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# **The Case for Investing In Canada**

*Accessing Excellence  
in Canadian Pharmaceutical  
Research and Development*



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The Pharmaceutical Working Group is composed of members representing:

The Canadian Drug Manufacturers Association (CDMA);  
The Industrial Biotechnology Association of Canada (IBAC);  
The Medical Research Council of Canada (MRC); and  
The Pharmaceutical Manufacturers Association of Canada (PMAC).

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# EXECUTIVE SUMMARY

**Canada** offers many advantages to companies seeking to pursue pharmaceutical research and development. The most important factors to be considered include:

- Canada's clinical, biomedical and biological research expertise, coupled with its internationally recognized expertise in the fields of molecular biology, immunology, cancer, neuroscience, diabetes and cardiology;
- Canada's excellence in the field of medicine and the delivery of quality health care;
- Beneficial federal and provincial tax incentives that include immediate write-offs for current and capital R&D expenditures, and federal investment tax credits of **20 per cent**;
- A nation-wide R&D infrastructure that promotes medical research and clinical trials including 16 universities with faculties of medicine affiliated with over 100 teaching hospitals and research institutions
- Funding, cost-sharing and partnering opportunities that exist with university, hospital, industry and government laboratories;
- Medical Research Council of Canada support for medical research totalling over \$240 million in 1994;
- Five Networks of Centres of Excellence concentrated on leading-edge research in the biomedical sector;
- Regulations that ensure safe products and clear approvals; and laws that strongly protect intellectual property rights but do not promote litigation for medical malpractice;

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- ❑ Labour costs that compare favourably to other countries;
  - ❑ A location that offers less-expensive set-up costs and access to a huge market, given Canada's membership in the North American Free Trade Agreement (NAFTA); and
  - ❑ A significant pharmaceutical industry made up of **more than 100** companies.

Other factors to consider when contemplating research and development in Canada include:

- ❑ Over **22 000** people were employed in the research industry in 1994. In the same year, **22 054** drug products were approved for sale, and drug sales totalled **\$5.94 billion**. Also, over **\$2 billion** was invested in the brand-name sector, and the generic sector grew by **47 per cent**.
- ❑ There has been a **600 per cent** increase in the amount of research funds given to faculties of medicine by private industry over the last seven years, and the pharmaceutical industry has become the largest funder of medical research in Canada, at **35 per cent**.

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# THE CANADIAN HEALTHCARE ENVIRONMENT

## II. 1 THE HEALTH CARE SYSTEM

The Canadian healthcare system provides universal access to quality health care. Within Canada, responsibility for primary health care rests with the provinces. They have authority over the availability and distribution of pharmaceuticals through provincial pharmacy legislation. The federal government transfers money to each province to pay a portion of health-care costs, thus ensuring that a national healthcare standard is maintained throughout Canada.

The federal government exercises its jurisdiction over health matters under the *National Health and Welfare Act* of 1944. Under the Act, the Minister of National Health and Welfare (now called Health Canada) has responsibility for, and authority over, matters relating to the promotion and preservation of the health, security and social welfare of Canadians.

Although government programs cover basic physician and hospital expenses, and provide financial assistance for the disabled, most Canadians also seek additional health coverage provided by private life and health insurance companies.

### **National Health Expenditures**

In 1993, Canada spent 10.1 per cent of its gross domestic product (GDP) on health (\$72 billion or \$2 507 per person). Government spending accounted for 72 per cent of all health expenditures. Private spending for uninsured or privately insured health services accounted for the balance.

According to a 1994 Health Canada Report entitled *National Health Expenditures 1975-1993*, 47 per cent of expenditures went to hospitals and other institutional care facilities (e.g. homes for the aged). Services by doctors comprised 15.1 per cent of the total, and other health professionals accounted for another 6 per cent. Prescription drugs amounted to 5.5 per cent, while over-the-counter drugs made up 4.8 per cent of total health-care spending. The remainder went toward distribution and operating expenses.

Like many other developed countries, Canada is now studying the cost-effectiveness of the present health-care system.

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## **Drug Regulations**

Pharmaceutical products are regulated in accordance with Canada's *Food and Drugs Act*, which is administered by the Health Protection Branch (HPB) of Health Canada.

The Drugs Program of the HPB is carried out by the Drugs Directorate. Essentially, this Directorate is responsible for protecting and improving public health by managing the risks and benefits associated with the use of drugs and cosmetics. The Directorate also develops and disseminates information that encourages the cost-effective use of drugs.

## **II. 2 RESEARCH AND DEVELOPMENT INFRASTRUCTURE**

The Canadian government recognizes the importance of successful research and development (R&D) for international competitiveness by funding organizations that play a vital role in pharmaceutical R&D. These include:

- The Medical Research Council of Canada;**
- The National Research Council of Canada; and**
- The Networks of Centres of Excellence.**

These government organizations are committed to the development of a strong pharmaceutical industry through the development of partnerships, networks and alliances. They form an interconnecting research "portfolio" that offers an established capability to conduct any and all stages of R&D: basic research; applied research; pre-clinical testing; phases I to IV clinical trials; post-marketing studies (PMS); and studies in pharmacoeconomics.

### **Medical Research Council of Canada**

The Medical Research Council (MRC) is the federal funding agency for a network of biomedical and clinical scientists in Canada. The agency promotes and supports basic, applied and clinical research in the health sciences. Further, the MRC provides research training and development to Canadian health-care researchers. Training is carried out in universities, healthcare institutes (mainly teaching hospitals) and research institutes.

In a single year, up to 10 000 highly skilled people, including scientists, technicians, nurses and support staff at universities, research institutes and teaching hospitals across Canada, are being supported by the MRC.

In 1994-95, the MRC's budget from the federal government was \$248 million. Of this, \$240 million was used to support research and research training, while the remainder (3.1%) supported the MRC's operations. Included in the 1994-95 budget was approximately \$5.3 million for funding five National Networks of Centres of Excellence.

### Areas of Medical Research Council Support

- bacteriology
- biochemistry
- blood
- cancer
- cardiovascular
- cell biology
- dental sciences
- drug research
- endocrinology
- gastrointestinal and liver
- genetics
- health services research
- hearing and vision
- imaging and nuclear medicine
- immunology and transplantation
- metabolism, including diabetes
- molecular biology
- musculo-skeletal
- nephrology
- neurosciences
- nursing
- nutrition
- population health
- psycho-social behavior
- reproduction (incl. pregnancy)
- virology

All MRC decisions on grant applications are made after careful assessment by a review panel comprising experts in the applicant's field. This panel is enhanced by experts drawn from the international research community. The process involves 38 different peer review committees composed of over 400 scientists spanning a wide range of specialties. This peer review process is fundamental in ensuring that R&D excellence is encouraged and supported.

Support for research is provided through two fundamental approaches: grants in support of specific research projects, and awards in support of people.

### Operating Grants by Area of Research 1993-94

Classification	Number of Grants	Funding \$ millions
Neuroscience	316	25
Cardiovascular	172	17
Biochemistry	131	14
Genetics	98	10
Molecular Biology	130	10
Other Disciplines (21)	1 151	89
<b>TOTAL</b>	<b>1 998</b>	<b>165</b>

*Average Grant: \$70 000/year for three years*

*Source: The Medical Research Council*

**Medical Research Council Awards  
for Salary Support  
1993-94**

	Number of Awards	Amount (\$ millions)
Scientists	407	22.7
Research Training*	1,598	24.8
<b>TOTAL</b>	<b>2,005</b>	<b>47.5</b>

*\*Includes Fellowships (Post-doctoral) and Studentships (M.A., Ph.D)*

*Source: The Medical Research Council*

**Partnerships**

The MRC has developed many partnerships with industry and private, governments and non-profit organizations. These partnerships provide a means for the partners to invest in research and training programs through the peer review process. Therefore, the MRC can be a valuable partner for foreign companies seeking to establish or increase their R&D activities in Canada by adding value through incremental funding and other forms of synergy such as:

- assuming the role of an objective third party to identify appropriate research teams;
- acting as an intermediary between the research community and industry;
- assessing and evaluating technologies and their development through its peer review process; and
- providing financial leverage to augment industrial investment.

As an example, the Health Program is jointly administered by the Pharmaceutical Manufacturers Association of Canada (PMAC) and the MRC. This Program, established in 1993, is a five-year, **\$200 million initiative** to promote biomedical research. It is designed to foster collaboration between researchers working in universities, affiliated hospitals, research institutes and the pharmaceutical sector. The Program provides support for a wide range of collaborative activities, including research and development grants; chairs in specialized disciplines at universities; clinical networks; and studentships, fellowships and scholarships in research and training.

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## **The National Research Council**

Within the federal government, the National Research Council (NRC) is active as a research partner with industry in biomedical research in life sciences, including biotechnology. Collaborative research is concentrated in the following five institutes, which are dedicated to specific sectors of the life sciences/biotechnology.

### *Biotechnology Research Institute, Montreal, Quebec*

The Biotechnology Research Institute (BRI) is strategically located in a cluster of pharmaceutical companies with head offices in the Montréal area. The mission of the BRI is to promote, assist and perform R&D in biochemical and molecular engineering. The BRI focuses on biochemical engineering, genetic engineering, protein engineering, pilot plant operations and pharmaceuticals.

The BRI plays a special role as a supplier of leading-edge biotechnologies for large pharmaceutical, and accomplished small and medium-sized biotechnology-based firms. The BRI works with industry and universities to create bilateral and multilateral collaborations, and provides licensing opportunities for technology transfer. Its multidisciplinary teams of scientists and engineers assist industry through collaborative research programs.

The BRI has created critical expertise in generic R&D programs in the environmental and biopharmaceutical sectors. It also has expertise in the identification and characterization of molecular targets for drug development. The Bioprocess Sector of the BRI represents one of only a few institutes in the world with the expertise, technology and instrumentation to carry out bioprocess innovation and technical development, from process inception to industrial-level production, using micro-organisms, animal cells and enzymes as biocatalysts.

### *The Montreal Joint Centre for Structural Biology, Montreal, Quebec*

In 1994, the BRI joined forces with researchers at the Université de Montréal and McGill University to create a structural biology research centre. The Centre's interests range from basic aspects of protein structure and structure prediction to the investigation of specific biological questions and the development of drug products. The Centre places special emphasis on creating ties with industry, either as users of the facilities, collaborators or full members of the Centre.

### *Institute for Biological Sciences, Ottawa, Ontario*

Working in partnership with industry, the Institute's focus is on immunochemistry, with applications in the development of immunotherapeutics and cell biology, vaccines and diagnostics, which are in turn focused on finding therapies for neurodegenerative disorders.

### *Stacie Institute for Molecular Sciences, Ottawa, Ontario*

The Steacie Institute has significant expertise in the areas of theoretical chemistry, molecular selectivity, and molecular structures and dynamics.

### *Institute for Biodiagnostics, Winnipeg, Manitoba*

This recently formed Institute employs magnetic resonance imaging and spectroscopy, infrared spectroscopy and computational analysis of biomedical data, as its core technologies for disease diagnoses.

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### Networks of Centres of Excellence

The Networks of Centres of Excellence (NCE) provide industry with the opportunity to access Canada's leading basic, applied and clinical researchers in an efficient and cost-effective manner.

Established by the federal government, the NCE program aims to increase research excellence and improve Canadian industrial competitiveness. The networks link world-class researchers and industry throughout Canada on key projects organized around a common area of interest. Participation in a network leverages the effectiveness of all members. For example, university participants can pool their expertise and resources for major investigations on a scale that could not be attempted by traditional approaches. Business participants gain up-to-the-minute awareness of discoveries and avenues of exploration that could affect their operations in a future global market. Not only are the NCEs a source of advanced technologies, they also provide a substantial contribution toward the training of Canada's next generation of scientists and engineers.

Currently, five NCEs are specifically aimed at conducting R&D in the biomedical sector, and one that aims to improve the efficiency of health informatics.

#### Networks of Centres of Excellence Budget and Number of Scientists

Network	Budget (\$M) 1994-98	Number of Trainees	Number of Scientists
Canadian Bacterial Diseases Network	7.4	51	131
Canadian Genetic Diseases Network	15.7	52	128
Neuroscience Network	22.3	104	81
Protein Engineering Network	8.7	54	76
Respiratory Health Network (Inspiraplex)	10.3	85	47
HEALnet*	8.6	60	N/A
<b>TOTAL</b>	<b>\$73.0</b>	<b>406</b>	<b>463</b>

\* HEALnet is not involved in biomedical research

Source: The Medical Research Council

The networks use state-of-the-art equipment. For example, the Canadian Bacterial Diseases Network and the Canadian Genetic Diseases Network have signed a joint three-year collaborative research agreement with SCIEX, one of Canada's developers of advanced instrumentation for bioanalysis, and the University of Alberta. This agreement is designed to facilitate the development of technologies that permit rapid characterization of the genes involved in bacterial and genetic diseases. It is expected to lead to advances in technology and the development of a faster (50-fold) and more efficient determination of DNA sequences.

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NCE research projects are subjected to rigorous scientific selection and evaluation. Not only do the projects have to meet strict scientific criteria, they also have to contribute to Canada's economic well-being and enhance the quality of life. Some of the projects being undertaken by NCEs in the biomedical sector are listed below.

*The Canadian Bacterial Diseases Network*

The Canadian Bacterial Diseases Network (CBDN) links top researchers in universities and government laboratories in the investigation of key aspects of bacterial attack and host response in humans and animals. The Network's program responds to the pressing demand for new vaccines, antibiotics and novel approaches to diagnostics. Through the CBDN, the biotechnology and pharmaceutical industries gain access to a unique source of expertise and intellectual property in current research. A notable recent advance by the CBDN includes the discovery of a new biochemical approach that may block the onset of chronic infections that kill most cystic fibrosis patients.

*The Canadian Genetic Diseases Network*

The Canadian Genetic Diseases Network (CGDN) brings together world-class researchers and industrial partners to focus on devastating and common genetically transmitted diseases. Network projects involve the investigation of genetic predisposition to diseases such as cancer and heart disease, and the identification of specific genetic abnormalities that can cause diseases such as cystic fibrosis, muscular dystrophy and Huntington's disease. Researchers within the CGDN have confirmed that a specific genetic error is associated with almost all cases of Huntington's disease.

*The NeuroScience Network*

This Network provides a unique spectrum of research capability to explore and test new strategies for neuronal repair in Canada. Canada has a long-standing reputation for world-class neuroscience research, and this Network has created a unique R&D resource by linking 125 research participants from 18 universities and research institutes across Canada. This linkage provides access to the leading neuroscience being developed in Canada and to the opportunities for developing products for a wide range of brain and central nervous system disorders.

*The Protein Engineering Network of Centres of Excellence*

The Protein Engineering Network of Centres of Excellence (PENCE) dedicates itself to cooperation and collaboration with industrial clients, particularly in the pharmaceutical and biotechnology sectors. It links 51 scientists from 18 institutes, companies and universities involved in protein engineering. For all companies, PENCE is a fertile source of new ideas and technologies. Current R&D is focussed on the medical applications of protein engineering. As a consortium of the leading applied protein engineers in Canada, it is able to provide assistance to industrial processing, and to many areas of drug discovery and early development.

*The Respiratory Health Network (Inspiraplex)*

This Network concentrates on respiratory health, as well as the development of innovative solutions and technologies for the treatment and prevention of breathing problems that are caused by diseases and environmental factors. Ongoing projects include a collaboration with industry to create drugs to overcome airway blockage in people with cystic fibrosis and asthma, and kits to test lung and diaphragm functioning.

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A further significant building block in the development of Canada's pharmaceutical industry is the outstanding nature of biomedical research that occurs in other Canadian institutions, namely:

#### **Universities and Teaching Hospitals**

For its size, Canada has a university medical research base that is second to none in the world. There are 16 medical faculties in Canadian universities, and these are affiliated with a network of over 100 teaching hospitals and research institutes.

When one looks at Canada's research performance as measured by the publication record of Canadian scientists and the impact of their work on other scientists worldwide, a remarkable picture emerges. Canada, with a population less than half of the next smallest G-7 country, has the highest research productivity, efficiency and effectiveness and ranks second only to the United States in total impact per capita. As a result, the efficiency and effectiveness of Canada's research, especially in the biosciences, is greater than its nearest competitor - the United Kingdom - by 35 per cent and 30 per cent, respectively. The majority of Canada's pharmaceutical-medical science publications arise from university research supported by extramural programs of the government through its granting councils.

#### **Contract Research Organizations (CROs)**

Canada has private-sector organizations that offer integrated packages of all the major services required by pharmaceutical and biotechnology companies to take a new drug through the developmental and regulatory process. Depending on their clients' requirements, these CROs can design and conduct some or all aspects of the development process. They offer services that include the whole development spectrum, from toxico-kinetic and metabolism studies through Phase I (human safety, pharmaco-kinetic and pharmaco-dynamic studies), to Phase II through Phase IV clinical studies. Bioanalytical support of each of these activities and the preparation of drug registration submissions to regulatory agencies in both the U.S. (Federal Drug Administration) and Canada (Health Protection Branch) can also be provided. As well, a large network of institutions can be accessed, where clinical trials can be conducted.

#### **Clinical Trials**

Canada has an enviable capacity to perform globally competitive, cost-effective clinical trials, especially since full-scale medical examinations are covered by Canada's health-care system, and this significantly reduces the costs of such research. In this way, Canada is rapidly demonstrating a world leadership in the development and application of pharmaco-economics. As well, innovative clinical trial networks provide industry with a direct entry into the drug delivery system for new pharmaceutical products.

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### II.3 THE CANADIAN PHARMACEUTICAL INDUSTRY

The Canadian pharmaceutical industry is characterized by an array of company sizes and types. The industry is composed of three main segments:

- ❑ **Brand-name** pharmaceutical manufacturers represented by the Pharmaceutical Manufacturers Association of Canada (PMAC);
- ❑ **Generic** drug manufacturers represented by the Canadian Drug Manufacturers Association (CDMA); and
- ❑ **Biopharmaceutical** companies represented by the Industrial Biotechnology Association of Canada (IBAC).

The commercial enterprises interact with a significant number of biomedical research institutions and networks located throughout Canada. The majority of the leading pharmaceutical firms engage in R&D in Canada, and most hold patents for their inventions.

In 1994, the pharmaceutical industry employed over **22 000 people**, of whom 19 300 were employed by manufacturing companies. Over 25 per cent of the employees in the pharmaceutical industry are university graduates.

In 1994, sales of pharmaceutical drug products in Canada totalled **\$5.94 billion**, an increase of 10 per cent over 1993. This figure includes shipments of \$4.45 billion, plus imports of \$2.06 billion, minus exports of \$0.57 billion. Over the past few years, imports and exports have remained at around 35 per cent and 11 per cent of total sales, respectively.

Forty per cent (\$2.39 billion) of the total sales were for patented drugs (including \$100 million for veterinary products) and sixty per cent (\$3.55 billion) were non-patented drugs (including generic products and brand-name products that are no longer, or never have been, subject to patent protection). Of the 22 054 drug products approved for sale, only 6 per cent are patented.

Between 1988 and 1993, the Canadian pharmaceutical retail market expanded from \$7.3 billion to \$11.8 billion. Of this figure, \$6.3 billion is for prescription medicines. Brand-name products account for approximately 90 per cent of this amount.

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Seniors are one of the fastest growing demographic groups in Canada. In 1971, people aged 65 and over made up 8.2 per cent of the population. Twenty years later, the figure was 11.6 per cent, and by the year 2031, this group will make up an estimated 22 per cent of Canada's population. This has tremendous implications for health-care costs, since seniors today consume some 25 per cent of all prescription medications.

### **Brand-name Sector**

This sector is dominated by multinationals, most of which have headquarters in the United States and Europe. In 1994, the 60-plus companies represented by PMAC accounted for 78 per cent of prescription drug sales, 70 per cent of unit volumes, and approximately 80 per cent of the industry's assets. The cumulative investment in R&D by Canada's brand-name pharmaceutical industry between 1988 and 1994 is over \$2 billion. PMAC members spent 13.8 per cent of total sales on R&D. The industry projects another \$3 billion in R&D spending by the end of the decade.

### **Generic Sector**

The generic sector, whose sales grew by 47 per cent in 1994, held 10 per cent of the wholesale market and 21 per cent of unit volumes. This sector is dominated by two large Canadian-controlled companies, *Apotex* and *Novopharm*, both located in Ontario, which together account for 75 per cent of generic drug sales in Canada. These two firms are now among the top 50 R&D spenders in Canada across all sectors. Both of these companies own stand-alone biopharmaceutical ventures and have joint ventures with companies in the U.S. and Europe.

### **Biopharmaceutical Sector**

Canada has over 100 companies active in health-care biotechnology. Many of these biopharmaceutical enterprises are still at the early growth stages, although about 20 have made the transition from R&D into various stages of the commercialization process. Biopharmaceutical companies in Canada are active in a wide range of product development, including vaccines, new drugs, gene therapy and diagnostics.

## II.4 MEDICAL RESEARCH ACTIVITY

Universities and the pharmaceutical industry are the two key performers of basic and applied research.

### Universities

In 1994, the 16 medical faculties in Canadian universities invested almost \$853 million in biomedical research. This represented 56 per cent of their total research investment of \$1.5 billion.

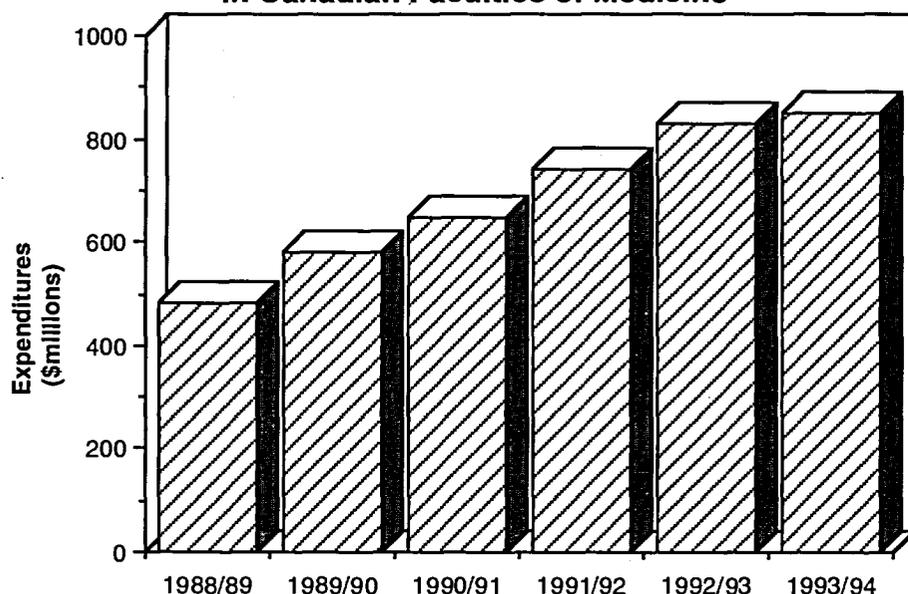
<b>Research Funding in the 16 Canadian Universities with Medical Schools 1993-94</b>			
<b>University</b>	<b>Total Research Expenditures, All Disciplines (\$ millions)</b>	<b>Amount in Health/Health Sciences (\$ millions)</b>	<b>Percentage in Health Sciences Research (%)</b>
Alberta	93.8	52.1	55.5
British Columbia	116.0	46.6	40.2
Calgary	60.5	35.7	59.0
Dalhousie	27.1	13.2	48.7
Laval	131.9	62.0	47.0
Manitoba	68.4	39.1	57.1
McGill	182.8	104.1	56.9
McMaster	76.2	46.1	60.5
Memorial	26.8	5.1	19.0
Montréal	222.1	144.3	65.0
Ottawa	57.0	25.0	44.0
Queen's	69.3	21.6	31.2
Saskatchewan	48.3	16.4	33.3
Sherbrooke	31.2	11.8	37.7
Toronto	249.3	176.3	70.7
Western Ontario	51.2	28.6	55.9
<b>Total</b>	<b>1,511.9</b>	<b>828.0</b>	<b>54.8</b>

*Source: The Association of Canadian Medical Colleges, 1995*

According to The Association of Canadian Medical Colleges in its 1995 Canadian Medical Education Statistics publication, the top six universities, ordered by their biomedical research expenditures during 1993-94, are as follows:

- University of Toronto \$177.3 million
- Université de Montréal \$132.9 million
- McGill University \$102.5 million
- University of British Columbia \$ 58.8 million
- Université Laval \$ 56.4 million
- University of Alberta \$ 48.6 million

### Expenditures for Biomedical Research in Canadian Faculties of Medicine



Source: *The Association of Canadian Medical Colleges, 1995*

The Association also reported a 600-per cent increase in the amount of research funds provided to faculties of medicine by private industry in the last seven years.

The MRC was the largest single source of funding for biomedical and health-care research of Canadian faculties of medicine in 1993-94. It provided \$211.1 million (24.8%) of total funding, which was mainly directed toward investigator-initiated research.

The pharmaceutical sector is also a key supporter of R&D at Canadian universities, hospitals and medical research facilities. Between 1988-94, expenditures in these areas amounted to \$770 million.

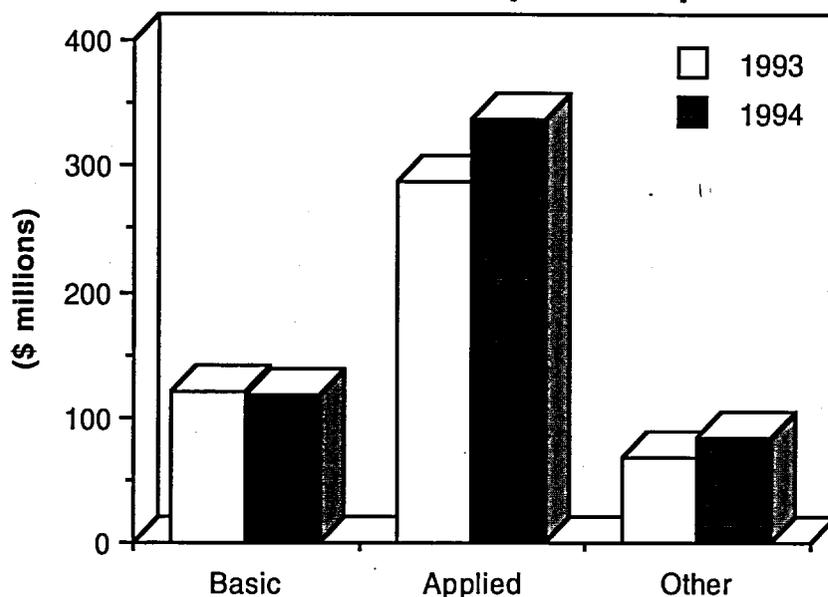
#### **Brand-name Drug Companies**

While the Canadian brand-name pharmaceutical industry is relatively small, representing less than 2 per cent of all shipments, employment, investments and value-added in the manufacturing sector, it accounted for 10 per cent of the manufacturing sector's R&D in 1994.

In the past seven years, the pharmaceutical industry has dramatically increased its R&D spending. By 1994, the pharmaceutical industry had become the largest funder of medical research in Canada, contributing 35 per cent of total health-care R&D gross expenditures, followed by the federal government with 21 per cent.

Excluding capital and depreciation expenditures, the application by type of research as a percentage of expenditures in 1993 and 1994 is shown in the following chart:

## Current Research and Development Expenditures



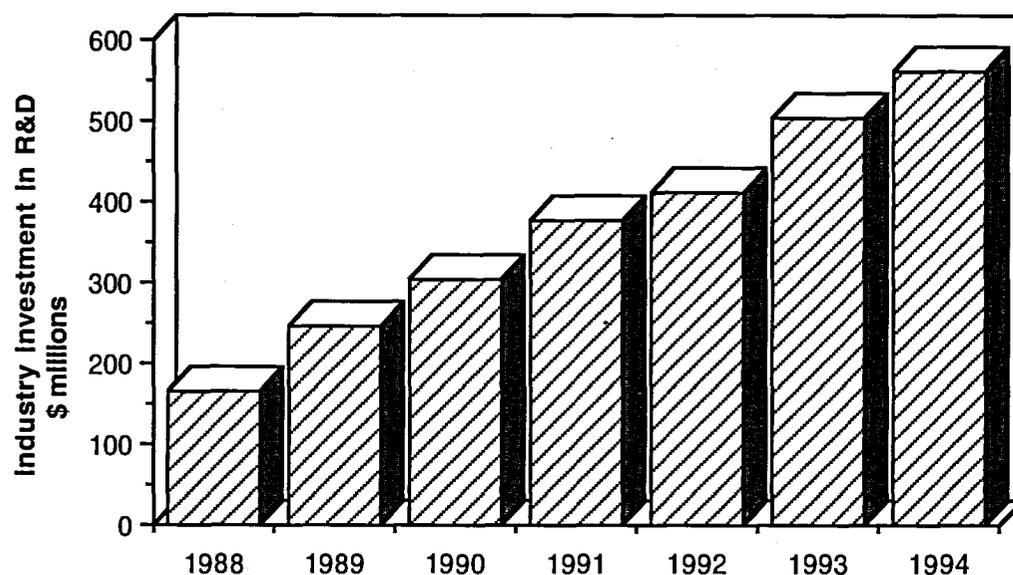
*Source: Patented Medicine Prices Review Board Annual Report, 1994*

Applied research in the Canadian pharmaceutical industry comprises clinical and preclinical trials. This emphasis on applied research is not surprising, since the Canadian healthcare system provides a strong infrastructure to undertake clinical trials.

Canada recently amended its patent legislation, which covers intellectual property protection, to equal that in other industrialized countries. In return, the brand-name pharmaceutical companies made a commitment to more than double the percentage of sales that they invested in R&D, from less than five per cent in 1986 to 10 per cent in 1996. This level was attained four years ahead of schedule, and continues to rise. Annual R&D investment in Canada by pharmaceutical companies exceeded \$500 million in 1994 - a threefold increase in just six years.

The principal reason for this development is that Canada provides an excellent environment for R&D.

## Brand-name Pharmaceutical Industry Investment in Research and Development



Source: *Patented Medicine Prices Review Board Annual Report, 1994*

Announcements of new capital investments by major pharmaceutical companies operating in Canada include the following:

- Astra Pharma Inc.** has invested \$150 million (1993-97) in a new Montreal research centre specializing in pain control drugs.
- Ciba-Geigy Canada** will triple its production for the North American, European and Australian markets by 1998.
- Eli Lilly Canada Inc.** broke ground in April 1995 on a \$25-million research and development centre at its headquarters in Scarborough, Ontario. The new facility will house the company's expanded Medical Division, along with the Lilly Analytical Research Laboratory. Space is also being provided for a new Bioanalytical Research Laboratory to conduct blood plasma analysis on new compounds in clinical trials. This lab will feature four state-of-the-art mass spectrometers developed and manufactured in Canada.
- Glaxo Canada Inc.** spent \$150 million (1993-97) in new administration and manufacturing facilities in Ontario.
- Merck Frosst Canada Inc.** poured \$50 million (1993) into the modernization of its Quebec manufacturing facility to produce selected drugs for domestic and export markets.

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- ❑ **Wyeth-Ayerst Canada Inc.** provided an \$80 million (1993) investment in capital expansion of its fine chemical plant in Brandon, Manitoba.

Since 1988, the private sector has increased its R&D expenditures in the area of university and institutional research in Canada. This has effectively leveraged the sector's R&D investment and has given it access to a variety of networks, which keeps the sector at the forefront of technology. Some examples follow.

- ❑ **Amgen Canada Inc.** has invested \$100 million to establish the Amgen Research Institute in Toronto. The Institute is affiliated with the Ontario Cancer Institute/Princess Margaret Hospital, Canada's largest cancer treatment and research centre.
- ❑ **Bayer Inc.** is investing \$1.35 million to support basic research in the progression and treatment of heart failure under the MRC/PMAC Health Program. The research will be carried out at The Toronto Hospital. The MRC will be donating an additional \$600 000 in funding support.
- ❑ **Bristol-Myers Squibb Pharmaceutical Group** gave \$10.3 million in January 1995 to the Samuel Lunenfeld Research Institute at Toronto's Mount Sinai Hospital. The funds will support the research by the Institute's molecular and development biologists, and will be used to establish the Centre for Human Genome Research and Molecular Medicine at the Institute. This initiative alone will create more than 150 research positions.
- ❑ **Ciba-Geigy Canada Ltd.** has given \$547 600 to the Mount Sinai Hospital, Toronto, toward research into osteoporosis.
- ❑ **Glaxo Wellcome Inc.** invested \$2.9 million in support of a study into the treatment of a form of lung cancer and establishment of a tumour bank. The company also pledged \$2.6 million over the next three years in support of the Glaxo Heritage Research Institute at the University of Alberta. This brings Glaxo's total investment in this new facility to \$7.6 million. The Institute is conducting medical research into better treatments for AIDS and Hepatitis B.
- ❑ **Merck-Frosst Canada Inc.** has donated \$200 000 to establish a Research Chair in Pharmaco-epidemiology at the University of Saskatchewan.
- ❑ **Sandoz Canada Inc.** has entered into a five-year, \$4-million agreement with The Toronto Hospital. The funding will support organ transplantation research and patient management, and will establish a research chair in transplantation.
- ❑ **Schering Canada Inc.** has donated \$559 000 toward clinical trials in HIV patients at various hospitals and universities across Canada.

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### Generic Drug Companies

Canada's generic pharmaceutical industry, consisting mainly of Canadian-controlled companies, is evolving into one of the most dynamic and fastest growing export-oriented industries in the country. Generic companies in Canada use competitive manufacturing technology to produce a broad range of lower-cost drug products.

Originally, these companies mainly focussed on manufacturing equivalents of pharmaceutical products, when these products had expired patents or were subject to compulsory licensing.

In 1993, Canada's patent legislation eliminated compulsory licensing to bring Canadian patent law into line with other G-7 countries. These companies then had to refocus their main activities. Despite this change, the Canadian generic industry has continued to expand. In 1994, according to **IMS Canada**, generic pharmaceutical sales reached \$720 million, which represents a 38-per cent increase over the previous year.

These results have been achieved partly as a result of cost-containment policies in health-care management programs, and partly through a commitment by the generic companies to focus on increased research and development, and export markets. The objectives of Canadian generic drug manufacturers are to become fully integrated pharmaceutical companies, including R&D in both generic and innovative products. The emphasis is on manufacturing and exporting for final dosage forms and fine chemicals. The success of these initiatives is reflected in the fact that, in the last year, generic drug firms have expanded their facilities and their areas of endeavour. There are recent examples.

- ❑ **Apotex** has expanded its facilities in Ontario and Manitoba. The company ranks 25th in terms of R&D spending for all companies in Canada and has seven new products under development in its Innovative Drug Development Program.
- ❑ **Genpharm** has expanded its staff by 50 per cent to conduct more R&D.
- ❑ **Novopharm** is undertaking a \$12.5-million expansion of its Ontario facilities.
- ❑ **Pharma-science** expanded its facilities in 1994 for increased R&D and production.

In 1995, the **CDMA** established the first Canadian Chair in Pharmacokinetics through a \$500 000 grant to the **Université de Montréal**. The creation of the Chair will allow the establishment of predictive models in pharmacokinetics, as a cornerstone of research into the bioequivalence of generic drugs. Another chair, endowed with the same amount, has also been established to study the effect of medicines on pregnancy.

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A \$4-million joint program involving **Apotex** and the **MRC** will be used to support scientists conducting basic research aimed at the discovery of new therapeutic agents.

The vast majority of R&D conducted by member companies of the CDMA is carried out in Canada. This includes synthetic chemistry, analytical chemistry, pharmaceutical formulation development, clinical testing, and both bioavailability and clinical efficiency, where relevant. The member companies have targeted more than \$750 million for R&D expenditures over the next 10 years.

The generic companies have a great deal of collective expertise in manufacturing, formulation, packaging and marketing of drug products and fine chemical manufacturing. It is these skills that are available for ventures into new technologies. The CDMA member companies have already entered into a number of strategic alliances with multinational companies, and this has given them significant global reach.

The generic industry in Canada is a success story, and, collectively, this sector has a great deal to offer foreign pharmaceutical companies: technology transfer arrangements; product licensing and distribution arrangements to secure product registrations; and joint venturing opportunities.

### **Biopharmaceutical Companies**

The biotechnology industry is of major and strategic importance to Canada. For this reason, the Government of Canada implemented its National Biotechnology Strategy in 1983 to support and encourage the growth of an internationally competitive industry. The industry, in just over 15 years, has grown from a handful to well over 200 firms.

The Canadian biotechnology industry is concentrated in centres with a strong university and hospital research base. The biotechnology/university relationship is expected to strengthen, as university technology assessment and transfer agents take a more active role in negotiating alliances between their institutions, and pharmaceutical and biotechnology companies.

Biopharmaceutical companies stress R&D. Five Canadian companies rank among the top 20 in terms of ratios of R&D investment to revenues: **Allelix Biopharmaceuticals**, **BioChem Pharma**, **Biomira**, **Hemosol** and **QLT Phototherapeutics**.

Biotechnology firms active in the health-care sector tend to dominate the industry, and now account for over 50 per cent of all firms in biotechnology in Canada. This industry sector dominance, according to Ernst & Young, is not likely to lessen in the near future. The top public biotechnology companies are biopharmaceutical and clinical diagnostics firms:

- ❑ **Allelix Biopharmaceuticals Inc.**, Mississauga, Ontario  
*Product focus:* therapeutics and biopharmaceuticals for the treatment of AIDS, osteoporosis, inflammatory diseases and disorders of the central nervous system.
- ❑ **BioChem Pharma Inc.**, Laval, Quebec  
*Product focus:* portfolio of therapeutics targeting viral diseases, cancer, AIDS, pain control and cardiovascular diseases.

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- ❑ **Biomira Inc., Edmonton, Alberta**  
*Product focus:* therapeutics aimed at stimulating the immune system to respond to synthetic cancer-associated antigens and targeting the corresponding human antigens with respective monoclonal antibodies.
  - ❑ **Cangene Corporation, Mississauga, Ontario**  
*Product focus:* blood-cell growth factors.
  - ❑ **Hemosol Inc., Etobicoke, Ontario**  
*Product focus:* development of a human blood-substitute.
  - ❑ **IBEX Technologies Inc., Montreal, Quebec**  
*Product focus:* heparinase-based hematology diagnostics and therapeutic heparinase for post-surgical heparin neutralization.
  - ❑ **ID Biomedical Corp., Burnaby, B.C.**  
*Product focus:* a nucleic acid probe amplification system - Cycling Probe Technology (CPT).
  - ❑ **IMUTEC Corp., Scarborough, Ontario**  
*Product focus:* biologic response modifier technology and products for the treatment of cancer and other diseases.
  - ❑ **QLT Phototherapeutics Inc., Vancouver, B.C.**  
*Product focus:* pharmaceutical products and applications for photodynamic therapy (PDT), an emerging medical field that uses light-activated drugs in the treatment of cancers and other diseases.
  - ❑ **Spectral Diagnostics Inc., Toronto, Ontario**  
*Product focus:* the development of a highly accurate cardiac panel test for chest pain diagnostics.
  - ❑ **StressGen Biotechnologies Corporation, Victoria, B.C.**  
*Product focus:* technology related to the broad application of stress proteins to vaccines and therapeutics (this corporation is the world's largest supplier of stress response reagents).

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The pharmaceutical industry has clearly recognized the importance of biotechnology companies for providing access to new and innovative health-care products. Some notable alliances have been formed with Canada's biotechnology companies:

- German health-care giant **Fresenius A.G. Oberusel** has partnered with **Hemosol Inc.** to develop, produce and market Hemolink™, the company's red blood-cell substitute. Fresenius is investing \$40 million in the alliance.
  
- **Hoechst-Roussel Canada Inc.** of Montreal and **Hoechst-Roussel Pharmaceuticals Inc.** of Somerville, New Jersey, have signed a five-year research and development alliance with, and investment in, **Allelix Biopharmaceuticals Inc.** The alliance is designed to accelerate the discovery and development of drugs for psychiatric disorders, particularly schizophrenia. The biotechnology-oriented research and drug discovery program will focus on the dopamine and serotonin receptors in the central nervous system. Novel drugs developed through this research should be useful in treating diseases such as schizophrenia and other psychoses. Under the terms of the alliance, Allelix will receive, from Hoechst-Roussel Canada, over the period of the agreement, annual R&D funding and clinical milestone payments estimated to be worth \$53 million.
  
- **Warner Lambert** has invested \$30 million in an alliance with **BioChem Pharma Inc.** involving anti-thrombosis research.

Demand for biotechnology applications is increasing in North America. According to a survey of this industry (*Canadian Biotech '94: Capitalizing on Potential*, Ernst & Young, September 1994), North American sales of human therapeutics and diagnostics are expected to increase from their current level of US\$8 billion to over US\$28 billion by 2004. Throughout North America, as a consequence of greater knowledge and maturing research programs, potential applications have been on the rise and are expected to accelerate.

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The same survey showed that the key factors that are accelerating the growth of the Canadian biotechnology industry include:

- increasing awareness of the sector's importance by investors;
- substantial government commitment to the biotechnology sector;
- continued success of the Network of Centres of Excellence program;
- strategic alliances with pharmaceutical companies; and
- harmonization of drug regulatory policies.

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## **III. THE CASE FOR INVESTING IN CANADA**

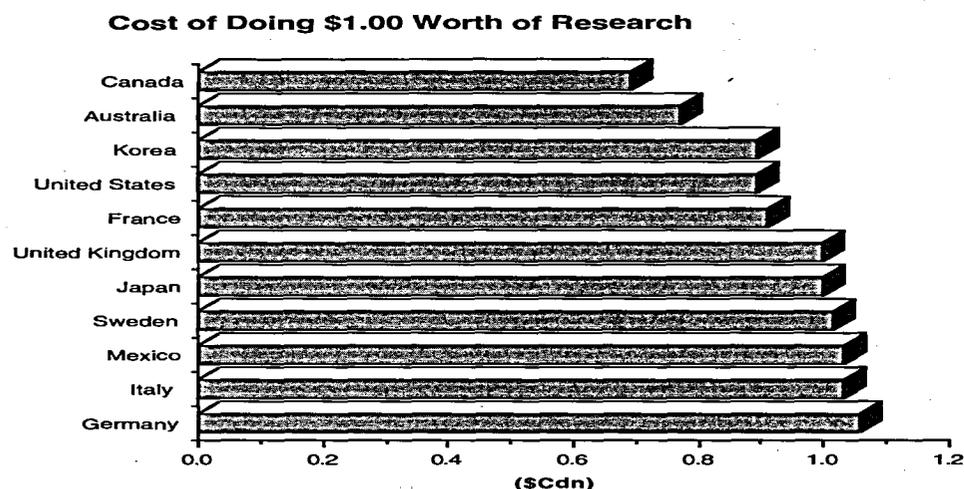
Canada offers many competitive advantages for investment in the pharmaceutical industry, and companies operating in Canada experience a range of economic and business advantages:

- tax incentives;
- the promotion of medical research and clinical trials;
- research funding;
- effective regulations, clear laws and less litigation;
- a quality work force and comparable labour costs;
- an advantageous location; and
- the presence of other multinationals.

### **III. 1 TAX INCENTIVES**

Tax in Canada is collected at both the federal and provincial levels. The federal corporate rate of 21.84 per cent, coupled with an average provincial manufacturing and processing tax of 13 per cent, offers an average combined tax rate of 34 per cent in Canada, which compares favourably to the average corporate taxation rates in the United States and other industrialized countries.

Canada offers the most attractive tax incentive package for manufacturing companies to engage in R&D when compared to the tax systems of such industrial countries as the United States, Japan and Western Europe. This is the result of a strong federal tax incentive package enhanced by the tax treatment of R&D in the provinces that offer it. The federal corporate tax, coupled with the varying provincial manufacturing and processing taxes, result in combined tax rates generally in the range of 18 to 23 per cent for small companies and 31 to 39 per cent for large companies. A 1994 study conducted by The Conference Board of Canada revealed that the Canadian corporate tax system provides greater overall incentive for companies to engage in R&D than do the tax systems of 10 other leading industrialized countries.



Source: *The Conference Board of Canada, June 1994*

The Conference Board of Canada determined that the after-tax cost of one Canadian dollar of research was C\$0.6, compared with C\$0.9 in the United States, C\$1.05 in Japan and C\$1.1 in Germany.

Similarly, in 1995, the International Information and Communications Tax Network of KPMG Management Consulting further confirmed the data obtained by the Conference Board of Canada study, when it reported in its 1995 edition of *Tax Treatment of R&D Expenses* that the after-tax cost of conducting R&D in Canada is lower than almost anywhere else. KPMG's analysis determined that the best place for any company to perform research and development is in Canada, because Canadian tax incentives ranked first among the 23 industrialized nations that they examined.

Canada offers significant incentives to R&D performers:

- Immediate write-offs for current and capital R&D expenditures made in Canada or, at the taxpayer's option, deferral of claiming such expenditures to a future year.
- Federal investment tax credits on current and capital expenditures (excluding buildings) of 20 per cent. The credit is increased to 35 per cent for small Canadian-controlled private companies (CCPCs) - companies with a minimum of 50 per cent Canadian ownership, whose shares are not traded on a stock exchange, and who are not controlled by any combination of non-resident or public corporations.
- For small CCPCs (those with total taxable income less than or equal to \$200 000) the applicable tax credit is 35 per cent on the first \$2 million of qualifying R&D expenditures. The tax credit is fully refundable to the corporation, to the extent that the credits are not used to offset federal taxes payable.

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- These tax credits are available on both incremental and non-incremental R&D expenditures as opposed to the United States, where only incremental R&D expenditures qualify.

In addition to the federal tax incentives, five Canadian provinces offer further incentives for R&D investments.

- **Ontario** offers a superallowance to companies based in, and conducting R&D in, that province. This allowance has two components: a base allowance, which is equal to 25 per cent of the qualifying expenditures for large corporations and 35 per cent for small companies; and an incremental component, which is equal to 37.5 per cent for large firms and 52.5 per cent for small firms.

Effective January 1, 1995, Ontario also provides a 10-per cent refundable innovation tax credit (OITC). This credit is intended to enhance the federal refundable 35 per cent investment tax credit for R&D that is carried out in the province by small and medium-sized businesses.

- **Quebec** offers a fully refundable tax credit of 20 per cent of the wages paid in Quebec for carrying out R&D. For small firms, this credit is increased to 40 per cent.
- **Nova Scotia** offers a 15 per cent refundable tax credit for corporations performing R&D in the province.
- **Manitoba** provides a 15 per cent non-refundable R&D tax credit, which is calculated on the expenditure that is eligible for the federal credit and applies to R&D carried on in the province.
- **New Brunswick** offers a 10 per cent non-refundable tax credit.

It should be noted that these tax incentives are available to any corporations performing R&D in Canada, including Canadian subsidiaries of foreign-based firms. In addition, foreign corporations that contract R&D to a Canadian firm can benefit from the lower costs of performing R&D in Canada. For example, if R&D is contracted to a small Canadian-controlled private corporation that is eligible for a 35-per cent R&D tax credit, the foreign firm could benefit from the reduced cost of performing the R&D in Canada. Joint-venture relationships with Canadian R&D companies can also lead to a substantial increase in R&D performed per dollar spent.

Significant cost savings are available to manufacturers that conduct R&D in Canada. The Canadian subsidiary of a foreign manufacturing company would realize substantial after-tax cost savings by doing identical R&D in Canada rather than in the United States. An October 1995 report prepared for Industry Canada by Deloitte & Touche, entitled *A Comparison of Tax Incentives for Performing Research and Development in Canada and the United States*, concluded that, although Canada and the U.S. have two main tax measures in common that are designed to encourage R&D activities - the R&D expense deduction and the R&D tax credit - their systems differ in three important ways: the timing of claiming the R&D ex-

pense deduction; the size of the R&D tax credits available; and the ability to access the R&D credits.

### **Comparison of Tax Incentives in Canada and the United States**

#### **Canada**

- R&D capital expenditures can be written off immediately
- There is an option to defer a claim
- The total cost of contracted R&D is eligible
- Equipment costs qualify
- Canadian travel costs qualify
- Employee benefits are eligible in certain circumstances

#### **United States**

- Assets are depreciated
- Only immediate write-offs are permitted
- Only 65% of contracted R&D is eligible
- Equipment costs do not qualify
- Travel costs do not qualify
- Only direct salary is eligible

The current Canadian system of R&D tax incentives provides Canadian corporations with a significant cost advantage over U. S. firms, when vying for R&D work to be performed in Canada.

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## III.2 MEDICAL RESEARCH

### Medical Research

For more than 50 years, Canadian medical research has enjoyed an outstanding international reputation. Canada is recognized for the delivery of health care, and for pioneering achievements in diagnostics and treatment in areas such as neuroscience, diabetes and cardiology. With such a strong medical tradition, it is not surprising that health care continues to be at the forefront of Canada's R&D agenda.

Canada's past achievements include:

- the discovery of insulin by Banting, Best and Collip at the University of Toronto;
- discovery of the carcino-embryonic antigen, produced by cancers of the colon, and development of the first immunological blood test for the presence of cancer (Université de Montréal);
- discovery of the defective gene that causes cystic fibrosis by Dr. Lap-Chi Tsui (Hospital for Sick Children, Toronto);
- discovery of the T-cell receptor gene (Dr. Tak Mak, University of Toronto);
- discovery of an anti-viral therapy for hepatitis B (Dr. D. L. Tyrell, University of Alberta);
- development of a new method for detecting prostate cancer at an early stage, thereby improving survival rates for patients through the use of combined anti-hormonal treatments (Dr. F. Labrie, Université de Laval); and
- identification of the genetic defect responsible for myotonic dystrophy (University of Ottawa research team).

More recent developments, during the 1990s, in pharmaceutical and health-care research are highlighted by achievements in fields such as biomedicine, immunology, gene therapy, and cancer diagnosis and treatment, to name but a few.

The additional examples that follow indicate that Canadian researchers are at the forefront of world research and have made major contributions to our understanding of biological and medical processes, and to the generation of new technologies and new industries.

### Molecular Biology

The work of Dr. Michael Smith, Biotechnology Laboratory, University of British Columbia, in site-directed mutagenesis, has helped to accelerate discoveries made through genetic engineering. He received the 1993 Nobel Prize for Chemistry for this pioneering research.

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### **Alzheimer's Research**

Dr. Judes Poirer of McGill University has developed a blood test to determine a person's chances of developing Alzheimer's disease. The test, available in Canada since May 1994, identifies people carrying the apolipoprotein E4 gene, which is linked to Alzheimer's disease.

### **Molecular Genetics**

Dr. Phillippe Gros, director of a biochemistry laboratory at McGill University, has been instrumental in two breakthrough discoveries in the area of molecular genetics. The most recent is the cloning of a gene, dubbed *Nramp*, in which mutations cause susceptibility to several infectious diseases such as tuberculosis and leprosy. The second is the cloning of the multidrug resistance *mdr* gene family, which controls resistance in the cells to anticancer drugs commonly used in chemotherapy.

### **Brain-cell Research**

Dr. Samuel Weiss, a University of Calgary medical researcher, has received more than \$3 million in funding for his project on brain-cell regeneration. His breakthrough research includes the discovery of stem cells in the mouse brain that produce new neurons like those found in the brains of adult mammals. This discovery, being the first demonstration of neural regeneration in the brain, has opened up the possibility for the repair of human brain cells damaged by strokes or head injuries.

### **Discovery of Diabetes Genes**

A University of Calgary research team, led by Dr. Leigh Field of the Canadian Genetic Diseases Network, has discovered two new genes that play an important role in the development of juvenile diabetes. This ongoing research could lead to the development of diagnostic techniques to help identify individuals at high risk of developing this disease. Ultimately, this research could be the key to the prevention of the onset of the disease, which affects one in 300 children by the age of 20.

### **Male Sterility Research**

Researchers at the Maisonneuve-Rosemont Hospital of the Université de Montréal have found a cause of male infertility that paves the way for a possible treatment for thousands of sterile men. Led by biochemist Gilles Bleau, the MRC-funded human reproduction research team has determined that, if sperm lacks a protein known as P34H, it cannot bind to the egg, which is a prerequisite for fertilization.

### **Identification of Spinal Muscular Atrophy Genes**

A research team at the Children's Hospital of Eastern Ontario (CHEO) and the University of Ottawa has identified two separate genes associated with spinal muscular atrophy (SMA), the most common genetic cause of death in Canadian infants. The CHEO team was able to clone a gene that is usually deleted in SMA cases. This gene contains a protein that could help to halt not only the death of motor neurons in SMA patients, but the killing of brain cells in diseases such as Alzheimer's and Parkinson's.

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### **III.3 RESEARCH FUNDING**

According to data issued by Statistics Canada (*Expenditures in the Health Field, 1994*) and the PMPRB (*Seventh Annual Report, 1994*), gross R&D expenditures in the health-care field amounted to over \$1.5 billion in 1994.

Health-care R&D expenditures in 1994 rose by 12.3 per cent over the previous year. Applied research absorbed the largest share with \$336.5 million or 62.7 per cent of total expenditures, followed by basic research (\$117.4 million or 21.9%) and other qualifying research (\$82.7 million or 15.4%).

Canada's health-care infrastructure and its associated R&D activities provide the pharmaceutical industry with an excellent means of leveraging its R&D investment. In 1994, almost \$3 of R&D was conducted in Canada for every \$1 invested by industry.

The innovative pharmaceutical industry was the leading contributor to health-care research, with expenditures at \$561.1 million in 1994. The balance of total expenditures, \$1.045 billion, represents leveraging opportunities in health-care research in Canada.

Although a significant proportion of public spending was not directed at specific industrial projects, Canadian universities, teaching hospitals and research centres are increasing their involvement with industrial partners at all stages of R&D activities. This trend is resulting in a wide range of opportunities for industry to maximize the impact of its R&D investment by collaborating with public institutions.

### **III.4 EFFECTIVE REGULATIONS, UPDATED LAWS AND LESS LITIGATION**

#### **Regulations**

Canada's regulatory system is applying high standards in determining safety and efficacy of pharmaceutical and related health-care products. The drug approval process is clear, logical and evolving to meet the industry's needs. As well, the current regulations are very similar in scope to those applied in the U.S. and other major producing countries.

The HPB has recently restructured its corporate management, and current initiatives include improvement in the resource allocation process, and an increased emphasis on partnerships and co-operation with stakeholders in the regulatory process.

#### **Performance Standards and Initiatives**

In 1994, the Drugs Directorate established performance standards for the drug submission review process. These are competitive with similar standards used by agencies in other countries.

New regulatory initiatives include:

- the harmonization of regulatory requirements with the European Union and the United States;
- a joint review process between the HPB and the Food and Drug Administration (FDA) in the United States;

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- ❑ a revision of current Good Manufacturing Practices (cGMP) for biological products;
  - ❑ an agreement with the European Free Trade Association (EFTA) Scheme for mutual recognition of evaluation reports on pharmaceutical products (PER Scheme), as part of an international effort to recognize drug evaluations completed by EFTA countries, as well as Australia and Iceland. (The PER Scheme provides members with a standardized system for the drafting and exchange of evaluation reports in order to reduce duplication in the assessment program);
  - ❑ an agreement with Australia, which provides for sharing of information on the chemistry, manufacturing, and preclinical and clinical trial portions of drug submissions (Canada allows the export of products that have not yet been approved for sale in its own territory);
  - ❑ Health Canada approval for the sale of 122 original medicines, between 1988 and 1993;
  - ❑ approval, during the same period, of 24 new chemical entities for cardiovascular diseases and 21 for anti-infective and anti-viral therapy, including five HIV therapies;
  - ❑ approval of 16 new compounds for the treatment of central nervous system disorders, and of 14 to treat cancer; and
  - ❑ introduction in 1994 of 80 new products, including 21 new chemical entities.

### **Emergency Drug Release**

The Drugs Directorate provides a service through which Canadian practitioners (physicians, dentists and veterinarians) can obtain the emergency release of a quantity of a drug that has not yet been approved for marketing or sale in Canada. This service is known as the emergency drug release program. Emergency drug releases are made for an individual patient or a specific group of animals, when a medical emergency exists and standard therapy is not effective.

### **Drug Evaluation Fees Regulations**

In 1995, the government started charging fees for the evaluation of submissions related to human pharmaceutical, radiopharmaceutical and biological drug products. In return, the pharmaceutical industry will have a more efficient, streamlined and effective drug review process.

### **Updated Laws**

The *Canadian Patent Act*, which legislates intellectual property rights, was amended in 1987 and again in 1993 to bring patent protection for new pharmaceutical products up to the world standard.

Under the 1987 amendment, a Patented Medicine Prices Review Board (PMPRB) was established. This independent quasi-judicial body ensures that the factory-gate prices of patented medicines charged by patentees in Canada are not excessive. It also reports annually to Parliament on pharmaceutical price trends, and research and development.

The *Patent Act* also requires the PMPRB to monitor and report annually on the ratio of R&D expenditures to revenues for each patentee, and for the patented pharmaceutical industry as a whole. For individual patentees, this calculation includes all revenues from Canadian sales of medicines, including revenues from licensing agreements.

### Less Litigation

The Canadian business environment is significantly less litigious than that of the United States. In general, the Canadian legal system does not promote the use of legal means to receive compensation for medical malpractice.

A study in the *New England Journal of Medicine* indicates that Canadian physicians are one fifth as likely to be sued as their counterparts in the United States. (Coyte et al. 1991-1 324: 89-93).

## III.5 A QUALITY WORK FORCE AND COMPARABLE LABOUR COSTS

### Work Force

Canada is rich in its availability of highly talented research professionals. Canadian physicians and hospitals are considered to be among the best in the world. The greatest growth area for new jobs has been in medical R&D in Canada. In this field alone, employment rose by 192 per cent or 1 773 new positions between 1987 and 1994.

Canada offers the highly skilled, educated work force demanded by knowledge-based, R&D-intensive industries. Canada's educational system, one of the world's finest, provides top-quality graduates to industry. Canada has 53 universities that award bachelor's degrees in the sciences as well as 26 universities that offer masters and doctoral degrees in the sciences and/or engineering. Because of this well-developed educational infrastructure, Canada is able to maintain a relatively high percentage of graduates in science and technology compared to the United States and other G-7 countries. In a recent survey, Canada ranked first among G-7 countries in per capita post-secondary education enrolment.

The following table provides a breakdown of graduates from Canadian universities and colleges in the fields of engineering, sciences and the health professions.

Discipline	B.Sc./B. Eng.	M.Sc./M. Eng.	Ph.D	Total
Engineering/Applied Science	8 309	2 111	552	10 972
Biological Sciences	7 722	993	397	9 112
Mathematics	6 580	1 301	615	8 496
Health Professionals	7 778	1 399	400	9 577
<b>Total</b>	<b>30 389</b>	<b>5 804</b>	<b>1 964</b>	<b>38 157</b>

Source: Statistics Canada, 1995

### Labour Costs

Professional and labour costs in Canada compare favourably with other countries. Between 1993 and 1994, Canada's labour costs decreased by 2.1 per cent and wage settlements, in the

manufacturing industry, increased only by 2.1 per cent. As well, estimated labour productivity in manufacturing was up by 1.2 per cent to reach 3.5 per cent in 1994.

**Salary Comparison for Engineers  
(1993)**

	Canada	United States
Senior Level	\$90 000	\$104 000
Starting Level	\$38 000	\$ 50 000

*Source: Association of Professional Engineers of Ontario*

The following table presents the national averages paid to selected job classes in biotechnology research in Canada

Job Class	Average National Salary (Annual)
Senior project manager	\$76,200
Project manager	\$58,200
Lab Manager	\$52,100
Research scientist	
Junior	\$41,500
Intermediate	\$59,500
Senior	\$71,100
Research associate	
Junior	\$35,700
Intermediate	\$42,600
Senior	\$45,700
Clinical research associate	
Junior	\$45,100
Intermediate	\$58,100
Senior	\$61,300
Research technician	
Junior	\$27,300
Intermediate	\$32,100
Senior	\$33,400
Quality assurance manager	\$67,500

*Source: Biotechnology Compensation Survey, Personnel Systems, Ottawa, 1995*

Not only is the cost of the Canadian work force relatively low, but the quality of the work force is second to none in industrialized nations. Canada has a very strong base of scientific competence, and has produced highly accomplished researchers in the areas of science and technology.

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### III.6 AN ADVANTAGEOUS LOCATION

A 1995 study, done by KPMG Management Consultants, entitled *A Comparison of Business Costs in Canada and the United States*, has shown that it is less expensive to do business in Canada than in the United States, especially for the pharmaceutical industry.

KPMG developed computer models to compare the relative costs of setting up and running a facility in a suburban industrial park in eight Canadian cities and seven U.S. cities. The scenario was from start-up to 10 years of operation. The study team compared a variety of cost components, from industrial land and construction costs, as well as operating expenses (electricity, transportation), to wages, benefits and tax credits for seven industries including pharmaceuticals. Each facility was assumed to have sales in excess of \$10 million, and a minimum of 100 employees.

The study revealed a definite Canadian advantage, which was found to be consistent among cities and regions. For the pharmaceutical sector, the report noted that initial investment in facilities showed a 17-per cent difference in Canada's favour. On average, \$3.5 million was spent in the Canadian locations, compared to \$4.1 million in the seven U.S. sites.

Labour costs, in the pharmaceutical model, including wages and salaries, and statutory and other benefits, were lower in all Canadian cities and overall showed an impressive 26-per cent difference in Canada's favour.

In addition, Canada presents an ideal gateway to the North American market for European and Asian companies. Through the implementation of the NAFTA, Canada is a member of the largest trading bloc in the world: 360 million consumers with combined annual health-care expenditures in the three countries approaching \$1 trillion.

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### III.7 THE PRESENCE OF OTHER MULTINATIONALS

Canada already has a significant number of major multinational pharmaceutical companies. The Canadian pharmaceutical industry includes over 100 companies involved in manufacturing and distributing a range of products, including human prescription and non-prescription drugs, and veterinary and biological products. Within this superior business environment, Canada encourages investment in the pharmaceutical industry to:

- establish research and manufacturing facilities;
- assign global mandates for R&D to international subsidiaries;
- establish collaboration and technology transfer between foreign partners and Canadian fine chemical and biopharmaceutical firms;
- subcontract pharmaceutical R&D to third-party research establishments; and
- form alliances, joint ventures or establish licensing agreements with Canadian pharmaceutical or biopharmaceutical companies.

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## APPENDIX

### LIST OF SOURCES

#### Canadian Biotech News

Weekly newsletter on the Canadian Biotechnology Industry

#### Canadian Drug Manufacturers Association

Miscellaneous press releases and fact sheets

#### Canadian Medical Discoveries Fund Inc.

*Prospectus dated December 7, 1994*

#### Department of Foreign Affairs and International Trade

*The Case for Investing in Canada - Canadian Pharmaceutical Industry, March 1994*

#### Ernst & Young

*Biotech 96: Tenth Annual Report on the Biotechnology Industry*

#### Health Canada

*Time to Act, November 1991: National Advisory Council on Pharmaceutical Research*

Health Protection Branch

*Food and Drugs Act and Regulations*

#### IMS Canada

*The Pharmaceutical Market - World Review 1995*

Strategic Information Services

*Pharma Marketing Canada, November 1994*

*PharmaFocus Canada 1997*

*PharmaFocus Canada 1999*

#### Industry Canada

*International Pharmaceutical Industry Study, March 1994: Prepared by Queen's Health Policy Team, Queen's University*

*A Comparison of Tax Incentives for Performing Research and Development in Canada and the United States, October 1995: Prepared by Deloitte & Touche*

#### KPMG Canada

*A Comparison of Business Costs in Canada and the United States, March 1995*

#### Medical Research Council of Canada

Annual Reports; miscellaneous reports and communications

#### National Research Council of Canada

Annual Reports; miscellaneous reports from NRC institutes

#### Patented Medicine Prices Review Board

*Seventh Annual Report*

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and International Trade**

**Industry Canada**