Features

Safe drugs: how safe are they?

CUP
Julian Betts and
Marc Tessier-Lavigne

On November 26, 1961, the Grunenthal drug firm withdrew its popular sleeping pill containing thalidomide from the market. Before thalidomide was withdrawn, the chemical produced deformities in 6,000 infants in West Germany alone. In the two decades that has passed since the thalidomide catastrophe, governments in North America have monitored the drug industry's research much more carefully. In 1973, the Canadian government, in conjunction with the U.S. government, published a detailed, 183-page set of drug test guidelines.

Despite compliance for these new regulations, the drug industry on several occasions has been found guilty of abuses and fraudulent practices in attempts to circumvent these stringent requirements, especially when sizeable profits are at stake.

The elaborate and expensive drug testing produce begins with a thorough pharmacological assessment of the drug. If the effectiveness study gives promising results, the company will being testing the drug on laboratory animals, usually dogs and rats.

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The first test procedure determines the acute toxicity of the drug, or in other words the amount of the drug which is lethal.

Secondly, the researchers check for sub-acute toxicity by adding the drug to the animals' diet during a 90-day period and observing any physiological changes. Some of the animals are then killed and thoroughly examined, while others are kept alive and put on a normal diet, to determine whether any side effects which appeared in the animals are permanent.

The third step of the procedure tests whether low dosages of the drug over long periods of time are toxic to the animals. The effects of the drug on three generations of animals are studied. These three sets of experiments require some two years for completion and cost an estimated $500,000. On the average only one or two per cent of all drugs tested will pass these tests.

If the studies reveal no major problems with the drug, the firm will then present the toxicity results to the Health Protection Branch in Canada or the Food and Drug Administration (FDA) in the United States. If the toxicity data meet the requirements, and if the company can provide evidence of the drug's potential benefit, the health protection branch will grant the company permission to test the drug on healthy human volunteers. The tests study the kinetics of the interaction between drug and body, and are eventually applied to consenting patients.

If the new drug produces no major side effects in the patients, and if it proves more effective in alleviating the condition than others drugs already on the market, the drug company may begin limited distribution of the drug to general practitioners. After this complex risk/benefit analysis, the drug firm finally puts the drug out onto the market.

Despite these elaborate safety precautions, unsafe drugs continue to appear on the market. Last November the National Cancer Institute announced that corticosteroid drugs used in the treatment of cancer and arthritis had been linked to a new strain of pneumonia. In March 1978, Japanese courts awarded $1.1 million in damages to 16 people who had taken an anti-diarrhetic drug called quinoform which resulted in paralysis. The drug allegedly affected 11,000 Japanese before its ban in 1970. Ciba-Geigy, one of the pharmaceutical companies that marketed quinoform, suffered a further setback in 1977 when the American government ordered phenformin, a prescription drug used by some 385,000 diabetics, off the market. Over an 18-year period the blood disorder it produced resulted in more than 100 fatalities in the U.S.

The first reason for such failures is the danger inherent in all drugs - the safety standards in the industry are not always to blame. Animal tests can only approximate how a drug will affect humans. Indeed, some drug's side effects may not manifest themselves even during the testing of humans. Carcinogens in particular may escape detection since cancer can take up to 25 years to appear.

Risk/benefit analysis comes into play at this stage to aid in deciding whether a drug's side effects are worse than the condition it cures. An example of such a problem arose in May 1979 when the National Cancer Institue (NCI) reported that reserpine, a drug used to lower high blood pressure, caused cancer. FDA and NCI officials agreed that the short term benefits of the drug outweighed the possibilities that it could produce cancer over the long term. Reserpine is still on the market; the final decision is left to the consumer, as it is with birth-control pills.

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According to Samuel Epstein of the School of Public Health of the University of Illinois, the drug industry has produced inadequate, biased and manipulated data, and has even gone as far as destroying compromising data.

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The greatest problem is that almost all the risk/benefit analyses from which regulatory decisions are made are produced and interpreted by the industry itself or by universities and commercial laboratories under contract to industry.

This high degree of self-regulation has resulted in low quality studies. In 1967, the FDA Commissioner Herbert Ley complained that "almost half of the petitions originally submitted to the Food and Drug Administration have been incomplete and, therefore, have required subsequent supplementation, amendment, withdrawal, or denial."

Financial pressures may adversely affect the quality of research performed by the drug industry. In 1979 the FDA published a list of 2,400 inexpensive generic equivalents of brand name drugs. Critics cited the industry's attempt to legally block this move as an example of profits coming before the public good. However, the drug companies say they opposed the list because firms which sell cheap generic drugs generally have no research expenses to pay. Professor D.S. Ecobichon of McGill's pharmacology deparment says that by marketing inexpensive drugs, these firms adversely affect the quality of other companies' research programs.

Whatever its effects on testing, the profit factor has undoubtedly influenced the marketing side of the industry. Critics write that the industry has created entirely new markets for its drugs where none existed before.

In Canada the monitoring of drug tests is further complicated, since most drugs sold here are imported. The Health Protection Branch does monitor imported drugs. But how well? Professor Ecobichon recounts the story of an assay he once performed on imported vitamin C. The tablets contained only one quarter the amount of usable vitamin C that the package claimed they contained. The government had not noticed.

The Health Protection Branch can impound drugs coming into the country for 60 days to test them. Ecobichon says that although the branch employees are "supposed to test" all incoming drugs, they "probably release the drugs unless they're suspicious. He believes that although branch is performing its job as well as possible, it is "overworked," and consequently "always looking at yesterday's problems.

But beyond mere negligence, or the production of inadequate data, industry has also indulged in fraudulent manipulation of data. Epstein cites the cases of the drug Dornwall, for which the Wallace and Tienan Company were found guilty of submitting false data, and the drug MER/29 for which officials of the Richardson-Merrill Company were criminally convicted. The drug Penalba was removed from the market in 1968 after an FDA inspector accidentally discovered hidden information proving its lack of efficacy as compared with its individual ingredients.

In response to such occurrences, governments have set out to ensure the quality control of the data used in regulation. In the U.S. in 1977, Congress allocated $16.6 million to the FDA for this purpose. The industry has responded by increasing its testing capacities, a move that brings new fears to critics. They believe the problem of data misrepresentation and abuse can be solved only by creating independent organizations to form what Epstein calls a "neutral buffer zone" between those who test and those whose products are being tested. They also advocate the widespread use of laboratory and professional malpractice suits modelled after medical malpractice suits, which are now widely accepted.

More recently, in 1977, Industrial Biotest Labs of Illinois, faced with a U.S. governmental investigation, destroyed files dealing with toxicological and carcinogenicity tests of thousands of federally approved products including drugs, food additives, pesticides and industrial chemicals. Officials subsequently admitted having ordered this destruction of documents.

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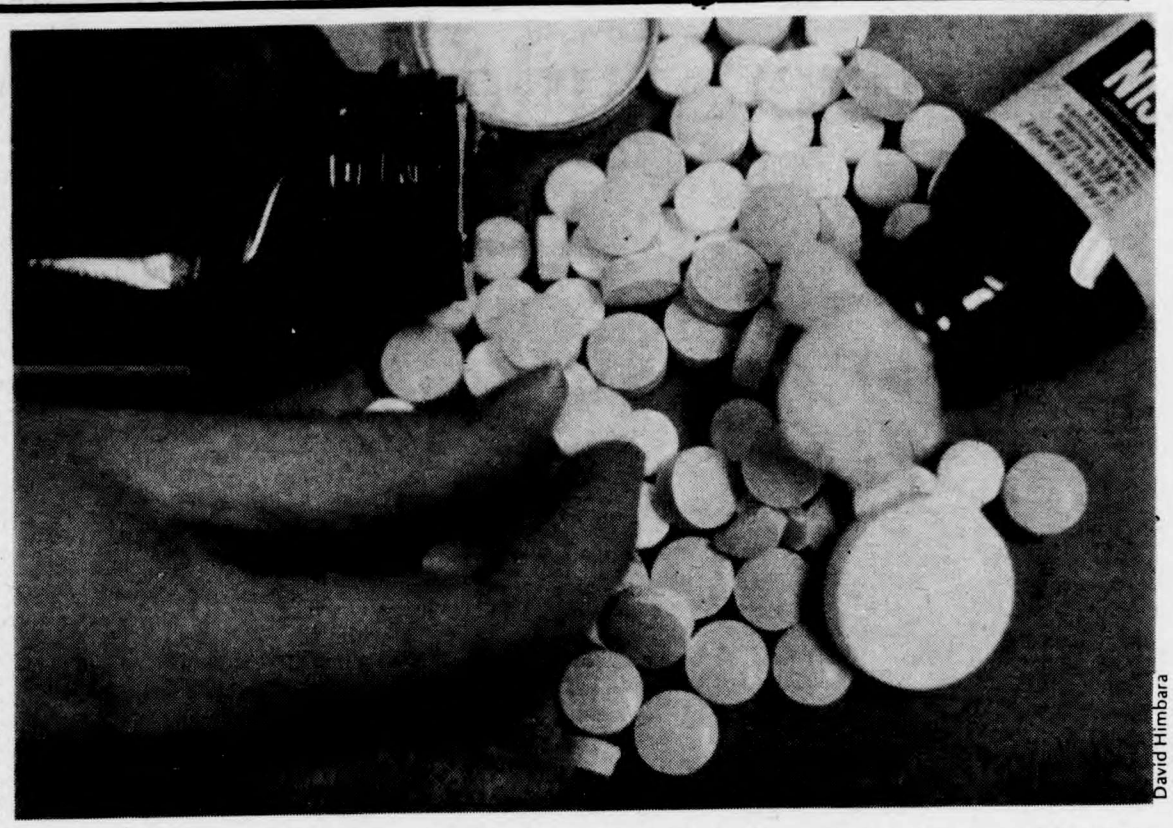
Data misrepresentation, combined with inadequate subsidizing of governmental inspection, have helped make the results of tests, if not totally unreliable, at least suspicious.

According to Ecobichon, one factor that can affect the safety of a drug is its "chronic abuse" by the consumer, either intentionally or by mistake. He said: "There are no safe drugs. There are only safe dosages...All drugs have unwanted side effects." For this reason he believes that no amount of testing can absolutely guarantee a drug's safety. High standards do, however, help.



David Himbara