MEDICAL REFORM GROUP OF ONTARIO

BRIEF

To
Commission of Inquiry on the Pharmaceutical Industry

August 1984

PREAMBLE

The Medical Reform Group of Ontario is a voluntary organisation of physicians . The Medical Reform Group believes in optimising the delivery of health care to the Canadian consumer, based on the experience and research of its members. It supports the principle of universal medicare and favors a high degree of public involvement in decisions about the health care system.

At the annual meeting of the Medical Reform Group on October 27th 1983 a resolution was passed on pharmaceuticals. This read:

"Whereas the prices charged for drugs by the multinational drug companies are excessive and Whereas the availability of generic drugs can result in substantial savings to the Canadian public and Whereas the proposed amendments to the Patent Act would reduce the future availability of generic drugs:

Be it resolved that the Medical Reform Group call on the Federal Government to abandon its plans to change the Patent Act as it applies to prescription drugs."

The appointment of the commission of inquiry is welcomed by the Medical Reform Group and is seen as an opportunity for a wide ranging probe into a number of important areas related to

prescription drugs. It is hoped that the inquiry will lead to an understanding in governing circles of the relative importance of pharmaceuticals in the health care system, the development of improved information for appropriate prescribing and some directions for the future of medical research. There are also important questions about the costs of drugs both to consumers directly and to governments and other payment agencies that pay for drugs.

The pharmaceutical industry is one that is highly concentrated in the hands of multinational companies. The inquiry should examine the effects that the ownership has for Canada; this raises many issues relating to Canadian control and ownership that have been identified in other industries and that are important for the overall future of the Canadian economy.

The Medical Reform Group has no outside funding and has no vested interest in any particular form of regulations regarding pharmaceuticals. It hopes that its analysis will be of value in furthering the best interests of the Canadian consumer.

Section 1.

THE PHARMACEUTICAL MANUFACTURING INDUSTRY IN CANADA: ORGANIZATION

The early Canadian drug industry was divided into domestically owned companies, the first one established in Toronto in 1879 by E.B.Shuttleworth, and foreign-owned subsidiaries, the original being started in Windsor in 1887 by Parke, Davis and Company. The branch plan operations were set up to take advantage of provisions in the Canadian tariff laws designed to protect domestic manufacturers from competition from foreign imports. Companies that made their finished products in Canadian facilities with 20 to 25 % of the value of the products being added in Canada qualified to have their drugs designated as "made in Canada." This designation meant that the fine chemicals used in the production process could enter the country with only a 15% duty or could come in duty free. Any foreign company importing a competing product which had no value added in Canada found its drug subject to a tariff of 20%. Therefore in order to undercut a competitor's price a company would establish a manufacturing facility in Canada. The size of the Canadian operation would then grow with sales and as new products were introduced. However, the branch plants usually confined their activities to secondary manufacturing and sales as there was no incentive for the backward integration into the manufacture of fine chemicals or for undertaking research or any other activities that could be done at the corporate headquarters.

In the 1940's, the Canadian industry underwent a dramatic

transformation. As potent new drugs, especially antibiotics, were rapidly developed and marketed the location of pharmaceutical preparations shifted from the drugstore to the factory where sophisticated technological processes were employed in the synthesis of the active ingredients in the new drugs. Economies of scale became possible in the manufacture of these drugs and production was centralized in a few centres. This centralization coupled with a reduction in transportation costs and an increasing openness of world trade spelt the end for many small domestic companies.

Unable to compete on the scale demanded by the new technology most of them fell under foreign control. Prior to World War II a significant portion of the industry had been Canadian controlled but the postwar wave of acquisitions left Connaught Laboratories the one domestically controlled company of any consequence.

Ayerst, McKenna and Harrison provides a good example of the fate of most of the Canadian firms. (2) In the prewar years, Ayerst had a large and vigorous research and development organisation that was quite successful in the Canadian context in discovering new products. However the Canadian market was too small to generate the gross profits necessary to continue this R&D activity. The testing, marketing and other requirements that would have been necessary for Ayerst to expand into foreign markets would have meant further investment that was large and risky in relation to the firm's size. At the same time the New

York based multinational American Home Products, a conglomerate known for its agressive marketing approach, had the resources and expertise necessary for entry into the American and other markets and was interested in entering the pharmaceutical field. Consequently Ayerst was purchased by American Home Products in 1943. Over the next 20 years, other large Canadian companies were also bought out: E.B.Shuttleworth Chemical Company by Pitman-Moore in 1957; Frank W.Horner by Carter Products in 1963; and Charles E. Frosst, by Merck, Sharp and Dohme in 1965.

In 1981 there were 138 companies competing in the Canadian pharmaceutical market. These firms can be divided into three distinct types: i. subsidiaries of multinational companies - tendentiously self-labelled as 'innovative'; ii. generic companies that manufacture drugs for which patents have expired and patented drugs for which they have obtained compulsory licences; and iii. biological companies, such as Connaught, that produce such products as vaccines, insulins and blood by-products. A number of the generic companies are Canadian controlled and there are two associations of domestically owned companies: The Canadian Drug Manufacturers Association with twelve members in Ontario, Quebec and British Columbia, and the Association des Fabricants du Quebec de Produits Pharmaceutiques representing about ten Quebec-based manufacturers. The subsidiaries of multi-nationals dominate the Canadian market, controlling over 90 percent of it. All of the large multinationals belong to the PMAC. Membership in the PMAC is overwhelmingly by

foreign-controlled corporations. The criteria for membership of PMAC do not appear to be public knowledge. It is a matter of conjecture who decides when a company is 'innovative'. In 1961 when the PMAC had 57 members , seven were Canadian owned, but by 1981 that number was down to four of 66. These 66 firms control about 90% of the dollar volume of prescription drugs sold in Canada. (3.)

Table 1: The 21 Largest Pharmaceutical Firms in Canada--1981

Rank	Company Name	Canadian Sales $(000,000)	Country of Ownership	PMAC Member
1	Merck Frosst Canada Ltd.	84.2	United States	Yes
2	Smith Kline & French Canada Ltd.	62.3	United States	Yes
3	CIBA-Geigy Ltd.	52.0	Switzerland	Yes
4	Ayerst Laboratories Inc.	47.5	United States	Yes
5	Wyeth Ltd.	45.3	United States	Yes
6	Parke, Davis Canada Inc.	40.6	United States	Yes
7	Abbott Laboratories Ltd.	38.7	United States	Yes
8	Travenol Canada Inc.	33.9	United States	Yes
9	Syntex Inc.	33.2	United States	Yes
10	Upjohn Company of Canada	32.3	United States	Yes
11	Glaxo Holdings Ltd.	31.8	United Kingdom	Yes
12	Schering Canada Inc.	27.2	United States	Yes
12	Ortho Pharmaceuticals (Canada) Inc.	27.2	United States	Yes
14	Sandoz Ltd.	25.1	Switzerland	Yes
15	Eli Lilly Canada Inc.	24.8	United States	Yes
16	Sterling Drug Ltd.	24.0	United States	Yes
17	Burroughs Wellcome Inc.	23.8	United Kingdom	Yes
18	Hoffman-LaRoche Ltd.	23.4	Switzerland	Yes
19	Pfizer Canada Inc.	22.7	United States	Yes
20	Searle Pharmaceuticals	21.1	United States	Yes
21	Squibb Canada Inc.	20.0	United States	Yes

Note: All divisions of a single parent company are combined under one listing for purposes of this table if the divisions all operate out of the same physical facilities. Companies that are owned by the same parent, but which maintain separate

Canadian corporate headquarters are listed separately. An example of the first case is Merck Sharp and Dohme and Frosst which are grouped under Merck Frosst Canada Ltd. An example of the second case is Ayerst and Wyeth, both owned by American Home Products but which are listed separately.

Table adapted from: R.C. Kennett, Profile of the Pharmaceutical Industry in Canada, Supply and Services Canada, Ottawa, April 1982, p.8.

Consumer and Corporate Affairs, Canada, Compulsory Licensing of Pharmaceuticals: A Review of Section 41 of the Patent Act, Ottawa, 1983, p.8.

Table 2: PMAC Membership 1982-- Nationality of Firm

American	Swiss	British	Canadian	Other
42	4	6	4	10

Sources

Who Owns Whom--North America 1977-8, Dun and Bradstreet, London, 1978

Inter-Corporate Ownership 1978-9 Statistics Canada, Ottawa, 1979

A Profile, PMAC, 1980

Drug Merchandising, 64:26-42, April 1983

Section 2: PRICES AND PROFITS

PRICES

The price of drugs is not an easy topic. All kinds of figures measuring different parameters clutter up the issue. The average cost of a prescription more than tripled between 1956 and 1980, but what does that mean? The price could have gone up because more expensive drugs were being prescribed; because there was more medicine per prescription; or because prescriptions were being written to cover longer periods of time. The rise in per capita expenditure could be similarly explained.

According to Peter Ruderman (1), if the outpatient prescription expenditure is revised to take into account changes in both population and prescription prices, then the number of prescriptions per capita exactly doubled between 1960 and 1971, thereby accounting for much of the rise in per capita expenditure.

The drug industry constantly refers to the Consumer Price Index (CPI), since that seems to indicate a remarkably slow rise in the price of drugs.(2) But the CPI should be used with caution. It measures the changes in prices of only a small "basket" of drugs. To be sure that it is an accurate reflection of drug prices we would have to know the answers to a number of questions. Are the products whose prices are being measured truly representative of what people are buying? Are the drugs patented,

Table 3: Changes in the Price of Drugs: 1956 to 1981

	Overall Consumer Price Index (1961=100)	CPI for Prescribed Drugs (1961=100)	Outpatient Prescription Expenditure (1960=100)	Personal Income (1960=100)	Per Capita Expenditure on Prescribed Drugs ($)	Average Cost per Prescription ($)
1956	--	--	--	--	5.69	2.49
1961	100	100	102	102	7.87	3.14
1966	111.4	97.9	175	156	--	3.34
1971	133.4	93.8	319	248	18.64	3.73
1976	198.6	113.6	--	--	31.66	5.02
1981	316.0	170.3	--	--	57.00 (est.)	8.19 (1980)

Sources: Restrictive Trade Practices Commission, Report Concerning the Manufacture, Distribution and Sale of Drugs, Queen's Printer, Ottawa, 1963, p.388.

Royal Commission on Health Services, Provision, Distribution and Cost of Drugs in Canada, Queen's Printer, Ottawa, 1964, p.68.

A.P. Ruderman, "The Drug Business in the Context of Canadian Health Care Programs", International Journal of Health Services, 4:641-650, 1974.

Maclean-Hunter Research Bureau, A Survey on Prescriptions 1977, Conducted for Drug Merchandising and Le Pharmacien, Toronto, July 1977, p.29.

Pharmaceutical Manufacturers Association of Canada, Background Information on the Canadian Pharmaceutical Manufacturing Industry, Ottawa, 1979, Appendices 1,4.

Consumer Prices and Price Indexes--October-December 1981, Statistics Canada, Ottawa, 1980.

Halifax Chronicle Herald, July 26, 1982, p.18.

which ensures a higher price, or not? Are brand name or generic name drugs being used? How often are the drugs changed which are used in the index? This last point would seem to be particularly important, because between revisions, the CPI would not reflect the introduction of any new drugs. In fact, the CPI covers only five drugs on a weighted basis, and as a result the index reflects price changes of only a small fraction of the thousands of drugs used today in Canada. The Royal Commission on Health Services concluded "any examination of drug prices requires more intensive inquiry than reliance on the general purpose price index on drugs currently used." (3)

On an international scale, three different studies between 1961 and 1972 concluded that Canadian drug prices were among the highest, if not the highest, in the world. (4) (Even representatives of the drug industry, such as William Robson, president and chief executive of Smith Kline and French Canada, conceded that "drug prices probably were higher than they should have been in the 1960s.")

How did the pharmaceutical industry respond to these studies? Sometimes the industry took the "drugs are inexpensive (relatively)" position. Drug costs in various countries were compared with the number of hours of work required to pay for prescription drugs. "Labor indices" were prepared which showed that Canadians were able to buy their drugs with fewer hours of work than people in most other countries. This argument, however,

is not acceptable because it avoids the question of whether the prices were reasonable with respect to manufacturing costs and profit levels.

Equally weak were claims about the comparative cost of drugs in relation to the benefits derived. Again we were told nothing about the reasonableness of the prices. By that standard we should be willing to pay a hundred dollars for a pint of brake fluid if our car breaks down on a remote highway in the middle of the night. After all, that brake fluid would provide relief from misery, permanent disablement or even death. (5)

The industry's third line of defence was to claim that costs for research and quality control were so high as to justify the prices charged. This argument will be explored later, but for now it should suffice to say that neither of these were considered significant by the Royal Commission on Health Services.

Since the early 1970s the multinationals have continued to maintain drug prices at artificially high levels. The explanation for the high cost of drugs in Canada seems to revolve around two themes-- competition or the lack thereof, and foreign domination of the Canadian industry.

1. Competition

The selling price of a drug does not reflect the cost of its production. Even the drug companies admit this. (6) Drugs are priced at the level of the product already on the market with which they must compete, regardless of the production costs. Tolbutamide is an oral antidiabetic drug produced by a relatively inexpensive process compared to the production costs for insulin. However, when it was introduced, its price was identical to that of insulin, because insulin was the competition.(7)

New semisynthetic penicillins were introduced into the Canadian market in the mid-1950s. Despite manufacturing costs which varied from $54 per kilogram to $196 per kilogram, they were all sold at almost the same price. A similar situation prevailed with the drugs of the tetracycline family.(8) The industry claimed that essentially identical prices were not the result of patent control, but represented exactly the result to be expected from active competition. "The Restrictive Trade Practices Commission , however, does not find this argument convincing...The Commission's view is strengthened by the fact that the prescribing physician does not pay for the drug and, according to the evidence before us...very frequently does not know either the price of the drug he prescribes or those of alternatives."(9)

In 1977, the PMAC published a table of the most frequently prescribed drugs in Canada.(10) The purpose of this

table was to show that drug prices had remained stable or decreased, since their introduction. Analysing this table differently, according to whether or not these products were subject to significant price competition, yields far different results. (Price competition, in this instance, was defined as a 25 percent difference between the highest and lowest priced brands of the same drug.) Of the eleven products where price competition existed, the price decreased on nine. Of the eleven where there was no price competition, the price increased on eight. This difference in price changes is a clear indication of the effect of competition on the movement of drug prices. Leslie Dan, president of Novopharm Limited, the largest Canadian-owned pharmaceutical manufacturing company, gives two further examples illustrating the effect of competition on drug prices. In the first example, he notes that for the first twelve years of Inderal's existence, Ayerst continually increased the price. In 1980 when a competitor was marketed, the price of Inderal suddenly dropped by 25 to 35 percent. Similarly, when a competitor to Smith Kline and French's Dyazide appeared in 1982, the price for Dyazide also dropped by 25 to 35 percent.(11)

Mr. Dan's observations are backed up by Patrick Tidball, the manager of British Columbia's Pharmacare program. According to Mr. Tidball: "The average per hundred price of multisource products has remained low and has actually declined from 1974 to 1979. Where products are available from only one manufacturer,

however, the average per hundred price has remained high and has increased during the same period."(12) The reality is that for most products there is only a single supplier. The July 1, 1982, edition of Ontario's Drug Benefit Formulary lists a total of 1,335 different preparations. (This figure includes different dosage forms of the same drug and different formulations of the same drug; for instance a drug may be marketed as pills, capsules, solution, creams or ointments.) Almost 75 percent of these preparations were available from only one manufacturer. In only 138 cases, or 10 percent of the total, was there significant price competition. (The definition of significant price competition is the same as that applied above.)

Finally, we can look at the effects of price competition on the prices of drugs in Canada as compared to prices internationally. A 1978 PMAC study (13) compaared the price of the nineteen top selling drugs in Canada with the price of the same drugs in seven other industrialized countries. Of the nineteen drugs seven were subject to competition. For those seven the Canadian price was, on average, 55 percent of the price in the other seven countries. For the twelve drugs protected from price competition, the Canadian price was on average, almost 75 percent of the international price. Clearly, if Canadian drug prices are dropping below those in other parts of the world, competition in Canada must be a major force in the drop.

According to a 1976 study of competition in the Canadian drug industry, price cuts in drugs are usually applied only during the last stages of the product's life cycle, when the decision to withdraw the product is being made.(14) This stability in prices exists because "the control exercised over the manufacture, distribution and sale of certain drugs through patents has virtually eliminated price competition in respect of such drugs."(15) Some industry representatives maintain that price competition is not necessarily undesirable from the social point of view. They argue that in a research-oriented industry the profits resulting from having a temporary monopoly on the drug through the mechanism of patent protection are needed to sustain a reasonable flow of innovations. However, this same study analyses the magnitude of the discrepancy between the prices charged by the large companies for their brand name products and the smaller companies for their generic equivalents. It concludes that the significantly higher prices charged by the research-oriented companies could not be accounted for by their research and development expenditures.(16)

In place of price competition, the industry has given us product competition. In product competition drugs are promoted not on the basis of being less expensive than other equivalent products, but on the grounds that they are superior in their action, whether or not that is in fact the case. Companies identify successful drugs sold by their competitors and then

expend large quantities of money in an attempt to invent new drugs that circumvent existing patents, and thereby secure their own product for which they can obtain a patent.(17) "Above all, regular new marketable discoveries are absolutely vital in the fight for...sales," was what one industry-oriented magazine had to say.

Product competition is a formidable entry barrier into therapeutic markets, especially for small companies. (A "therapeutic market" consists of drugs used in the treatment of a particular problem or disease, such as arthritis or ulcers. All drugs can be placed into one, or more, therapeutic markets, depending on how many uses the drug has.) In order to develop a new patentable product a company must be able to expend substantial capital, first to research and later to marketing. Smaller companies lack the necessary funding and therefore are denied entry into the market. The strength of the entry barrier into the pharmaceutical manufacturing industry is illustrated in a 1974 study of 71 Canadian manufacturing industries. The entry barrier was measured against the following five characteristics: empirically observed ability to meet capital requirements, advertising intensity, research and development intensity, risk and level of concentration within the industry. Of the 71 industries, the pharmaceutical industry had the twelfth highest entry barrier.(18)

The net result, has been a high level of concentration within therapeutic markets. Among the large firms,a pattern of specialization has emerged that tends to break the companies into smaller, rather exclusive groups. Each group shares a market such as antibiotics or steroids. In the late 1960s, an economist who has closely studied the industry concluded that "while the exact order of firms in a market may change, the positions of leadership are effectively preserved for the large firms specializing in that area. Concentration thus tends to be both high in degree and stability."(19) In other words the marketing oligopoly approach found in consumer products such as food and household products prevails. Not surprisingly, therefore one of the most recent entrants to the field (by takeover) is Proctor and Gamble.

The PMAC tries to hide this type of market concentration by talking about overall industry concentration statistics instead. In 1976, the latest year for which figures are available, the top four drug manufacturers, all foreign controlled, accounted for less than 25 percent of total pharmaceutical industry shipments. The PMAC compares these figures to the comparable figure of 50 percent for all Canadian manufacturing industries and proclaims that "drug manufacturing is relatively unconcentrated."(20) However, these figures ignore the relatively high degree of concentration in therapeutic markets just referred to. In 1982, in 28 out of 38 major therapeutic markets, two companies accounted for more than 50 percent of sales. For

Table 4: Concentration in 14 Therapeutic Markets

Therapeutic Market	Percent of Market Controlled by Top Four Companies		Percent Change in Market Concentration 1964-1976	Number of Companies in Top Four in 1976 That Were in Top Four in 1964
	1964	1976		
Bronchial Dilators	51.8	72.9	40.7	1
Ethical Cough and Cold Preparations	42.9	54.3	26.6	3
Hormones, Plain Corticoids	60.2	72.3	20.1	2
Penicillin	78.8	89.7	13.8	3
Hematinics	34.0	38.1	12.1	1
Ethical Laxatives	43.8	46.8	6.8	3
Sex Hormones	81.0	82.2	1.5	2
Hormones, Corticoid Combinations	64.9	63.5	-2.2	3
Ethical Analgesics	69.4	67.0	-3.5	3
Other Hypotensives	104.8#	98.1	-6.4	2
Nutrients	74.7	68.1	-8.8	1
Tranquilizers	77.6	64.7	-16.6	2
Antibiotics, Broad and Medium Spectrum	55.7	46.0	-17.4	1
Vitamins	44.5	33.2	-25.4	2

#There appears to have been an error in these figures and therefore concentration movement in this market cannot accurately be assessed.

Source: J.J. Friedman & Associates, Pharmaceutical Prices in Canada: Guiding Principles for Government Policy, PMAC, Ottawa, 1981, pp.177-204.

example, two companies had 100 percent of the respiratory stimulant market; two had 66 percent of the diuretic ("water pill") market; and two had 60 percent of the anticonvulsant market.

A look at Table 4 shows that by 1976, the top four companies controlled over 50 percent in ten of the fourteen markets listed. Moreover, in at least seven of these markets concentration had increased between 1964 and 1976. Finally, there was a high degree of stability in terms of company leadership in these fourteen markets between 1964 and 1976. Of the top four companies in each of these markets in 1964, three were still in the top four, in 1976, in five markets; two were still in the top four in another five markets; and in four markets one company was left in the top four.

Since patents inhibit competition, it is also reasonable to assume that they allow companies to maintain prices at unduly high levels. The prices of antibiotics during the 1950s provides an example of this practice. By 1953, there were three patented broad spectrum antibiotics on the market: chlortetracycline, manufactured by Lederle, chloramphenicol, manufactured by Parke-Davis, and oxytetracycline, manufactured by Pfizer. All three sold at exactly the same price, $5.10

for sixteen capsules of 250 milligrams. Between 1953 and 1960, two more patented broad spectrum drugs were introduced and both sold at $5.10 for sixteen capsules. During the seven year period to 1960, the price of all five drugs remained unchanged. When it eventually did drop in 1960, the reason was the importation of lower cost European drugs which introduced a measure of price competition. According to the Restrictive Trade Practices Commission, "it was as if the price established in 1953 had come to be regarded as the right price."(21) During this same period, the price of "old" penicillin, which was unpatented, went down 80 percent. Considering that the costs of producing broad spectrum antibiotics fell by about as much as the costs of producing penicillin did, it seems that the difference in their price reductions can only be due to the presence or absence of patent protection. Commenting on the difference in price changes between the broad spectrum antibiotics and penicillin, the report issued under the Combines Investigation Act said "it would appear that the larger drug manufacturers have in recent years attempted to avoid a repetition of the experience with penicillin...and any manufacturer discovering a new drug has sought to control its sale and distribution."(22)

Eventually other companies are able to market competing drugs either as a licence to manufacture or import a drug in return for payment of a royalty fee to the patent holder, or the patent has expired or by developing a therapeutically

similar product. But even under these circumstances the first firm to offer and promote a new type of product has a substantial and enduring sales advantage. According to a study done for the U.S. Federal Trade Commission:

> In each market the success of the first brand did stimulate other firms to enter with therapeutically substitutable products. Yet such follow-on brands failed to dislodge the early entrant from a dominant position.(23)

The market power gained by being first permits the companies that introduced the drugs to continue to charge higher prices than their competitors and still maintain a dominant share of the market. Due to the higher prices of brand name drugs, the multinational companies end up with about 80 percent of the market share, based on dollar sale. A 1980 survey of pharmacies across Canada dealt with the question of which drug was used in filling a prescription when selection was allowed. (Product selection means that a pharmacist is allowed to substitute one therapeutically identical drug for another.) For eight of thirteen drugs, the first brand on the market, and still the one with the highest price was either the most frequently or second most frequently used product.(24)

II Foreign Control

Foreign control is a fact of life for the Canadian industry. In 1981, of the 21 largest companies, by sales, none was Canadian-owned (see Table 1). Foreign companies controlled about 92 percent of the industry in 1972. That figure is probably several percentage points higher by now; according to a 1980 report from the Department of Industry, Trade and Commerce, the percentage of assets under Canadian control has been declining since 1975.(25) Domestically owned companies supplie only 15 percent of the Canadian pharmaceutical market in 1975, ranking us below countries such as Mexico, Iran, India and the Philippines. Any concerns that may be voiced about such a high degree of foreign ownership are dismissed by the PMAC as the result of "a brooding insular sense of nationalism, which pervades political thought."(26)

In 1981, Canada had a trade deficit of over $301 million in pharmaceuticals versus a $29 million deficit in 1968. Between 1968 and 1979 the fraction of the Canadian market served by imports origination from parent countries or other subsidiaries abroad increased from 13.9 percent of sales to 26.3 percent, while the fraction of the market served by Canadian subsidiaries fell. The PMAC would like us to believe that the 1969 changes in the patent laws have lead to a decline in the growth of pharmaceutical manufacturing in Canada and therefore a more rapid increase in imports than in exports. According to James Doherty,

PMAC chairman, the bill "has created the impression that Canada is not a good host country and has meant a reduction in plant investment here... The industry has geared down to the Canadian market only."(27)

The PMAC is right about the increase in the trade deficit but at least part of the blame for that growth can be laid at the door of the multinationals. Foreign parent companies, for example, often charge their Canadian subsidiaries exaggerated prices for raw materials, thereby falsely elevating the value of the imports. According to Gorecki the effect of compulsory licensing on the balance of trade for prescription drugs was of minimal importance.(28)

The PMAC is also right about drug manufacturing in Canada; it is declining relative to total world production of drugs. Between 1967 and 1981, Canada's contribution to the world output of pharmaceuticals fell from 2.6 to 1.6 percent of the total. But the slowdown in manufacturing has little to do with any patent law changes, since these have affected less than 17 percent of total 1981 drug sales.

To begin with, even in the late 1960s drug manufacturing, in Canada was minimal. Eighty-five percent of manufacturing was confined to the conversion of imported material into final-dosage form. As well, the Canadian industry imported an

important number of finished products which were just packaged and marketed here. (Packaging of a drug product in Canada, including merely labelling it for reshipment to pharmacists, apparently qualifies a product for the designation "made in Canada.")(29)

The real reason why growth in the manufacturing of drugs in Canada is decreasing from its already low level is that the multinationals are finding that they can generate greater profits by consolidating production in other countries.(30) An analysis of the import and export figures confirms that the multinationals are centralizing their production. Between 1968 and 1977, the country which had the largest relative gain in exports to Canada was Puerto Rico. The rise in imports from Puerto Rico is the result of U.S. companies moving their manufacturing operations there to take advantage of tax concessions. Gordon and Fowler conclude:

> For Canada, importing fine chemicals had been the rule, but what took place during the seventies was the massive transfer abroad of the secondary stages of drug manufacture, including the production of the end product.(31)

Accompanying this shift in production was a predictable decline in production and non-production employment in Canadian establishments as a percentage of total employment.(32) The employment shift may also account for the failure of wages in Canada to rise as rapidly in the drug industry as in other Canadian industries.

The companies claim that in addition to the patent laws, another reason for discontinuing manufacturing activity in Canada is because the small size of the Canadian market makes production uneconomical. However, studies have shown that manufacturing costs do not decrease as plants get larger, and that only a relatively small plant is required for economical production. Because of the high level of imports, the effect of dumping duties becomes an important consideration in the price of drugs in Canada. Dumping duties are applied to drugs imported into Canada if the import price is less than the "fair market value" of the equivalent drug sold in the exporting country. In order to avoid this duty the parent may jack up the price to its Canadian subsidiary. The Special House of Commons Committee on the price of drugs concluded that "for this reason, imported finished dosage forms of drugs might well be priced higher than would normally be the case, especially in those instances where the importer was a subsidiary of the parent exporting company."(33)

The ability of Canadian branch plants to export drugs is also limited by foreign control. With most patents on drugs foreign-owned, subsidiary companies of the parent patentees control the market within their own jurisdictions. Export activity has to be confined to world areas where patents are not taken out; areas that are commercially insignificant. As a representative of the Canadian subsidiary of one U.S. company said, "We have so many

plants all over the world I just do not know where we would export to." (34) Finally, having a successful Canadian operation takes second place to achieving an optimal overall international performance. This situation leads to the finding by the Department of Industry, Trade and Commerce that Canadian subsidiaries are usually "not encouraged or permitted by the head office to assume responsibility for exports of their products."(35)

Foreign domination and a lack of price competition are the factors that allow the pharmaceutical industry to maintain prices in Canada at artificially high levels. However, even if these conditions were changed, there is no guarantee that prices would drop.

PROFITS

If the prices run high, can profits be far behind? According to a 1980 report from the Department of Industry, Trade and Commerce, "pharmaceutical manufacturing remains among the more profitable manufacturing activities in Canada."(36) A 1983 report by the investment firm of Walwyn Stodgell Cochrane Murray Ltd. of Toronto called the pharmaceutical industry " a particularly attractive area for long-term investment. The field is characterized by high profitability and consistent growth. Favorable demographics assures that this growth will continue well into the foreseeable future."(37)

In all their publications the PMAC tries to obscure the true rate of profit in the industry by referring to profits after taxes, when comparing the pharmaceutical industry to other businesses. But in order to compare the profits in the drug industry with all other manufacturing industries , the before tax figures should be used. The after tax rate of profitability of two companies may differ solely because of variations in the rate of income tax depending on the scale of corporate income. The U.S. Task Force on Prescription Drugs suggests that the most useful measure of profitability is probably the rate of return based on invested capital, since the most important consideration for stockholders is generally the relative success of their investment in a company. The Consumers' Association of Canada agrees that this is the best index to use and so did the PMAC.

Using this criterion, we examined the rate of return on capital employed from 1968-1980. (Statistics Canada does not report profit as a percentage of capital invested. The closest category is capital employed.) The results can be seen in Table 5. The pharmaceutical industry is much more profitable than manufacturing in general. The average over the thirteen year period for the drug makers is more than 80 percent higher than for all manufacturing. During the entire period under consideration the pharmaceutical industy has always been among the top fifteen manufacturing industries.

Table 5: Rate of Return on Capital Employed, Before Taxes, 1968-1980 Profit and Loss Companies

Year	All Manufacturing (%)	Pharmaceuticals (%)	Ranking of pharmaceutical industry of 87 manufacturing industries
1968	10.6	24.9	4
1969	10.7	22.1	6
1970	8.2	20.9	3
1971	9.5	23.8	2
1972	10.8	23.8	3
1973	15.2	22.3	11
1974	17.3	25.0	8
1975	13.4	22.6	10
1976	11.7	19.4	13
1977	10.8	18.7	13
1978	12.8	20.4	12
1979	16.2	24.9	10
1980 (Prelim.)	14.7	27.0	4
Average	12.5	22.8	

Source: Corporation Financial Statistics--Detailed Income and Retained Earnings Statistics for 182 Industries, Statistics Canada, Ottawa, Various Years.

One major factor contributing to the high rate of profits was the advent of medicare. While the multinational companies cry loud and long about the patent law changes of 1969, they fail to mention that medicare, which started around the same time, gave a substantial boost to their fortunes. More patients visiting doctors meant more prescriptions being written and that of course translated into greater sales. A look at the annual increase in the number and dollar value of retail pharmacy prescriptions bears this out. Between 1966 and 1969, the annual growth in the number and value of prescriptions was 4.4 and 7.8 percent respectively. Between 1970 and 1973, the increases were 9.7 and 12.8 percent respectively. In 1970 the changes were most dramatic. The number of prescriptions filled grew by 14.9 percent and their value grew by an incredible 22.6 percent.(38)

As robust as these profits seem, it is quite likely that they are an underestimate of the industry's true profit picture. To start with, the profit figures take into account non-prescription drug making activities, which usually yield lower rates of profit. In 1964, the rate of profit (before taxes, royalties and management fees) on total resources employed, was 18.2 percent for the total operations of drug companies in Canada, but their profit on just the manufacturing of pharmaceuticals destined for human use was 24.5 percent.

The 1964 Report of the Royal Commission on Health Services said that "the earnings of the Canadian drug industry are not a satisfactory test of the overall pricing policies of the industry because they are understated."(39) This statement recognizes that multinational firms tend to charge the most advantageous "cost" of raw materials supplied by their plants in other countries, so as to have lower profits in high-tax countries than in low-tax countries. For example, support for this view is found in the Restrictive Trade Practices Commission Report. In the early 1960s, the average rate of profit on sales, before taxes, was 15.7 percent for nine Canadian pharmaceutical branches or subsidiaries, compared to 25.0 percent for their American parents. This trend would appear to be continuing. From 1970 to 1975, the profits of the American pharmaceutical industry on stockholder's equity, after taxes, averaged 16.2 percent , while in Canada, it was only 13.3 percent.(40) Figures for 1979 yield the same result: after tax profit on equity in the U.S. was 18.0 percent compared to 16.1 percent in Canada.

Still more evidence on the same topic is provided by Gordon and Fowler. They conclude that the terms under which resale products (finished products that are imported into Canada for sale) new materials and business services were transferred from foreign parents to Canadian subsidiaries were designed to transfer profits out of the Canadian subsidiaries. In 1976, the cost to

Canadian subsidiaries for resale products was 73.4 percent of sales. This figure which is more than twice the production cost in the United States on these products, provides the parent companies with substantial profits. Furthermore, the 26.4 percent gross margin did not begin to cover the selling and other overhead expenses incurred by the Canadian subsidiaries, with the result that no profit was reported in Canada. (In 1976, resale products accounted for almost 20 percent of sales in Canada.)(41)

In 1980, the Department of National Revenue launched an industry-wide audit of the international transactions of the pharmaceutical industry. A sampling of fourteen major drugs in Canada, covering the period 1977 to 1979, revealed that prices charged by one subsidiary to another subsidiary of the same company were more than three times higher than the prices paid for the same drugs when the transaction was between two independant companies.(42) Findings of this sort led a representative of the department to comment that "profits were not being reported in Canada but some where else."(43) It is believed that because of the government audit, $20 to $25 million in additional tax reassessments were filed and promptly paid by several companies in order to avoid court action. The opinions of the Department of National Revenue were also echoed by Statistics Canada, which felt that many non-arms length import transactions between multinationals and local subsidiaries did not follow the free trade pattern which should normally apply; in other words, these

transactions were not based on factors such as production costs and foreign exchange movements that normally favor trade with one country over another. The Statistics Canada report concluded that: "Widedspread tied trade [trade between subsidiaries of the same company] means that there is a considerable scope for transfer pricing, which may work to undermine tax revenues in Canada."(44)

Looking at the figures in Table 5 and all the evidence just presented suggesting that these figures are an understatement of the industry's true profits, it would seem difficult to deny that there are huge profits to be derived from making pharmaceuticals. But deny it the PMAC does. The claim is repeatedly made that the high profits are an accounting illusion created by the standard accounting practice of treating research and development expenditures as expenses against current income rather than capitalizing these outlays as an investment item. However, as Gary Gereffi, assistant professor of sociology at Duke University, makes clear, the accounting explanation of high profitability is inadequate for several reasons.(45) First, the accounting bias is not just confined to the pharmaceutical industry but is present in "discovery-intensive" industries such as oil and gas and industries with high levels of research and development expenditures. Under certain circumstances the accounting rate of return could actually <u>understate</u> rather than overstate the "real" or economic rate of return. Second, as we have just seen, under any method of calculating profitability, the

declared profits of the industry in Canada are likely to be artificially depressed. Finally, by allowing pharmaceutical companies to treat research and development costs as a current accounting expense, the government, in effect, is granting them an indirect fiscal subsidy to encourage their risk-taking efforts. This accounting method thus serves to raise the drug firm's profitability in fact as well as on paper. In two U.S. studies even after "correcting" profits by treating research and development expenditures as an investment the drug industry was still one of the most profitable industries around.

The pharmaceutical companies' main justification for needing high profits, is that theirs is an inherently high risk industry.

> The industry is characterized by a fairly high degree of risk, in the sense that there is a continual introduction of new products, which generally operate to displace existing products... This leads to an indicated rate of product obsolescence of a fairly high order...A fairly high rate of profit is to be expected under such conditions in order to induce the firms to continue to invest in what is an uncertain environment... High risk is

> expected to bring higher rewards, to compensate for the taking of risk. And it is risky. Almost 200,000 substances are investigated each year, but only one in every 1,000 compounds yields a usable drug--after seven years' research and an investment average of $7,000,000!(47)

The contention that "profits" are needed to supply the funds to finance research and development is not consistent. Profits, by definition , are the residual left after all costs, including those for research and development, have been met. To add to costs an additional element for future research, which, of course, will also be paid for by future sales, is to charge consumers twice for the research component. Charging the consumer twice, means that the consumer pays the stockholder twice, one in dividends and again in plant and equipment. These payments are added to the stockholder's holdings, although the investment comes out of the patient's pocket. Who ends up paying twice for the research costs? The elderly and the ill, the ones who use proportionately more medicine, and the ones who can least afford the cost.

Dr. Dale Console, a former medical director of Squibb, has testified about the risk involved:

> They [the drug firms] stress that there are many failures for each successful drug. This is true since it is the very essence of research. The problem arises out of the fact that they market so many of their failures.
>
> I doubt that there are many other industries in which research is so free of risks... with a little luck, proper timing, and a good promotion program, a bag of asafetida with a unique chemical side chain can be made to look like a wonder drug.(48)

According to evidence presented by Cyanamid, to the Restrictive Trade Practices Commission, there is strong degree of brand loyalty among doctors, and superior products do not easily replace older ones. "Achromycin...has been widely used by many physicians." "When Declomycin, which we think is an improvement, became available we set out thinking that physicians were entitled to know about this new drug... We encountered the most conservative form of loyalty to Achromycin that you can imagine."

A drug's lifespan is another concept thrown into the debate on industry profit. The initial marketing costs of new drugs are usually recovered about 8.8 years after the drug first appears. According to an estimate from the president of the PMAC,

the average lifespan of a drug from its introduction to its withdrawal is about ten years, and a study commissioned by the PMAC states that the average product life is fifteen years and that most drugs remain in the market for considerably longer periods. The average drug, therefore, enjoys a range of one to six years of pure profit. (49)

In one study, 71 Canadian manufacturing industries were ranked on the basis of risk. The drug industry was 67th, showing itself to be almost the lowest risk industry in Canada. The Special House of Commons Committee on the price of drugs concluded:

> A review of the evidence before this Committee seems to indicate that, in comparison to manufacturing in general, the effects of losses on the pharmaceutical firms as a group does not indicate the presence of greater risk. In fact the rates of return on investment demonstrate that, over the period 1953-1964, the pharmaceutical industry in Canada has been increasingly less risky as compared with manufacturing in general.(50)

Analysis of the profits of the drug industry for the 1970s, suggests nothing to indicate that it is any riskier now than it was in 1964.

Section 3 - RESEARCH

THE CONTRIBUTION OF DRUGS TO HEALTH

In almost all the literature published by the PMAC, there are charts and tables showing decreases in the death rate from various diseases, increases in life expectancy and drops in the number of people in psychiatric institutions, all of these changes being attributed mostly to the wonders of modern pharmaceuticals made available through research. As doctors we in the Medical Reform Group write prescriptions every day, so it would be foolish of us to deny that drugs can be useful or even, at times, life-saving. We use drugs for the benefit of our patients. It is striking what a small number of drugs out of all those on the market we prescribe. Still it would be interesting to examine the claims of the drug industry.

By 1971, Canadian life expectancy at birth, for men, had increased by over nine years since 1931 and for women by over fourteen years as the PMAC claims. But between 1931 and 1971, the lifespan for men who reached forty years of age went up less than 1 1/2 years and for women just slightly under six years.(1) The nine and fourteen year increases in overall life expectancy were largely due to a sharp decline in infant mortality rates. Infant

mortality decreased because of improved overall living and nutritional standards. Infant mortality is strikingly unrelated to pharmaceutical innovation.

The PMAC cites statistics to show that the mortality rate from diphtheria dropped from 9.7 per 100,000 population in 1926, to 0.1 in 1956. The implication is that this fall was due to the availability of antibiotics and vaccinations. Immunization against diphtheria was introduced in Ontario in the eaarly 1930s, but again, we have to put this fall in perspective. In the 1880s, mortality from diphtheria was 90 per 100,000. So before we had medical therapy for diphtheria, there had already been a decline of almost 90 percent in the death rate from the disease. Furthermore, once you caught the disease, your chances of dying were the same in 1955 as they were in 1900, despite antibiotics and any other medicines available to doctors.(2) Similarly, the decline in death from rheumatic fever, lobar pneumonia, tuberculosis and scarlet fever, had started long before the era of vaccinations and modern drugs. Again, the reasons lie in better nutritional and hygiene standards and better living conditions in general. One study analyzed U.S. mortality statistics and concluded that, at most, 3.5 percent of the total decline in mortality in that country, since 1900, could be ascribed to the introduction of vaccines and antibiotics.

Citing more statistics, the PMAC points to a 35 percent

drop in the number of patients in Canadian psychiatric hospitals from 1963 to 1974 due to the introduction of psychoactive drugs such as the phenothiazines and asserts that "the availability of an armamentarium of psychotherapeutic drugs...has made revolutionary progress into the overall treatment of the disease (of mental illness)."(3) But once again the PMAC is choosing to use selective statistics. The inpatient psychiatric population may be dropping but according to an Ontario Public Service Employees Union (OPSEU) financed study of Ontario's mental health care system readmission rates in that province climbed from 25 percent in 1941 to 70 percent in 1971, and currently two thirds of all admissions to psychiatric hospital units are readmissions. (4)

The polio vaccine has been of great benefit; antibiotics have drastically reduced the length of illnesses and have saved many lives; and drugs to lower blood pressure help to prevent heart attacks and strokes. But the usefulness of drugs must always be examined in perspective. We have to take into account other changes in society, and we have to carefully examine the evidence that is cited in favour of drugs.

While the usefulness of some drugs is in question, the uselessness of others is not. In the mid-1960s, the U.S. Food and Drug Administration set up expert scientific panels from the National Academy of Sciences and the National Research Council (NAS/NRC panels) to evaluate the claims made for all drugs introduced into the U.S. prior to 1962. (Significantly, the

Canadian government has never undertaken a similar review, largely due to budgetary restrictions.) Of the 4,000 products considered, 2,000 were cleared as "effective", but 760 were categorized as "ineffective" or "ineffective as a fixed-ratio combination." The remainder were classified as "probably effective" or "possibly effective". Six hundred were banned from the market, and hundreds of others required substantial changes in their labelling.(5) The large companies' products did not escape being labelled ineffective: 29 came from Squibb, 27 from Upjohn, 21 from Pfizer, 20 from Lederle, 19 from Lilly, 15 from American Home Products' Wyeth and 14 from Merck. Of 16,000 therapeutic claims made for the products under investigation, 66 percent could not be scientifically substantiated. (6) The NAS/NRC panels concluded:

> Many of the presentations submitted by manufacturers in support of the claims made for their drugs were far from convincing. The lack of evidence based on controlled studies by seasoned investigators was conspicuous. In its place, we were asked to evaluate bulky files of uncontrolled observations and testimonial-type endorsements. Moreover, independent searches of the medical literature indicated that there exists little or no scient-

ifically convincing evidence to support many of the claims made for many drugs that have acquired a significant place in medical practice.(7)

One group of drugs that came in for particular criticism, was the fixed dose combinations. They were ruled against for the following reasons:

1. The fixed dosage form made rational therapeutics difficult or impossible since necessary titration of one ingredient was made impossible by the presence of others.
2. Some of the formulations had no rational basis.
3. Some ingredients were present in too small a dose to be effective.
4. Though several ingredients were active and contributed to the therapeutic effect, a similar effect could be obtained by the use of one of the ingredients if used in a normal dose.
5. The therapeutic effect of one ingredient ran counter to the therapeutic effects of another.
6. An ingredient was present for which

there was no evidence of effectiveness.

7. The combination is often given a trade name distinct from the names of the component drugs, and often bearing no relation to them, and thus does not readily identify the components to the physician.

8. Although savings are achieved in some cases, in others the fixed combination is significantly more expensive than the total cost of the ingredients dispensed separately.(8)

Forty antibiotic combinations were found to be ineffective, by reason of being no more effective then their components used singly. Fifty antibiotic combinations were judged dangerous, not just to the individual user , but also to the public at large, because they could permit resistant strains of bacteria to proliferate.

Significantly, of a total of 2,131 new products introduced into the American market between 1958 and 1967, 1440 were combination products, more than two thirds of the total. Since the Canadian market is such a carbon-copy of the American one, it is safe to assume the same situation prevailed here.

Fixed dose combination drugs are still a problem as far as the Quebec Order of Pharmacists is concerned. In 1982, its president, Jean-Claude Marquis stated: "Because it is better and safer to prescribe individual drugs, we are not in favor of any fixed combination drug products."(9)

WHAT RESEARCH GETS DONE AND WHY

Why were so many combination products developed and marketed? Or, to put the question more broadly, what motivates the drug companies to undertake the research that they do? Jim Russo, a representative in the U.S. for the Pharmaceutical Manufacturers Association, has admitted that drug companies do not readily undertake research on relatively uncommon diseases, because drugs for them would generate insufficient profits.(10) These same sentiments were echoed in 1980 by Joseph Williams, president of Warner Lambert, who said: "Our focus is to develop major drugs for major markets."(11)

A key influence on the direction, or misdirection, of pharmaceutical research, is whether or not the product can be patented. New uses of already existing chemicals cannot be patented and therefore industry research tends to ignore these substances. This point was supported in testimony by George Wright, a professor of chemistry at the University of Toronto, before the Special House of Commons Committee:

> Some significance must be attached to the observation that new drugs emanating from commercial drug research laboratories are almost always new-and-therefore-patentable

compounds, despite a reservoir of about two million known chemicals, the majority of which have not been examined pharmacologically.(12)

Again the reason for the companies' lack of interest is related to profits. Two examples of how existing chemicals are not developed by the drug industry involve lithium and L-dopa, medications that may be very beneficial in manic-depressive disorders and in Parkinson's disease respectively. Reports of lithium's effectiveness began appearing as long ago as 1949. But lithium is a naturally occurring element and cannot be patented. Only when it was found that lithium could be compounded into a patentable slow release form did the drug companies start researching and manufacturing it. The existence of L-dopa has been known since the early 1930's but for two reasons its development was delayed until the late 1960s. First, the pharmaceutical industry considered the potential U.S. market of 1.5 million Parkinson's sufferers to be too small. Secondly L-dopa is derived from fava beans and as a natural substance could not be patented. When the Swiss multinational Hoffman-LaRoche devised a way to make L-dopa synthetically they could get a patent on it and as with lithium it was then manufactured commercially.

The Royal Commission on Health believed that much of the research done by companies was directed towards duplicating already existing drugs; in effect, inventing around other

companies' patents to capture a share of the particular market. Frequently the new products are no better than the old ones and may have new and more dangerous side effects. In its brief to the Special House of Commons Committee, the province of Alberta severely criticised the effect of patents on the allocation of resources within the industry:

> Hence patents have ... induced wasteful duplication of effort and the misdirection of effort toward rivalry-oriented molecular manipulation, the development of often irrational combinations of existing drugs, which lack flexibilty and compound the problems of dosage and toxicity, and the devising of additives which represent often questionable and perhaps unnecessary flourishes in the direction of increasing the absorption rate of a drug, guarding against side effects and the like. (13)

Predictably, the drug industry opposes that line of thought. Its claim is that patents provide the incentive for significant research discoveries. However a U.S. Senate Antitrust Subcommittee could not substantiate that claim. It found that a majority of 176 important drug discoveries were made either in countries that did not grant product patents or in non-commercial U.S. laboratories.

In Canada, it is hard to see how the existence of

patents has done anything to encourage research and development. This was the conclusion of the Restrictive Trade Practices Commission in the early 1960s.(14) A few years later, the Royal Commission on Health found that of 395 patents on fourteen "important pharmaceutical products", only nine, or less than 3 percent, were held by genuine Canadian firms.(15)

The stress placed on the discovery of new processes and patents, means that properties and therapeutic possibilities of existing medicines are not studied intensively. A good case can be made that this is likely to be more cost effective. Patients and doctors would benefit from more exact knowledge of the use and possible disadvantages of established drugs. There are many instances of extended uses of old established drugs -- the case of ASA in circulatory disorders being one good example.

In an industry, however, where product--not price--competition is the chief form of rivalry, it is essential to keep introducing new products. Pierre Garai, who was an advertising executive and a staunch supporter of the pharmaceutical industry, and the free enterprise system in general, wrote that "to continue to thrive in the highly competitive sphere in which they exist, the drug companies will have to remain essentially in the business of new products. <u>That is where the greatest profit opportunities lie.</u>" (16) Elsewhere

in his article, Mr. Garai was candid enough to explain what the emphasis on new products means:

> No manufacturer of drugs can afford to restrict his production to genuinely significant pharmaceutical innovations. There simply aren't enough of these around in any given fiscal year or, for that matter, for any dozen fiscal years. It should therefore surprise no one that we find slight modification of existing products marketed by the bushel, a veritable blizzard of parity products slugging it out as each company strives to extend its share of the market, endless polypharmaceutical combinations of dubious merit and a steady outpouring of new chemical entities whose advantages, to say the least, remain to be established.

The drug companies argue that they often cannot know which slight changes in existing drugs will yield great therapeutic benefits. That line of reasoning is not generally accepted. Dr. Dale Console, former medical director of Squibb, counters with testimony that "with many of these products, it is clear while they are on the drawing board that they promise no utility. They promise sales. It is not a question of pursuing them because something may come out of it....it is pursued simply because there is profit in it." The cost of this kind of research is not negligible either in terms of talent or money. Haskel

Weinstein, former acting medical director of the J.B.Roerig Division of Pfizer, deplored what he regarded as a waste of scientific talent:

> A great many extremely fine scientists are employed by these manufacturers. Their talents should not be expended on patent by-passing chemical manipulations, on ridiculous mixtures of drugs, or inconsequential additives to established drugs. Since the number of well-trained capable scientists is severely limited, their potential should not be wasted. (17)

Dr. Console emphasized before a U.S. Senate subcommittee what happens once a drug company decides to market a compound that has no significant therapeutic advantage over products already available. The decision sets in motion a cumulative process resulting in further waste in the stages of animal and human evaluation : "This may take one or two years, or more, requiring many man-hours of time contributed by experts in various disciplines. Most if not all this research is wasted as is the time of scientists who might be better engaged in producing something worthwhile." In 1982, of approximately 800 new molecular entities in the clinical testing process in the U.S., less than 5% were judged by scientists in the U.S. Food and Drug Administration to have the potential for important therapeutic gain.

The U.S. Task Force on Prescription Drugs concluded that

of all the new products introduced onto the market in any one year, only 10 to 25 % represent important new chemical entities and only a fraction of those are important therapeutic advances. According to one estimate, of 1,848 new products marketed in the U.S. between 1959 and 1968, only 30 were important therapeutic advances -- about three a year. The New York Academy of Medicine puts the figure at about six a year. The Task Force concluded :

> To the extent that an industry devotes a considerable share of its research program to the development of what have been termed duplicative and noncontributory products, there may be a waste of skilled research manpower and research facilities, a waste of clinical facilities needed to test the products, a further confusing proliferation of drug products promoted to physicians and a further burden on the patient-consumer who, in the long run, must pay the costs. (18.)

Consider the situation with the benzodiazepine class of minor tranquillizers, the group of drugs that includes chlordiazepoxide (Librium) and diazepam (Valium). Librium from Hoffman-LaRoche was the first of the class on the market, and was the most popular minor tranquillizer available until Valium came along. Roche's marketing produced winners in Valium and Librium; we now also have flurazepam (Dalmane), clonazepam (Rivotril), bromazepam (Lectopam) amd nitrazepam (Mogadon) from Roche itself,

along with lorazepam (Ativan), oxazepam (Serax), chlorazepate (Tranxene), triazolam (Halcion), temazepam (Restoril) and alprazolam (Xanax) from other companies seeking to cash in on the "benzodiazepine bonanza". Authoritative medical opinion is that there are few, if any, substantial clinical differences that distinguish one of these drugs from another.

RESEARCH IN CANADA

In 1969 PMAC member companies were spending about $9.5 million a year on research, but only $3.35 million of that was applied to work being done in Canada. The rest was money charged to Canadian subsidiaries by their multinational parents for research done abroad. Based on the amount of money actually spent in Canada, the Royal Commission on Health concluded that expenses for research and development did not play a major role in the price of drugs.

By 1982, $75 million was being spent on research by PMAC companies. PMAC publications devote pages to describing the industry's research effort here, but they are also careful to remind readers that "research in the pharmaceutical industry is virtually 'an investment in faith' since there is little tax incentive nor effective patent protection to do so." The PMAC is also careful to boast of the large number of scientists engaged in pharmaceutical research in this country, but compared to other countries in the Organisation for Economic Cooperation and Development (OECD), Canadian R&D employment is not very impressive. In 1975, Canadian companies employed 155 full-time workers in research for every $100 million (U.S.) in pharmaceutical production. That level of employment ranked Canada last on a list of nine OECD countries.

Of the 134 companies listed in the 1975 Census of Manufacturers of Pharmaceuticals and Medicines, only 36 carried

out any research in Canada in that year, and by 1982 only six companies were doing any significant amount of research in Canada. (19) Canada's share of worldwide pharmaceutical research and development is one of the lowest among the industrialialized countries. Pharmaceutical research carried out in Canada is only about 40% of that which could be expected based on Canada's share of the world market for drugs.

The standard myth propagated by representatives of PMAC and the drug companies is that the 1969 changes to the patent laws are to blame for the low level of research in this country. They begin by claiming that drug research was flourishing in the 1960s. They cite support by the Canadian Medical Association's director of publications (20) (one David Woods, who is not medically qualified and whose authority on this subject is questionable), by the head of Canada's Medical Research Council (21) and by various figures in the Canadian scientific community.

For the sake of argument let us ignore the fact that drugs so far affected by the patent law changes account for less than 17% of total 1981 drug sales. In the 1960s, before the patent laws were changed, research in the pharmaceutical industry was already growing at a rate slower than that for all industries. The amount spent on drug research did almost triple between 1963 and 1969, from $6.2 million to $17.3 million. But during this period the government imposed much stricter requirements for the approval of new drugs; requirements which necessitated a sizeable increase in the documentation to be submitted before a drug could be

marketed. It was these new requirements that lead to the increase in research spending in Canada, not any sudden altruistic desire on the part of the drug companies to do more research in Canada.(22)

As regards the assertion that drug research has suffered from the patent law changes this is a myth resting on a trio of claims: that the 1969 patent law changes have reduced the profits of the industry to such an extent that there is no money left to invest in research; that drugs developed in Canada are somehow treated differently from drugs developed outside of Canada; and that economically it really matters to a multinational company if it loses 20 % of the Canadian market for a particular drug. Earlier we saw that profits in the industry during the 1970s were close to double those of manufacturing industries in general.

As far as the location of the research goes, if a drug is sold in Canada it does not matter where the research on it was done --in Canada, the U.S. or Switzerland-- a compulsory licence can still be issued against it. There is no advantage to be gained, as far as compulsory licencing is concerned, by doing research outside of Canada.

Finally, as Canada only represents 1.6% of the world pharmaceutical market, and less than 10% of the North American market, it is obvious that no company would spend $50 to $75 million to develop a drug just to meet Canadian needs (even assuming such needs could be identified). The major incentive to do research and development in Canada lies in the profits to be

derived from selling pharmaceuticals in the major world markets, Western Europe, the U.S. and Japan, which represent 33, 25 and 17 percent of world sales respectively. The prospect of losing 20 % of the small Canadian market to a generic company would not deter a multinational from doing research in Canada if the company truly had any commitment to promoting research here.

The lack of any factual support for these three claims renders this myth just that, a myth. According to Gorecki: "There has <u>not</u> been a massive reduction in R&D activity in Canada ... Indeed, the weaker inference that R&D activity has declined is not supported." If account is taken of inflation, then the growth in research spending stopped in 1973, dropped slightly, and subsequently levelled off, before declining somewhat in the late 1970s. However, the amount spent on R&D in 1980, in real terms, was above that spent in 1969. This pattern of spending in fact just mirrors what happened in R&D expenditures in Canadian industry generally.

It is doubtful whether tax incentives play any major role in the level of R&D activity. Indirect evidence makes the authors of a report on Canadian pharmaceutical R&D sceptical about its importance. Their viewpoint is substantiated by the dearth of reserach activity which still exists despite government incentives to promote commercial research. In 1978, substantial new tax incentives were approved for research done in Canada. In 1979, investment tax credits for research were increased. In all the federal government has provided assistance to firms engaged in

industrial research and development through six different programs over the years. (23) However the pharmaceutical industry has made relatively limited use of all but one one these programs; contrary to the PMAC claims about "little tax incentive" for research the government has been providing substantial research incentives. (24)

One of the main reasons for the past and present lack of research is the foreign control of the Canadian industry. A 1980 study for the federal Department of Industry, Trade and Commerce reported that the degree of foreign ownership of a country's drug industry exercised a strong negative effect on the R&D intensity in that country. Dr David Bond of the federal Deparment of Consumer and Corporate Affairs contends that : "where a company does research isn't a function of the patent laws, you can do research anywhere." However the multinational firms are inclined to maintain strong centralised research establishments. Donald Davies, chairman of the American Home Products' subsidiary Ayerst McKenna and Harrison agrees: "Virtually all companies do most of their research in their home country....German companies do the bulk of their research in Germany and French companies do their work in France. That's just the way it is." (25)

The reason for this centralisation is that substantial economies of scale appear to exist in conducting research into new drugs. One estimate suggests that the critical mass for a research facility is between 200 and 300 personnel and that the scale economies begin at that level. Including all drug companies, there

were only 930 people employed in research in Canada in 1980.

Where the centralised research activities occur depends on a variety of factors, including: the country of origin of the multinational; in many foreign countries drug prices are controlled and multinationals are allowed to charge higher prices only if R&D activities are increased; in some European countries drugs are approved by the health authorities much faster than in North America, that is with much less documentation, therby providing a faster return on investment; significant income tax exemptions and tax holidays are offered in countries such as Ireland and Puerto Rico; some countries, such as France require companies to conduct research within their borders if they wish to market their products there; finally the technical and educational development of the staff plays a role in the selection of a research site. Since Canada lacks any large indigenous drug companies research and development allocated to Canadian subsidiaries is generally devoted to product introduction activities, with only limited new product development.

The case of Anturan, a drug marketed by the Swiss multinational Geigy in 1959 for the treatment of gout epitomises a number of the above contentions about research in Canada. In the mid-1960s, Dr. Fraser Mustard, working at the Toronto Sunnybrook Medical Centre, began to suspect that this drug might be useful in the secondary prevention of myocardial infarctions in people with arteriosclerotic disease ("hardening of the arteries"). He approached the management of the Canadian subsidiary of CIBA-Geigy

to get funding for clinical trials to test this hypothesis, but neither the Swiss parent company, nor the U.S. subsidiary were interested and consequently there was no money forthcoming. Although CIBA-Geigy did not consider this research to be worthwhile the Medical Research Council of Canada, through a process of peer review, did and gave Dr. Mustard's team three quarters of a million dollars.

In 1974, the Trial Drug Screening Program was set up by Canadian Patents and Development, a government agency. According to the Department of Industry, Trade and Commerce:

> The underlying concern which prompted this trial program was a perceived lack of interest by Canadian pharmaceutical firms in evaluating chemical compounds produced in Canadian universities and government laboratories for their possible therapeutic and commercial value... The results of the Trial Drug Screening Program tend to support the view that multinational research-based pharmaceutical firms keep fully informed of the basic and applied research done by Canadian government and universities, but fail to pursue comprehensive drug development programs for this research in Canada due to the limited R&D assignments of their Canadian subsidiaries. (26)

It is the larger firms that do the bulk of the research in Canada, but the effects of foreign control still limit their contribution. When the amount of money spent on research and development in Canada is compared to the value of sales in Canada, the figures show that as the dollar volume of sales increases proportionately less, relative to sales , is spent on research and development. Therefore, the companies with the greatest sales in Canada are substantially dependent upon research obtained from their foreign parents.

The former president of Bristol Laboratories, (a subsidiary of the U.S. packaged goods company Bristol Myers) Edward R.Rowe did not seem to see anything wrong with so little research being done in Canada: "I think we are very fortunate in Canada to have all of these marvellous drugs made available to us through the efforts of people around the world." (27) We may indeed get the benefit in drugs, of foreign research, but Canada does not get the economic advantages of research. Scientific employment is reduced; there is no impetus for students to pursue careers in pharmacology research; and the industries that are attracted by research do not develop here. Furthermore, we become dependent on the research priorities of another country, priorities which may not coincide with Canada's.

Research and development expenditures have actually been declining in relative terms. As a percentage of total sales of human pharmaceuticals, they went from 8.5% in 1969 to 5.7% in

1976. During the period 1971 to 1977, research and development expenditures by pharmaceutical firms continued the trend of the previous seven years, and grew at a slower rate than expenditures for all manufacturing industries: 1.6 percent per year versus 2.3.

The little research money that is spent in Canada is divided into three areas. Eight percent goes to basic research which seeks to discover new concepts of drug therapy or totally new drug products; 35 percent is used for applied research which consists of testing potential drugs on animals and humans; and 56 percent is applied to product development, which encompasses areas such as developing new dosage forms or different forms of the drug, such as pills, tablets, creams or solutions. The absence of basic research is apparent, when we consider that Canada originated only 0.5 percent of all new chemical entities introduced by the world pharmaceutical community in the period 1958-1970. This performance ranked Canada last on a list of nine OECD countries. Much of the applied research and development that is carried out by Canadian subsidiaries is done for one of two reasons: either to take advantage of tax concessions, or to satisfy the Health Protection Branch's regulations about clinical testing of new drugs. Applied research and development also assumes a highly routine character, which tends to make these tasks unappealing to university scientists. Furthermore, in a profit- motivated firm, there is always a latent conflict between an atmosphere of freedom, which is necessary for good scientific endeavour, and the necessity of direction from those who are

responsible for the conduct of the firm. When product development is the predominant research activity, both the goals and procedures become relatively well defined, and an atmosphere of completely free inquiry is not crucial. These considerations may explain the fact that although the pharmaceutical industry provided approximately 21 percent of the total funds for health care research in 1977, it utilised only 11 percent of the total number of medical researchers in this country in that year.

Section 4: PATENTS

The respect to industrial property rights as represented by patents and trade marks is the essential foundation for progress in research and therapeutics in the pharmaceutical industry.

--PMAC Principles and Code of Marketing Practice (1)

The pharmaceutical industry regards patents as sacrosanct. As previously shown, patents can keep drugs at artificially high prices, thereby keeping profits high. The Canadian Drug Manufacturers Association has calculated that the 1969 changes to the Patent Act, which facilitated the entry of generic products in the Canadian market, has reduced Canada's drug bill by between $85 and $165 million. This money would have wound up in the coffers of the multinationals, but for the presence of generic drugs.

During the lifespan of the patient, companies have a monopoly on the product and can modify the dosage forms of the drug; combine it with other drugs; and make up special preparations like liquids, sprays, creams, ointments, capsules and intavenous solutions. By covering all bases, even if a new drug comes along to supplant the initial basic drug, the manufacturer continues to profit from the modified forms of the drug. The patent life of a drug can be extended by taking out additional process patents at a

later date. For example, Hoechst received its first Canadian patent on furosemide, a diuretic, in 1962. The patent was to expire in 1979, but because further patents were granted in 1967, the expiry date was extended to 1984. Large firms can patent everything in sight, thereby not only monopolizing the best products and processes for their own use, but also precluding the use of second-best products and processes by potential competitors.(2)

A former director of research for an American multinational, Dr. Calvin Kunin, enlightened a U.S. Senate committee on methods by which companies can exploit patents to their advantage: "If I were in the industry, and I were in danger of losing my patent with which I have reaped my fortune over many, many years and I wanted to retain that patent then I would combine that drug with some thing else so that I have a new proprietary agent. This is the way of keeping this with one's pocket." (3)

These are not the reasons that the industry gives for wanting patents retained and strengthened. Drug companies claim that they need exclusive rights to a drug in order to recover the enormous development costs.

The claim is open to attack on at least three different grounds. First when the drug companies say that it costs, for example, $50 to $75 million to develop and market a drug, they are not just referring to Canadian costs, but world-wide costs. Since Canada represents about 2% of the world market, the Canadian share of development costs that needs to be recouped is $1.0 to

$1.5 million. The second point that needs to be examined is the extent to which development costs can actually be attributed to any particular drug. According to at least one expert observer, Paul Talalay, professor of pharmacology at the Johns Hopkins University School of Medicine, "It's naive to accept what the large-scale drug companies say regarding the cost of any given drug. On the whole, because most firms are involved in so many different investments and products, and because as a result their bookkeeping is so complex, no drug can be clearly defined as profitable or nonprofitable." (4)

Perhaps surprisingly, this viewpoint is backed up in a PMAC sponsored study:

> The usually high proportion of unallocable common costs in the total structure of pharmaceutical costs makes it impossible for prices charged for individual drugs to be directly related to costs of producing those specific drugs. Common costs, such as outlays for research and development or similar overhead activities, are applicable to all products in their totality but not traceable to any product individually and can not be allocated to individual products except in the most arbitrary manner. (5)

In other words drug companies cannot reasonably claim that they need a certain period of time to recover the costs of

developing a new drug because these costs cannot be determined. But it would be wrong to mystify the pharmaceutical companies finances. If the bookkeeping makes it difficult to assign specific figures to specific drugs, overall figures can be applied to the range of drugs; and that leads to the final basis for challenging the industry's contention that patents are necessary for the recovery of development costs of a drug.

Research by the Center for the Study of Drug Development in Rochester, New Mexico, calculated that on the average it takes about 8.8 years to recoup development costs. (6) Under the current patent laws the average time that a company has a monopoly on a drug in Canada is about 8.5 years. Earlier it was pointed out that drugs stay on the Canadian market for at least fifteen years and that even after competitors bring out their own brands the original drug still retains the lion's share of the market. Therefore, even granting the big assumption that costs are allotable, an individual drug company is still in a monopoly position long enough to recover development costs and then go on making a profit on the drug for many years after.

According to the PMAC, patents are one of the most important incentives for research and are "an internationally accepted instrument for the transfer and sharing of technology." But Alan Klass in his book <u>There's Gold in Them Thar Pills</u> argues that from the point of view of scientists, patents are a foreign concept. They developed not because of anything within the nature of science, but purely for commercial reasons. Patents

impede the free flow of ideas, which is the life blood of science. Once a discovery is patented, other scientists can use it only with the permission of the patent holder. However, no scientific discovery stands by itself, but is built upon the work of other researchers. If the man who discovered the method of growing polio virus had patented his idea instead of freely publishing it, the polio vaccine might never have been developed. As Klass says: "It was only when corporate interest became dominant that the right of a party claiming a patent for a discovery became prominent. Patents serve the industry much more than the individual discoverer and certainly much more than society." (7)

Since 1923, Canada has had a system of compulsory licensing, by which a company may apply to the Commissioner of Patents for a licence to manufacture a particular drug by the patentee's process, upon payment to the patentee of a royalty. Theoretically, the provision for compulsory licences to manufacture should have had a tendency to reduce the monopolistic situation in the drug industry. It gives companies the opportunity to market drugs which are enjoying substantial sales. Unfortunately, that is only the theory. Between 1923 and 1949, there were no applications for a compulsory licence. The lack of applications up to this time probably reflected the absence of any drug "winners," that is drugs which were major advances and which forecast volume sales with record profits. In addition the industry was perhaps more rightfully styled "ethical", producing drugs legitimately required, rather than the market building, mass

market approach characteristic of corporate business in the post-war period. After 1949, there were significant developments in a number of therapeutic fields -- antibiotics, corticosteroids and tranquillizers being three prime examples. From 1949 until 1966, however, there were only 34 applications made, an increase which the Restrictive Trade Practices Commission did not consider significant in light of the potential.

The drug industry claimed that their willingness to issue licences voluntarily accounted for the paucity of applications for compulsory licences. The Director of Investigation and Research for the Combines Investigation Act, however, did not accept this claim. Companies may be reluctant to apply for compulsory licences beause a licensee who has been forced to grant a licence may withhold technical knowledge required in producing the drug in question. (8) The Commissioner of Patents, Mr J.W.T.Michel, pointed out one of the economic realities involved with patents: "The reason why the foreign patentees don't want to grant licences voluntarily is because they make much more profit by selling themselves than just by collecting a royalty."

Most of the applications for compulsory licences were made by small Canadian firms turning out products under generic names. These companies were among the few who could benefit from acquiring a licence. Their small size did not allow them to advertise to the extent of the major companies. Consequently, the only sector in which they could compete was in the supply of drugs

to hospitals and institutions where purchases were made under a tender system.

Licence applicants were further deterred by the requirement that the drug must be manufactured in Canada, with all the costs inhererent in manufacturing and quality control even if small quantities were being produced. The patent holder on the other hand, typically imported the raw material in bulk form and then simply prepared the dosage form in Canada. The Commissioner of Patents emphasized to the Restrictive Trade Practices Commission that foreign companies holding Canadian patents objected very strongly to the granting of licences. In fact over the years, it was a well established policy among the large multinational companies to delay applications as long as they could, to the point where it was hardly worth the trouble and barely within the capabilities of most of the existing small manufacturers to successfully pursue an application. The large companies never went after one another's patents for fear of the free-for-all that could have developed.

The Director of Investigation and Research summed up the situation:

> At the manufacturer's level, prices of certain drugs are affected by the control over the manufacture, distribution and sale of such drugs exercised through patents. The provisions of the Patent Act relating to compulsory liceces appear to have proved ineffectual to

combat this situation and the clear intent of the Act has been frustrated. (9)

The Restrictive Trade Practices Commission argued that patents were keeping Canadian drug prices higher than they should be, distorting research efforts and not contributing substantially to Canadian scientific advancement. It therefore recommended in 1963 that Canada should abolish all patents on pharmaceuticals.

In 1962, the House of Commons had established a special standing committee (the Harley Committee) to examine various aspects of prescription drugs. By 1965 it began to consider the relative quality of brand name drugs and their generic equivalents; from there it was a logical step to the question of patents. The PMAC mounted a campaign to preserve the existing patent system. The cost of that campaign is estimated to have been between $200,000 and $250,000 annually. This figure does not take into acount expenses incurred by individual PMAC members. It is believed that the PMAC's main concern was to stop the Canadian government from setting any precedent on patents and compulsory licences that would have been an example for other countries, particularly those with large domestic markets for pharmaceuticals.

The Conservatives were in opposition at the time, and the PMAC supplied the Tory members of the committee with ammunition to use against anti-industry witnesses. At least one representative of the PMAC was present at all meetings of the

committee to relay further questions and facts to these members. The Harley Committee reported in April 1967. While it stopped short of recommending the abolition of patents, it did recommend that the government allow compulsory licences to be issued to enable firms to import drugs into Canada which were already manufactured here under patent.

Having a compulsory licence to import a drug into the country would be a major boon for small companies since they would be able to forego the major expenses involved in establishing manufacturing facilities. Such a change to the patent laws was anticipated to introduce substantial competition into sectors of the drug market and as such brought about a vigorous denunciation from the drug industry. The president of the PMAC, Dr. William Wigle, a past president of the Canadian Medical Association, wrote to the Canadian Medical Association Journal threatening that if this recommendation was acted upon the large companies operating in Canada would close down their plants. While in Florida, Dr Wigle observed: "The Canadian parliamentary committee was willing to put Canada at the mercy of foreign nations in the event of world wide epidemics." (10) H.C.Balmer, president of Glaxo, warned in an open letter to M.P.s that: "The saving to Canadians won't match the cost to government of controlling the influx of hitherto unknown products...[and] if additional resources to secure such control are not planned, we will have chaos indeed." The letter concluded: "Anyone importing Glaxo products manufactured by a related company ...does so at his own peril and

at the peril of the Canadian public " (emphasis in original)

Immediately after the Patent Act changes passed at the end of March 1969, American Home Products Ltd. proceeded to oppose the legislation through the courts. At first, the company attempted to prevent the application of the law by seeking an order of prohibition against the Commissioner of Patents. That action delayed the implementation of the legislation for a year. When the case reached the Ontario Court of Apeals in March 1970, it was dismissed within fifteen minutes. Then other companies, such as Roche, started challenging the Commissioner's decisions on the basis of the royalty allowance. These cases were also decided in favour of the government. By 1971, of the 69 licences issued, there had been 43 appeals before the courts. These court battles acted as a disincentive to companies seeking licences, since they could anticipate up to a two-year court fight and a cost of about $100,000 in court fees. The use of court appeals as a delaying tactic was eventually recognized by judges, as the followiwng section from a ruling shows:

> ...there is ... ground for thinking that many appeals under s.41 of the Patent Act are brought regardless of any considered opinion that there is, under the authorities, any valid ground for attacking the Commissioner's decision. (11)

Other methods to forestall or limit competition from licensees were also tried. Hoffman-LaRoche issued statements questioning the quality of the licensee's products. In a letter,

sent to doctors by the President of Roche, J.S.Fralich, the following section appears:

> To our knowledge none of these imitators had to duplicate the enormous amount of work which is necessary in the compilation of a new drug application. Likewise, no clinical investigation activities of any consequence by these companies have come to our attention. (12)

When this type of approach seemed unsuccessful, Roche switched to price cutting on sales of Valium and Librium to hospitals. Finally, Roche used a technique known as "filling the pipes": just prior to the entry of the licencee's product, the patentee floods the market, usually in combination with a price special, so that the licensee cannot establish its product in the market for some time.

In 1982, American Home Products' subsidiary Ayerst lost a two-year court battle with Apotex, a Canadian generic manufacturer. Ayerst was trying to force Apotex to change the colour, shape and size of its tablets of propanolol, a widely prescribed anti-hypertensive drug. (The drug incidentally is a discovery of Britain's Imperial Chemical Industries and is produced by Ayerst under licence.) The Supreme Court of Ontario dismissed Ayerst's claims, noting that "there is not even the whisper of a suggestion that the appearance of Apotex's version of propranolol has adversely affected the plaintiff company in the slightest degree. Apotex won, but had to pay $100,000 in court costs. (13)

By 1983, over 290 licences had been granted. Absent from the list of licence holders were any of the companies against which a compulsory licence had been issued. Gorecki explains the reasons for this situation:

> The economic self interest of the patentees explain their absence from the list...Should each patentee decide to take out a licence against all the remaining patentees then price competition much greater than currently exists between licensee and patentee, would result. Given the extreme insensitivity of the demand for drugs to price changes, the price and profit margins of the patentee would fall. Hence, as a group, patentees would experience considerable adverse economic consequences from a policy of acquiring compulsory patent licences. (14)

What kind of an impact has compulsory licensing had? To begin with it does not appear to have promoted Canadianization of the drug industry. Of all the licences issued, almost half have gone to non-Canadian firms, or to firms that have been acquired by non-Canadian owners. Five companies that have received licences are owned by four multinational pharmaceutical firms, including licensees ranked first and third (by number of licences owned).

Although the presence of generics may have forced the multinationals to reduce the selling prices of their products to the tune of $85million to $165 million, it does not seem to have significantly affected their profit levels. In the decade ending

in 1980, the average before tax profit on capital employed for the pharmaceutical industry was 22.8% or 73 % higher than that for all manufacturing industries.

Despite all the uproar, compulsory licensing has affected only a relatively small part of the drug market. Between 1970 and 1978, 142 compulsory licences were issued for 47 prescription drugs. Five drugs alone, chlordiazepoxide (Librium), diazepam (Valium), furosemide (Lasix), ampicillin (Penbritin) and thioridazine (Mellaril), accounted for 48 of these licences -- over 80% of all licences granted were for drigs in just three out of nineteen therapeutic categories: anti-infective, cardiovascular and central nervous system drugs. Even where there is competition, the companies that have obtained licences have been able to make only minimal inroads into the market. An analysis of twenty drugs against which compulsory licences had been issued showed that the licensees drugs averaged less than 20% of the market share of sales. (15)

The drugs affected by the close to 300 licences that have been granted so far do not begin to account for a majority of the sales dollars in the Canadian market. In 1981, total sales of drugs under compulsory licence were $170 million, of which only about $35 million represented sales of firms holding compulsory licences. that year the total value of the Canadian human pharmaceutical market was $1.01 billion, meaning that drugs affected by compulsory licensing represented less than 17% of the market. Six different studies have appeared analysing the effect of compuslory

licensing on drug prices. (16) All have concluded that compulsory licences bring down the price of those drugs affected, and in some cases the reduction is substantial. It must be remembered, though, that the great majority of drug sales in 1981 were untouched by compulsory licensing.

However minor the impact of compulsory licensing, the multinationals use it to grind many of their already sharp axes. For instance, the patent law changes are being used as an excuse to keep drugs of questionable medical value on the market. "Why should we take these products off the market since there is no incentive to do research and improve them?" asked a disingenuous Bill Robson, president of Smith Kline and French Canada Ltd. (17) Terry Mailloux, a corporate vice-president of Hoechst Canada, bemoans the need for strategies to counter the impact of generic companies on his company's profits. One way to "let money come in to keep things going", he said, is to keep the company's older and largely obsolescent products on the market. Guy Beauchemin of the PMAC agrees that keeping outdated drugs on the market is a "defence mechanism against unjust laws." Mr Beauchemin also admits that the drug companies use the existence of the patent law changes to charge higher prices for some of their products. Claiming that they have lost profits as a result of compulsory licences being issued on some drugs, the multinationals increase their prices on drugs still under their monopoly.

Mr.Beauchemin's statement illustrates that in spite of government controls, the pharmaceutical companies contine to enjoy

substantial freedom to raise prices in order to maintin profit levels. Controls appear to be no more than a minor nuisance, one that can even be used by the multinationals as an excuse for flexing new muscles.

In 1979, Ciba-Geigy used the existence of compulsory licensing as an excuse to cancel a $500,000 research project in Montreal. The company claimed that it was unprofitable to continue researching a certain drug since other manufacturers could market the drug without the bother of research. The drug in question was Anturan, the same one that Ciba-Geigy had refused research funds for a few years earlier. (18)

Interestingly, as one observer points out, the companies did not consider compulsory licensing so much of a disincentive as to force their complete withdrawal from the Canadian market. "They went on selling their drugs to us, and they went on making good profits. They wanted to turn the clock back to pre-1968 conditions...but even the tighter conditions of the '70's didn't drive them out of the market."

A particular aspect of compulsory licensing that the PMAC has repeatedly attacked is the size of the royalty rate paid to the originating company by the licensee. This rate has been established at 4% of the licensee's sales. The 4% figure was set by the Commissioner of Patents in 1969, just after the law was changed and has been subject to attack ever since. The multinationals have argued for a higher rate all the way up to the Supreme Court of Canada, and have lost. Through all their

protestations, the companies have never been able to present a persuasive case that the rate is too low. Presumably if the claim had merit, the multinationals should have been able to prove it by now either to the Commissioner or before the courts. (19)

In 1980, in their lobbying efforts to have Section 41(4) of the Patent Act modified, the PMAC and the multinationals promised that if modifications to the Act were made the industry would be prepared to increase its manufacturing and research activity in Canada. When the industry's package was analysed by the federal Departments of Industry, Trade and Commerce and Consumer and Corporate Affairs, "it became apparent that most of the new R&D and manufacturing promised by the industry was either already planned or was to be financed through government incentive programs." (20)

The PMAC and the multinationals are still issuing promises and/or threats, depending on what happens to Section 41(4). The promises, consequent to a repeal, include: an increase in local manufacturing and employment, a voluntary system of price controls and increased expenditures on research. Among the threats, if the law remains unchanged, are: continued plant closings resulting in a loss of employment, and a further reduction in current levels of research and development.

It is difficult to believe the PMAC's promise of increased Canadian manufacturing in the light of remarks made by the Pharmaceutical Manufacturers Association in the U.S. in a submission to a congressional committee. Member companies were

surveyed regarding the reasons for establishing foreign affiliates. The leading considerations given were tariff and trade restrictions (listed by 95 percent of respondents as "important"), legal requirements for local production (85 percent) and "better servicing of existing work" (81 percent). (21) Apparently patent protection was not a major factor. This conclusion fits with material presented earlier where we examined the multinationals' aversion to doing research in Canada and showed that the 1969 patent law changes had no bearing on these decisions to do research. The Canadian Drug Manufacturers Association has studied the other promises and threats. According to the CDMA, voluntary systems of price controls would be ineffective and impossible to monitor, and furthermore, since most companies are branch plant operations, their promises about prices could simply be over-ridden by their overseas parents. The PMAC points to the 1982 and 1983 closings of facilities in Quebec of American Home Products' Ayerst and Hoffman-LaRoche, respectively, as examples of how the patent law changes are eroding, and will continue to erode, pharmaceutical research and manufacturing in Canada. But the CDMA analysis offers a different perspective on these closing. The shutdown of Ayerst's research and development division was a consequence of American Home Products' worldwide failure to produce significant innovations. (A.H.P. is known for its low ratio of expenditure on research and development. The Montreal plant which lacked the capacity to expand, was only one of the many foreign casualties. At the same time American Home Products, like many other

multinationals, is expanding its offshore operations in Puerto Rico for tax reasons. Donald Davies, chairman of Ayerst, concedes that Canada's patent laws were not among the main reasons for closing their research facilities in Montreal. (22)

Hoffman-LaRoche shut down its manufacturing operation in Quebec because it too was suffering from a lack of new products (and presumably had failed to anticipate the widespread decline in Valium consumption partly as a result of strong feminist pressure against over prescribing). Roche apparently made a serious strategic error in overexpanding its Quebec physical facilities well beyond its requirements. Ninety R&D jobs were cut at Roche's Swiss corporate headquarters in 1981. Roche has also moved to expand in Puerto Rico.

Finally the CDMA points out that because the pharmaceutical industry is not labor intensive, it is unlikely that employment levels wil increase proportionately to increased sales in the future. The Association concludes that "even in the absence of compulsory licensing it is very unlikely that significant increases in employment could be expected."

Lee McCabe of the federal Department of Consumer and Corporate Affairs reinforces the CDMA's cautionary note: "People seem to take it on faith that because this industry has a fairly high level of research and development it must be a winner...But I have to ask myself whether we wouldn't be better off putting our bucks elsewhere...." (23)

CONCLUSION AND RECOMMENDATIONS

Our brief has looked at the pharmaceutical industry and found it to be almost totally foreign dominated by multinational corporations. We have shown that this foreign control is largely responsible for the lack of any significant pharmaceutical research and development in Canada. Foreign control and the domination of therapeutic submarkets by a small number of companies are the major factors in keeping drug prices at unacceptably high levels. Foreign control limits the amount of domestic manufacturing, the opportunities for exports and thereby the opportunities for increases in employment in the industry.

Profits in the drug industry consistently run at a level of about 80 percent above those in other manufacturing industries, making it impossible to accept the claims of the industry that the patent law changes of 1969 have had many substantial effect on the economic viability of the industry. Compulsory licensing is the main reason why Canadian drug prices are no longer the highest in the world as they were in the 1960s. Abolishing or modifying the compulsory licensing provisions of the Patent Act would not result in more manufacturing or more investment in research and development; it would just mean higher drug prices for Canadians and higher profits for the drug companies. For these reasons the Medical Reform Group passed the resolution referred to in the Preamble, calling on the Federal Government to "abandon its plans to change the Patent Act as it applies to prescription drugs."

Although the Medical Reform Group has no other specific

policy about the pharmaceutical industry we would suggest that the commission might ask the government to look to the need for action in the following areas:

An Essential Drugs List Would it be as beneficial for a country like Canada as for Third World countries to have an essential drugs list. Could this be easily developed from the content of provincial drug benefits formularies?

Would it be possible or desirable to only grant patents to truly innovative drugs? Should the inclusion of a new drug on an essential drugs list give the right of the originator to an exclusive patent, or conversely is the right to a compulsory licence even more compelling in such circumstances? Might it be desirable to have incentives to encourage truly original research?

The absence of a Canadian equivalent of the British National Formulary is becoming an increasing problem to the practicing physician. Could the commission identify the government departments and the sources of independent drug information that have the responsibility for producing such a reference? The need will increase with the growth of non brand-name prescribing and the increasing number of generic off-patent drugs.

The commission would be advised to look into the place of drug company funds in the total picture of financing medical research.

It would be desirable to see what proportion of medical research in Canada is supported in this way and what the consequences are. The biases produced by the search for new marketable compounds should be examined, and contrasted with the need for research into established drugs and alternative, including non-drug, forms of treatment. The proportion of such moneys spent on post-marketing surveillance and the means for communicating such research to the practicing physicians should also be looked into.

The discretionary degree of research by pharmaceutical companies should be looked into. Are the self-styled innovative companies truly innovative? Should all companies be compelled to devote a certain proportion of their revenue to research? Would companies and the Canadian public benefit by the option of companies giving a pre-arranged amount to institutionalised non-industry Canadian medical research?

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