say in answer to that is I know the way in which I am using the results of the inspections and the way in which it is being interpreted for purposes of establishing my list. What the food and drug directorate does on its own side is not my concern.

Mr. MITCHELL: I did not say that. The same result of the inspection is going to the two sources

Mr. SHOWALTER: Yes.

The CHAIRMAN: Are there any further questions, gentlemen?

Gentlemen, before we adjourn the meeting, is it the feeling of the committee that we would like to have Dr. Morrell come back to us either this Friday or a week from Friday? A week from today we will have Dr. Brien from London. If it is the wish of the committee we might have Dr. Morrell this Thursday or Friday, or next Thursday or Friday.

Mr. MACKASEY: Thursday is preferable to Friday.

The CHAIRMAN: There are six or seven committee meetings listed for this Thursday.

Mr. MACKASEY: Friday is becoming impossible because we have the house at 11 o'clock and we only get started and then have to leave.

The CHAIRMAN: If we could get started at 9.30 a.m. we should have time. Should we have Dr. Morrell a week from Thursday or Friday?

Mr. MITCHELL: There would not be any more committee meetings next Thursday than there are today and we managed to have a quorum.

The CHAIRMAN: I am in the hands of the committee.

Mr. MACKASEY: The point is that the later Dr. Morrell comes in the proceedings, the better opportunity we will have to review things which come up in the meantime.

The CHAIRMAN: We are having Dr. Brien a week from today. It was on the Brien committee's report that the amendments to the regulations were made. Perhaps we should hear Dr. Morrell after we have heard from Dr. Brien to see whether Dr. Brien is satisfied with the changes which have been made. I would suggest that Dr. Morrell appear a week from Friday.

Mr. MACKASEY: I would prefer a week from Thursday.

Mr. ENNS: I would not be able to be here a week from Thursday.

The CHAIRMAN: Is it the opinion of the remainder of the committee that we would like to have Dr. Morrell a week from Thursday? There will be no meeting later on in this week. The committee will adjourn until one week from today when we will have Dr. Brien.

I would like to thank Dr. Showalter for coming today and giving us his testimony which has been very interesting and informative to the committee. We thank him very much for coming forward.

APPENDIX "A"

NOTE—*Original pagination of this Standard is indicated in margin*

CANADIAN GOVERNMENT SPECIFICATIONS BOARD

STANDARD ON MANUFACTURE, CONTROL
AND DISTRIBUTION OF DRUGS
74-GP-1a
7 FEBRUARY 1964

Supersedes 74-GP-4
22 September 1961

This Standard applies to the Manufacture, Control and Distribution of Drugs for Supply to Agencies of the Government of Canada

NATIONAL RESEARCH COUNCIL, OTTAWA, CANADA
Comments and enquiries regarding this publication
should be addressed to the CGSB secretary

COMMITTEE ON STANDARDS FOR DRUG MANUFACTURERS AND DISTRIBUTORS

(Membership at date of approval by the Committee)

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McCalla, W. R.	Parke Davis and Company Limited
Stewart, W. R.	The Upjohn Company of Canada

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Turnbull, J. B.	Executive Director

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Wood, E. S.	General Purchasing Branch

Department of National Defence

Featherston, Major R. W.	Surgeon General Staff
Showalter, Dr. H. A. (Committee Chairman)	Inspection Services
McCarten, W/C W.T.	Surgeon General Staff

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Matthews, J. E.	Emergency Health Services
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Brooks, G. E.	Attorney-General's Laboratory

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Canadian Government Specifications Board

Wolochow, D. (Committee Secretary)	Secretary

74-GP-1a
7 February 1964

Supersedes 74-GP-1
22 September 1961

CANADIAN GOVERNMENT SPECIFICATIONS BOARD

STANDARD ON MANUFACTURE, CONTROL AND DISTRIBUTION OF DRUGS

1. SCOPE

1.1 This standard applies to the manufacture, control and distribution of drugs for supply to agencies of the Government of Canada.

1.2 It applies to primary manufacturers of drugs, primary distributors of drugs, importers and commercial testing laboratories.

1.3 The supplier is responsible for ensuring, and for demonstrating to the satisfaction of the purchaser, that material he supplies is manufactured, controlled and distributed in conformity with this standard.

1.4 The decision as to conformity rests with the purchaser.

2. GLOSSARY

2.1 *Supplier*—Any person or firm that undertakes to contract for the supply of a drug.

2.2 *Drug*—Any substance or mixture of substances manufactured, sold or represented for use in:

2.2.1 The diagnosis, treatment, mitigation or prevention of disease, disorder, abnormal physical state or symptoms thereof in man or animal.

2.2.2 Restoration, correction or modification of organic function in man or animal.

3. APPLICABLE ACTS AND REGULATIONS

In addition to complying with this standard, the manufacture, testing and handling of all drugs shall conform with the relevant provisions of the following:

3.1 The Food and Drugs Act and Regulations.

3.2 The Proprietary or Patent Medicine Act and Regulations.

3.3 The Narcotic Control Act and Regulations.

3.4 The Pest Control Products Act and Regulations.

3.5 Animal Contagious Diseases Act and Regulations.

3.6 Municipal and Provincial Regulations that apply in the area where the plant of the supplier is situated.

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4. INSPECTION AND CRITERIA OF CONFORMITY

4.1 Anyone wishing to supply a drug may request through the purchaser an inspection of the system of manufacture, control and distribution of the drug.

4.2 *Rating System*

The degree of conformity with each of the detailed provisions within Sections 5 to 15 shall be indicated by a figure based on the figure shown in the right-hand column of this standard, which represents full compliance with that requirement. The final rating is obtained by expressing the aggregate of all such individual figures as a per cent of the maximum.

4.3 The supplier shall be deemed to have conformed with the standard if the final rating obtained in the manner described is not lower than 90 per cent provided, however, that no individual rating is less than 70 per cent of that indicated in the appropriate requirement in Sections 5 to 15.

5. PREMISES AND EQUIPMENT 50

5.1 The construction, fittings and furnishings of the area in a building where the drug is processed and packaged shall be of such material and finish as will:

5.1.1 permit the ready and efficient cleaning of all surfaces

5.1.2 prevent the introduction of extraneous materials into drugs during their processing and testing

5.1.3 prevent the migration of dust, having regard to the nature of the operation being performed.

5.2 In accordance with good pharmaceutical practice, the following requirements shall be met:

5.2.1 All processing, packaging, testing, storage and distribution areas shall be of material, construction and finish that will permit the ready and efficient cleaning of all surfaces.

5.2.2 All ceilings, floors and walls of the building shall be reasonably dust-tight, to the extent that dust cannot migrate through the floor or walls, or from one room or operation to another.

5.2.3 All ceilings and walls shall be constructed, finished and maintained to prevent the introduction of extraneous materials into drug products.

5.2.4 Drains shall be of adequate size and suitable type; and where connected directly to a sewer, they shall be equipped with traps.

5.2.5 Adequate ventilation shall be provided in all working areas.

5.2.6 Adequate light shall be provided on all working surfaces except where conditions demand darkened areas.

5.2.7 All packaging and processing equipment shall be subject to a clean-up procedure following the manufacture of each batch or lot of drug.

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5.2.8 All manufacturing equipment shall be operated and maintained in a manner that will prevent contamination of drugs with extraneous materials.

5.2.9 All processing and packaging equipment shall be designed to permit ready and thorough cleaning, and shall be of materials and construction that will not contaminate or add extraneous materials to drugs with which it is used.

6. SANITATION 100

6.1 The premises used for the processing, testing, finishing, distribution and storage of the drug, and all auxiliary facilities, shall be maintained in a clean, sanitary and orderly condition free from vermin, infestation, accumulated waste and debris.

6.2 No household pets nor vermin shall be permitted in a drug plant.

6.3 Evidence shall be presented that the establishment has a proper written program for maintaining the conditions specified.

6.4 Toilet facilities of an approved sanitary type shall be provided for male and female employees, and kept in satisfactory condition at all times, according to the following minimum scale:

No. of Employees	*No. of Toilets*
1 – 9	1
10 – 24	2
25 – 49	3
50 – 100	5

For each additional 30 employees over 100, 1 additional toilet.

6.5 A supply of toilet tissue shall be available for each toilet.

6.6 An adequate number of sanitary wash basins near working areas with a satisfactory supply of hot and cold water, liquid or powdered soap, air dryers or single-service towels shall be provided. Hand-washing procedures shall be carried out before commencement of work and after each absence from duty.

6.7 No eating, smoking nor spitting shall be permitted in working areas.

6.8 Only material required for the particular manufacturing operation in progress at any one time shall be stored in an immediate working area.

6.9 Clean working garments shall be worn over, or in place of, street clothing for work in processing and packaging areas.

6.10 Premises shall be clean, sanitary, orderly and free from accumulated waste and debris.

7. PARENTERALS 300 Page 4

7.1 In the event that parenteral drugs are processed, all fillings and aseptic processes shall be carried out in a separate and enclosed area designed for the processing and filling of such drugs and operated in a manner that will prevent contamination of the drugs.

7.2 All processing and filling procedures for parenteral drugs shall be carried out in a separate room specially designed for this purpose and under the direct responsibility of personnel complying with the requirements of 8.2, provided such personnel have had training in microbiology.

7.3 The filling and processing area for parenteral drugs shall be designed and equipped to ensure the safety and, where necessary, the sterility of the drugs compounded and filled; the equipment shall, where necessary, be provided with a supply of filtered "sterile" air under positive pressure, disinfectant sprays or disinfectant wipe-downs; and the area shall be subject to limited access of personnel.

7.4 Where applicable, the operators before entering the filling and processing area for parenteral drugs shall scrub with antiseptic soap and be dressed with sterile outer garments, rubber gloves, face mask, and coverings for the head and shoes; or the shoes shall be treated with a germicidal preparation immediately before entry to the filling area.

7.5 The filling operation for parenteral drugs shall be checked routinely by performing plate counts, or by other suitable tests, on the air in the room, by performing routine checks on the efficiency of the sterilizing procedures used and, when necessary, by carrying out normal filling operations with sterile thioglycollate medium or other suitable medium.

7.6 Records shall be prepared and retained of the processing and filling of parenteral drugs, and of the sterilizing procedures used, including sterilizing charts and/or in-out sterilizing time, temperature and pressure reports where applicable.

7.7 No clinical nor diagnostic procedures and no other unrelated operation shall be carried out in the filling area for parenteral drugs.

7.8 Nonpyrogenic water shall be used in all aqueous parenteral drugs, and records shall be maintained of the routine pyrogen tests.

8. PERSONNEL 125

8.1 *Health of Personnel*—No person known to be affected with a disease in a communicable form or to be the carrier of such disease, and no person with open lesions on the exposed surface of the body, shall be employed in the processing, packaging, testing or storage of drugs.

8.2 *Qualified Personnel*

Technically qualified personnel shall be used as supervisors in the formulation, processing, testing, packaging and labelling of the drug. They shall have such technical training as is deemed necessary (see 8.2.1 and 8.2.2), having reasonable regard for performance of the duties and the responsibilities involved. Technically qualified personnel are considered to be:

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8.2.1 Graduates in Science from a university of recognized standing, with a degree requiring the study of chemistry, biochemistry, pharmacology, pharmacy, microbiology, chemical engineering, medicine or veterinary medicine, with adequate practical experience after graduation in the formulation, processing, packaging, labelling or testing of drugs.

8.2.2 Persons qualified by training or experience to carry out the supervision of formulations, processing and testing of drugs provided these operations are under the direction of a person complying with the requirements of 8.2.1.

8.3 *Maintenance Personnel*

8.3.1 Suitably qualified personnel shall be responsible for the maintenance of machinery, equipment and sanitation.

8.3.2 There shall be responsible, suitably qualified personnel in charge of the maintenance of machinery, equipment and sanitation.

9. RAW MATERIAL TESTS 100

9.1 Each lot or batch of raw or bulk material used in the processing of the drug in dosage form shall be tested to ensure identity and purity of such raw or bulk materials.

9.2 Raw or bulk materials are considered to be any ingredients of a drug and shall be tested by methods of pharmacopoeial or equivalent status.

9.3 Records of the tests carried out shall be available in a lucid form.

10. FINISHED PRODUCT TESTS 200

10.1 Each lot or batch of drug in dosage form shall be tested to ensure identity, potency and purity for its recommended use. In addition, where necessary to ensure the quality of the finished product, testing of ingredients or in-process testing may be required.

10.2 The tests carried out shall be of pharmacopoeial or equivalent status.

10.3 Records of the tests carried out shall be available in a lucid form.

11. PLANT OPERATION 250

Adequate production controls shall be used, having regard to the nature of the drug.

11.1 *Records*

11.1.1 Production Control Records shall be available in lucid form.

11.2 *Supervision*

11.2.1 The formulation and processing procedures shall be supervised by personnel complying with the requirements of 8.2.

11.2.2 The packaging and labelling processes shall be supervised by personnel complying with the requirements of 8.2.

11.2.3 Each ingredient to be added to a batch shall be subjected to one or more checks for identity and quantity by personnel complying with the requirements of 8.2. Page 6

11.2.4 Addition of each ingredient to a batch shall be confirmed by personnel complying with the requirements of 8.2.

11.2.5 Preparation of master formula cards shall be done by, and subjected to independent checks by, personnel complying with the requirements of 8.2.1.

11.2.6 The initials of personnel performing and checking operations in each step of the process shall be recorded on the work order.

11.3 *Raw Materials*

11.3.1 All raw materials used in processing shall be covered by detailed written purchase specifications.

11.3.2 All raw materials shall be precisely described on work orders used for processing, and work orders shall be issued by personnel complying with the requirements of 8.2.

11.3.3 Each raw material used in processing shall be identified by a lot number, receiving number or laboratory control number, which shall be recorded on the work order.

11.3.4 Generally, all raw material stocks shall be kept in an area separated from the immediate manufacturing area.

11.3.5 All raw materials shall be held in quarantine until released by the Quality Control department.

11.3.6 All raw materials shall be stored in such a way as to preserve potency and quality.

11.3.7 All raw materials shall be adequately labelled as to identity.

11.3.8 All raw materials dispensed for processing shall be labelled as to identity and quantity, and, where possible, grouped for batch.

11.4 *Processing and Packaging*

11.4.1 All processing operations shall be performed according to comprehensive and detailed written procedures.

11.4.2 All processing and packaging operations shall be performed only following the issuance of individually numbered work orders.

11.4.3 All packaging operations shall be performed according to comprehensive and detailed written procedures or specifications, and shall include disposal procedures for surplus labels.

11.4.4 All bulk and packaged drugs shall be held in quarantine until released by the Quality Control department.

11.4.5 Each lot of packaged drug shall be identified by a lot number.

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11.4.6 All containers of semi- or fully processed bulk shall be adequately labelled as to identity.

11.5 *Packaging Materials and Labels*

11.5.1 All printed packaging materials and labels shall be under the supervision of a person complying with the requirements of 8.2.

11.5.2 Printed packaging materials and labels shall be stored in limited access area as follows:

11.5.2.1 Wherever possible, limited access shall be understood to mean a fully enclosed area under the supervision of personnel conforming with the requirements of 8.2, and with access restricted to designated personnel.

11.5.2.2 Where the bulk of the printed packaging materials is so great as to prevent compliance with the above, limited access shall then be considered to mean a designated area under the supervision of personnel conforming with the requirements of 8.2, and with access restricted to designated personnel.

11.5.3 Withdrawal of printed packaging materials and labels shall be done as follows:

11.5.3.1 Printed packaging materials and labels shall be withdrawn for use against written work orders issued by personnel conforming with the requirements of 8.2.

11.5.3.2 Printed packaging materials and labels issued for use against written work orders shall be checked by personnel conforming with the requirements of 8.2.

11.6 *Storage*—All raw materials and finished stocks of bulk and packaged drugs shall be stored under conditions approved by the Quality Control department to preserve potency, quality and safety of the drug.

12. QUALITY CONTROL DEPARTMENT 100

12.1 The manufacturer of drugs shall have a Quality Control department under the direct supervision of a person complying with the requirements of 8.2.1 and responsible only to the Management.

12.2 The function of the Quality Control department and personnel shall be separate and distinct from the Processing, Packaging, and Sales departments.

12.3 The Quality Control department shall have or employ a quality control laboratory. Such control laboratory shall have equipment and facilities for inspecting and testing to ensure the quality, identity, potency and safety of all ingredients used in the production of drugs as well as of the finished drugs supplied.

12.4 All material used in packaging of drugs shall be quarantined upon receipt from the supplier and shall be subject to release by the Quality Control department only after inspection.

12.5 Where necessary to control quality during processing, samples of each lot or batch of the drug shall be submitted to the Quality Control department for inspection or testing for compliance with process specifications.

12.6 The Quality Control department shall be responsible for determining the stability of the finished drug.

12.7 The Quality Control department shall be responsible Page 8
for checking to see that the requirements of all process and storage specifications are carried out.

12.8 A formal written record shall be maintained by the Quality Control department of every complaint, on each finished drug originating within its manufacture, that arose during or after its distribution, along with the action taken in dealing with the complaint.

13. RECALL SYSTEM 35

13.1 A system of control shall be used permitting a complete and rapid recall of any lot or batch of the drug from the market.

14. RECORDS—PRODUCT INFORMATION 20

14.1 Records shall be maintained relating to the drug in a form, manner and content satisfactory to the Purchaser, showing all information received pertaining to the quality or hazards of any drug. This includes letters from all Regulatory Agencies and what action has been taken on this information.

15. RECORDS AND SAMPLES—MAINTENANCE OF 20

15.1 Records required to be maintained in respect to a drug shall be kept until the expiration of five years from the date of the testing of the drug, *or* the expiration date of the drug, whichever occurs first.

15.2 A sufficient sample of each lot of the finished drug in dosage form shall be kept by the manufacturer under suitable conditions of storage until the expiration of five years from the date of the testing of the drug, *or* the expiration date of the drug, whichever occurs first.

16. INSPECTION

16.1 Where all or part of the inspection must be carried out in a foreign country, the necessary living and travelling expenses related to such inspection shall be provided by the supplier.

17. PENALTY FOR NONCONFORMITY OF SUBMITTED MATERIALS

17.1 If material submitted to a purchaser is found either before or after delivery not to conform with the requirements of the contract, the following demerits shall apply to the rating arrived at in accordance with 4.3:

17.1.1 *First Rejection*—two percentage points shall be deducted from rating established.

17.1.2 *Second Rejection*—an additional three percentage points shall be deducted.

17.1.3 *Each Additional Rejection*—a further five percentage points shall be deducted.

17.2 If as a result of rejections described in 17.1 the rating obtained by a supplier falls below the required 90 per cent, the supplier shall be deemed not to comply with the requirements of this standard.

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18. REINSTATEMENT

18.1 The penalties laid down in Section 17 shall remain in effect for a period of not less than 90 days. A supplier may apply for reinstatement by presenting to the purchaser a submission indicating appropriate corrective action.

19. ENQUIRIES

19.1 Any correspondence or negotiations regarding the application of this standard shall be directed to the purchaser.

20. NOTES

The publications referred to in 3.1 to 3.5 inclusive are available as follows:

20.1 The Food and Drugs Act and Regulations—The Queen's Printer, Ottawa, Canada.

20.2 The Proprietary or Patent Medicine Act—The Proprietary or Patent Medicine Division, Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Canada.

20.3 The Narcotic Control Act—The Narcotic Control Division of the Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Canada.

20.4 The Pest Control Products Act—Plant Products Division, Canada Department of Agriculture, Ottawa, Canada.

20.5 The Animal Contagious Diseases Act—Health of Animals Division, Canada Department of Agriculture, Ottawa, Canada.

Correspondence regarding this standard should be addressed to the Secretary, Canadian Government Specifications Board, National Research Council, Ottawa, Canada.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 17

TUESDAY, NOVEMBER 24, 1964

WITNESSES:

Dr. F. S. Brien, B.A., M.B., F.R.C.P. (Lond.), F.R.C.P. (Canada), F.A.C.P., Professor of Medicine, and Head of the Department, University of Western Ontario, London (Ont.); and Dr. C. A. Morrell, Director of the Food and Drug Directorate, Deparment of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21268—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jones (Mrs.)
Jorgenson
Macaluso
Mackasey
Marcoux
Orlikow
Prud'homme
Roxburgh
Rynard
Slogan
Wadds (Mrs.)
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

TUESDAY, November 24, 1964.
(22)

The Special Committee on Food and Drugs met at 9.50 a.m. this day. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Asselin (*Richmond-Wolfe*), Côté (*Longueuil*), Harley, Mackasey, Mitchell, Prud'homme, Rynard, and Willoughby.—(9).

In attendance: Dr. F. S. Brien, Professor of Medicine and Head of the Department, University of Western Ontario, London, Ont.; and Dr. C. A. Morrell, Director of the Food and Drug Directorate, Department of National Health and Welfare.

The Chairman announced that Dr. Morrell will be able to appear as requested on Thursday, November 26th. He informed the Committee that he had received a letter from the General Manager of the Canadian Pharmaceutical Manufacturers Association asking that the General Legal Counsel of the Association, Mr. F. R. Hume, Q.C., appear before the Committee to discuss registration and/or licensing of drug manufacturers.

The Committee agreed to hear Mr. Hume after Dr. Morrell's appearance.

The Chairman introduced Dr. Brien who was the Chairman of the Special Committee on New Drugs appointed in 1962 by the Royal College of Physicians and Surgeons of Canada, at the request of the Minister of National Health and Welfare.

Dr. Brien made some opening remarks.

Both Dr. Brien and Dr. Morrell were questioned.

The questioning concluded, the Chairman thanked Dr. Brien for his presentation and Dr. Morrell for the information supplied.

At 11.45 a.m. the Committee adjourned to 9.30 a.m. Thursday, November 26.

Gabrielle Savard,
Clerk of the Committee.

21268—1½

EVIDENCE

TUESDAY, November 24, 1964.

The CHAIRMAN: Gentlemen, there is now a quorum.

I would like to say that at the request of the committee the next meeting will be held on Thursday, instead of Friday, and Dr. Morrell, the director of the food and drug directorate will be in attendance.

There is one piece of correspondence in which the Canadian Pharmaceutical Manufacturers Association express their wish to come back before the committee to give their view on the revisions on the subject of licensing and registration. If the committee will agree, I will request that they come back, if possible, one week from today.

Some hon. MEMBERS: Agreed.

The CHAIRMAN: Is there any discussion on that suggestion?

Gentlemen, then if we could get right down to the meeting, I would like to introduce Dr. Brien, who is from the University of Western Ontario, and who has actually appeared before this committee, I think, at its original meeting in 1962—No. 4, he corrected me. He was the chairman of the special committee on new drugs which was appointed in 1962 by the Royal College of Physicians and Surgeons of Canada, at the request of the then minister of national health and welfare, Mr. Monteith.

So, without any further ado, I will introduce Dr. Brien, and I know he has some opening remarks to make.

Dr. F. S. BRIEN, B.A., M.B., F.R.C.P. (Lond.), F.R.C.P. (Canada), F.A.C.P., *of the University of Western Ontario*: Well, as your Chairman has intimated, and as some of you know, along with two other physicians, I chaired the committee that was set up in the manner indicated, and reported on the situation with respect to new drugs as it pertained at the end of 1962, and this, of course, is available in No. 4 of the proceedings which was printed on February 5, 1963. *(Reproduced in No. 1 of Thursday, Aug. 1, 1963, 1st session of 26th Parliament).*

A number of recommendations were made in this report, and I would just like to briefly mention a few of them. The first was with respect to the need for expansion in the food and drug directorate, in order to just keep up to the ever-increasing work that it is called upon to carry out. The recommendations made by the committee with respect to personnel were passed. It was noted at the time that it was perfectly obvious to the other two members of the committee and myself that this would not be a simple matter, to recruit them, and we tentatively noted that three years would be a very optimistic view, if I remember correctly, and actually this has proven to be the case. It has not yet been possible, so Dr. Morrell informs me, to recruit the directorate up to the level which we thought would be capable of performing satisfactorily and expeditiously.

One other recommendation that was made was that a working,—and this is italicized if you look at the report,—a working standing drug committee be formed, either from the Canadian drug advisory committee, which is a fairly large committee of 15 or 16, or thereabouts, or partly from it and partly outside, or from completely outside.

As we had gone through the business of compiling this report, the members of the committee knew exactly what they were talking about when they underlined, or italicized, the words "working committee", and in subsequent

discussions, in No. 7 of the Minutes of Proceedings and Evidence of Friday, June 19, 1964, on page 166, there is a reference to this problem, where the matter of this committee was being discussed and wherein it is stated that the alternatives were to go ahead and set up the working committee, realizing that it might be very difficult to get people to serve on it in the way that the Royal College committee meant it to operate on the one hand, or to use the other alternative, which is to call together a series of special committees, and this is completely within the terms of reference of the C.D.A.C. to deal with various specific problems as they arise, or have arisen, and I believe that to date about four, or possibly five of these committees have met, and consulted about specific problems with the directorate. Whether this is a satisfactory method of handling the problem or not, I am not at the present in a position to accurately state, because my connections with the directorate technically ended with the submission of this report. However, I have visited it on at least one or two occasions since then, at the request of the director, and with the approval of the Royal College, which actually appointed me to that committee.

The next item in the College report that I would like to mention was that certain revisions in the regulations under the Food and Drug Act were suggested. The net result of this was that actually a new Section 8, or Division 8 rather, which is now pages 126B to 126F, deals with new drugs, and revokes the old sections C.01. 301 to 307 inclusive. I shall come back in a moment, if I may, to make some remarks relative to the new regulations, but first I would like to mention that the other point, the other recommendation of great interest was with respect to the need for increased clinical trials of new drugs, and I would also add old drugs too, in this country.

I would like to report that, as has also been mentioned in No. 7 of the proceedings, that with the assistance of the Canadian Pharmaceutical Manufacturers Association, and the help of their medical section, or its medical section, a body known as the Canadian Foundation for the Advancement of Therapeutics has been chartered. Its honorary president is Doctor Ray Farquharson, who is known to you all, and currently in charge of the Medical Research Council. The chairman is myself. Along with this we have a number of directors who have been selected for geographical reasons to permit ease of meeting, roughly from Quebec city to Winnipeg, and in addition we have two representatives of the medical section of the C.P.M.A. This body has met on several occasions. It is doing the following things with the rather limited funds that are presently at its disposal: First, it is providing a number of student summer fellowships to be given to students in the various medical schools in this country, to assist them through a summer doing work which, we hope will enhance the science of therapeutics in the future. Secondly, we have provided postgraduate fellowships for again a limited number of physicians to take training that will fit them especially for the teaching and practice of therapeutics, and the evaluation of drugs, and so forth. Also, because of the time of year when this program was initiated, we had to act as our own project supporting body, for the simple reason that we wanted to get the program off its feet as rapidly as possible, and it was not feasible to apply to the ordinary fund granting agencies at this particular time of year. So that, in a limited way, we then gave certain project support.

It is our hope as time goes on, and this Foundation prospers, and we certainly hope it will, to be able to assist in the setting up and the operation of

clinical pharmacological units in connection with the teaching hospitals and universities. At the present time we can only do this to a very limited degree, because of the funds at our disposal.

The last activity of this foundation to which I would like to refer at this moment concerns a conference that was held at Ste. Adèle, in Quebec, on the 22nd and 23rd of October last, on human pharmacology. This was attended by between 90 and 100 persons, representing departments of medicine, pediatrics, pharmacology and other interested persons within universities, some deans; some other clinical investigators; and they came from the University of British Columbia to Dalhousie. A most worth-while program was put on, that went into all aspects of the evaluation of drugs, and we had three outstanding speakers in this general area from the United States, and as well had a discussion on the medico-legal, even ethical and moral aspects of drug testing, that was carried on by Mr. I. C. Rand, who has just retired as the dean of law at the University of Western Ontario, which position he had occupied for five years, and prior to which he served with distinction on the bench of the Supreme Court of Canada. I think that this meeting was of the greatest value to us as a foundation; I hope that it has stimulated, I am sure it has, interest in the fields which were alluded to in the report, and certainly our American visitors were most complimentary and said they hope they can get such a meeting together in the United States.

While this meeting was in progress, I learned for the first time—and I may say I heard it repeatedly—of certain dissatisfaction with some of the new regulations. In fact, just one line, almost, would cover the point. I talked to Dr. Allmark of the directorate, and asked him to give me information relative to this on the one hand, and I might say I got gratuitously, without any asking, comments from the Canadian Pharmaceutical Manufacturers Association, who feel that at the moment some of their efforts, particularly with respect to new drugs, are being stifled.

Now, I am not in a position to comment with complete accuracy about all aspects of this problem, but I think that it would be proper, or at least not improper, for me to make just a remark or two at this time.

Now, the item that is causing the difficulty is from Division 8, which deals with new drugs, and actually it is C.08.002(1)(a), which reads as follows, and it is just two lines: The Manufacturer of the new drug—"No person shall sell or advertise for sale a new drug unless (*a*) the manufacturer of the new drug has filed with the minister, in duplicate, a new drug submission relating to that new drug in a form and having a content satisfactory to the minister."

Now, actually, the problem would appear, as I see it, to revolve about just the last phrase here: "—in a form and having a content satisfactory to the minister."

Dr. C. A. MORRELL (*Director, Food and Drug Directorate*): Mr. Chairman: Dr. Brien, do you mean to point out the objections to C.08.005(1)(a)? I think you read 002; are you not talking about what we call notice of compliance?

Mr. BRIEN: Yes, I am sorry. Well, at any rate this has to do with the fact that industry feels that the directorate has been a bit slow on the one hand, and I could understand this just by sheer volume of work, and I would not be hypercritical at all about this, because my investigations several years ago led me to the inevitable conclusion that the directorate just has not got the manpower to carry on expeditiously, and this is the case, or so I believe. The other side of this is that these regulations have been in effect since October a year ago; in other words, about 13 months, and I would presume that any new regulations relative to a wide variety of things, quite apart from drugs, might have growing pains, if I may use this terminology to refer to the troubles that attend the introduction of new regulations of pretty nearly anything.

However, the point that the manufacturers are upset about is that a notice of compliance must be given to them with respect to these investigational new drugs before they can be released for clinical trial. Actually in the United States such a notice, at least at the present time I gather, is not necessary to enter a drug into clinical trials. I would be the last person in the world to suggest that just because the United States does it that way, we should follow suit. This is no argument at all, as far as I am concerned. However, I do think, and again I am speaking here as an individual who is neither in the manufacturing business, nor in the regulating business, but I am interested in the testing of drugs, and I participate in this in so far as I can.

I do feel that there might be times when it might not be necessary, nor indeed desirable, to force this issue, and I also realize that if I were appointed to a committee, or asked to serve on one, that would advise the director as to whether they should go further, or it would be safe to release for investigation a particular drug at a given time, that this might be a very difficult position to be in. I realize this too.

Now, one last point, though, that I would like to make about this is that I am sure that this is a period where there are probably growing pains on both sides. I know from Dr. Allmark's remarks to me that it is impossible to write down a clinical guide relative to a wide variety of things, and send it to manufacturers, and say that you must have this, this, this, and so forth, before a notice of compliance will be given. However, I think that from the one side it might be possible for the directorate to perhaps give a little more information that might help to speed this up. This is my observation from that side of the fence, and on behalf of the people that make them, the agents that are being tested, or are about to be tested, I think again that one might, when there are reports about which there can be no doubt at all emanating from either the United States or the United Kingdom, I think that I would be perfectly willing to enter such certain drugs into trials with a little less stringency as far as our own application of the regulations is concerned.

Now, I will go back to the point that you have heard from all sorts of sources, that no drug is safe. If you want to have no reactions to drugs, it is simple: You abolish drugs. That is the only way. In other words, then, we face calculated risks every day. Three times in the last year I have seen people very close to death as the result of ingestion of acetylsalicyclic acid, or more commonly it is called aspirin, once as a deliberate attempt to commit suicide, and you can commit suicide with aspirin. If you can keep your stomach from regurgitating the pills, all you have to do is take enough of them, and hang on to them, and it will work. It takes about 100 in an average adult, thereabouts, 70 to 100. Once where an accidental overdosage occurred in an adult that had an illness that simulated influenza; and then, of course, the inevitable child who got into the pills, that should not have been where he could reach them.

Iron, whether it comes in the form of pills, or in the form of blood, is a lethal material which is seldom questioned, save in the case of children who accidentally are poisoned by it, but people who have severe refractory anaemia that arises, or that can arise from a variety of causes, and for which rarely the ingestion of large amounts of iron will help, but usually is given in the form of transfusions, and of course as the transfused blood cells disintegrate, as they do in a maximum of 100 days, then they release the iron from the hemoglobin, and this is not excreted unless the person is bleeding, and it rises up, and if the condition giving rise to the anaemia does not kill the patient, then the patient will die anyway—in other words, from the blood, or the iron really.

So, what you are doing, you see, is taking a very calculated risk, and buying some time. The longest time I have been able to buy with anybody with severe bone marrow failure is 7½ years, and this man received the equivalent of 75

grams of iron, and if you translate that into liquid blood, that is about a bath-tub full, transfusions, over a period of seven years, but he died from the results of my therapy. But, on the other hand, of this 7½ years, five of them were tolerably happy. So that this goes on in medicine all the time.

I would like to quickly refer to something for which I have the greatest commendation for our director, namely, that is the setting-up of an adverse drug reporting program. Have you been able to have the initial meeting yet?

Mr. MORRELL: Yes sir, a week ago Monday.

Mr. BRIEN: The people that have been selected to do this chiefly are in the large—not necessarily all, but a good many of them are—teaching hospitals, and a good many of them are interested right now in the examinations of the Royal College of Physicians and Surgeons of Canada, usually in medicine, or perhaps pediatrics, and the orals are taking place this week, so I did not know whether he had been able to hold the meeting or not, but this is the first time that a really good, organized attempt to get at the adverse reactions to drugs in hospitals has been gotten under way, and I am most happy, Dr. Morrell, that you have been able to get it off the ground, because I hope that they are not going to report too many—certainly of the type that would—reactions of the type that would give us concern, but at least we have got a mechanism now in being that is infinitely better than anything else that we have had heretofore.

In this particular regard I might also say right now that some of you who are in the Canadian pharmacological society, or the pharmacological society of Canada—I can never remember which is the proper terminology—have been advocating a committee on drug safety for a number of years, and I know that at the moment the Canadian Medical Association, and therefore the provincial ones through it, are being asked to contemplate whether they might, together with the pharmacologists, with members of the Royal College, and members of the department, look into the setting up of such a national committee on drug safety. Now, whether or not this will come into being, I cannot say, but I think that it is worthwhile for the members of this committee to know that people in various bodies are thinking about it.

Now, the last thing I would like to say, just a little bit about how drugs are handled in a large hospital, and particularly in the hospital in which I worked, because this is the one I know most about. The Victoria Hospital in London has about 1,000 beds; we have, according to our pharmacist, 5,000 items in our stock, and we spend at the present time something like $400,000 a year on buying it. In the case of about between 50 to 60 of the items, we have invited people to tender on drugs of various sorts, and not all the people whom we ask to tender do so, for one reason or another.

We have found that in the case of small products, like tablets or capsules, that it is of great advantage to buy them in lots of 50 to 100,000 and this is our practice, from 50 to 100,000 in some 50 to 60 of these items, and this, of course, has resulted in very substantial savings to us as a hospital, and to the country, or at least the province, because the Hospital Services Commission is, in Ontario, intimately concerned with this. The amount of the total that we buy by tender is somewhere around a seventh or an eighth of the total.

Now, to my knowledge, or at least with respect to a question which I asked our chief pharmacist the other day, these drugs are purchased from people who sell drugs to federal institutions who require them. From the standpoint of our own handling of investigational new drugs, I would like to just make one last comment and then I will sit down: We handle these drugs by having them sent to the doctor who is to be responsible for the investigation, but in care of the pharmacy; they are not sent to the pharmacist; they are sent to the doctor, in care of the pharmacy. Some of them have to be refrigerated, but

the majority of them, of course, do not. We handle those drugs substantially in exactly the same fashion that narcotics or other controlled drugs are handled; the pharmacist keeps sheets on them, similar to those that are kept for Mr. Hammond, and then any time he can give an accounting to the last pill or ampoule or whatever form the drug is in, which of course is one of the requirements in the revised regulations.

However, before these drugs are sent for investigation to the pharmacist, the investigator must present either a detailed account of what he proposes to carry out, or fill out a pro forma of our own devising, which is then scrutinized by our pharmacy and therapeutic trials committee, and if we do not like it, he will not be investigating the drug. If he does, it will be on a controlled basis such as I have outlined.

We have a great advantage, being a university hospital, that we have the professor of pharmacology at Western University on this committee, and indeed he comes to all the pharmacy committee meetings of the hospital, for the simple reason that it is good for us in the clinical field to have him there, and it is good for him in the basic science field to be there, because we are both engaged in the teaching of undergraduate and postgraduate students.

Thank you for your indulgence. I will attempt to answer such questions as are within my competence, and if they are not, I will just say so.

The CHAIRMAN: Thank you very much, Professor Brien.

Gentlemen, the meeting is open for questions.

Mr. WILLOUGHBY: I think, Mr. Chairman, that we all appreciate the problems that they are faced with in those very important questions, and we appreciate the work of Dr. Brien's committee, and also Dr. Morrell. It looks to me as though we have two problems: one is shortage of staff; and the other is probably an excessive investigation in some ways, so that things are being held up in two ways.

Now, in the first place, in the question of staff, you have mentioned the fact that you are offering scholarships in connection with the clinical investigations, which I think is an excellent idea. Do you think that we could help Dr. Morrell to increase his staff, because I realize that he has not been able to fulfil the suggestions that you have made in your previous report. Could we assist him in some way by recommending federal scholarships to people who are prepared to go into his department and would guarantee that they would stay with his department for a period of years after they were assisted in their clinical work?

I would suggest that that might be a way that we could improve it.

Then we have the question of investigation. I understand we sometimes are as long as six months longer in approving a drug here, due to some extent to the shortage of staff, but to some extent, probably, to our excessive thoroughness in not accepting some of the preliminary reports fully, and you have also suggested that we should probably improve that by expediting the work, and accepting these reports earlier before we permit them for clinical investigation.

But would licensing companies in Canada, particularly, would that assist us in some way in accepting their reports, so as to expedite the work in the department here?

That is two questions. Another question I would like to know is, do you consider that provincial investigation is justified, such as I understand is being set up by the department of national health and welfare in Ontario, or should we encourage, rather, that the whole matter be taken over by the federal authorities, and not use the provincial organizations as well?

My last question, and I will leave these questions with you, is this: Is it complicated to have food and drugs investigation in the same department?

Probably Dr. Morrell can answer that better. Would we expedite certain drugs if we had two departments investigating separately, investigations going on separately?

I think probably that is all the questions I had in mind from your report.

The CHAIRMAN: Your last question, Dr. Willoughby. Do you mean that the food and drug directorate should be divided?

Mr. WILLOUGHBY: Yes, decidedly; so as to give them less complications.

Mr. BRIEN: To deal with the problem as I see it relative to the provision of additional staff, we are starting out trying to interest some young men that are perhaps one, or conceivably two, but so far it has just been a year from graduation. Before that chap would be useful to Dr. Morrell, assuming that he went straight ahead to do this, it would require a minimum, I should think, of about five years of training. Well then, on top of that, he is gaining some practical experience at the same time, but still even though he has completed his, if you like, formal training, after he graduates he is still not useful to Dr. Morrell. I have found out a good deal about the operations of the directorate in the course of getting at the information that is contained in the report, and I think that there is a training period that would be necessary there, so he gets to know what the problems really are.

Now, I think that certainly it is in the interests of the country for us to try and get some people into this field and bring them along, but they are not going to be producing dividends until considerably past the time Dr. Morrell and I both have retired.

Mr. WILLOUGHBY: Well, if we do not start, we will not get there.

Mr. BRIEN: No, of course we will not, and we should certainly make a start on this, but what he needs right now is some expert help, and the only way I can see that you can get it is buy it, and you buy it from one of two sources: Either industry or the teaching, the academic professions, and I think that it was intimated in the original report, and actually I spoke to the then minister about this very point, that I did not go in—I do not know the complete range of salaries that are involved in this, but I know that if you wanted to get somebody to do a job for you in a given field, that one way to do it is offer him more than he is getting now, plus certain other considerations. You certainly will not attract him if you offer him less, I can tell you that; and I think we need to go on, by all means, and try to encourage people to come up into this field, but also I think that by one means or another you have to get into active and successful competition with the people that have the kind of man Dr. Morrell needs working for them now, and he can tell you where they are, and what they are doing, and I think you have got to lure them away from that. This is what happens to my staff when another university wants some of them. The first thing I know he says: "I have an offer that is just too good to turn down," and he is down in Alabama, you see. This has happened to me just in the last few months, and there has got to be a bit of this to get what he needs right now.

Now, with respect, and I said this very carefully, realizing that he might just put me on the spot some day about one of these things, I do think that there might be, after the growing pains straighten out, that there might be a bit of judicious relaxing of the requirements in certain cases, and I think I cannot state it more specifically than that I would be—Dr. Morrell is in a position that if anything happens he will be crucified, period. Those of us who practice medicine are not in quite that same position, and any one who has not made a mistake either has not much of a practice, or he is a liar.

Now, relative to this, I cannot give any sensible comment at all about this provincial investigative business, because I do not know the details, even though I come from Ontario. We noted only in the report that it had been advocated in certain areas, that the food and the drug divisions be separated.

Now, I would like not to go again into this at great length, but I do think there are certain things we ought to bear in mind, that there are times certainly when something has happened in the food line, and they have had to just drop everything in the drug line to go out and look into something that has cropped up suddenly with respect to food, and we are just as interested in that from the standpoint of public safety as we are the drugs.

Certainly if they were separated, then they would not be able to call upon him, or I presume they would not, unless there were some liaison.

However, I think that before anyone contemplates separating this directorate a tremendous amount of thought ought to go into it, from the standpoint particularly of the duplications of laboratory facilities with respect to testing for many things, both in the drug and food. It is very difficult, I think, at times to sort them out and I see no point in building two empires when one good company will do the job.

Certainly it is embarrassing to Dr. Morrell right now to have to get into any detailed, unexpected examination in either food or drugs with his present facilities. What he needs, certainly, is more people at the present time. I would not advise separating the two without a great deal of thought and a most careful look at the laboratory side of things, because this is tremendously expensive from the standpoint of just the physical space, the equipment, and also the people to operate it, and there are people—there have been arguments made that people who do the work in drugs should not be doing it in food, and so on. Now, they may have certain validity but this depends on the qualifications of the man on the one hand, and the types of work you are asking him to do on the other.

Mr. WILLOUGHBY: What about the licensing? Would that expedite the department if we had nothing but licensed organisations supplying our drugs?

Mr. BRIEN: I do not know; I do not know, it would depend on—there would be trmendous difficulties in, I should think, seeing that everyone lived up to the requirements. I cannot answer that, sir; I do not know.

Mr. WILLOUGHBY: Surely we could make it a little more difficult for these, as we call them, fly-by-night organizations to sell inferior products.

Mr. BRIEN: I would be all for doing that, but it would have to be done by a licence.

Mr. WILLOUGHBY: I do not know of any other way in which it could be done. Do you know of any other way?

Mr. BRIEN: I suppose there is one argument in favour of it. I have listened to people who know much more about the technical or legal aspect of it than I do, and I have heard that it can be done and that it cannot be done; I do not know. However, if you had certain requirements in respect of people selling drugs, whether you call it a licence or anything else, I think the important thing is they are adequately scrutinized by our federal directorate.

Mr. WILLOUGHBY: Under the present organization is Dr. Morrell allowed to control the smaller companies which are operating?

Mr. BRIEN: From my conversations with him I am led to believe he has the power to do this, but you are in a technical field which is a little beyond me. I would like to hear from Dr. Morrell about that. How do you do it, Dr. Morrell?

The CHAIRMAN: Dr. Morrell will be here on Thursday.

Mr. BRIEN: I would like to hear what he has to say right now.

Mr. MORRELL: There are many things I could say in respect of a number of points which have been raised this morning as a result of Dr. Brien's statement. In answering the last question first, of course we have authority over a company, and it has nothing to do with its size. I think, Dr. Willoughby, that some-

times it is difficult to find them. If I do not know of them, if they have been in existence only a few months and we may not know they are in business, this is the main weakness in not having some requirement for prior notification that they are going to be in business and the kind of business they are going to carry out. There is nothing to prevent anybody in this room setting up a drug business tomorrow if that person should wish to do so. He would not have to tell me. I presume they have to tell somebody; perhaps the local municipality gives them a licence.

Mr. WILLOUGHBY: They should have to have a licence and should have to apply to your department to obtain one.

Mr. MORRELL: I believe this was the point in your statement.

Mr. WILLOUGHBY: Yes.

Mr. MORRELL: Nevertheless, when we find them through our own efforts, or through somebody telling us that Smith, Brown and Morrell are in business down the street, we would soon go down to see what they are doing, and in that way catch up with them. In the law there is nothing which says we cannot do that. In fact, the law says we can do it, and we think our responsibility is that we should do it.

Mr. BRIEN: It also is written in the law that you must have a licence to do this the same as to drive your automobile, but I still think they might do it without a licence.

Mr. MORRELL: We would still have to find those who did not obtain a licence; then we would have something to take them to court on. They would have broken the law by starting without a licence. When we found this company we could charge it in court with operating a pharmaceutical business without having received a licence under the Food and Drugs Act. However, Dr. Brien, you are quite right; we still have to find them.

Now, if we find them we cannot charge them at once with anything; we have to find some reason for taking objection to whatever they are doing. It seems to me, along that line, that we can start right away working on them and perhaps seize all the products they have, and so on, because the act gives us authority to do this.

Mr. BRIEN: This is a little bit like trying to define the practice of medicine. There really never has been a satisfactory definition of this. It includes, among other things, that you do certain things for hire, gain or hope of reward. If you said, "Now look; I do not want any money, I am not working for anybody, I do not hope for any reward at all except maybe to go to heaven when I die", and you treat somebody, could you be charged for doing this without a licence? Are you practising medicine? The courts never have answered this.

Mr. MACKASEY: We already have had one manufacturer here whose sole motivation was to go to heaven; he did tell us he was not in it for profit.

Mr. BRIEN: There are areas in which it is terrifically difficult. It is like buying a licence to drive your automobile. You see the odd automobile in the back fifties which does not have a licence in a province as advanced as is Ontario.

Mr. RYNARD: I would like to compliment Dr. Brien on the very lucid and painstaking explanations he has given us. Most of my questions have been answered. I would like to say that perhaps through the county health unit and medical health officers you could have all drug firms licensed and it would not be necessary for the federal authorities to run around hunting up those people. We do it in other areas and surely we can do it in this.

I took from Dr. Brien's remarks that he felt now our food and drug directorate is slow in getting a release for new drugs. On the one hand he states he feels they need more staff and on the other hand, if I understood him correctly,

he feels that the only testing time there is is when they are put on clinical trial I also understood that he believes we are a little slower in this regard than they are in other countries, namely the United States, Great Britain, and probably Europe.

I would like to ask Dr. Brien whether he feels there should be certain limitations put on the length of time a drug can be held up before it is released for clinical trial in order to avoid the sometimes long delays which apparently we have now.

I also would like to ask Dr. Brien whether he feels that it now is necessary to have a standing committee when we have a committee which is going to report on adverse reactions of drugs?

Why was the drug parstelin taken off the market for so long and why did it take so long to set up a committee to study it; why was there such a delay in bringing in the report? Surely, in the hospitals across Canada the effects of parstelin were known. They were using this drug. My point is that in practice we had a great many complaints of people being cut off this drug. I know of one doctor who had to go to an institution in order to get it; this seemed to be ridiculous to me. After doing all this work, they bring the drug parnate back and allow stelazine to be used; but now we have to prescribe them in two separate prescriptions which adds cost to the patient. I would like to ask what is gained by dividing it up. Surely a medical man has to take the responsibility for what he is prescribing. He would prescribe parnate if he wished, or he would prescribe stelazine. I am just wondering why the committee brought in this report.

Mr. BRIEN: Dr. Rynard, I will go back to the beginning in respect of parstelin. I had nothing to do with this committee, but I would be glad to tell you a little bit about my own experiences in respect of it. Basically, I do not like to see multiple drugs in the same basket or the same capsule, for the very obvious reason that it stifles your manipulation of the two and you end up putting in more of either one. Basically, I do not like particularly those things they have in vitamins—all the trite elements and tram car tickets. In most instances people do not derive benefits from a good many.

Mr. MITCHELL: You call that gunshot.

Mr. BRIEN: Of No. 12 bore or even 10, sometimes.

Anyway, stelazine is in use in the particular Ontario mental hospital in which I consult and where I was yesterday afternoon. There are over 2,000 patients in this hospital; it is the Ontario hospital in St. Thomas. There is no need for me to withhold its name. Stelazine is not the only drug that is used, but it is a most useful one, and I can attest to this from my own observations. To my reasonably accurate knowledge they do not use a great deal of the combination of it with parnate. I just do general consultation on the medical aspects of the illnesses of any people they want me to see, but I have been going there at least monthly since 1946 and I have a pretty good idea of the trends in therapy.

I am in no position to comment on the reason it took so long to process this business. The business of bringing back parnate to a controlled environment and forbidding it on an outpatient basis, of course, is one of the problems. When we set up our own therapeutic trials committee we said the same thing knowing perfectly well we would be changing it. Initially, however, we just said these drugs will be used only in an inpatient service. It became perfectly obvious it is reasonable in the case of some of them to use them on an outpatient basis, because it would be absolutely ridiculous and impracticable to bring the people in just for the sake of having them under the roof, so to speak, provided the man who is testing knows what he is doing and has an

intelligent co-operative patient. All these things are ingredients to successful drug testing. Without them the thing is fraught with danger and apt to produce inconclusive results or lead to wrong conclusions.

Basically, I think it is far safer to have parnate separated from stelazine for the simple reason that it will not be used nearly as much on the one hand, and along with the information which has gone out about parstelin and like drugs, it would make a man think carefully before he prescribes it; it will make him think in terms of possible ill effects.

Actually, one of the most practical explosive responses in the hypertensive realm—actually it was parstelin and not parnate alone—which I observed was in respect of a patient for whom I was prescribing the drug myself. These are in the minority. However, they are very dangerous; they are potentially dangerous and look exactly like the explosions of a pheochromocytoma which would cause a stroke in plain English.

With regard to the standing drug committee versus the adverse reporting program, I think these are two entirely different things. The adverse reporting program is a peripheral attempt to get prereporting on this. This is only as good as the person who is nominated to do it and the co-operation which he has from all the doctors who use the hospital. He cannot go around and quiz 1,000 patients every day to find out whether this, this, or this is good. It requires the co-operation of everybody in the program, including your nurses too.

The other problem is right here in this city; it is the problem of whether you can obtain better results by having a group of ad hoc committees which have special interests relating to the particular subject under study, and made up entirely of, for the sake of argument, half a dozen persons versus a committee that has a certain amount of continuity and has men with principally but not necessarily entirely medical interests in the drug field who would come to do the kind of work we did. It requires an awful lot of time to make this work.

With regard to the Canadian drug advisory committee as it is presently constituted—leaving out these special ad hoc committees—I think it would be fair to say, Dr. Morrell, that you directed it be called together at intervals of perhaps several times a year prior to the thalidomide difficulties, of course, to deal with certain problems that it could solve in an afternoon or a day, and not as a continuing thing which would go on for months. This is the real problem about this working committee; that is, to obtain personnel who are able to do this, not only just from the standpoint of their motivation, but from the standpoint of having the time away to do it. I was a pretty ineffective teacher for several months while this was going on. This was done with the indulgence of my university, because they thought it was a good public service.

It is difficult to get a committee of even half a dozen persons that would be capable of dealing with the entire question. It was our feeling that if you got such a committee together it should have people coming on it and going off each year, preferably for terms of something up to three years, or two anyway. You can get excellent men to serve on C.D.A.C.; I have no doubt of that at all. It meets relatively infrequently and for short periods of time. This is sort of a compromise which came about as a result of talking to various people here in Ottawa. In some respects I think it is better, and in others I think it is inferior.

I think again, just as there have been certain disagreements between the manufacturers and the directorate, this is a time of testing—I think this will become pretty apparent in the near future. You have had a certain amount of ex-

perience; I do not know how much you need to get a really good judgment on this, Dr. Morrell, but sooner or later you will see that it is obvious you should go one way or the other. Is that correct?

Mr. MORRELL: I think so.

Mr. BRIEN: This is the way I read it right now.

Mr. RYNARD: I have one supplementary question. I take it you do agree that a standing committee should be set up in view of the fact that you waste a good deal of time getting a committee appointed and getting people to act?

Mr. BRIEN: Yes. This is a real problem. Time is wasted just trying to get the thing together. If Dr. Morrell had a pretty good and sound committee organized he could say we will call in Dr. so and so because he is an expert in this field and get down to work there, even if it is just for two hours, as I am here this morning. I think this would help him a good deal. This is my feeling.

Mr. RYNARD: As I understand it it took weeks to get three persons to act this year on the drug parstelin. If your standing committee was set up it could go to work straight away.

Mr. BRIEN: Yes; and if it were properly constituted, it could deal with perhaps seven out of ten or nine out of ten of the problems, depending on what they were.

One last answer I omitted was in respect of whether I thought we should loosen up grossly on the supply of materials for clinical testing. I think Dr. Morrell's job is to be just as sure as he can be that the thing is safe and that it is reasonable to release it. If I were asked to make the decision, I think there are times when I perhaps would release some things a little sooner. I do not want you to get the idea that I am finding fault with him at all; I am not. I think there are times when this might be done, provided I personally knew the people who had done the particular piece of work. I could name some persons who most of you would know, and all the medical men would know immediately whose advice I think would be better than, for instance, what I might give you. This is the time when I would loosen it up a little bit.

Mr. MACKASEY: Dr. Brien, I share your enthusiasm in the adverse reporting program being set up, particularly the inclusion of Dr. Genest from the Montreal area for whom the committee has high regard.

Mr. BRIEN: So do most other people.

Mr. MACKASEY: I noted your earlier remarks pertaining to the particular hospital with which you are associated and its policy of buying drugs in a very impressive amount of dollars. You mentioned you obtained tenders for 50 or 60 of these particular drugs. I lost track of your testimony there. Am I right in inferring that you were very selective in respect of whom you invited to tender? I suppose you were selective for reasons of increasing the safety factor. Would you care to elaborate on this a little?

Mr. BRIEN: Yes. One time I went down to the pharmacy and I counted 47 different kinds of cough medicine; that is at least 43, 44 or 45 too many depending on your point of view. What we did was try to reduce the products or streamline the operation. I might say we do have tenders for as many as between 50 and 60 of this large list. In most but not all cases the bid that is accepted comes from people within the C.P.M.A. In fact, we have right here in this room the director of a firm which gets a very substantial part of our business with regard to one drug.

We try to keep two or three representative agents of a particular type in the pharmacy. However, any doctor on our staff—and this totals nearly 300 when you take them all in—can prescribe any drug that is offered for

sale in Canada if he will name it by its brand name and indicate the name of the manufacturer. If we do not have that in the pharmacy, we have an arrangement whereby it is obtained from the local wholesale distributor in the city and it will be delivered just about as quickly as it would had it come up from the pharmacy to the floor. So, in the main our staff people are content to use the drugs that are there and we have had nobody object, or at least suggest that they were not efficacious.

Mr. MACKASEY: I would like to return to your analogy, which I appreciate as a layman, of the 47 brands of cough syrup. Do you feel, at least from the safety point of view, that it is not efficient to simply ask for cough syrup? You would like to be doubly certain and specify the type or brand.

Mr. BRIEN: Yes, and it is ridiculous to have 47 when you can get along with about three. You can put an awful lot of other things in the space they occupy. A cough syrup will do one or two things for a cough, and so long as it does that safely and well I am not worried about who makes it so long as it does what it is supposed to do and does not do harm. We have reduced the 47 brands of cough syrup down to three.

Mr. MACKASEY: In other words the main criterion in respect of cough syrup is not the price so much as the reputation of the person producing the cough syrup.

Mr. BRIEN: Actually, as I say, cough syrups act in different ways. There are a multitude of people who make these. If we wanted one that suppressed, then we would want maybe two or three people to tell us what they would provide us with that type of medicine for. As I say, we have deliberately tried to pick on people about whom there could be no question. I might add that we do inspections of our own occasionally. We have sent, at my instigation, a party down to a plant. He has been into a good many plants in the last year and he knows exactly what is going on. It has been very good for us as a hospital to have him do this.

Mr. MACKASEY: I have gathered from your evidence and from the evidence of other expert witnesses here, including the gentleman who was here last week, that everything being equal, the products of the manufacturers who make up the Canadian Pharmaceutical Manufacturers Association are in general a little better than those from firms which do not belong to this association; in other words, they do a fairly excellent job in general in policing their own association, and perhaps the public is indebted to them. I say this because there have been certain headlines which have been taken out of context which have castigated the industry in general. I do find more and more that the Canadian public do have a lot to be thankful for in respect of the high degree of integrity of their members in general. Do you agree with that?

Mr. BRIEN: I certainly do, and this is based on opinions of other people whose judgment I regard and it also partly is based on inspections I made personally. I might say, these have shown the most intimate details of how they do things, right down to the work books where they put their data down in its roughest form. That is the place to look when you are looking into some of these things.

Mr. MACKASEY: Thank you very much.

Mr. MITCHELL: Mr. Chairman, I have just a couple of questions to ask Dr. Brien. In your submission, doctor, you suggested that there might be less stringent inspection of drugs from certain countries, and you named two, the United States and the United Kingdom. You suggested that less stringent inspection could be used by the directorate in respect of processed chemicals or finished preparations entering Canada from other countries. I believe your

suggestion here, if I understood correctly, would be that there could be more possibility of an inferior chemical or product coming in from countries other than those two you named.

The other matter I would like to bring up is that you are quite aware of the setting up a couple of years ago of the select committee on drugs by the Ontario government. I had the privilege and pleasure of being there myself. In their findings they recommended we could save X number of dollars in supplying generic drugs to government institutions under the directive of the Ontario government. I realize we are not going into the cost of drugs now. Do you consider that this type of drugs, being supplied in this case to mental and t.b. institutions, would have the same therapeutic value in respect of the patients receiving them; that is, overlooking the financial complex entirely and merely taking into consideration the efficacy of these preparations. Could you say whether they are supplying that type of medication at the present time?

Mr. BRIEN: What I had in mind when I made the specific reference to the United Kingdom and the United States was to an earlier release, Dr. Morrell, of your clinical investigation in this country.

Mr. MORRELL: Yes; I understood that.

Mr. BRIEN: I told you that at the moment I am investigating a drug which I might say is highly efficacious and which currently is on the market over there and is not yet here or was not here a few days ago. There was not the slightest doubt in my mind about this agent. I will be surprised if you do not release it in due course; I would be amazed.

My point, Mr. Mitchell, was this. With regard to this particular agent, I know very well it was going to work before I got it for the simple reason that it was through the efforts of some men in the United States whom I know personally and well, and for whom I have the greatest regard, that it has been released and is available on the open market in the United States. There are times when reports of that nature are available to me, and if I were asked to give an opinion on the release of a drug as an investigational new drug, I would be favourably disposed, perhaps, to allow it out a little sooner than would appear to be the case at the moment. That was the whole point I was trying to make. It is not a blanket suggestion that everything be released without careful scrutiny. However, I think I would be prepared to believe some outside people who played a part in this.

Now then, so far as the situation in Ontario is concerned in respect of some of the generic drugs, the only time I ever took it on myself to question something and have it sent down to the directorate because I had some doubt about whether the material had in it what it was supposed to contain, Dr. Morrell or his department reported that it had exactly what it said on the label. This, however, does not prove that it was absorbed at the same rate as the same product made by somebody else might be absorbed; but at least it had in it what the people said it had. This business of selective or different absorption I am sure can vary from one firm to another with a lot of things.

In a general way, relative to tuberculosis, I am sure there is some generic material being used there. I have a limited personal contact with tuberculosis; this is usually in respect of diagnosing it and getting the person under sanitorium auspices. However, in a few instances I do participate actively and treat the person. One of the agents you referred to as a generic compound is being used and it is very satisfactory.

Mr. MITCHELL: You mean P.S.A.

Mr. BRIEN: And I.N.H. It is perfectly satisfactory in this particular instance of which I am thinking. There are others about which I have my own strong feelings from having seen them. I believe I have heard Dr. Morrell suggest there is much less likelihood of a well known brand of a particular agent failing to

produce the effects that are desired than perhaps some of the others. I think this might or might not be true. I do not think all generics, by any means, do not live up to their advance billings.

Mr. MITCHELL: You say you do not believe they live up to their advance billings?

Mr. BRIEN: No, I think that you cannot say that just because it is marketed as a generic it is not going to be any good. That is what I mean, in plain English.

Mr. MITCHELL: But you are not taking the whole group of generics.

Mr. BRIEN: Oh, no, I will be very cautious about this. If you wanted me to write it down and sign my name to it, I am afraid I would end up going and doing a lot of personal work. I would not even take Dr. Morrell's word on some of these; I would go and look at it myself in some ways.

Mr. MORRELL: Yes, I think, Mr. Chairman, if I were in Dr. Brien's position I would want to prescribe drugs that were made in places that I knew.

Mr. BRIEN: Exactly.

Mr. MORRELL: I do not give tuppence, Dr. Brien, about a brand name. All I would say—

Mr. BRIEN: No, neither do I. It is the place it is made.

Mr. MORRELL: If a person goes and pays $25 or $50 to get a brand name, that does not confer any quality on his drug. A brand name is not what I talk about. It is where and who made it.

Mr. BRIEN: That is right; I agree.

Mr. MORRELL: That is what you want to know.

Mr, BRIEN: I agree with you sir.

Mr. CÔTÉ (*Longueuil*): Mr. Chairman, first I apologize for being late but I am just back from the Canada pensions plan committee meeting.

I just wanted to ask one question: Dr. Brien, you said that in a drugstore you see 47 different kinds of cough syrup.

Mr. BRIEN: This was in our hospital pharmacy; it was not an ordinary drugstore.

Mr. CÔTÉ (*Longueuil*): And as far as you are concerned, three would be enough. Do you think, personally, that we have too many drug manufacturers in the country?

Mr. MITCHELL: No.

Mr. BRIEN: Well, that is just the same as asking me are there too many automobile manufacturers, is it not?

Mr. CÔTÉ (*Longueuil*): Personally, do you think it would be better if we did not have so many drug manufacturers?

Mr. BRIEN: No; I do not care how many people make it, so long as they make good products, and they are acceptable to us from all the points of view that all of us are interested in.

There are something getting towards 500 manufacturers are there not?

Mr. MORRELL: Yes, getting up that way.

Mr. BRIEN: It is a very large number, and whether or not we would be better off if we had 50 instead of 500, I think is beside the point. You can argue that from economics and all sorts of things.

The thing that really matters is the end product, and our ability to make sure that it is as safe as we can make it, and as efficacious as we can make it.

Mr. CÔTÉ (*Longueuil*): Would you place in that category the manufacturers who make safe products, the manufacturers who could not qualify to sell to the government by the new rules?

Mr. BRIEN: I will answer that question as soon as you tell me why they did not qualify.

Mr. CÔTÉ (*Longueuil*): Do you know the reason?

Mr. BRIEN: Oh, I have read the newspapers; I have brought a clipping here, and I was just waiting for this one.

Mr. CÔTÉ (*Longueuil*): I am not referring to the newspapers.

Mr. BRIEN: I want to know why they did not qualify, and I will answer your question. It might have been because the ceiling was not high enough, or they were one bathroom short for a hundred people.

Mr. CÔTÉ (*Longueuil*): Yes, that is what I said last week, too.

Mr. BRIEN: It has nothing to do with whether your drugs are good, bad, or indifferent.

Mr. CÔTÉ (*Longueuil*): Well, would you say that the rules the government are asking for the factories to qualify are too strict, too rigid?

Mr. BRIEN: As a matter of fact, I cannot answer that question completely honestly, because I do not know all their requirements, but I know, as I say, just what I saw in the paper the other day, and I suspected somebody would sooner or later get around to this, and the press release that I saw just said that a considerable number of people did not measure up to the requirements, and it did not state anything more than that, and I would like to know why they did not measure up before I answer your question.

Obviously, there are certain standards laid down, and they failed to meet the over-all requirements. These deficiencies might be very serious, or they might be inconsequential, and this is the old problem that you get into, for instance, in saying that a doctor might not be, should not be on the staff of a hospital if he is over, for the sake of argument, ten miles away, or 25, because of the difficulty he would have getting to see the patient. Well, you see, two miles in a crowded city might take four times as much time—it certainly would in London right now, with the main street torn up with its sewer project —as 25 on an open highway.

So, before you can answer the question intelligently you have got to know all the reasons, and I do not know them, and therefore I cannot give you what I would consider an intelligent answer.

If you make certain stipulations, and to use the one that is commonly used, with respect to doctors, that they should be within a reasonable distance of a hospital, as soon as you start to define that there is going to be one fellow who is 100 yards farther, and if you stick to the rule, then he cannot belong, and if you let him in, the fellow that is 250 yards farther, he works it, you see, so this is a most difficult thing to answer. Their reasons for refusing to approve somebody might be that they were just grossly not measuring up, or it might be some simple thing, that they could fix and meet the requirements a month later.

I do not know; there was no information available to me on this point. I did ask our pharmacist if he bought any drugs from people who were not permitted to sell to the government, and the answer I got was no, and he said that right now if people are so approved it does not take them long to let you know.

Mr. CÔTÉ (*Longueuil*): We do not know the list ourselves.

Mr. BRIEN: I know you do not, but the fellow who makes them knows, I am sure. He either sells them or he does not, but if he does and you contemplate buying from him, he lets you know that very quickly. This has happened, in fact, recently.

Mr. CÔTÉ (*Longueuil*): I think that some of the rulings that were asked, some of the requirements, I would say, were very little things.

Mr. BRIEN: Well, that is what I say; I do not know what they were. I am just being perfectly honest.

Mr. CÔTÉ (*Longueuil*): This is the reason why I think these firms should qualify, if those are such little items.

Mr. BRIEN: Well, if they are minute things, then they should be correctible without much trouble, and either the requirements are reasonable, or they are not.

Mr. MACKASEY: Mr. Chairman, Dr. Brien very wisely anticipated this line of questioning. I intentionally stayed away from it because I did not think this was your purpose in being here this morning.

Mr. BRIEN: No, it is not.

Mr. MACKASEY: We are having Dr. Morrell on Thursday and I am sure Dr. Morrell will be able to give us adequate explanation of whether perhaps they should use bar soap over some other type of soap, and things of this nature.

What I would like to say is that poor Dr. Morrell—we are off the record at this stage of the game—but he is in the type of job where he is damned if he does, and damned if he does not. On one side, the industry blames him for being over-cautious and we on the committee are creating the impression, through the press, that possibly we are not cautious enough.

So, I do not know how Dr. Morrell—he must have an awful degree of dedication to put up with it.

The CHAIRMAN: Dr. Morrell will be able to go into this. I am sure he is well prepared for questioning on Thursday.

Mr. BRIEN: I might just read one line from the last part of this 1962 report, and it dealt with this point, and it reads as follows:

> Beset on the one hand by manufacturers requesting speedy action, and on the other by a duty to protect the public from hazards of which they (and he) might be unaware, his course of action deserves the highest commendation.

I have no reason to change that. I have seen none in the intervening time, since that line was written.

The CHAIRMAN: I do not think there are any more questions from the committee.

I would just like to thank you, Professor Brien, for coming down from London to appear for an encore performance before the committee.

The meeting is adjourned until Thursday at 9.30 a.m. when we will have Dr. Morrell before the committee.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 18

THURSDAY, NOVEMBER 26, 1964

WITNESSES:

Dr. C. A. Morrell, Director of the Food and Drug Directorate; Dr. G. D. W. Cameron, Deputy Minister of National Health; Mr. A. Hollett, Director, and Mr. Robert Ferrier, Field Inspection Unit, both of the Bureau of Operations of the Food and Drug Directorate, Department of National Health and Welfare.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21270—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong	Horner (*Jasper-Edson*)	Prud'homme
Asselin (*Richmond-Wolfe*)	Howe (*Hamilton South*)	Roxburgh
Basford	Jones (Mrs.)	Rynard
Côté (*Longueuil*)	Jorgenson	Slogan
Enns	Macaluso	Wadds (Mrs.)
Francis	Mackasey	Whelan
Gauthier	Marcoux	Willoughby—24
	Mather	

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

Note: Mr. Mather replaced Mr. Orlikow on November 25.

ORDER OF REFERENCE

WEDNESDAY, November 25, 1964.

Ordered,—That the name of Mr. Mather be substituted for that of Mr. Orlikow on the Special Committee on Food and Drugs.

Attest.

LÉON-J. RAYMOND,
The Clerk of the House.

21270—1½

MINUTES OF PROCEEDINGS

THURSDAY, November 26, 1964.

The Special Committee on Food and Drugs met this day at 10.15 a.m. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Armstrong, Harley, Howe (*Hamilton South*), Macaluso, Mackasey, Mather, Roxburgh and Willoughby—8.

In attendance: Dr. C. A. Morrell, Director of the Food and Drug Directorate; Dr. G. D. W. Cameron, Deputy Minister of National Health; Mr. A. Hollett, Director, and Mr. Robert Ferrier, Field Inspection Unit, both of the Bureau of Operations of the Food and Drug Directorate, Department of National Health and Welfare.

The Chairman referred to correspondence received from Nordic Biochemicals Ltd. of Montreal. It was agreed that the Chairman answer the letter on behalf of the Committee.

Mr. Mackasey moved, seconded by Mr. Macaluso,

That the committee recommend that its quorum be reduced from 8 to 5 members for this meeting only;

Thereupon Mr. Howe moved, seconded by Mr. Willoughby, that the motion be amended by replacing the words "for this meeting only" by "starting today". The amendment carried on division: YEAS, 7; NAYS, 1.

The question being put, the Chairman declared the motion carried as amended.

The Chairman welcomed back the Director of the Food and Drug Directorate. Dr. Morrell made a short statement about standards for drug manufacturers in Canada, and related matters. The witness answered questions and was assisted by Messrs. Ferrier and Hollett, and by Dr. Cameron.

The Committee agreed that the Trade Information Letters and amended Food and Drug Regulations referred to by Dr. Morrell and which had been distributed to the Members, be appended to this day's proceedings. (*See Appendix "A"*)

The Chairman thanked Dr. Morrell and the officials of the Department of National Health and Welfare for the information supplied to the Committee, and at 11.25 a.m. the Committee adjourned to 9.30 a.m. Thursday, December 3rd.

Gabrielle Savard,
Clerk of the Committee.

EVIDENCE

THURSDAY, November 26, 1964.

The CHAIRMAN: There is a quorum present.

As the first item of business I would like to have a motion to reduce the quorum from eight to six members.

Mr. MACKASEY: I move we ask permission to reduce the quorum for this meeting only to five members.

The CHAIRMAN: For this meeting only?

Mr. MACKASEY: Yes. I think the other members have a duty to be here, or to arrange their affairs so that the meetings do not coincide. I mean this meeting only.

Mr. MACALUSO: I second the motion.

Mr. HOWE (*Hamilton South*): I move an amendment to the motion to read five members starting today.

Mr. WILLOUGHBY: I second the amendment.

The CHAIRMAN: Are there any further amendments or discussion on it? The question then is on the amendment first that the quorum of this committee be reduced to five members starting today. All those in favour? All those against?

Amendment agreed to.

I declare the motion carried as amended.

Gentlemen, there is one piece of correspondence from Nordic Biochemicals, pointing out some of the evidence in this committee implying that there was a direct relationship between the size of the manufacturing establishment and the quality of the drugs manufactured. They have included a brief which they have presented to the Restrictive Trade Practices Commission.

I have read this over carefully, and I do not think that it adds anything to the testimony which has been presented to this committee. If it is your wish, I will write to Nordic Biochemicals and tell them that I do not think their brief adds anything to the testimony. If they wish to appear before the committee, they will be welcome to do so.

Is that satisfactory to the committee?

Agreed.

The CHAIRMAN: Gentlemen, this morning we have Dr. Morrell and some of the people from his department before us. Would you like to come up, Dr. Morrell?

Dr. C. A. MORRELL (*Director, Food and Drug Directorate*): May I bring Mr. Ferrier with me?

The CHAIRMAN: Most certainly. Bring anyone you wish. Dr. Morrell wants to make a short statement before the meeting is open for questioning.

Mr. MORRELL: Mr. Chairman, in view of what has been said, and the headlines, I think, in the papers, I want to make something quite clear: There are really no two standards for drug manufacturers in this country. Dr. Showalter has specifications which he uses for purchasing drugs for the government departments, and the Food and Drugs Act has regulations governing the same area, which are regulations under a law, and that law happens to be part of criminal law.

Now, there is considerable difference with regard to what can be written in specifications for the purchase of drugs and what can be written in regulations under the Food and Drugs Act, and these differences are evident if you compare the specifications of the Canadian government specifications board and the regulations under the Food and Drugs Act. For example, I think you all have the standard under 74-GP-1a, and I have given this morning to, I think, each one of you a copy of the regulations, which is attached to one of those trade information letters, and you could compare, for example, C.01.052(b) and 6, or C.01.052(c) and 7. The first is the regulation, and the second one is the paragraph pertinent to it in the specifications.

Now, in addition to there being a difference in the wording, and the detail, and so forth, there are an awful lot of differences in respect to what you can do with them. Specifications can be enforced, and are enforced, by a board which considers an inspection report and makes a decision. That is what the board does, and that is their business, I presume, as to what they decide, but reinforcing of the regulation is something entirely different. If you are going to enforce a regulation, you must be prepared to go to court, and when you go to court you have to produce evidence that is acceptable to the court, and evidence that can stand up to a thorough going over by a defence lawyer, and I assure you that that is very difficult.

Now, this may lead to the disqualification, if you want to use the word, for purchasing, but the evidence may not be there at all that would be of any use in a court of law. So that what can be done with them is quite a different matter, I assure you.

Now, we carry out the inspections; the reports of our inspections, or a summary of the reports may be sent to Dr. Showalter, if he asks for them, but in carrying out the inspection our inspectors base their inquiries on the food and drug regulations, and advise the manufacturer where it is felt that conditions might contribute to violations of the act. Coincidental with the inspection for our purposes, all aspects of the standard 74-GP-1a are examined, in order that a report can be made, if and when required, to the interdepartmental committee, or to Dr. Showalter's committee. All inspections are carried out by the same group of inspectors, using an identical system, and there is no differentiation whether firms sell to government agencies or to the general public, of course.

A marking system can be used, and is used, in which certain deductions are made from a perfect mark for failures to meet certain specific requirements, and the total can be examined by the inspection board, Dr. Showalter's board, and he can decide, or his board can decide, whether or not they accept the products of that company.

We have to decide whether we have sufficient evidence to go to court, and this is a very different thing.

I think that is all; I wanted to make that clear, because it needs to be made clear.

Mr. ROXBURGH: Dr. Morrell, you make a statement here, and as I have it, right I hope, you say, it is quite a different matter what can be done with them. In that you are referring to the manufacturers of the drugs when they are brought up in court, provided they have a strong defence lawyer. Is that the idea?

Mr. MORRELL: Well, that is part of it, Mr. Roxburgh. What I mean is that there is quite a difference in what can be done with the information we have received in inspection. Dr. Showalter can examine the marks, and decide what they wish to decide in his committee.

We can go to the legal branch and say: "We think we have something here which will stand up in court and is worth going to court about", and they may, or may not, agree with us, and then we go to justice, if they agree, and they too may say: "We think you have a case", or: "You have not a case", and then

a lawyer is appointed, and it takes a little time to brief him, and he too says: "I think you have a case," or: "I do not think you have a case", and then you have to go to court, and produce all your evidence, and it is heard by a magistrate or a judge, and the company, if they wish, will have their lawyer properly there to attack the evidence of the witnesses.

Mr. ROXBURGH: If they have a pretty smart lawyer they may get away with it.

Mr. MORRELL: Well I do not want to say that, but it could happen.

Mr. MACKASEY: Dr. Morrell, it has often been said in the committee here that you are short of personnel. There have been two reasons advanced: one has been the lack of funds; and secondly, the lack of trained personnel available for this type of work. The last witness yesterday said it almost reduced this country to winning away people by bigger salaries, and other incentives. Do you feel you are short of personnel in general?

Mr. MORRELL: Yes, I do.

Mr. MACKASEY: Now, in the last request of the department, how many people would you have asked for, approximately?

Mr. MORRELL: Well, we have asked for more always than we have received.

Mr. MACKASEY: Do you know specifically how many?

Mr. MORRELL: Yes; for this current year, the fiscal year 1964-65, we asked for 136 positions, and we were granted 99 in the Food and Drug.

Mr. MACKASEY: Is this a better average than usually was the policy?

Mr. MORRELL: Yes, that is better than we used to get.

Mr. MACKASEY: Now, do you ask for more than you expect to receive, or—

Mr. MORRELL: We ask for what we think we need.

Mr. MACKASEY: Exactly. Now, these 135 people are not all Ph.D.'s, are they?

Mr. MORRELL: No, no.

Mr. MACKASEY: There are some down to menial jobs?

Mr. MORRELL: We have to have them, yes.

Mr. MACKASEY: But they are just as important to the over-all picture?

Mr. MORRELL: Yes, I think so.

Mr. MACKASEY: In other words, you would be better off—I do not want to put you in the position of answering this, but you did need 135, and you were permitted to engage 99. In other words, these 99 will work harder to perform the role of 135, or some phase of your operation will be put in abeyance, or put aside?

Mr. MORRELL: The answer is quite obvious, I think.

Mr. MACKASEY: Now, we have before us your amendments to the existing rules. Can, under present circumstances, a drug company be formed—now, I am not talking about bootleg companies; I am talking about a company being formed—can it be formed, go into operation, produce and sell drugs, before you with your limited staff had an opportunity to make certain that the building and facilities going into the production of drugs met these standards?

Mr. MORRELL: A drug company can be formed and go into operation without notifying us that they are going to do so, and that means that we either learn about it by observation, we happen to see it, or we see their advertisements, or we hear something, or somebody tells us that they are in operation.

Mr. MACKASEY: Now, doctor, I sense from your remarks that you have carried out all the tests that the Department of Industry have asked you to carry out amongst those people who decided to tender?

Mr. MORRELL: I believe we did, yes.

Mr. MACKASEY: And the Department of Industry are then free to set up whatever standards they set up?

Mr. MORRELL: Correct.

Mr. MACKASEY: But, in your own conscience the standards you set up are sufficient and adequate?

Mr. MORRELL: Yes, I think they are.

Mr. MACKASEY: Now, of 23 firms who did not pass the very stringent rules of the Department of Industry, did you find any of them that did not meet with your requirements? Without mentioning names; I do not think names are important.

Mr. MORRELL: Well, I can give you a run down of that, because I thought this would be coming up. Actually we did find that there were 31, not 26 or 28. I think 28 was the figure given. There were 31 firms that did not conform. It depends on the day, I think, of the week, but we dealt with 31. Now, of this 31, 16 were subsequently reinspected, and of the 16 that have been reinspected, 11 had certainly improved to a great extent.

Now, that left five of the ones that we had reinspected that had not improved. One of them has been prosecuted for unsatisfactory products; another one, whose failing was in his control department, where he did not have a qualified man in charge, made this correction by hiring a control chemist; the third one, we are analysing the products preparing for action; the fourth one no longer manufactures. They could see, perhaps, the writing on the wall. It would cost them too much, so they went out of it. The fifth one was bought out, sold out to one who was a bigger firm, and who had been a satisfactory producer.

Now, that takes care of the 16 that were reinspected out of the 31 that were referred to as not having met the specifications. The other 15 have not been reinspected yet. They will be when we can get to them.

Now, I think this all refers to the 31. I have got a few more figures here, if you would like to hear them?

Mr. ROXBURGH: Just in the way of information, with the staff which you have got—and Mr. Mackasey has sort of brought out there is a lack—how long will it take you to do an inspecting job on one of those? You did those 16 now.

Mr. MORRELL: Well, it takes about 2½ to three days. Mr. Ferrier has been in the field doing inspections, and has been transferred to our staff in Ottawa, but he has had a lot of experience in this. He is a pharmacist. He tells me that it takes between 2½ to three days to do an average factory inspection, not the biggest. They will take longer. You can see, then, the number of days, but there are plants, am I correct, that we have not yet been in?

Mr. R. T. FERRIER (*Inspector, Food and Drug Directorate*): Yes.

Mr. MACKASEY: In other words, perhaps the committee was a little hasty in presuming, or jumping to the conclusion that the 31 firms who could not necessarily meet the Department of Industry standard were not perfectly legal in selling drugs, or morally right in selling drugs to the public. They did maintain what you believe to be satisfactory standards, the big majority?

Mr. MORRELL: I think so. As I say, we prosecuted one, and we have been around to see 11 of the 16, to see what corrections they have made. They were all told at the time of inspection where their failings were, and told that we we would be back later.

Mr. MACKASEY: Doctor, just to clear up another misapprehension, perhaps these firms would have been subject to your regular inspection eventually?

Mr. MORRELL: Oh, of course, of course.

Mr. MACKASEY: It is just that they desire to sell the industry?

Mr. MORRELL: That put them a little higher on the priority list for inspection.

Mr. MACKASEY: You earlier agreed with me that despite the stringency of your rules here a firm can set itself up in the interval until you get around to inspect it. This, I presume, is because under the present day circumstances there is nothing in our rules and regulations, the laws of the country, that makes it necessary for a manufacturer of drugs to obtain some form of registration certificate from you that they have the proper facilities, the physical facilities, the proper help, before they manufacture their first tablet. Am I right in that, or wrong?

Mr. MORRELL: You are right, in that there is no offence committed from our standpoint if a manufacturer goes into business.

Mr. MACKASEY: Do you feel that this is right from a safety point of view?

The CHAIRMAN: I am not sure that that is a fair question. Dr. Morrell only follows the regulations as government has laid them down.

Mr. MACKASEY: I have a very high regard for Dr. Morrell, and every time we have Dr. Morrell here, I feel he is dedicated to his job, and is one of these Canadians who is interested, and I wonder why he has not had a nervous breakdown before this.

I am not interested in the rules of the government. I am interested in safety, and one of the things about this committee is that there is no party line here; we are out to do business.

Do you think it is right and proper, in this day, and in this country, that a man can set up this type of operation without first having you approve this operation? Do not you think that with the safety of this country involved he should mark time until you give him a clean bill of health?

The CHAIRMAN: Perhaps it would help Dr. Morrell to answer if you took out the word "proper" and said would it help his job.

Mr. MACKASEY: I am not interested in helping Dr. Morrell's job; I am interested in preventing any firm from producing one aspirin without having first got a clean bill of health from Dr. Morrell's department before he starts. That is what I am interested in.

Mr. MORRELL: Well, Mr. Chairman, I cannot help but feel that we would like to see it before it gets into operation. Now, this raises a lot of side issues, but I would still like to see it before it got into operation.

Mr. MACKASEY: In other words, it is up to your legal department to find ways around it.

Mr. MORRELL: Well, there is more than that. This gets, as somebody told me this morning, into big government, and whether or not you want it tied up into little bundles, and the big daddy kind of thing, but as I feel it I would just like to know who is going into business, and what they have got to conduct their business, what people, and what they are going to make.

Mr. MACKASEY: You do agree with me, then. One last question, because with a lot of the inferences that are made sometimes to the public, and I as a layman have come out of this meeting with a much greater regard for the doctor and the druggist, and people like you than I had when I first came here. There has been a lot of controversy about our drug industry in general, and particularly the Canadian Drug Manufacturers' Association. There are two schools of thought, and I would like your honest opinion: Are they simply an organization to cover up for each other in the matter of safety, or do you feel they have been an association which has worked with you, and made your role a little easier?

Before you answer, I would like you to incorporate this: Are their standards as a group collectively lower, even, or better than the national average you would find, taking all drug companies in Canada?

Mr. MORRELL: Well, I would like to start out with a little discourse on this: I do not know what the Canadian Pharmaceutical Manufacturers' Association would be covering up. If they are covering up something, they have done it pretty well, but I do know that one of the qualifications for membership in the Association is that the company concerned must have quality control procedures in operation, and there are some members here who could correct me if I am wrong, but I do think I have been told that members of the association will inspect a new member who is applying for membership, to see whether they agree that he has quality control procedures. I think that that is a fact.

Now, I wanted to say this too, however, and I think the Canadian Pharmaceutical Manufacturers' Association will agree with me: There are firms who are not members of that association, who have adequate quality control procedures. For some reason or other, they do not want to belong, or they do not belong. I do not know whether they want to; they do not. So that you cannot say that all the people in that association have adequate controls, or produce good drugs. That is not so, but I think it follows, and we have some indication that their standards are higher than the average.

Mr. MACKASEY: What about co-operation, doctor?

Mr. MORRELL: Well, we have our differences, as they well know. I find it easier to deal with an association than with 54, or whatever it is, individual companies, with 54 individual ideas, or suggestions, or complaints, and I have found this not only in the pharmaceutical industry but in the food industry, and all other industries that we deal with.

Mr. HOWE (*Hamilton South*): Dr. Morrell, when Dr. Showalter was here, one of my questions was why were the names of these drug firms not made public, because I felt several things: first, that possibly some of the drug companies were being protected, over and above the public being protected; and I also felt that through Dr. Showalter's department there was a segment of the public being protected, where the entire public was not being protected; and at the same time, realizing that there are certain companies, unnamed, who do not need to conform to certain standards, that you are casting doubts, or aspersions, on reputable firms leaving an element of doubt with regard to which companies were the bad ones, and which companies were the good ones, and it is my contention still that these companies should be named. The public should have the names of the companies made available to them, one way or another, by having a stamp of approval that they are allowed to use this in their advertising as an approved company, or some such standard, that the public is going to be protected, and the good drug companies are also going to be protected.

Mr. MORRELL: I think your question should be directed to Dr. Showalter.

Mr. HOWE (*Hamilton South*): I directed it to Dr. Showalter, and now I am asking you in your capacity.

Mr. MORRELL: I will talk about the food and drug regulations then. That is what I have to deal with. If we find something wrong with a manufacturing plant, a drug company, that in our opinion will convince a magistrate that there is a violation of the regulations, and that will cause a hazard to the public, we can take him to court, and we do.

Now, when it gets to court, it becomes public knowledge. It often gets in the paper. If it does not get in the paper, it is because nobody has taken the trouble to go over and listen.

But suppose somewhere along the line we are told we have not a case. I personally do not think we should tell the public about that, because we have

not a case, and it seems to me unfair, and perhaps it could lead to a form of blackmail, if we gave out these names. We cannot take them to court, but we do not think they are good, or as good as they should be.

Now, I do not think that we should, and furthermore, I think there is more than that; there is the Official Secrets Act. We have the authority to go into plants, and make inspections. We can get information, by virtue of the law, that other people cannot get, and I think that is considered as confidential until we find that there is some violation. Then we can go to court, and it becomes public knowledge at that time.

Mr. HOWE (*Hamilton South*): Well then, in a negative sense, could the conforming companies not be listed, and omit the other companies? This is a negative approach, but could this not be done, and then if one of those conforming companies were to slip in the standards, this would be made public by your legal procedures.

Mr. MORRELL: Well, somebody could easily make a list of those companies that have been in court. Now, mind you, within a month after that they may have corrected the whole thing.

Mr. HOWE (*Hamilton South*): Yes, but why this veil of secrecy?

Mr. MORRELL: I do not consider it a veil of secrecy, Mr. Chairman. I think it is just what everybody does who enforces a law. If they have a just complaint, something that can be proven, or they think it can be proven—they may lose the case, mind you—they go to court with it, which is the proper procedure, I think, under our system of law and government, rather than to have a bureaucrat like myself issue lists of people that I do not think meet certain requirements.

Mr. HOWE (*Hamilton South*): Well, it seems to me that there are other forms of business much less important to public health that have to conform to standards before they can have a licence issued to sell and distribute certain products.

Mr. MORRELL: We do not have a licence system.

Mr. HOWE (*Hamilton South*): That is my point.

Mr. MACKASEY: Dr. Howe brought out a point of at least giving a stamp of approval, or a signature of some sort to those people who can meet the Department of Industry standards now. However, a witness from the Department of Industry, Dr. Showalter, did admit to me that many responsible, reputable, and highly efficient firms do not care to sell to the Department of Industry, because their structure is too small, and the volume involved is too big for them.

Therefore, I think that in that event these firms would suffer some inference that they cannot wear this badge of approval, not because they do not meet the standards, but they chose not to sell. This, I think, is a dangerous aspect.

Mr. MORRELL: Yes, I think it is.

Mr. HOWE (*Hamilton South*): Is it allowable for companies that have passed the standards to advertise this?

Mr. MORRELL: Well, I have nothing to do with this, Dr. Howe. Did not we hear from Dr. Brien on Tuesday that they bought only from companies that sold to the government?

Mr. HOWE (*Hamilton South*): So it is conceivable, then, that companies could in their advertising to doctors or druggists state that they have conformed to standards laid down by the government?

Mr. MORRELL: By the specifications board.

Mr. HOWE (*Hamilton South*): By the specifications board, that this would not be disallowed?

Mr. MORRELL: Not in so far as I am concerned.

The CHAIRMAN: I think Dr. Brien made the point companies wo do meet the specifications have no hesitation in telling people they have done so.

Mr. WILLOUGHBY: It seems to me that we are trying to lock the stable door after the horse has gone, and then tell the horse he was wrong. Surely to goodness there must be some way that we can suggest that a proper licensing system can be given to these people before they start to manufacture all these drugs.

I other words, we should not have to have a police organization going around finding out that somebody started a drug firm down a back alley somewhere. Sure to goodness it is within the power of our government to organize a licensing system to ensure that these people have reasonable standards before they start turning out a second rate product.

That is what we have got to recommend to the government. I do not know whether we are within jurisdictional power, but I think that is our one big step, and I wonder whether Dr. Morrell agrees with that? I have another question I wish to ask him too.

The CHAIRMAN: Dr. Morrell said he would like to have the opportunity to inspect these plants before they sold products.

Mr. MORRELL: I would like to know who is going into business, and who they are going to employ, and what their products will be.

Mr. MATHER: Would the doctor like to make that compulsory?

Mr. WILLOUGHBY: Could we have a federal act to cover that situation?

Mr. MORRELL: Well, you referred to a police organization. That is what food and drug is.

Mr. WILLOUGHBY: Yes, but you do not have an organization insisting on a licence from the department before they start to manufacture.

Mr. MORRELL: Well, it is not quite so easy, I think. If a company started business, I think this was mentioned the other day, without a licence, we would still have to find them, would not we? We would have something, perhaps, to charge them with when we did find them, but we still have to find them.

Mr. WILLOUGHBY: Well, how could they set up manufacturing if they did not have a licence if it was an act that says you have to have a licence, and be approved by the board before you start to manufacture?

Mr. MORRELL: You have to have a licence to operate a motor vehicle, and from what I see in the papers there are quite a few people operating cars without a licence, which may have been suspended. You have to catch them at it. This is a police action in itself.

Mr. WILLOUGHBY: Yes, but it is not illegal to manufacture drugs, apparently.

Mr. MORRELL: No.

Mr. WILLOUGHBY: And yet it is illegal to drive a car without a licence?

Mr. MORRELL: Yes.

Mr. WILLOUGHBY: Well, anyway I presume that you agree that a licensing system might be of assistance to your department?

Mr. MORRELL: Well, it might make enforcement easier.

Mr. WILLOUGHBY: Well then, another question that I had, in relation to the shortage of staff. It seems to me that this is another very important thing, because if the department is going to function properly we obviously have to try and supply the necessary funds, and the personnel, to maintain that staff.

Now, we have a situation developing here in Ontario, I understand, where they are putting up an institution for the checking of drugs, somewhat a duplication of the service that is being done by your own department. It would seem

to me that that is an unnecessary duplication, if they are going to be able to staff their institution while you have not got enough staff in your institution. Why should not we have one institution for all of Canada, that is really worth while, and make it worth while to get a proper staff? I cannot see where the duplication is going to help the situation at all. I think it is a waste of personnel, as well as a waste of money. Do you agree with that?

Mr. MORRELL: Well, the one in Ontario, Dr. Willoughby, is in the attorney general's laboratory. I have visited it; they have a section there that tests certain drugs. Now, they are testing to specifications that have been set up by the Ontario, I think it is by the Ontario department of health, for purchasing drugs for the hospitals. The variety of drugs that they have is much less, of course, than are available on the market. They buy only certain types of drugs, and they buy in very large quantities, and this laboratory tests these drugs according to the specifications that are laid down by the Ontario government. I know some of the requirements, and they are not requirements that we would have in the Food and Drugs Act, and I do not think necessarily improve the safety or potency of the drug.

Mr. WILLOUGHBY: But just the same, Dr. Morrell, you must admit that that personnel is being used.

Mr. MORRELL: Yes, there are a few people there that we could employ.

Mr. WILLOUGHBY: Exactly. In other words, we could amalgamate this into one organization, and do a better job. I mean a better job as far as your department is concerned.

Mr. MORRELL: The kind of people they need are the kind of people we need. That is obvious.

Mr. WILLOUGHBY: Yes. Now, one other point: If we can get increased grants in some way, would the suggestion that we were discussing last time, of scholarships in the department, to bring in young people apply? I know that the argument the other day was that it will take years to develop this. That is fine. Well, this country will be existing for years, I hope. Why should not we establish a scholarship system that would induce these young people to get into this type of work with the department?

Mr. MORRELL: Well, this is one thing we are considering. I think there is a possibility that we can hire a few young people at the bachelor's level who have a good, proper background, and send them off to university for post-graduate training.

In one or two of the sciences they are very scarce: that is pharmacology and pharmaceutical chemistry of a high order. One difficulty is obviously that apparently there is nothing that compels them to come back to the government after they have had their training period.

Mr. WILLOUGHBY: Yes, but these scholarships would be specific for the idea of bringing them back. They would have to stay a certain period of time.

Mr. MORRELL: We have in the past, you may know, sent some of our laboratory people away for graduate training on half pay, and some of them have stayed on, and are still with us after years, and others stayed a year or so, and were tempted away by industry, or universities.

Mr. WILLOUGHBY: My last question I have for a minute is: Would there be any advantage, as your research department is concerned, to separate the department of food and drugs?

Mr. MORRELL: I do not think there would be, certainly at that level, no, because there is an awful lot of overlapping. For example, the toxicology, both for foods and drugs, and we have been through the pesticides, but there are other toxicologies in foods. That is all done in the one division in the laboratory. The pharmacology and toxicology do that for both sides of the

picture, and I do not see any point in splitting them. Then you are going into the Ontario business again. You are dividing up your resources. Vitamins, for example, are naturally present in foods, and are also present in pharmaceutical preparations. Now, both foods and pharmaceuticals are again in the same division, so far as vitamin content, and so on, is concerned. You would have to split that in two.

Now, there is a lot of management business, overhead if you like to say, in connection with our inspection services, and it is all managed through the one group, both the drug inspection and the food inspection, but I will say that we have done quite a bit in recent years to make the separation.

Mr. Ferrier, who is sitting on my right, was hired, I think, for drug inspection from the beginning. He was a graduate in pharmacy; he was put out to learn the techniques, of course, that are common to both food and drug inspection, and he learned his business there, and then went into the drug, as a specialist on factory inspection, because we need someone here in Ottawa who has had this field experience, and it hurts to take him out of the field, where there are so few, but we have brought him here to help guide us on programs of inspection and enforcement in the drug field, because he has had the field experience, and knows what it is all about.

To get the best out of our resources, we have to organize and plan it pretty carefully. We just cannot go from place to place, and hit or miss, and this is what he is here for, and in our bureau of operations we have a drug unit and a food unit in the office here at headquarters. We have pharmacology and toxicology sections, pharmaceutical and chemistry sections, narcotic and chemistry sections in the laboratory, which are basically drug sections, and we have food sections in the laboratory, which are basically food sections. Food chemistry, for example, is in the food section.

Then we have services for both of them, animal pathology, which is needed for both, because with experimental work with animals we want to know the pathology of it. The pathological section can do the tissue of it, and diagnose them for either a food or a drug experiment.

So there is a lot to be saved by having them together.

Mr. ROXBURGH: I was just going to say, Dr. Morrell, that so far in this meeting the thing that has struck me that is most disturbing is the fact that individuals, or groups, are allowed to go into the manufacturing of drugs without any previous check at all, and yet there are all sorts of other products, and such a thing as driving cars has been mentioned, but others as well that I know of that they have to have an inspection before they go into business. They are not allowed to go into business, and quite franfly, to an ordinary layman like myself it is rather appalling that we are dealing with a product that has to do with the health of the people, and anybody can go down the back alley and manufacture it. Remember, as you say, they cannot necessarily always be caught; but if there were a law, and an individual went into the manufacture of drugs without a licence and was caught, convicted and imprisoned or assessed a terrific fine, there would not be so many wanting to do it.

I was just wondering, as I sat here thinking about it, is there anything to prevent us, Mr. Chairman, from passing a motion here and now that the present government take steps to set up a licensing bureau to deal with persons going—and this may not be right, this is just the idea—into the manufacturing of drugs?

The CHAIRMAN: This would be the function of the committee when it makes its report.

Mr. ROXBURGH: Good. I would like to bring that suggestion to the committee.

The CHAIRMAN: It has already been suggested several times.

Mr. ROXBURGH: All right.

Mr. MACKASEY: Dr. Morrell, the hiring of personnel for your department, I presume, is part of the Civil Service Commission function?

Mr. MORRELL: Yes.

Mr. MACKASEY: Do you know of any particular case, or any particular individual that you would like to have in your department, for instance on an executive level, who is willing to come, but because of the stringent salary levels of the Civil Service Commission it prevents this man from so doing? Without mentioning any names, can you tell me what the difference is between what you could give this man under the present regulations, and what he would like, or what he feels his talents are worth to you?

Mr. MORRELL: Well, about $5,000 a year.

Mr. MACKASEY: You feel that we are not being pennywise and pound foolish in the case of these few individuals?

Mr. MORRELL: Well, as you know, we are competing—this was talked about last session, Mr. Mackasey—we are competing with universities, and with industry, and I suspect the industry has more flexibility. Speaking of this man, I have thought of three possibles, or four. I have no assurance that if I manage to get this $3,000 to $5,000 for these individuals, that the companies would not just say: "Well, you are worth another two or three thousand to us", and we would be back where we were.

Mr. MACKASEY: Do you feel that any of these people have indicated salary and money would not be their sole motivation in their way of life?

Mr. MORRELL: Well, they have talked of coming at a lower salary, but not too low, by any means.

Mr. MACKASEY: Certainly not. In other words, the present standards, despite the fact that we are dealing with people's health and safety of drugs, do make it virtually impossible to get the people you would like to get?

Mr. MORRELL: Well, at the present time I think that is true.

Mr. MACKASEY: And do you think we have got to face this fact sooner or later?

Mr. MORRELL: I think so.

Mr. HOWE (*Hamilton South*): Dr. Morrell, does your department have any control over the so-called patent medicines, and their advertising? In other words, medicines and drugs, so-called, that are sold directly to the public?

Mr. MORRELL: Yes.

Mr. HOWE (*Hamilton South*): Do you not feel that there is a lot of falsification in the advertising, capitalizing on public ignorance?

Mr. MORRELL: We have some safeguards, doctor, in that respect. Radio and television broadcasts, commercials relating to foods, drugs, are subject to prior examination by people in the food and drug directorate here.

Mr. HOWE (*Hamilton South*): All advertising?

Mr. MORRELL: All commercial advertising on radio and television for foods or drugs. I think we did about 30,000 of these last year, and about 5,000 would be drugs. Is that right?

Mr. A. HOLLETT (*Director, Bureau of Operations, Food and Drug Directorate*): Something over 5,000.

Mr. MORRELL: Now, these come in through use and by virtue of a clause in the regulations under the Broadcasting Act, which says that they must be, they use the word approved, although we never do, they must be approved by the Department of National Health and Welfare before they are used on the air.

Mr. HOWE (*Hamilton South*): Do they use the word truthful?

Mr. MORRELL: No, they do not; they say approved. Now, our people look at them, and if you have got any time some day, I know you have not, but I wish you had, we could show you some of them, what we do to them. You can hardly see them for blue pencil marks, so that they are very much watered down, in a sense, and I think if you listen to American television and radio you will notice a distinctive difference between the Canadian and the American.

Now, there is only so much we can do on the advertising, and if you are going to have advertising, and after all, where are we? We are in a capitalized, free enterprise democracy, where it is all right to advertise; there is nothing bad about it. You do it. So that a man has the right to say something about his drugs, or his food product, and I think we have to allow that, but if he says something that we know to be false, or misleading, we can take it out, and we do, and this is not altogether accepted happily by the industry. We have them down there for testing, and trying to argue around the thing, but I think we get our way most of the time.

So that there is a good deal of deletion and, I hate to use the word censorship, I should not, but bringing it down to the facts as we know them.

Now, we cannot control the tone of voice of the announcer, or his emphasis. We have only got the words in front of us.

Mr. HOWE (*Hamilton South*): Of this 5,000, are many of them also eliminated?

Mr. MORRELL: Some of them are eliminated, or rejected out of hand, are they not Mr. Hollett?

Mr. HOLLETT: Some of them do not get through at all.

Mr. HOWE (*Hamilton South*): Is this simply because there are out and out lies as to the properties they are said to have with regard to healing properties?

Mr. HOLLETT: The whole tone is misleading; the message is unacceptable; it is in contravention of the act and regulations.

Mr. MORRELL: There is another aspect: Section 3 of the act itself prohibits the advertising to the general public of any food, cosmetic, drug, or device as a treatment or cure for a list of diseases. This is listed in a schedule to the act, and there you just cannot advertise.

Now, that is done for a specific reason which you, I think, would appreciate because the list of diseases is one that includes the serious diseases and it is proper, I think, to not encourage people to diagnose those diseases and treat them themselves. They should go to a doctor, and get proper diagnosis and proper treatment.

Mr. HOWE (*Hamilton South*): In other words, the majority of these drugs are for symptomatic alleviation of self diagnosis?

Mr. MORRELL: Yes, they are what you see on the T.V. for colds, and aches, and pains, and so on.

The CHAIRMAN: Dr. Morrell, if I may ask you a couple of questions to clarify a few points here, you mentioned that you in the 1964-65 request asked for 137.

Mr. MORRELL: It was 136.

The CHAIRMAN: Yes, 136 positions, and you had been granted 99?

Mr. MORRELL: That is right.

The CHAIRMAN: How many of those positions did you actually fill with the personnel?

Mr. MORRELL: We have now throughout the directorate, which has about 600 positions—

Mr. HOLLETT: It has 550 to 600.

Mr. MORRELL: I was told about two or three weeks ago about 70 vacancies.

Mr. HOLLETT: They vary from day to day.

Mr. MORRELL: They vary, people leave; some left yesterday, and some may leave next week, and we may get a new man, and so on, but that is the number of vacancies that we have now. Of course, it varies; stenographers, I think, are just about as hard to get as pharmacologists, and we have always a demand for that level.

The CHAIRMAN: You mentioned that you are always requiring more personnel. How many personnel would you ideally like to have under the present regulations to fulfil the requirements that you have to meet?

Mr. MORRELL: Right this minute, cut them off, no more added, please?

The CHAIRMAN: Yes.

Mr. MORRELL: Well, we did lay out for the Civil Service Commission and the treasury board a ten year plan of what we would hope to have at the end of ten years. This goes back two years, so it is now around eight years, and I think it was around 1,200 that we thought would be enough to do an adequate job at this level, not when the country has increased and there are more responsibilities.

The CHAIRMAN: In other words, double your present staff?

Mr. MORRELL: About double, yes.

The CHAIRMAN: There was one other question I wanted to ask you: Do you think it would help the department, and perhaps you do not want to answer this. You get your people now through the Civil Service Commission?

Mr. MORRELL: Yes.

The CHAIRMAN: Are these people hard to convince of your requirements for special training? Would it help if your department was moved out of the control of the Civil Service Commission and dealt with directly by your own department?

Mr. MORRELL: Well, actually, I do not really know; I have not had any experience of being outside of the Civil Service Commission. Recruiting, when you recruit for high level, technical qualifications, you cannot recruit by sending out a poster in a post office; you have got to know where the people are, and you have got to go and see these people, and deal with them on a personal basis. Now, that we do, and we are allowed to do it but when the offer comes, it has to go through all the boards, and so on, and that is done through the Civil Service Commission. We cannot offer a man a job, but we can tell him that there is a job, and what the job amounts to, and what the salary level for that job is, and get him interested, and tell him, perhaps, what his future will be with the department, and the kind of work, and the facilities he will have to work with. This often interests a man almost as much as the money; not perhaps quite, but almost. Then we can go back. We tell him to put in an application for this job; it goes to the Civil Service Commission, and then it is dealt with by a board, on which our own technical people sit. There are Civil Service Commission people there, and personnel people there, and if he is acceptable, then the notice goes back to him through the Civil Service Commission.

Mr. ROXBURGH: In a case like that, are your recommendations taken into consideration by the Civil Service Commission? Say that you are the man who interviews this chap, and you give him these ideas, and then he goes before the Civil Service Commission to try for his examinations, or to be approved; are any recommendations by the department taken into consideration?

Mr. MORRELL: Well, our men are on that board.

Mr. ROXBURGH: Oh, I missed that.

Mr. MORRELL: Yes, they are represented on the board.

Mr. WILLOUGHBY: An associated question, and I certainly do not want to ask a question in any way that suggests that we have not got complete confidence in what you have told us, but would there be any advantage in our committee asking the head of the personnel section, I understand his name is Mr. Preston, to sit here with us and discuss the problem, too?

Now, I do not in any way suggest that what you have told us is not completely correct, or anything else. I just wondered whether he might have some other way of assisting us in this problem.

Mr. MORRELL: I do not know whether Dr. Cameron would want to say anything there?

Dr. G. D. W. CAMERON (*Chairman, Dominion Council of Health*): Mr. Chairman, it is difficult to answer that question. I do not think the problem here is one of selecting personnel, or supervising personnel, which is the job of the head of the personnel division. The limitation on the employment of staff is largely a matter of planning the estimates for the year; it is a matter of size, not only of the food and drug directorate, but of other parts of the department, and this is inherent in the whole system of government, determining how the funds available are to be raised, or to be distributed. So that, while Mr. Preston could explain in greater detail how these people are employed, how they are found, and so on, I do not think it would really contribute a great deal to the point you are making.

Mr. MACKASEY: Mr. Chairman, I have an emergency call. I do not want to embarrass the committee, but I just have to leave.

The CHAIRMAN: All right. Are there any other questions of Dr. Morrell?

Mr. WILLOUGHBY: I have one, outside of Dr. Morrell's problem; this is purely within the committee, and that is I was rather astounded at the last meeting to hear Dr. Brien say that in the hospital in London—and this may be purely an internal problem in their hospital, I am sure it must be, I just wondered whether we have any jurisdiction whatever—they have 5,000 items in the drug department there. Is there any way that—I am afraid we might be outside of our field altogether—we could co-operate in some way, by bringing in one of these large hospital pharmacists to discuss this problem with us?

It is absolutely appalling to me when he said 5,000 items in a drug department in a hospital.

The CHAIRMAN: Well, this would be up to, really, the committee whether they wish to do this, and as you know, the bigger the hospital, the more doctors, and each doctor has his own particular drugs he likes to use, and it does not take long to add up to 5,000.

Mr. WILLOUGHBY: Is there any way we can co-ordinate the duplication? I know they have got committees in hospitals who set up these things, but 5,000, that was amazing.

The CHAIRMAN: I think the federal government would not have any jurisdiction in this area, neither would the provincial government. This would be completely within the bounds of the individual hospital.

Gentlemen, if there are no other questions I would like to thank Dr. Morrell and his departmental officials for coming here today, and we will adjourn the meeting until Thursday, December 3, at which time Mr. Hume, the general legal counsel representing the Canadian Pharmaceutical Manufacturers' Association, is coming to discuss registration and/or licensing.

There is one other matter: It has been suggested that we might want to incorporate the regulations of the food and drug directorate as part of our minutes of today. Would somebody so move?

Mr. ROXBURGH: I move that the regulations of the food and drug directorate be appended to the minutes.

Mr. HOWE (*Hamilton South*): I second the motion.

The CHAIRMAN: The committee is adjourned to one week from today.

APPENDIX "A"

FOOD & DRUG

DIRECTORATE

Department of National Health and Welfare, Ottawa, Canada

Trade Information Letter No. 218
Date: April 18, 1963

To: All Drug Manufacturers and Distributors

Re: Amendments to the Food and Drug Regulations—
Drug Manufacturing Facilities and Controls.

Further to Trade Information Letter 191, I am pleased to inform you that the Food and Drug Regulations were amended by P.C. 1963-449 of March 18, 1963, in accordance with the attached Schedule No. 33. These were published in the Canada Gazette, Part II, of April 10, 1963.

C. A. Morrell,
Director.

Attachment: Schedule No. 33

SCHEDULE NO. 33

1. The *Food and Drug Regulations* are amended by adding thereto, immediately after section C.01.047 thereof, the following heading and sections:

"Manufacturing facilities and controls.

C.01.051. No manufacturer shall sell a drug in dosage form unless the drug has been prepared, manufactured, preserved, packaged, processed, stored, labelled and tested under suitable conditions, as provided in section C.01.052.

C.01.052. For the purpose of section C.01.051, suitable conditions in respect of a drug require

(*a*) that the construction, fittings and furnishings of the area in a building where the drug is processed and packaged shall be of such material and finish as

(i) will permit the ready and efficient cleaning of all surfaces,

(ii) will prevent the introduction of extraneous materials into drugs during their processing and testing, and

(iii) will prevent the migration of dust,

in accordance with good pharmaceutical practices;

(*b*) that the premises used for the processing, testing, finishing, distribution and storage of the drug and all auxiliary facilities shall be maintained in a clean, sanitary and orderly condition free from vermin, infestation, accumulated waste or debris;

(*c*) in the event parenteral drugs are processed, that all fillings and aseptic processes shall be carried out in a separate and enclosed area designed for the processing and filling of such drugs and operated in a manner that will prevent contamination of the drug compounded and filled;

(*d*) that qualified personnel shall be used as supervisors in the formulation, processing, testing, packaging and labelling of the drug, who shall have such technical training as is deemed necessary by the Director, having reasonable regard for performance of the duties and the responsibilities involved;

(*e*) that qualified personnel shall be responsible for the maintenance of machinery, equipment and sanitation;

(*f*) that each lot or batch of raw or bulk material used in the processing of the drug in dosage form shall be tested to ensure identity and purity of such raw or bulk materials;

(*g*) that each lot or batch of drug in dosage form shall be tested to ensure identity, potency and purity for its recommended use;

(*h*) that quality controls shall be used that are adequate having regard to the nature of the drug;

(*i*) that a system of control shall be used permitting a complete and rapid recall of any lot or batch of the drug from the market; and

(*j*) that records shall be maintained relating to the drug in a form, manner, and content satisfactory to the Director showing

(i) the tests of each lot or batch of raw or bulk materials used in the processing of the drugs,

(ii) the tests of each lot or batch of drugs in the dosage form,

(iii) the quality controls,

(iv) all information received pertaining to the quality or hazards of any drug,

(v) the results of tests to determine the stability of the drugs, and

(vi) the measures taken to ensure the recall of lots or batches of drugs from the market.

C.01.053. The records required to be maintained by paragraph (*j*) of section C.01.052 in respect of a drug shall be kept

(*a*) until the expiration of five years from the date of the testing of the drug; or

(*b*) until the expiration date of the drug,

whichever first occurs, and certified copies of any of the records shall be sent to the Director on his request.

C.01.054. A sufficient sample of each lot of the finished drug in dosage form shall be kept by the manufacturer under suitable conditions of storage

(*a*) until the expiration of five years from the date of testing of the drug, or

(*b*) until the expiration date of the drug,

whichever first occurs, and an adequate portion thereof for analyses and examination shall be submitted to the Director on his request.

C.01.055. In the case of a drug sought to be imported into Canada, the Director may require

(*a*) information and evidence satisfactory to him that the conditions of manufacture described in section C.01.052 have been met in respect to such drug, and

(*b*) before such drug is released for sale, the testing in Canada of the drug by an acceptable method in the form in which it is sought to be imported,

and if, in the opinion of the Director such drug or any lot or batch thereof does not conform to the requirements of these Regulations, the drug or lot or batch thereof shall not be admitted into Canada for use as a drug."

FOOD & DRUG

DIRECTORATE

Department of National Health and Welfare, Ottawa, Canada

Trade Information Letter No. 247
Date: November 18, 1964.

To: All Drug Importers

Re: Analytical Data and Information for Imported Drugs

The Food and Drug Regulations were amended in March, 1963 by the addition of sections that specify the manufacturing facilities and controls required for all drugs sold in Canada, both domestic and imported. A copy of these Regulations is attached. As an aid in determining if imported drugs comply with these requirements, the following information should be available in Canada for each shipment of drugs being imported:

1. *Specifications for the Product*

A quantitative statement of all ingredients and physical characteristics such as size, shape, colour, disintegration time, pH, clarity, etc. should be included.

2. *Limits of Variability*

The variation permitted by the manufacturer from the standard specifications should be stated and should include variations such as ranges for percentage of required potency, disintegration time, pH and other established characteristics.

3. *Methods of Analysis*

The analytical methods used to test the drugs for identity, potency, purity, and where applicable sterility and pyrogens should be outlined. If the methods used are those designated as official in the Food and Drug Regulations or in the standard reference texts designated in Schedule B to the Food and Drugs Act, it is sufficient to indicate the source.

4. *Certificates of Analysis*

A certificate, signed by a qualified official of the firm, must state the actual results obtained when each lot of the drug was tested and such certificates must be supplied with each shipment.

The information referred to in items 1, 2 and 3 must be supplied for inspection with the initial shipment of each drug, and retained by the importer for subsequent shipments. This information need not be repeated for subsequent shipments if there is no change in formulation. However, the Certificate of Analysis referred to in Item 4 must be supplied for each shipment.

Importers are advised to have the above information available for all drugs being imported into Canada after April 1, 1965.

C. A. Morrell,
Director.

Enclosure
Sections C.01.051 to C.01.055

Manufacturing Facilities and Controls

C.01.051. No manufacturer shall sell a drug in dosage form unless the drug has been prepared, manufactured, preserved, packaged, processed, stored, labelled and tested under suitable conditions, as provided in section C.01.052.

C.01.052. For the purpose of section C.01.051, suitable conditions in respect of a drug require

(*a*) that the construction, fittings and furnishings of the area in a building where the drug is processed and packaged shall be of such material and finish as

(i) will permit the ready and efficient cleaning of all surfaces,

(ii) will prevent the introduction of extraneous materials into drugs during their processing and testing, and

(iii) will prevent the migration of dust,

in accordance with good pharmaceutical practices;

(*b*) that the premises used for the processing, testing, finishing, distribution and storage of the drug and all auxiliary facilities shall be maintained in a clean, sanitary and orderly condition free from vermin, infestation, accumulated waste or debris;

(*c*) in the event parenteral drugs are processed, that all fillings and aseptic processes shall be carried out in a separate and enclosed area designed for the processing and filling of such drugs and operated in a manner that will prevent contamination of the drug compounded and filled;

(*d*) that qualified personnel shall be used as supervisors in the formulation, processing, testing, packaging and labelling of the drug, who shall have such technical training as is deemed necessary by the Director, having reasonable regard for performance of the duties and the responsibilities involved;

(*e*) that qualified personnel shall be responsible for the maintenance of machinery, equipment and sanitation;

(*f*) that each lot or batch of raw or bulk material used in the processing of the drug in dosage form shall be tested to ensure identity and purity of such raw or bulk materials;

(*g*) that each lot or batch of drug in dosage form shall be tested to ensure identity, potency and purity for its recommended use;

(*h*) that quality controls shall be used that are adequate having regard to the nature of the drug;

(*i*) that a system of control shall be used permitting a complete and rapid recall of any lot or batch of the drug from the market; and

(*j*) that records shall be maintained relating to the drug in a form, manner and content satisfactory to the Director showing

(i) the tests of each lot or batch of raw or bulk materials used in the processing of the drugs,

(ii) the tests of each lot or batch of drugs in the dosage form,

(iii) the quality controls,

(iv) all information received pertaining to the quality or hazards of any drug,

(v) the results of tests to determine the stability of drugs, and

(vi) the measures taken to ensure the recall of lots or batches of drugs from the market.

C.01.053. The records required to be maintained by paragraph (j) of section C.01.052 in respect of a drug shall be kept

(*a*) until the expiration of five years from the date of the testing of the drug; or

(*b*) until the expiration date of the drug,

whichever first occurs, and certified copies of any of the records shall be sent to the Director on this request.

C.01.054. A sufficient sample of each lot of the finished drug in dosage form shall be kept by the manufacturer under suitable conditions of storage

(*a*) until the expiration of five years from the date of the testing of the drug, or

(*b*) until the expiration date of the drug,

whichever first occurs, and an adequate portion thereof for analyses and examination shall be submitted to the Director on his request.

C.01.055. In the case of a drug sought to be imported into Canada, the Director may require

(*a*) information and evidence satisfactory to him that the conditions of manufacture described in section C.01.052 have been met in respect to such drug, and

(*b*) before such drug is released for sale, the testing in Canada of the drug by an acceptable method in the form in which it is sought to be imported,

and if, in the opinion of the Director such drug or any lot or batch thereof does not conform to the requirements of these Regulations, the drug or lot or batch thereof shall not be admitted into Canada for use as a drug.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

MINUTES OF PROCEEDINGS AND EVIDENCE

No. 19

THURSDAY, DECEMBER 3, 1964

WITNESS:

Mr. F. R. Hume, Q.C., of Toronto, General Legal Counsel of the Canadian Pharmaceutical Manufacturers Association.

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21615—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jones (Mrs.)
Jorgenson
Macaluso
Mackasey
Marcoux
Mather
Prud'homme
Roxburgh
Rynard
Slogan
Wadds (Mrs.)
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

MINUTES OF PROCEEDINGS

THURSDAY, December 3, 1964
(24)

The Special Committee on Food and Drugs met this day at 9.45 a.m., the Chairman, Mr. Harry C. Harley, presiding.

Members present: Messrs. Armstrong, Côté (*Longueuil*), Enns, Harley, Howe (*Hamilton South*), Mackasey, Marcoux, Mitchell, Prud'homme, Roxburgh, Rynard—11.

In attendance: Mr. F. R. Hume, Q.C., of Toronto, General Legal Counsel of the Canadian Pharmaceutical Manufacturers Association.

The Chairman read into the record a letter dated December 2, 1964, sent by Dr. H. A. Showalter, Chairman of the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers, Distributors and Agents, regarding the publicity which followed his appearance before the Committee on November 17. The Chairman and the members commented thereon.

Mr. Hume was introduced. He read a prepared statement on the legal aspect of licensing and registration, and was questioned. Mr. Hume retired.

At 11.25 a.m. the Committee adjourned to the call of the Chair.

Gabrielle Savard,
Clerk of the Committee.

21615—1½

EVIDENCE

THURSDAY, December 3, 1964.

The CHAIRMAN: Gentlemen, we now have a quorum present. I will call the meeting to order. The first item on the agenda this morning is some correspondence. I have received a letter from Doctor Showalter, who appeared before the committee approximately three weeks ago. Doctor Showalter has written a letter which I would like to read to the committee.

December 2, 1964.

Dear Dr. Harley,

Use of 74-GP-1 Standard for Pharmaceutical Suppliers to the Government of Canada.

This is in response to your telephone call to me on 30 November 1964, concerning the publicity which followed my appearance before your committee on 17 November. I am writing solely in my capacity as chairman of the interdepartmental advisory board on pharmaceutical standards, and not as a departmental officer. Reports and discussions in the press seem to have created the impression, which was never intended in my statement to the committee, that the Canadian pharmaceutical manufacturing industry is in a deplorable state, and that the products on sale to the public are generally of dangerously low quality.

The statements of my brief were correct, that is, in the first round of inspections of the companies, none showed full conformity with all requirements of the standard, but as I explained (pages 427 and 428), the standard itself proved in its use to be somewhat unrealistic. Therefore, the first round of inspections became also a testing period for the standard, following which we revised it to what we considered to be a more reasonable but still adequate level. I also explained that the inspection methods and interpretations required development in order to accomplish full objectivity and consistency. At the same time, also the operations of many of the companies were being improved, in some cases to a considerable extent, partly due to the impetus given by these inspections.

Our effort was oriented towards the problems of government procurement, and in this sphere, while one is certainly concerned with safety and efficacy in the products, one is also responsible to obtain the specified "merchandise value" for the price paid, particularly when buying by tender and contract. The principal difficulties which had led us to the creation of this standard were those of workmanship and the more superficial aspects of quality, such problems as would disturb a purchasing agent but would cause less concern to a user.

Contrary to the impression which has been received, we have in Canada, in my opinion, a considerable number of highly competent and responsible pharmaceutical manufacturers. At the same time, there have been companies who have not employed the best modern manufacturing and control methods. This latter fact certainly gives rise to concern. Government buyers had come to believe that due to the necessary

practice of inviting competitive bidding, the goods that were received, while competitive in price, were often not competitive in quality, as is generally the case in the public market.

The standard cannot ensure delivery of perfect merchandise, but it does attempt, though admittedly in an imperfect manner, to define a company with reasonable competence and a highy responsible attitude. The results of our effort show that a majority of companies in the Canadian pharmaceutical industry exhibits these qualities, and at the same time, that a standard of this kind can have a very useful effect upon all.

Yours truly,

H. A. Showalter, Chairman,
Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers, Distributors and Agents.

I telephoned Doctor Showalter because I felt there were some areas of his testimony that had been misunderstood and I asked him if he would wish to write us a letter rather than come back as a witness, and thus try to save the time of the committee.

Mr. RYNARD: This lengthy epistle just shows that you are getting what you pay for. This is the crux of the whole thing. Doctor Showalter says that the quality may not be bad but the way the drugs are put up might be a little wrong. In other words, you are getting exactly what you are paying for.

Mr. ROXBURGH: Does not the letter say that there is a considerable number of these manufacturing plants which are all right? He also says that it is not necessarily true that others have reached the high standard of quality reached by some plants. He still acknowledges the fact that there are some manufacturers of drugs in Canada who do not come up to the standard.

Mr. HOWE: I still think these companies should be named.

Mr. ENNS: I think the whole reason for the letter was the unfortunate publicity that came out of the committee. I suppose Mr. Mackasey and I probably used the word "shocking" when we responded to some of the evidence that was given. We have also been to drug companies where we were certainly not shocked; we were impressed. It is just the way these things come out in the papers sometimes.

Mr. MACKASEY: I agree with that. I think the letter re-emphasizes what most of us know, that there are going to be certain degrees of efficiency. One firm is bound to be better than another. This is true in any line of endeavour. Our main purpose is to see that the firm with the lowest standards still maintains a sufficient calibre and standard so that the safety of the public is ensured. Doctor Showalter's letter is, I think, refreshing. He admits that some of his statements are not as accurate as I would like to think his testimony was.

Several pages later he mentions in his testimony that the standards are not too realistic. I do not remember him using these words but I am happy he is using them now. If the standards are unrealistic, it is unfair to the industry that after several months of trial he should come and speak into the record without mentioning the fact that the standards were unrealistic. This is the source of the whole problem. The only way Doctor Showalter could have found the standards unrealistic is by trial and error. I agree he had no other means at his disposal, but by the time he got here that lack of realism should have been more apparent to him and he should have said so at the outset, or else not have read that into the record at all.

The CHAIRMAN: Are there any other comments on this?

We shall now hear the witness whom we have this morning. This morning we have with us Mr. F. Hume, Q.C., who actually appeared briefly before the committee on one occasion with the Canadian Pharmaceutical Manufacturers Association. Mr. Hume is the general legal counsel of the Canadian Pharmaceutical Manufacturers Association and he came to the committee this morning prepared to discuss the legal aspects of licensing or registration.

Mr. F. R. HUME. Q.C., (*General Legal Counsel, Canadian Pharmaceutical Manufacturers Association, Toronto*): Mr. Chairman, ladies and gentleman, as the Chairman has advised you, my name is Hume and I am in the general practice of law in the city of Toronto. I mention that so that you, gentlemen, will understand that in putting questions to me on my few remarks you will be aware of the fact that the little knowledge I have about the pharmaceutical manufacturing industry has only been picked up as I have acted from time to time for the association, and it has been accumulated on a solicitor and client basis. Therefore, if you put a question to me with respect to my remarks to which I do not have an answer, I will certainly make a note of it and attempt to supply the answer through the Chairman.

As the Chairman has advised you, the association appeared before this committee on June 19, and at that time you will recall that I had the privilege of being present, just with a watching brief, with a delegation of medical, scientific and technical personnel. The matters under consideration at that time were related to drug safety. Brief reference was made in that submission to the fact that in order to achieve a better measure of safety with respect to people who manufacture or distribute pharmaceutical products in Canada, some sort of certification or registration was required.

Since that time I am advised that others have appeared, and you have heard other comments with respect to the subject. For that reason the association, I think, has requested permission to discuss with you, in slightly more detail, its views with respect to this matter, and have asked me to prepare some remarks.

Approximately six years ago the association became vitally concerned in the need for some more stringent inspection and control, and they undertook an extensive study of the subject. The results of the study were completed and submitted to the food and drug directorate. The association, in its appearance before the Restrictive Trade Practices Commission in 1961, submitted the following:

> A considerable amount of work has since been done by our association in this respect, and it is interesting to note that our companies are unanimously in favour of strong and enforceable regulations. There can be no doubt that it is in the best public interest, and we believe that every product imported or made in Canada should be produced in conformity with a sound manufacturing principle and under proper quality control procedures.

Mr. Chairman, then as now some manufacturers maintain proper manufacturing controls, as you have heard, but this does not necessarily apply to everyone in the industry. It was the opinion of the association, therefore, that the government should take strong and effective action in this area. I am instructed that the situation remains very much the same today.

It has been intimated before this committee that there are some 400 manufacturers in Canada. I think perhaps it should be noted that the greater majority of these companies or individuals are agents or distributors; some formulate small quantities of drugs for local distribution, and a somewhat smaller number are actually pharmaceutical manufacturers in the accepted sense of the term. However, when one of these manufacturers runs afoul of

the law or the regulations, then the entire industry is condemned through inference, and apart from the harm that this does to those manufacturers, it is the association's submission that this is not in the public interest. A good example is the one to which you have heard reference already this morning, the publicity given to the testimony of Doctor Showalter. I was not aware of his letter until I arrived here this morning, and I sought some instructions with respect to the matter. I will not make any further reference to it except to indicate that the Canadian government specification board who compiled these standards, I understand, did so in collaboration with the association, and that the first set of standards proved to be rather unworkable. Subsequent standards had been worked out and inspections had been made.

These standards however, Mr. Chairman, ladies and gentlemen, as I understand it, apply only to government purchases of drugs, and, from the standpoint of the association, do not answer the need which we expressed in the form of a recommendation that the association made to the royal commission on health services in May of 1962. May I gave you a brief quotation?

> That it be made mandatory that no drug be offered for sale in Canada unless it has been manufactured under controlled conditions by or under the supervision of qualified personnel, and that representative samples of each and every batch of product be tested for potency and safety by the manufacturer before release. In other words the high standard of pharmaceutical manufacturing attained by leading manufacturers should be made compulsory for all engaged in the industry, and these same standards should also apply to drugs manufactured abroad and offered for sale in Canada.

From the testimony offered to this committee by government representatives it appears that the food and drug directorate is working towards this objective. It is the association's contention, however, that no inspection system can be entirely effective unless those in charge of the system know of everyone engaged in the business. It is for this reason that the association recommends registration of all companies selling pharmaceuticals in Canada. The association believes that during the committee's deliberations this point about registration has been somewhat confused with licensing which we submit is another matter entirely.

Mr. Chairman, I should like to make it clear that the association is in favour of registration and not licensing.

While some persons have used the words "licensing" and "registration" as synonymous, these words are not understood to be similar by the association. Regulations requiring a licence imply, in this context, a system under which a manufacturer requires to obtain a licence as a condition precedent to the carrying on of a business and it would follow that a revocation of that licence by the authority would remove the right of the manufacturer to continue in its business.

Registration, on the other hand, implies a system under which each manufacturer would be required to register and the failure to do so would only result in the imposition of a penalty in place of a prohibition against continuing in business.

The registration favoured by the association would mean that every person or firm owning an establishment in which drugs are manufactured, prepared, compounded or processed must report the name, place of business and such other information as the authorities require. The same would apply to non-manufacturing agents or distributors. The purpose of such registration would be to assist the food and drug directorate to identify and inspect all places where drugs are made. Registration, however, would not be a condition precedent to the right to carry on business.

If a licence is required to carry on a particular business, the failure to obtain such a licence renders the person or firm liable to a penalty and to some form of prohibition order or injunction to prevent the continuance of the activities. Failure to register under a system favoured by the association would render the firm or person liable to a penalty but would not take away that person's right to continue in business provided that the other requirements and regulations of the food and drug directorate were satisfactory.

The association is of the opinion that the necessity for registration becomes apparent in matters affecting quality, manufacturing controls and adequate inspection by the authorities. Without registration the food and drug directorate has no way of ascertaining those persons or firms who are engaged in the manufacture (or distribution) of pharmaceutical products under its jurisdiction. Registration would ensure that all manufacturers would be known to the directorate and would provide a greater measure of safety and control in the public interest.

Some difference of opinion has occurred as to the jurisdiction of Parliament to enact regulations requiring this type of registration. This committee heard R. E. Curran, Esquire, Q.C., legal adviser to the Department of National Health and Welfare, on Thursday, July 16th, 1964. It is noted that Mr. Curran, in his prepared statement, referred throughout to "licensing" of drug manufacturers and stated that he had been asked to appear "to attempt to explain the legal position, both Provincial and Federal, insofar as it relates to licensing of a drug manufacturer as a condition of carrying on his business". It is therefore assumed that Mr. Curran was using the word "licensing" in the sense referred to above as being a necessary condition precedent to the privilege of engaging in the manufacture of pharmaceutical products.

Mr. Curran implied that registration would present no problem by his remarks as follows:—

> I think, however, a satisfactory result could be achieved by a regulatory requirement for returns to be made by drug manufacturers. The type of regulation that I have in mind would be one requiring a manufacturer to file regularly and from time to time showing such information... as might reasonably be required for the purpose of administering the Act. The requirement would be entirely separate from his right to carry on business and failure to file the return would not imperil his right to engage in business but which would subject him to a penalty.

Mr. Curran confirmed that lawyers in the field of constitutional law differ in their interpretation of these matters and he stated that it might well be other lawyers would not agree with his views.

Because of the possibility of confusion arising from the emphasis placed upon licensing by Mr. Curran and because I do not completely share Mr. Curran's view as to the inability of the Parliament of Canada to impose one or the other, I was requested to present my views to the association and to this committee.

The competence to enact valid legislation is divided in Canada between the federal parliament on the one hand by Section 91 and the provincial legislatures on the other hand by Section 92 of The British North America Act. In the United Kingdom this division of authority does not exist and English jurisprudence is not of much assistance in determining the question as to whether a statute or the regulations under it are intra or ultra vires.

The Food and Drug Act has been found to be within the competence of the federal parliament as being criminal law.

I respectfully disagree with the implication in Mr. Curran's remarks that, merely because a matter relates to criminal law, it is not possible for parliament to pass legislation authorizing the making of any regulation which is regarded as necessary for the proper enforcement of the Statute. Mr. Curran expressed the view:—

> To find a basis for federal licensing of the drug industry under The Food and Drug Act it would be necessary... that licensing was so directly related to the protection of the public health in the prevention other than to make it an integral part of the purpose of the regulations. In other words, it would be necessary to show that there are such hazards associated with the manufacture and distribution of drugs, regardless of their kind or purpose, that cannot be controlled other than by the licensing of the manufacturer.

It is respectfully submitted that the whole purpose of The Food and Drug Act is concerned with the protection of the public health and that it has been demonstrated that there are hazards associated with the manufacture and distribution of drugs. If the Statute is necessary and desirable in the public interest any regulation under or requirement of that Statute, which is necessary for the due carrying out of its purposes is, in my opinion, valid.

Mr. Curran stated:—

> The licensing of a particular product is, generally speaking, within the exclusive jurisdiction of the provinces.

Acting under the legislative heading of "Property and Civil Rights", many provincial statutes require licensing and/or registration. There are, however, many precedents under which licensing and/or registration is required under federal legislation. The following are some examples of statutes requiring licensing:

Licensing of Trustees under The Bankruptcy Act (R.S.C. 1952 Cap. 14 S.5)

Licensing of Elevators, commission merchants etc. under The Canada Grain Act (R.S.C. 1952 Cap. 25 S.79)

Licensing of Radio Stations under The Radio Act (R.S.C. 1952 Cap. 233 S.5)

Licensing of certain seeds under The Seeds Act (R.S.C. 1952 Cap. 248 S.8)

Licensing of money lenders under The Small Loans Act (R.S.C. 1952 Cap. 251 S.5)

Examples of registration are as follows:—

Registration of aircraft under The Aeronautics Act (R.S.C. 1952 Cap. 2 s.4(1) (b))

Registration of medical practitioners under The Canada Medical Act (R.S.C. 1952 Cap. 257 s.17)

Registration of ships under The Canada Shipping Act (R.S.C. 1952 Cap. 29 s.6 and ff.)

Registration of insurance companies under The Canada and British Insurance Companies Act (R.S.C. 1952 Cap. 31 s.50)

Registration of shipping services and the particulars of vessels under The Canadian Maritimes Commissions Act (R.S.C. 1952 Cap. 38 s.7)

Registration of premises for the storage of explosives (R.S.C. 1952 Cap. 102 s.2(1))

Registration of children under The Family Allowances Act (R.C.S. 1952 Cap. 109 s.4)

Registration of Indians under The Indian Act (R.S.C. 1952 Cap. 149 s.5)

Registration of persons transporting or shipping livestock under The Livestock and Products Act (R.S.C. 1952 Cap. 167 s.32(n))
Registration of loan companies under The Loan Companies Act (R.S.C. 1952 Cap. 170 s.13)
Registration of manufacturers of maple products under The Maple Products Industry Act (R.S.C. 1952 Cap. 172 s.10)

The above is an outstanding example of a federal statute requiring registration of a particular type of manufacturer and so far as I am aware this requirement has not been challenged as being beyond the legislative jurisdiction of the federal parliament.

The above examples are sufficient to indicate that in cases where the public interest required it, licensing or registration of an undertaking has been invoked many times.

The interpretation of the legislative heading "Trade and Commerce" in Section 91 of The British North America Act does not extend it to the regulation by a licensing system of a particular trade by the Parliament of Canada. (Attorney General for Canada vs. Attorney General for Alberta and others (1916) A.C. 588). However, I submit that nothing in the decision of the judicial committee of the privy council in that case denies the right to license or require registration with respect to matters over which parliament has jurisdiction.

Your committee should be aware that prior to the 1953 amendment the provisions of the Food and Drug Act contained a section for the making of regulations which opened with the following words:—

> The governor in council may make regulations.

There then followed some fourteen headings under which regulations could be made.

Special attention is drawn to the very restrictive provisions of this Statute for the making of regulations and unless a regulation under the former statute came within one of the fourteen headings, such a regulation would not have legislative sanction.

The Food and Drug Act passed as chapter 38 of the Statutes of Canada 1952-53 has vastly different provisions with respect to the making of regulations. The present Statute introduced the section on regulations (Section 24) in the following words:—

> The governor in council may make regulations for carrying the purposes and provisions of this Act into effect and, in particular, but not so as to restrict the generality of the foregoing may make regulations etc.

It will at once be recognized that the provisions of the present statute give wide powers to the governor in council to make any regulations which that body deems necessary for carrying the purposes and provisions of the act into effect and it is much broader than the previous restrictive provisions. There follow some thirteen headings but these headings are stated to be merely particulars and are not to restrict the generality of the power of the governor in council to make any regulations for carrying the purposes and provisions of this act into effect. It is therefore submitted that any regulation which the governor in council deems necessary for the purpose of carrying the act into effect may now be passed and it is not necessary to look for a specific heading in the section in order to justify a regulation.

It is therefore submitted that if the governor in council deems it necessary to pass a regulation requiring manufacturers of pharmaceutical products to register with the food and drug directorate, such a regulation would be valid,

it being presumed that the governor in council was of the opinion that registration was necessary for carrying the purposes and provisions of the act into effect.

It is also respectfully submitted that the courts would not inquire into the validity of such a regulation beyond ascertaining whether the making of the regulation was authorized by the statute and whether it had been issued in accordance with the provisions of the statute.

In Attorney General for Canada vs. Hallet & Carey Limited (1952) A.C. 427 the question before the judicial committee of the privy council involved certain actions taken by the governor in council under The National Emergency Transitional Powers Act. The governor in council ordered that certain grains be vested in the Canada wheat board. This was challenged and the court held that it was not competent for the courts to canvass the considerations which lead the governor in council to deem it necessary to make the order. The action taken was of a nature that the Governor General in council, not the courts, deemed necessary or advisable. In the Supreme Court of Canada The Honourable Mr. Justice Rand made three conclusions:—

1. That the governor in council had not exceeded his authority conferred upon him by the act;
2. That the courts should not attempt to substitute its judgment for that of the executive, and
3. That there was no bad faith on the part of the governor in council in making the order.

It is respectfully submitted that the only question to be asked is—does the statute give the power? If so, it is submitted that the courts would not interfere with the regulations nor attempt to subsitute its opinion.

While the 1953 statute does not specifically empower the governor in council to make regulations requiring the registration of manufacturers of pharmaceutical products, if the governor in council, on the recommendation of this committee, deems it necessary for carrying the purposes and the provisions of the act into effect that manufacturers register with The Food and Drug Directorate, then it is our respectful submission that such a regulation would be valid and the discretion of the executive would not be interfered with by the courts.

Mr. Curran indicated as his view that he thought section 24 of the act would provide authority for a regulation requiring registration. For the reasons set out above, I am of the opinion that the broad provisions clearly provide the authority for such regulations and that no further amendment is required.

Most of Mr. Curran's remarks were related to "licensing" of manufacturers and distributors. It may be that he would agree with my remarks about "registration". I take issue with him in his broad assumption that "licensing" presents a legal problem in the circumstances, but as the association I represent here is strongly in favour of "registration" the question is somewhat academic.

Registration of the nature referred to here would give the food and drug directorate information with respect to all of those engaged in the supplying of drugs; provide the possibility of adequate inspection of all and (if I interpret Mr. Curran's views correctly) would remove any doubt as to the constitutional validity of such regulations, at least between Mr. Curran and myself.

It is therefore urged that this committee recommend registration of manufacturers and distributors of pharmaceutical products. This would not affect the status of a manufacturer to engage in the business of his choice but would require him to make disclosure of his activity, location, facilities,

quality control procedures and any other matter which the governor in council deemed necessary for carrying the purposes and provisions of the Food and Drugs Act into effect.

The CHAIRMAN: Thank you very much, Mr. Hume.

The meeting is open for general questioning.

Mr. MACKASEY: Mr. Chairman, I would like to congratulate the witness on the fairness of his remarks and at the same time to express regret that we did not have advance copies. This is a very interesting document that answers many of the questions that had occurred to most of the members, I think. It might be necessary to have Mr. Hume back again in view of the fact that many of us would like to study that brief a little more exhaustively. I have tried to keep notes—at least, mental notes—as we have gone along here this morning but many things will occur to me, and I am sure to many of us, after we leave.

I think, Mr. Hume, that in my mind the question of registration and licensing has been a matter of semantics. I think we are all looking for some form of control or policing, although I do not like to use the word "policing".

It seems to me that two things have become evident, and maybe I am wrong as a layman in presuming these things. Several times you intimated in the earlier part of your brief that the penalties that could be imposed in conjunction with registration would be much easier than those that would necessarily be associated with licensing. I think on two occasions you mentioned that one of the reasons for which licensing is objectionable is the possibility that it could actually close down a manufacturer who did not meet certain requirements whereas registration—and again I may be wrong in my interpretation of some of your remarks—would invoke penalties but would not provide the government with the right to close a factory.

Am I right or am I wrong in that assumption?

Mr. HUME: Yes, Mr. Chairman.

First of all I would like to say that I am sorry if I misunderstood your procedure but I did not regard the document from which I read as a brief. I did not even follow it. While I did read parts of it I spoke from rough notes and partly extemporaneously.

I realize this will appear in your proceedings and if there is any further question on which I can be of assistance you have my assurance that I will be delighted to come back. I did not supply advance copies because I did not realize I would be expected to do so and because I really prepared it, as I do most things of this nature, just from notes.

The confusion in this matter may be a question of semantics, and therefore what I have tried to do is to decide what my clients regard as the difference.

In connection with licensing the *Citizens Insurance* case is the one, I am sure, that worries Mr. Curran and worries others who are concerned in this matter.

The *Citizens Insurance* case of 1916 used licensing in the sense of the licence being a condition precedent to doing what you wanted to do. In other words, if you did not have a licence you could not fly your airplane, you could not run your motor and you could not manufacture pharmaceutical products. In that case there was an attempt to prevent insurance companies from carrying on business without a licence, and it was decided that it was not within the legislative competence of parliament and the government of Canada under trade and commerce. This has been the cause of some concern since that time.

What I tried to do was to separate any confusion if I could by ascertaining first of all from my clients what they meant, and I will now try to express it simply as follows. Requiring this licence as a condition precedent is one thing.

Registration does not deny a person the right to be in business; it admits his right to be in business. If he does not register, however, he is subject to penalties; and you can make the penalties as severe as parliament wants to make them; you can make them so severe that one could not very well carry on without registering. It does not deny that inherent right that the Canadian has of entering into the pharmaceutical manufacturing business.

Mr. MACKASEY: On this point—and my example may be far fetched—could a man begin a plant and then register one day, two days or ten days later?

Mr. HUME: That would depend upon the way in which the regulations were worded, but I would think this might be possible. You would have to start your operation and probably you would register at the same time. There are, I am sure, examples of statutes, and some to which I have referred as a result of some research I did by going through the Revised Statutes of Canada to pick out examples. I do not know what the regulations say about the manufacture of maple products, for example, but a manufacturer of such products has to register, and whether he has to register before he starts his operation or a month after starting his operation would depend upon the way in which the regulation was worded.

Mr. MACKASEY: I asked this question because we have constantly emphasized to Dr. Morrell our displeasure or our amazement that anyone can begin a business and produce drugs and sell to the public not only for a month but, in theory, at least years before Dr. Morrell or his department gets around to inspecting the facilities of his particular manufacture.

Mr. ENNS: Or even learns about them.

Mr. MACKASEY: Yes. I think in the liquor industry where the government is so interested in getting their pound of flesh by way of excise taxes we still have bootleggers. Legislation and licensing would eliminate the bootleggers in the drug industry.

The important thing is that in Canada a man should not be able to manufacture drugs and take advantage, intentionally or unintentionally, of the size of Dr. Morrell's operation for a day, a week, a month of even a year before the directorate have been around, enabling some flagrant abuse of rules and regulations because of some lack in the control department and things of this nature.

I have no objection to registration—or call it anything you like—that would prevent this type of thing. For instance, Dr. Brien was here and I did review some of his testimony to the effect that many of the drug companies have legitimate products and if they want to start on the road to legitimate manufacture they are being held up by the Food and Drug Directorate for abnormally long periods of time. I think this is unfortunate for the association in general.

I am equally vehement about the possibility of people going into business without first having their facilities checked and some stamp of approval being put on them by Dr. Morrell, either by certificate or by registration or licensing—and I prefer registration only because it does not imply in a democratic country too great a degree of political or government interference in a free enterprise. Nevertheless, I would hate to see registration without one of the conditions being that one cannot produce one aspirin tablet or one of anything until Dr. Morrell's department has put its stamp of approval on the whole operation.

Mr. HUME: I think it would be possible to prepare—and I am sure Mr. Curran as legal adviser to the department would have no difficulty in preparing—a regulation requiring registration at any time either before or within a day or a week, depending on what the governor in council would think right or what the committee would recommend. You could make registration obligatory either before manufacture or within a reasonable time after commencing.

I do not know whether I am answering your question satisfactorily.

Mr. MACKASEY: The only thing that worried me in your brief—and I think you have allayed those fears now—was that the switch from licensing, on which our emphasis has lain for the last several weeks, to registration implies a certain loss of control or supervision to Dr. Morrell's department, and there was mention of the big stick that was waved by Dr. Showalter to the effect that you do not sell me if you do not meet my requirements.

Dr. Morrell has not this type of authority at his disposal. Other than by dragging the manufacturer to the courts which, as you know, can take years, and the fact that the manufacturer is subject to fine at any time he is in business, Dr. Morrell does not have the power that Mr. Showalter had.

I am prepared as an individual to accept registration provided someone satisfies me—and I think you have done so—that at the same time we are not sacrificing some of the authority Dr. Morrell needs.

Mr. HUME: I did not intend to sacrifice any authority. What I intended to indicate was that right now there is nothing, and that registration would give Dr. Morrell information as a result of which he could conduct whatever investigations and searches he wished to conduct and could ask as many questions as he thought necessary for the purpose of carrying the act into effect. I think at least this would give him information as to who is in the game and who is not.

Mr. MACKASEY: I have one last question.

Any factory not registered would be violating the law, and right now they are not. At least this would be another impediment to unreliable products.

Mr. PRUD'HOMME: Mr. Hume, I express myself better in French than I do in English, but as we have no interpretation facilities here this morning please do not hesitate to ask me to explain anything that I do not make clear.

You mentioned imported products and products manufactured in Canada. Will you give us the approximate proportion of any pharmaceutical products produced outside of Canada? I remember when we visited some place in Montreal and some place in the United States we were told that many pharmaceutical products were made out of Canada and imported into Canada. A problem may arise because even though we are very attentive to the way in which the products are manufactured here in Canada we would have no means of paying the same attention to the drugs which are produced out of Canada.

Mr. HUME: I understand your question perfectly. My difficulty is that I cannot answer your question though I am sure the information is available.

What I intended to imply here was that one does not register merely the manufacturers, one also registers the distributors, the importers or whatever you want—anybody dealing with a pharmaceutical product that is intended for use, in the view of the association, should be registered.

The Food and Drug Directorate would know those who were actually manufacturing and those who were only importing and those who were doing some of both, and by asking the appropriate questions I think they could find out a great deal more about how much is being processed here, how much is being brought into the country in bulk and turned into dosage form and how much of the product is being sold as it is imported, and so on.

Again, I cannot answer your first question with regard to the percentages because I have no idea. I do not think what I have suggested this morning would do other than to provide information to Dr. Morrell and his people on those who are engaged in the importation business.

Mr. PRUD'HOMME: Would you believe then, as far as the second point you mention, that licensing under federal or provincial jurisdiction would be the easiest form of regulation. Since it is of high importance would you think it would be easy if they were to have a meeting of both authorities to arrive

finally at a conclusion? I am not a member of your association but I strongly believe they should be both registered and licensed. This matter is of too great importance to have lengthy debates on the subject of whether it is provincial 92 or federal 91. I am sure the authorities concerned would agree that parliament should as soon as possible legislate concerning licensing of both manufacturers and distributors. Do you believe it would be easy to have such an understanding?

Mr. HUME: Mr. Chairman, this is perhaps a little difficult for me to answer because, being a lawyer, I am well aware of the fact that for many many years the Canadian Bar Association and others have been seeking to persuade the provinces to achieve more uniformity in matters of company and commercial law.

I think one of the difficulties involved in this matter would be the problem of persuading the provinces to agree to some uniform system, but I certainly agree that it is not impossible and I think I give a very good example of co-operation—if that is the proper word—by citing the judgment of the Privy Council in what is known as the Winner case. They decided that the federal parliament had exclusive jurisdiction over interprovincial and international bus and highway operations. The Motor Vehicle Transport Act was passed by the federal parliament and in effect constituted provincial boards and regulatory authorities as federal authorities for the purpose, and this has now been in operation for almost ten years. This is an example of a matter which was under federal jurisdiction and which is now being controlled and regulated by the provinces.

So I think it is quite feasible; but any question of its practicability is beyond my scope. I would think if this committee indicated strong views upon its desirability and if this is the only way to achieve the purpose, it would certainly appeal to me as a Canadian that the provinces and the federal government might unite as they have in the case of highway operation.

Mr. PRUD'HOMME: If such legislation were passed by parliament, do you think it is important that they should register before commencing their operations?

Mr. HUME: I strongly believe that as long as there is control of what is put on the market it does not matter. As long as it is accepted by the Food and Drug Directorate I do not see the necessity of making too clear a regulation saying that you should register before opening any kind of business.

In my 20 odd years of practising law I have incorporated many companies and I know that no company started in a new venture without a great deal of preparation and thought ahead of time. I do not know why, if this is a requirement and if this committee feels it necessary, it should not be possible to register at the same time as they file their letters patent for incorporation. I see no reason why they should not. One does not suddenly decide that one is going into business and go into it immediately. I presume there is a great deal of thought put into the undertaking, and I would assume it would be quite reasonable to require registration if this is what those who know more about it feel is necessary. I am a little out of my depth in the practical problems involved in starting up a new pharmaceutical manufacturing concern, but I would think it would be possible.

Mr. ROXBURGH: Mr. Hume, you have certainly given us a lot of information in regard to the registration or licensing and the legal part of it. As you know, we are laymen. The detail of whether it should be a licence or it should be registration I think we can well leave to the head of our government, to lawyers, and representatives of drug companies. We are here on behalf of the people of Canada and what worries me as an ordinary individual as we talk of this now is that we should be more concerned about the imports from countries outside of Canada—

Mr. PRUD'HOMME: That is what I had in mind.

Mr. ROXBURGH: —than whether there should be licensing or registration. It looks to me—and Mr. Mackasey brought up this subject—that one can still manufacture although one has been fined, but could you still do so when you had to manufacture under rules and regulations?

Mr. HUME: There are a great many rules and regulations presently in effect, as you are well aware. My attention was only directed to the problem arising from failure to register. He would still, of course, be subject to the present rules and regulations and those which will be promulgated in the future as a result of the regulations in respect to how he manufactures and so on.

I am only attempting to concern myself this morning with this single question of the legal ability. I may have misread Mr. Curran's ideas. It is one thing to read a sermon after Sunday morning and another thing to hear it delivered. I may have misread Mr. Curran's intention, but as I understood his testimony he was indicating some considerable doubts of the power of parliament to do certain things. This is the matter to which I was drawing attention.

I agree with you, of course, that all the other regulations presently in force would have to be complied with.

Mr. ROXBURGH: Therefore if we decide there shall be registration—which I think is something all of us have agreed must be done—if it is properly handled along with the present regulations it would do everything that a licence would do as far as preventing unscrupulous companies getting a drug on the market—unless they were bootlegging, and that is a matter with which we have to deal separately. I am speaking here of getting a drug on the market legitimately.

Mr. HUME: Yes, the association believes that registration will do everything that licensing will do.

Mr. ROXBURGH: I have another question and I have an idea it was answered before, but I am not sure.

Have you personally any knowledge now of how many manufacturers do not belong to the Canadian Drug Association?

Mr. HUME: I do not know, sir, how many there are in Canada. I think this is one of the problems. I can indicate the number who are members.

The CHAIRMAN: I can probably answer that. Dr. Morrell said that there are 485 manufacturers and distributors of drugs in Canada, of which I think some 55 belong to the association.

Mr. HUME: I am told that the 55 represent about 85 per cent of the production.

Mr. ROXBURGH: Eighty five per cent of the manufacturers in Canada?

The CHAIRMAN: No, they put 85 per cent of the products on the market.

Mr. ROXBURGH: Therefore, if registration were brought in through parliament every one of these companies would be forced to make themselves known by registering and, as you say, the law could be made sufficiently strong so that if they did not register it could stop them actually from manufacturing.

Mr. HUME: Most statutes that require registration—in fact all statutes at which I have looked that require registration—provide penalties for failure. Depending upon how serious is the failure the penalties that parliament impose are correspondingly stiff. This committee could recommend such a severe penalty in dollar fines or what have you that it would be extremely unhealthy not to register. We could therefore make sure that those who deliberately do not register would be subject to extreme penalties.

Mr. ROXBURGH: You have voiced the opinion to this committee that the regulations put into any registration legislation could—apart from bootlegging with which we have to deal separately—practically bring under control the manufacture of drugs in Canada?

Mr. HUME: It would certainly give the authorities knowledge of those who are in the business. It would provide an opportunity to inspect premises if that is felt desirable, and all the other things that go with the concern which the authorities and this committee has with respect to this matter, yes.

Mr. CÔTÉ (*Longueuil*): You said there were 485 manufacturers. How many of these are registered?

The CHAIRMAN: They do not have to register at the present time.

Mr. HOWE (*Hamilton-South*): Mr. Chairman, in an attempt to distinguish between registration and licensing Mr. Hume alluded to doctors as being registered rather than licensed. I was always of the opinion myself that I was licensed because certainly I could not practise medicine before I acquired whatever was necessary which could be removed as a penalty for malpractice or anything that was done on an unethical basis.

The CHAIRMAN: Are we not licensed provincially and registered federally?

Mr. HOWE (*Hamilton-South*): So it is the provincial law that provides the penalty of removal of licence. Could the penalties here not be severe enough for the drug manufacturers so that if they were malpractising, so to speak, they could have their registration removed or they could be deleted from the list of registered pharmaceutical manufacturers? Could the penalty be so severe that actually these drugs can be stopped being put on the market rather than having a situation in which the drugs would still be put on the market because of penalties which many firms would not mind continuing to pay if they were making enough money out of unethical manufacture?

Mr. HUME: There is the reference which I gave of the Canada Medical Act, Revised Statutes of Canada, 1925, Chapter 257, section 17. I think your licensing provisions are probably under provincial statute.

A second point with respect to penalties: I am sure it must seem to laymen a difference without much of a distinction, but the jurisprudence on the subject, in my submission, makes the very clear distinction that the licence is the condition precedent. Without the licence you cannot even start. Once you start, if your licence is taken away you cannot continue. That is implied in licensing. Registration can have the same practical effect if you have a penalty of, let us say, a substantial fine for the second offence so that if a person is faced with a substantial fine he will comply.

I think it is similar to the situation in regard to fines for parking one's vehicle on a rush hour route. Originally those fines were rather nominal, but when this became a problem the municipalities made the fines so substantial that it now does not pay to park one's car on certain routes in rush hours. The regulations can achieve the same purpose. I suppose it is possible to make the fine so severe for flouting the provisions that one virtually can put a man out of business because one's fines become prohibitive.

There are penalties in some provincial statutes. Under the Companies Act in the province of Ontario there are penalties for failure to file certain returns. There are penalties that are calculated on a per diem basis. If it runs at $20 a day and you let the thing go for several months it is a substantial fine. So there are ways of accomplishing this purpose, and the authorities have the right to impose any fine they wish. This I think will achieve the purpose of making sure that everybody will register except those who intend to operate outside the law in any event. There is always the man who is not aware of it or something like that, but I am sure after due publicity these matters do

come to their attention. I think one can accomplish one's purpose by providing a penalty that makes it unhealthy not to comply with the law.

Mr. HOWE (*Hamilton South*): But it still does not stop the act of manufacture. What is the disadvantage of licensing as opposed to registration?

Mr. HUME: Mr. Curran seems to have some doubts—and I recognize him as the legal adviser to the department and therefore presumably a specialist in his field—whether or not this is possible. I have attempted to indicate that in my view I do not completely share those doubts. But Mr. Curran and I both agree that there are many differences of opinion on this subject, and I am not attempting on behalf of my association to point to the easy way out; I am merely indicating to the committee that as I interpret Mr. Curran's remarks there is no doubt in the world—and this is certainly my view—about a system of registration.

If I am wrong and Mr. Curran is correct, then the recommendations of this committee, if you impose licensing, will be subsequently thrown out by a court as being ultra vires.

Mr. HOWE: So this is merely a legal technical procedure which prevents the act of licensing, not a lack of advantage in having it?

Mr. HUME: Yes, I think that is a fair statement. It is a technical matter, a constitutional law matter. I do not wish to be prejudicial on this but in my view I think a statute is necessary in the public interest. The statute gives, as it does in this case, the power to the governor in council to make regulations necessary for carrying it into effect. If that is so, then any regulation that the governor in council deems necessary for carrying it into effect is a valid regulation. I do not think Mr. Curran goes that far, and this is where the difference of opinion arises.

Mr. ENNS: If Mr. Hume has come here for a purpose of persuading the committee that registration is a valid means of providing an enforceable control over the drug industry, then he certainly has convinced me. I want to congratulate him on his learned dissertation. Before today the committee has shown real concern over the lack of control of manufacturers, and I suppose we were alarmed at the way people could go into this business without the knowledge of the food and drug directorate.

Mr. Hume, you said that one of the things that would make this an effective measure of control would be that it had to be enforceable. I suppose the act of registration meets this condition. Is this correct? I suppose that under a mandatory registration you cannot manufacture drugs without being registered.

Mr. HUME: The practical way it would work would be something like this: if the regulations are amended and are given due publicity, then those persons who are legitimate manufacturers and/or distributors who handle pharmaceutical products would, no doubt, register within a reasonably brief time, and then there would be some who would either defy it or would not be aware of it. Eventually I would assume that those persons would become known. I agree that there is a possibility that a person could be operating in a garage somewhere without anybody knowing about it. This is the kind of person to whom one of the committee members referred earlier, that is the bootlegger. Somehow or other these people get discovered in the end and they are brought to task and prosecuted.

Mr. ENNS: I will take the cue from you, sir. You said that somehow or other they will get discovered, but really your own words were "enforceable regulations are necessary". Is this an enforceable regulation? We were shown before that the food and drug directorate does not have sufficient staff for

a patrol of the industry. My biggest concern is in this area: Can the government enforce this? Maybe I am not fully informed on this.

Mr. HUME: If I interpreted your question correctly, I think it is possible for parliament to empower the directorate and to give them sufficient funds to provide the personnel necessary to carry out adequate inspection. It is possible. As to whether it will be done, I suppose this is a political decision which somebody will make in the future. If you have the regulation, then presumably you are going to provide the food and drug directorate with the personnel and funds with which to carry out the purposes of the act. I would therefore assume that if this committee recommends such a thing, it would also recommend that the food and drug directorate be enlarged, if that is the proper word, to a size which would permit it to carry out the purposes of the act.

Mr. ENNS: I have just one last question. I am wondering if there is any way of providing a penalty on the users of unregistered products. This is attacking the manner from quite another angle, but if I were a physician—which I am not—and if I were prescribing medications that were not manufactured under registered conditions, would this be a fair penalty on me?

Mr. HUME: You are asking me a question to which I am very happy to give a personal and private opinion. I think this would be quite impracticable. It would put an onus on the physicians and the pharmacists to ascertain all the sources of supply which are properly registered. This would be an impossible onus. This is my personal view. I would hate to be in a position where I was purchasing a law book for my law library and I had to ascertain that the sales tax was paid on it. This is the same sort of thing, and it would be impossible.

Mr. RYNARD: Mr. Chairman, I would like to ask Mr. Hume how many of the provinces have registration or licensing now?

Mr. HUME: I know of none. I am not informed on this outside of Ontario. This is a question to which I am sure I can find an answer. I am told that there are none.

Mr. RYNARD: This is an interesting point in that we have in the medical profession registration from the federal government and yet we cannot practise without a licence from the province. We all handle drugs, so that this brings up an interesting point to me. If this is true, then at present the provinces have no control over the drug situation. I thought you intimated a few minutes ago that they did have control, or that the province of Ontario did have control. This is why I am wondering how they could have control without a licensing system.

Mr. HUME: Mr. Chairman, I do not recall that I indicated that. I think my replies may have been slightly misunderstood. I think the only reference I made to the provinces was to say that Mr. Curran had indicated in his submission to the committee that licensing is generally a provincial matter. I have in effect agreed with him that, under property and civil rights, licensing is a very common situation in provincial legislation, but I did not mean to imply that any province in this particular industry had taken any steps.

Mr. RYNARD: I apologize for misunderstanding you. I will go a little further then and ask you if you are suggesting to this committee that it would be better to license provincially.

Mr. HUME: Rather than having a federal agency?

Mr. RYNARD: Yes.

Mr. HUME: Again I have no instructions on this, so I am going to give you my personal view as a Canadian. I think that if you have the facilities here in Ottawa under the food and drugs directorate for carrying out that act, which is a valid and proper act, it would be my personal view that the

registration should be with the federal government. After all, if you do it through the provinces, then the directorate is, I suppose, in the position of having to go to each of the provinces to find out who is in the business in order that they may carry out whatever their duties are. I would think it would be preferable if that were done through one central agency.

Mr. RYNARD: In other words, the pharmacists are licensed provincially, are they not?

Mr. HUME: Yes, sir.

Mr. RYNARD: It seems to me there is a little incongruity there. There are doctors and pharmacists who are licensed provincially, but the doctors are also registered federally. Maybe it would be worth while to have the drug firms registered federally but licensed provincially. I do not know.

Mr. HUME: As I understand it, there is no federal pharmacy act. The matter of regulating pharmacists, their training, their education and their duties, is all provincial. This is a strictly provincial matter; whereas the Food and Drug Act is a concern of the federal parliament. I think there are probably other examples where a portion of an undertaking was under provincial jurisdiction and another portion under federal jurisdiction. I suppose this must be so in a country like Canada which is a federation with divided jurisdiction.

It does not upset me as a Canadian that the pharmacists and the doctors are under provincial jurisdiction, whereas the Food and Drug Act is found to be valid under federal legislation. I feel personally that in matters of this kind you want to have a federal uniform set of statutes, regulations, schedules, and so on.

Mr. RYNARD: I could not agree with you more, but I am wondering, in this day and age when we are giving the provinces more control, if we possibly should not leave licensing to the province. Should we not pursue that course of action? I am just bringing it up here as an idea. I am not suggesting it at all.

Mr. HUME: Under the British North America Act the provinces can license manufacturers in any industry without any further requirements, if they wish to do so. There are certain restrictions which the law imposes, whatever the requirements may be. For instance, they must be uniform, and so on. I see no reason why any province, if it wished to, could not require a manufacturer, in any line who is located in a province, under property and civil rights, to be registered.

Mr. RYNARD: Can a pharmacist move from one province to another, and does he have to register or does he have to get a licence? What is the score on this?

Mr. HUME: Again, as I am practising in Ontario it is my understanding of the Ontario Act that a pharmacist coming in from another province must register. I do not know what the situation is in other provinces. I imagine it would probably be the same.

Mr. RYNARD: They are then accepted in any province and licensed?

The CHAIRMAN: I think last year parliament passed in Bill No. C-7, a pharmacy examining board which was to be uniform across Canada with the exception of the province of Quebec.

Mr. HOWE: I have a question which is supplementary to that. Would this not mean, if they are going to be licensed in a province, that each company would have to be licensed in each province where it distributes its product? If registration were federal, would this not create a complication?

Mr. HUME: Not really. An insurance company can be incorporated under a provincial statute or a federal statute. If it is incorporated under a provincial statute, then if it wants to do insurance business in other provinces it

must apply to the provincial authorities there. I do not know whether the correct word is registered or licensed. On the other hand, a federal company has the power to do business across Canada. A federally incorporated company has no power to own land in a province unless it applies to the province and gets a license. If you have a manufacturing concern with a federal charter located in Montreal which wants to open factories in five other provinces, it must go to each of the provinces.

Mr. HOWE: I was speaking of a concern distributing from Montreal to the other provinces. If you are going to license distribution of imported drugs from the outside, and you are going to have provincial licensing for distribution, then a drug manufacturer manufacturing in Quebec would have to have a distributor's license within the other provinces.

Mr. HUME: That is right. This does happen in other endeavours today.

Mr. MITCHELL: Mr. Chairman, Doctor Rynard has taken some of the wind out of my sails with some of the questions he asked. Maybe I could enlarge on two of them.

Mr. Hume, do you feel that registration—and I will use the word "registration" rather than licensing—would be more reasonable under provincial control than under federal control, and these regulations regarding registration would be different in each province; in other words, they would not be uniform throughout the country?

Mr. HUME: I am sorry. I believe you have turned my statement around. I think I stated that registration is preferable federally rather than provincially. I indicated that, I think, quite clearly, or I hope I did.

Mr. MITCHELL: I agree with you there.

Mr. HUME: But the way you put it your question implied that I stated the matter the other way around.

Mr. MITCHELL: I wanted to have it clarified. The use of the word "registered" instead of "licensed" has been brought up as reflecting on the pharmacists. It is my impression that the pharmacists are licensed by their graduating bodies for practice in whatever province they may be in.

I think I used the word "licensed" correctly in this case. I am wondering why the manufacturers are stating through you that licensing would be more proper in regard to them than licensing of pharmacists who handle the same products.

Mr. HUME: I think I understand you, Mr. Mitchell. In my understanding a pharmacist is a professional man who is required to got to the university and acquire a degree. To me this is clearly a matter of property and civil rights and I am not surprised to find it is a matter of strictly provincial concern, whereas a manufacturer is in a completely different category. I think it is a matter of opinion, but the clients I represent feel that as manufacturers the same results for the enforcement of this act—which is after all under the criminal law—can be obtained by registration without some of the disadvantages of licensing, and Mr. Curran may be completely and entirely right as to his interpretation of the constitutional law aspect of the matter. I am trying to answer the question properly. I find it difficult to compare the two. I have had very little connection with pharmacists in my professional life and I am not really competent to discuss their problems and why they are registered or why they are licensed. I am only speaking from general knowledge.

Mr. MITCHELL: Let us then say that registration is not as rigid as licensing. Would the pharmacist then be within his right in asking for the same regulation under the word "registration", rather than "licence"?

Mr. HUME: I suppose that if they felt that, then they would be within their rights to ask for something less rigid than they now have. It would be quite within their rights to do so.

Mr. ROXBURGH: Mr. Chairman, I have a supplementary question. Is not licensing just a matter of opinion between you, representing the manufacturers of drugs, and the lawyer of the government, on whether the government could enforce registration as easily as licensing? As you indicated earlier on, you could make registration even harder on the individual, and more restrictive than licensing, if you put in the rules and regulations. It is just a matter of opinion between, let us say, the top lawyers in Canada, and one could be as effective as the other. In other words, whether it is registration or licensing, the pharmacist would not be any better off. Is that not right?

Mr. HUME: I could not answer that question until the pharmacists saw what kind of registration they were getting.

With respect to your main question, I agree it is a matter of opinion. We finally solved these problems in the Supreme Court of Canada. As many federal statutes as provincial statutes have been ruled ultra vires. There is a continuous process of evolution here. I think that there is something to be said about the legal situation. I am sure you can get many different legal opinions on it. I adhere to the view that if the statute is proper and in the public interest, and if the statute is broad enough to give the governor in council power to carry this into effect, then whatever the governor in council deems necessary, however you compose it, would be held to be valid. If not, then surely the whole statute would be invalid. This is where Mr. Curran and I perhaps part company. He indicated that in his view you had to tie such a thing down to a particular product and show great danger to public health. I have a slightly different view on it.

Mr. ROXBURGH: Again it is a matter of legal opinion.

Mr. MACKASEY: I think that Doctor Curran, if I remember rightly, did agree—as the result of a question I posed to him—that if he could tie the question of licensing to the criminal law, then there would be no argument and it would be a federal matter.

Mr. HUME: I agree.

Mr. MACKASEY: Are there any restrictions in the case of registration and in the case of licensing on the type of penalties that could be enforced? Is registration, for instance, limited to matters of civil action, and could it be tied in with criminal action?

Mr. HUME: There are no restrictions. Parliament has supreme power to impose any penalty it wishes. Criminal law is granted to the federal government under section 91, but in order to put teeth into the provincial statutes it was recognized—and it is now the law of the country—that a provincial statute can impose a penalty. That is not really regarded as criminal law, and it is called quasi criminal law, but to the fellow who pays the fine it is the same.

Mr. MACKASEY: Suppose we did not want to fine him, but we wanted to put him out of business for repeated abuses, what would happen then?

Mr. HUME: The penalty would either have to be a fine or imprisonment.

Mr. MACKASEY: Could we do both under the guise of registration?

Mr. HUME: Yes, under registration you could put any penalty you like, either a fine or imprisonment. However, when you get into the area of putting him out of business, you are entering into the civil aspect of the matter under which a prohibition order is included. Under the Combines Investigation Act, for example, which is criminal law, there is a provision, which has not been successfully challenged, for what they call a prohibition order. This is a type of thing which, I presume, if it is valid for the Combines Investigation Act, would be valid for the Food and Drugs Act, both of them being under the criminal law.

Mr. MACKASEY: If we were to adopt a registration system, and if, later on, we felt it was not stringent enough, would it be possible to revise the law and impose licensing?

Mr. HUME: No, sir.

Mr. MACKASEY: In your remarks you referred to products coming into the country. I presume you were talking about dosage form rather than bulk form.

Mr. HUME: I do not recall indicating the source of the product. I did refer to imported goods. Again you are on a subject on which, as a lawyer, I feel I am not too competent to speak, but from the little bit of knowledge I picked up from the association I can say that the goods come in a variety of ways, as raw material, later processed and put into dosage form, as bulk, tested and packaged, and in the form in which it is finally sold. As to the details, I am afraid I cannot answer your question.

Mr. MACKASEY: You did mention imports. I gathered from the evidence submitted here by various people at various times that raw materials in dosage form, or finished form, come in from countries with whom we have some reciprocal agreements in so far as the standards of these firms are concerned. However, I fail to see what advantage you are going to get at present from registering some firm in Poland or Russia, apart from it being of academic value because of the unknown source of their raw material. If Doctor Morrell has no way of checking that source of material either through reciprocal agreement or otherwise, then what advantage is there in registering such a firm?

Mr. HUME: I have great doubts as to your ability to require a company in a foreign country to register as such. You do have complete control over your imports because you could actually require the person who is doing the importing and distributing to register, and that is the person we are talking about.

Mr. MACKASEY: What is the next step?

Mr. HUME: You are now getting into a technical field. Let us say you know who is importing. It would then be up to the food and drug directorate to decide what inspection if any they wanted to make of that product, as it came to the border or before it is sold in Canada. They would at least know who is importing, and I understand Doctor Morrell does not know who is importing drugs. Incidentally, he does get the information.

Mr. MACKASEY: It is not fair to Doctor Morrell to say that because he does have a certain check at the customs. He made this point emphatically, that all raw materials coming into the country under the Customs and Excise Act are reported to him. He then makes a spot check on the strength of these reports and this is within his jurisdiction.

Mr. HUME: I was not aware of that.

Mr. MACKASEY: However, I may say this, that Mr. Hume's testimony has been very helpful this morning but this committee must not lose track of the fact that in the final analysis, whether it comes to licensing, registering, or doing nothing at all, the safety of the drugs is going to depend, to a great extent, on Doctor Morrell's department. While registration will, I think, increase from the 485 known suppliers to perhaps 700 or 800, I am in favour of this registration. I do not want my remarks to be misunderstood, but this is also going to emphasize the need to put at Doctor Morrell's disposal more personnel and larger funds. At present, there are only 485 firms which are supervised once every three years at the rate of 160 a year, but when registration is invoked and the number of legitimate suppliers jump from 485 to, say, 907, then I hope this committee will be prepared to emphatically suggest to parliament that Doctor Morrell's staff should be doubled or tripled if necessary to put some teeth into the registration that will be required.

Mr. PRUD'HOMME: It is all very well to tie this to the criminal law, as one of the members suggested, but there could easily be a discussion about whether or not it is right to tie it to criminal law. That is why, whether Doctor Morrell's staff is doubled or tripled, I still strongly believe that we should urge that this committee recommend a meeting of federal and provincial authorities on this matter. Maybe the provincial authorities, in agreement with the food and drug directorate, could come up with some recommendations, such as increasing provincial staff under the supervision of the food and drug directorate.

I do not believe all of this should be the sole responsibility of Doctor Morrell and that it should only be the directorate who should be investigating production in say, British Columbia or Newfoundland. It seems to me that the provincial authorities should be consulted. If there is no such meeting, then I do not see how we as a committee can ask parliament to double or triple the directorate's personnel so as to enforce better control. We should recommend a meeting of federal and provincial authorities because it is in the interests of the general public that such a meeting take place to see what the provinces and what the federal authorities could do. Some people might argue that the provinces could do more since they are nearer to the source of production.

The CHAIRMAN: There is one question which I would like to ask Mr. Hume. At the present time the Food and Drug Act is considered to be criminal law and not civil law. Is that right?

Mr. HUME: Yes. My understanding of the historical development is that when the first Food and Drug Act was passed, it was challenged as being a matter of property and civil rights, a matter of provincial concern. I think this was confirmed by Mr. Curran's testimony. It had to be brought under some heading, and it was brought into the criminal law. I read the case some time ago, I forgot the details, but it was decided to be valid federal legislation. That is the end of the matter. It is not likely that the courts will reverse their judgment after these long years, so it is now valid federal legislation.

Mr. MARCOUX: I have a few comments which I would like to make. Surely it is a question of semantics because, as was said a few minutes ago, doctors are registered federally and licensed provincially. I do not agree with that because those who take the examinations and pass them are licensed by the Medical Council of Canada.

With these licenses, we are registered in the official federal registry, so that it can be ascertained that we are available. We have permission to practise anywhere on the condition that we have a licence provincially, but without examination. That means that if we want to practise anywhere in Canada, we are already registered and we can apply for a licence from the province, and we will have it immediately. But we cannot practise only with our own registration. That is what I want to emphasize. We are licensed by the Canadian medical council. We are not merely registered by them. We are licensed, so therefore we are licensed by a federal body. However we cannot practise under this licence. We have to have another provincial licence to do so.

Mr. HUME: The statute to which I referred uses the word registration, but it may be different in that regard, so there might be some difference in the matter. I went through the statutes in order to assist the committee to find examples that might be of assistance in this category federally. Under the Canada Medical Act the word used in section 17 is registration. This could be regarded as a licence. As lawyers we are licensed in a particular province, but we cannot register anywhere federally. If we want to move to another province we have to comply with the provincial requirements involved, and we have to pay a fee, and submit to an examination on the local provincial statutes.

Mr. MARCOUX: Our licence states that we have met the equivalent status, and that we have been examined.

Mr. HUME: I suppose the reason is that measles would be the same in any province, whereas a lawyer has to be acquainted with local provincial statutes.

Mr. MACKASEY: We want to keep aspirin the same in every province.

The CHAIRMAN: We really should not get into that field, Mr. Marcoux. Some doctors are registered to practise in only one or two provinces, and if they wish to practise in other provinces, then they have to write examinations.

Mr. MARCOUX: Some members seem to be mixed up in the matter of registration. We have been talking about the registration of manufacturers, not of the products which are manufactured.

Mr. HUME: That is right.

Mr. MARCOUX: Because in the food and drug trade it is possible to have those products, and we have to realize that many of the big companies are good companies and most of them are in the manufacturers' association, and we do not worry about them. We know that they are making their own tests for purity and for integrity, and we know that they do import raw material from other places, and that they make tests. So we are not concerned about them. Those we are concerned with are the others, and I think that registration would be a very good means at least of ascertaining who is using those raw materials and who is making other materials, other than those who are already in the association. That is all.

Mr. CÔTÉ (*Longueuil*): Can you tell me whether the 55 members of the association who are represented here today can actually sell their own products?

Mr. HUME: I am sorry but I do not have that information. However, it is information which I am sure can be obtained from the association and perhaps I might be permitted to forward it in the form of a letter to the Chairman of the committee as an answer to your question. I do not have any idea. I am making a note of your question. What you want to know is what members of the association can actually sell their own products, and how many?

Mr. CÔTÉ (*Longueuil*): Yes, how many can actually sell?

Mr. HUME: You mean sell to the government?

Mr. CÔTÉ (*Longueuil*): Yes, or can sell.

Mr. HUME: I hope all of them can, but I do not know the answer.

Mr. MITCHELL: They cannot unless they meet the tender price.

Mr. MACKASEY: Did you not say the standards set up by the Department of Industry are arrived at in co-operation with your association or with members of your association?

Mr. CÔTÉ (*Longueuil*): I know that your association was asked for it.

Mr. HUME: I understand that the Canadian government specifications board in developing these standards did work closely with us. My instructions are that they worked closely with the association, but as to the extent, I was not any part of it, so I do not know how closely they did work.

Mr. MACKASEY: I think on page 2 of the report they did list the people who sat down with them, and I think that among others Parke, Davis was mentioned.

The CHAIRMAN: Are there any further questions to ask of Mr. Hume? If not, we would like to thank him for appearing on behalf of the C.P.M.A. He has given us a very learned and interesting discussion this morning.

I suggest that we adjourn at this time to meet again at the call of the Chair. I shall have a steering committee meeting at the first of the week.

HOUSE OF COMMONS

Second Session—Twenty-sixth Parliament

1964

SPECIAL COMMITTEE

ON

FOOD AND DRUGS

Chairman: Mr. HARRY C. HARLEY

PROCEEDINGS

No. 20

WEDNESDAY, DECEMBER 16, 1964

THURSDAY, DECEMBER 17, 1964

Including

FOURTH AND FIFTH REPORTS TO THE HOUSE

ROGER DUHAMEL, F.R.S.C.
QUEEN'S PRINTER AND CONTROLLER OF STATIONERY
OTTAWA, 1964

21617—1

SPECIAL COMMITTEE ON FOOD AND DRUGS

Chairman: Mr. Harry C. Harley

Vice-Chairman: Mr. Rodger Mitchell

and Messrs.

Armstrong
Asselin (*Richmond-Wolfe*)
Basford
Côté (*Longueuil*)
Enns
Francis
Gauthier
Horner (*Jasper-Edson*)
Howe (*Hamilton South*)
Jones (Mrs.)
Jorgenson
Macaluso
Mackasey
Marcoux
Mather
Prud'homme
Roxburgh
Rynard
Slogan
Wadds (Mrs.)
Whelan
Willoughby—24

(Quorum 8)

Gabrielle Savard,
Clerk of the Committee.

REPORTS TO THE HOUSE

The Special Committee on Food and Drugs has the honour to present its

Fourth Report

Your Committee recommends that its quorum be further reduced from 8 to 5 members.

Respectfully submitted,

HARRY C. HARLEY,
Chairman.

Note: This report was presented to the House on Thursday, November 26, but was not concurred in.

Friday, December 18, 1964.

The Special Committee on Food and Drugs has the honour to present its

Fifth Report

On March 9, 1964, your Committee was constituted with the following Order of Reference:

"*Resolved*,—That a Special Committee be appointed to continue the enquiry into and to report upon (*a*) the hazards of food contamination from insecticides, pesticides, and other noxious substances; and (*b*) the safety and cost of drugs, begun by a Special Committee at the past Session;

That the Committee consist of 24 Members to be designated later by the House;

That the Committee be empowered to send for persons, papers, records, and to report from time to time, and to print such papers and evidence from day to day as may be deemed advisable;

That the minutes of proceedings and evidence of the Special Committee at the past Session be referred to the said Committee and be made a part of the records thereof;

That the provisions of Standing Orders 66 and 67(1) be suspended in relation thereto."

Your Committee in the last Session dealt with the matters referred to in part (*a*) of its order of reference.

Although your Committee has held 24 meetings this Session, heard statements and recorded expert evidence, it was possible to consider only the portion of its order of reference dealing with the safety of drugs.

Your Committee examined the officials of the government department of National Health and Welfare, particularly the Food and Drug Directorate, and the Chairman of the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers, Distributors and Agents.

Representatives of various drug manufacturers were called and several drug manufacturing plants were visited. Representatives of the medical, pharmaceutical, and pharmaceutical manufacturers associations were heard. Academic witnesses from the teaching hospitals appeared, as well as a consumer organization.

21617—1½

I. General Remarks on the Safety of Drugs

The Committee feels that generally speaking, at the present time the dangers from the use of drugs are small in proportion to their value. One must balance the potential harmful effects of any medication against its value in relieving pain and suffering from disease and preventing death. This balance is always under consideration by the medical profession.

Each and every drug has side effects because drugs act on the body as a whole and are not usually selective for one site of action. Each medication is a risk to the patient and the decision has to be made as to whether such a risk is worthwhile. The evidence heard indicates that the risk is small and that the treatment of disease is advancing rapidly as evidenced by the increasing life span of the individual. In summary one has to consider the risks of treating the patient with a certain drug against the risk of not treating the patient with this drug. In a severe illness a doctor may have to use a very dangerous drug for treatment but does so in the knowledge that without it the patient may succumb.

The above does not mean however that we should accept these risks without care. The Committee feels that the legislation of Canada and its administrators, along with the drug manufacturers, druggists and doctors have all played a significant part in keeping Canada relatively free of drug catastrophes such as was evidenced in Europe, and to a smaller extent in Canada, after the use of thalidomide. As the drugs in common usage are becoming more and more potent and more and more specific in their action, it is most important that our regulations regarding drugs be studied with all these factors in mind and that these regulations be such as to maintain the highest standards of drugs available for the use of Canadians and that they be as safe as is possible.

After the thalidomide tragedy a Commission was appointed to make recommendations regarding regulations under the Act. This Commission reported to the Minister and changes in the regulations were made particularly regarding preclinical submissions, stoppage of clinic trials and drug recall. These new regulations have been in force for approximately one year and appear to have improved the safety procedures involving the introduction of new drugs.

II. The Food and Drug Directorate

The legislation and regulations governing the safety of drugs are the responsibility of the Department of National Health and Welfare, and are administered by a branch of that Department, the Food and Drug Directorate. Your Committee would first like to recognize the high calibre of the work of the Food and Drug Directorate as carried out by their capable and conscientious staff. The people of Canada are fortunate to have these devoted civil servants dedicated to their safety and the Committee gratefully acknowledges this fact. Detailed discussion of this Directorate will be done under various headings.

1. Staff Requirements

It is obvious that the present Food and Drug Directorate are understaffed. The services that are required under the present regulations are delayed due to a shortage of staff. This delay has been accentuated by the new regulations which place further responsibility on the Food and Drug Directorate.

They now have to examine in detail pre-clinical studies of each new drug before it can be released for clinical testing by the manufacturer. It is probable that it is too early after the introduction of these new regulations to accurately predict what effect they will have on the introduction of new

drugs and the time that the Directorate will need to process these new submissions. It is therefore recommended

> that the new regulations of the Food and Drug Directorate concerning preclinical trials of new drugs be reviewed in one year.

The problem of staffing the Food and Drug Directorate is not merely a question of numbers of employees. The majority of the staff required have professional training of one type or another and these people also require further training in the Department itself before having the ability to do the job required by the Directorate. It is obvious that the wage scale at present offered by the Civil Service Commission is not in keeping with wages in a similar non-governmental position. Your Committee recommends

> that the wage scale offered professional people by the Civil Service Commission on behalf of the Food and Drug Directorate be increased to be in line with similarly employed professionals in a non-governmental setting. Some consideration should also be given to allowing the Food and Drug Directorate to hire directly in emergency situations with the concurrence of the Civil Service Commission.

Your Committee recognizes that this revision of salaries upwards would help to solve the problem on a short term basis but the long term solution is to attract to the Directorate those young undergraduates soon to finish their training. Thinking of the means by which the Department of National Defence attracts undergraduates into military service and keeping in mind the training even graduates need before employment in the Food and Drug Directorate your Committee recommends

> that the Food and Drug Directorate be authorized to accept undergraduate students as employees in their Department, to attend their University courses in the winter and to be trained in the Directorate in the summer, and on graduation to serve in the Directorate for a period of time similar to the scheme of the Department of National Defence.

Some of the recommendations of this Committee discussed later in the report will give the Directorate further responsibilities and cause further shortages of skilled, qualified personnel in a Department already grossly understaffed to do the job required.

Your Committee recommends

> that the staff of the Food and Drug Directorate be doubled and that future additions be made to the Staff as their responsibilities and duties grow.

2. Drug Information

At the present time the Food and Drug regulations require that a brochure be included in the drug package, listing all the known effects of the particular drug. The Food and Drug Directorate aid in the dissemination of drug knowledge regarding safety in additional ways:

(*a*) Poison Control Centres throughout Canada are given detailed knowledge by the Food and Drug Directorate of medications on the market and the method of dealing with cases of poisoning.

(*b*) An adverse drug reaction committee has been set up just recently by the Food and Drug Directorate composed of university and teaching hospital representatives, to report on unexpected drug reactions. This is an important

beginning; however the Committee would point out that the majority of medical practitioners are not attached to university or teaching hospital staffs. Your Committee recommends

> that the Food and Drug Directorate ask the co-operation of the Canadian Medical Association, the Canadian Dental Association, the Canadian Pharmaceutical Association, the Canadian Pharmaceutical Manufacturers Association, the Provincial Colleges of Physicians and Surgeons and the College of General Practice to report adverse drug reactions to the Directorate, and to facilitate this end the Directorate design and distribute a form suitable for reporting such reactions.

Your Committee also recommends

> that drug reaction reports be studied by the Food and Drug Directorate and reports made to the interested professions, at regular intervals, as well as to similar departments in governments of other countries and to the World Health Organization.

(c) The Advisory Drug Committee is a standing committee appointed by the government advising the Food and Drug Directorate on drug matters. This is composed of recognized experts on whom the Directorate calls for advice. In addition the Directorate has on occasion set up special committees to consider specific problems such as the recent committee on monoamine inhibitors. The disadvantage of a special committee is the time required to set it up and the advantage of such a special committee is that the Directorate can call on very noted specialists on any particular drug in any particular field. The Committee feels that both these factors can be used to good advantage by recommending

> that the Department of National Health and Welfare employ permanent staff
>
> (*a*) to study the Adverse Drug Reaction reports,
>
> (*b*) to draft suitable reports to the medical and related professions concerning drugs,
>
> (*c*) to form a nucleus of any special committee set up to consider any particular drug problem.

3. Infractions of Regulations

In order that the public be more aware of infractions of the regulations of the Food and Drug Directorate as they concern the safety of drugs your Committee recommends

> that any seizures of any material under Food and Drug Regulations and any prosecutions be published at regular intervals by the Food and Drug Directorate.

4. Quality Control

Under the present regulations all drug manufacturing firms are required to have quality control in their manufacturing processes. Those firms that are distributors of drugs and not manufacturers have the quality control inspection done wherever the drug they distribute is manufactured. The main problem in this area is the drugs that are imported into Canada and distributed without further processing. Here the Food and Drug Directorate have to be satisfied that quality control is adequate in the plant that is manufacturing them outside Canada. If the Directorate are not satisfied an inspector can be sent to the

country of origin to see first hand the quality control employed there. This is of course done in the field of biologicals as a once yearly inspection of sources outside Canada, but this has never been done as yet in the field of drugs other than biological products. Your Committee feels that quality control is most important and therefore recommends

> that inspection of quality control methods here and abroad should be carried out by the Food and Drug Directorate. If felt necessary by the Food and Drug Directorate this quality control check should be carried out by any importer before the drug is released for use in Canada. If this inspection is not carried out or does not meet our standards the imported drug would not be released for use in Canada.

III. Control of Drug Manufacturers

The Committee has considered in great detail the question of licensing or registration and whether or not such a procedure should be carried out. The major concern of the Committee is to see that drugs are provided as safely as possible for the people of Canada. It is the feeling of the Committee that licensing or registration should only be done if it adds to the safety of the drugs. The new regulations in force approximately one year provide for examination of drugs before they are tried on patients (pre-clinical submission), give the Food and Drug Directorate the right to stop clinical trials of drugs and the power to recall drugs. A company that produces a new drug has to comply with new drug regulations, but a company that wishes to produce and sell a drug not classified as a new drug can do so without permission or even knowledge of the Food and Drug Directorate. The Committee feels that this is unwise and could possibly lead to the production of unsafe drugs and therefore recommends licensing or registration of all drug manufacturers and distributors, in order that the Food and Drug Directorate may have full knowledge of all those engaged in this business, and have the opportunity to inspect their premises.

In respect to which of these two procedures should be carried out it seems to be apparent that registration could be implemented without legal complications and be as effective as licensing because of the penalties for failure to comply with the requirements of registration. As far as licensing is concerned there is some difference in legal opinion we have heard as to whether this could be carried out within the terms of the Food and Drug Act. Lack of license would prohibit drug manufacture while lack of registration could invoke a penalty but not prohibit manufacture and is more in keeping with the free enterprise system. Taking all these matters into consideration your Committee recommends

> that all drug manufacturers and distributors be registered, such registration of existing companies to be carried out as soon as is possible by the Food and Drug Directorate, and in the case of new companies such registration to be applied for prior to the sale of their products on the open market. In view of possible delays in inspection by the Food and Drug Directorate, if inspection of new companies does not take place within a limited period of time, such products may be marketed.

If registration were to be carried out by the Provinces it is obvious that many varying standards would be in effect across Canada. As the safety of drugs is under the Food and Drug Directorate, of a federal government department, and authority is under the Criminal Code it is recommended

> that such registration take place on a Federal basis.

Because of the necessity for making sure of continued high standards it is further recommended

> that re-inspection of registered drug manufacturers should take place at regular intervals to be prescribed by regulations.

IV. Medical Research

Medical research has to be encouraged in Canada by the drug industry and by government. The majority of drug firms in Canada are foreign owned and the basic research is usually done in the country of the firms' origin. It is noted however that these Canadian subsidiaries are performing an increasing amount of separate research in Canada and are to be commended for this. In this field the Committee recommends

> that the government continue the present tax incentives for research carried on in Canada and study further methods of encouraging medical research in Canada.

Government contributions to research through the Medical Research Council should be increased. It is noted that the per capita expenditure on medical research in Canada is much below that of other countries with comparable medical standards.

The current position of medical research is aggravated by the decision of the National Institute of Health discontinuing grants to Canada for medical research. The facilities required for research are deficient and at the present time government grants are not available for capital purposes such as construction. Your Committee therefore recommends

> that the federal government increase substantially the present monies available to the Medical Research Council and further that a separate fund be created for the construction and furnishing of research facilities under the direction of the Medical Research Council.

V. Proprietary and Patent Medicines

No significant evidence was produced of any reason to change the marketing practice of proprietary and patent medicines. It is apparent that a secret formula is of no real value to anyone and may in fact on occasion constitute a danger if such medication were ingested in large doses. With this in mind your Committee recommends

> that the full contents by ingredient and quality of proprietary and patent medicines be listed openly on package and label.

VI. Generic vs. Brand Name Drugs

Generally speaking drug manufacturers may be divided into two types—the producer of brand name drugs and the producer of generic drugs. This is not quite correct as a brand name company may market some of their products under the generic name only. However you may wish to classify them, there are two different types of drug manufacturers:

(1) a drug manufacturing company that develop their own products, do the research, original manufacture, create the market and distribute the product;

(2) a drug manufacturing company that manufacture and distribute a product originally produced by some other firm and do not take part in the drugs research. They in other words produce a drug for which a market has already been created.

These latter are usually referred to as generic firms. Because they have contributed nothing to the primary research or continuing research on a drug they can of course produce this drug at less cost. This does not necessarily mean that the drug they produce is dangerous or any less potent than a trade name drug. It is known however that the so-called generic firms present greater problems for the Food and Drug Directorate.

It is obvious that if all drugs in Canada were manufactured in this way that research in the pharmaceutical industry would cease and be confined to the hospital and university setting which the Committee feels is undesirable. As an example the Committee points out that penicillin was discovered outside of the drug industry but the drug industry had to be asked to help to develop means of mass production of penicillin. This factor then reinforces our previous recommendation

> that the government continue the present tax incentives for research carried on in Canada and study further methods of encouraging medical research in Canada.

VII. Drug Usage—Public vs. Government

Some question has been raised regarding a double standard for drugs—one fit for government use and one fit for public use. Your Committee would point out that the inspection on all drugs is the same in Canada, and all inspections are carried out by the same branch of the Department of National Health and Welfare, the Food and Drug Directorate. The only difference lies in the interpretation of the same inspection, the government specifications board going into detail not directly related to the safety of drugs and the regulations of the Food and Drug Act. The reason for the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers is that they perform the same service for the government patient that the doctor normally does for his own patient. When one of the public requires a drug, the selection of the drug is made by the doctor based on his knowledge of the drugs available, their cost, safety and all other factors. When the government patient is given a drug, this drug selection is made by the doctor, from government drugs bought by tender on advice of the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers. As the government purchases under the tender system, these are usually the cheapest drugs available, and this extra precaution is felt to be necessary to ensure safety. This is also true where other governments or agencies purchase by tender, that inspection services in addition to the Food and Drug Directorate are usually employed by the purchaser.

Your Committee feels that the same safety standards are used for government and public. In time if the recommendations of this Committee are agreed to by the government and implemented the need for the Interdepartmental Advisory Board on Standards for Pharmaceutical Manufacturers will disappear.

VIII. Summary of Recommendations

Your Committee summarizes its recommendations in the same order of their appearance in the report and not necessarily in the order of their importance to the question of safety:

1. That the new regulations of the Food and Drug Directorate concerning pre-clinical trials of new drugs be reviewed in one year.
2. That the wage scale offered professional people by the Civil Service Commission on behalf of the Food and Drug Directorate be increased to be in line with similarly employed professionals in a

non-governmental setting. Some consideration should also be given to allowing the Food and Drug Directorate to hire directly in emergency situations with the concurrence of the Civil Service Commission.

3. That the Food and Drug Directorate be authorized to accept undergraduate students as employees of their Department, to attend their University courses in the winter and to be trained in the Directorate in the summer, and on graduation to serve in the Directorate for a period of time similar to the scheme of the Department of National Defence.

4. That the staff of the Food and Drug Directorate be doubled and that future additions be made to the staff as their responsibilities and duties grow.

5. That the Food and Drug Directorate ask the co-operation of the Canadian Medical Association, the Canadian Dental Association, the Canadian Pharmaceutical Association, the Canadian Pharmaceutical Manufacturers Association, the Provincial Colleges of Physicians and Surgeons and the College of General Practice to report adverse drug reactions to the Directorate, and to facilitate this end the Directorate design and distribute a form suitable for reporting such reactions.

6. That drug reaction reports be studied by the Food and Drug Directorate and reports made to the interested professions, at regular intervals, as well as to similar departments in governments of other countries and to the World Health Organization.

7. That the Department of National Health and Welfare employ permanent staff.
   (*a*) to study the Adverse Drug Reaction reports,
   (*b*) to draft suitable reports to the medical and related professions concerning drugs,
   (*c*) to form a nucleus of any special committee set up to consider any particular drug problem.

8. That any seizures of any material under Food and Drug Regulations and any prosecutions be published at regular intervals by the Food and Drug Directorate.

9. That inspection of quality control methods here and abroad should be carried out by the Food and Drug Directorate. If felt necessary by the Food and Drug Directorate this quality control check should be carried out by any importer before the drug is released for use in Canada. If this inspection is not carried out or does not meet our standards, the imported drug would not be released for use in Canada.

10. That all drug manufacturers and distributors be registered, and such registration of existing companies to be carried out as soon as is possible by the Food and Drug Directorate, and in the case of new companies such registration to be applied for prior to the sale of their products on the open market. In view of possible delays in inspection by the Food and Drug Directorate, if inspection of new companies does not take place within a limited period of time, such products may be marketed.

11. That such registration take place on Federal basis.

12. That re-inspection of registered drug manufacturers should take place at regular intervals to be prescribed by regulations.

13. That government continue the present tax incentives for research carried on in Canada and study further methods of encouraging medical research in Canada.

14. That the federal government increase substantially the present monies available to the Medical Research Council and further that a separate fund be created for the construction and furnishing of research facilities under the direction of the Medical Research Council.

15. That the full contents by ingredient and quantity of proprietary and patent medicines be listed openly on package and label.

Your Committee would like to thank all those organizations, industries and individuals who appeared before the Committee or submitted material for consideration. In addition, your Committee would like to thank those who made it possible for its Members to see the manufacture and processing of drugs.

The Committee finds that it will not be able to complete, at the current Session of Parliament, its inquiries into the matters referred to it for report and accordingly, recommends that this Committee be re-established in the next session of this Parliament to resume the study of the remaining term of reference, namely the cost of drugs.

A copy of the Minutes of Proceedings and Evidence (*Issues Nos. 1-19*) is appended.

Respectfully submitted,

HARRY C. HARLEY,
Chairman.

MINUTES OF PROCEEDINGS

WEDNESDAY, December 16, 1964
(25)

The Special Committee on Food and Drugs met *in camera* this day at 3.45 p.m., the Chairman, Mr. Harry C. Harley, presiding.

Members present: Messrs. Armstrong, Asselin, (*Richmond-Wolfe*), Côté (*Longueuil*), Enns, Francis, Harley, Howe (*Hamilton South*), Marcoux, Mather, Mitchell, Prud'homme, Roxburgh, Rynard, Whelan, Willoughby (15).

The Committee considered a Draft Report to the House recommended by the Steering Subcommittee on Agenda and Procedure.

Mr. Willoughby moved, seconded by Mr. Rynard,

That the second recommendation, on page 4, be amended to read as follows:

> "that the wage scale offered professional people by the Civil Service Commission on behalf of the Food and Drug Directorate be increased to be in line with similarly employed professionals in a non-governmental setting. Some consideration should also be given to allowing the Food and Drug Directorate to hire directly in emergency situations with the concurrence of the Civil Service Commission.

The motion carried on the following division: YEAS: 7; NAYS: 1; ABSTENTIONS: 4.

The recommendation was adopted as amended on the following division: YEAS: 7; NAYS: 1; ABSTENTIONS: 4.

The study of the draft report continuing, at 5.15 p.m. the Committee adjourned to 10.00 a.m. Thursday, December 17.

THURSDAY, December 17, 1964
(26)

The Special Committee on Food and Drugs met *in camera* today at 10.20 a.m. The Chairman, Mr. Harry C. Harley, presided.

Members present: Messrs. Enns, Francis, Harley, Howe (*Hamilton South*), Mackasey, Marcoux, Rynard, Willoughby (8).

The Committee resumed consideration of a Draft Report to the House recommended by the Steering Subcommittee on Agenda and Procedure, and further amended it.

On motion of Mr. Howe, seconded by Mr. Marcoux,

Resolved, (unanimously),—That the Draft Report be adopted as amended.

The Committee instructed the Chairman to present the said Report to the House as the Committee's Fifth Report.

At 11.15 a.m. the Committee adjourned.

Gabrielle Savard,
Clerk of the Committee.