A STUDY OF THE EFFECTS ON RESEARCH AND DEVELOPMENT IN THE CANADIAN PHARMACEUTICAL INDUSTRY FROM THE 1969 PATENT ACT AMENDMENTS

by

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All remaining errors, omissions or non-clarities are the sole responsibility of myself.

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ABSTRACT

Considerable controversy resulted from the 1969 amendments to the Patent Act concerning the regulation of ethical drug prices in the Canadian pharmaceutical industry. It has been argued that research spending in Canada has been adversely affected.

This paper examines the impact of government policy on the level of research and development (R and D) expenditures in Canada since the amendments to the Patent Act took place. Quantitative results obtained from the econometric models formulated fail to support the hypothesis that the amendments reduced the level of R and D performed in this country.

1.0 INTRODUCTION

In 1969, the Canadian Patent Act was amended through bill C-102, to permit the issuance of compulsory licenses to import in the pharmaceutical industry. Compulsory licenses are the granting of a license to allow a party not holding the patent to use the patent holder's processes prior to the expiry of the 17-year patent term. This amendment has long since been a major source of concern for patent-holding firms, particularly, to foreign-owned multinationals operating in Canada. The situation prevailing before the 1969 amendments took place is discussed in a thorough analysis of the subject by R.W. Lang, in his book The Politics of Drugs. However, this paper will focus on the examination of the impact of the 1969 changes on R and D expenditures in Canada.

In Canada, Section 41(4) of the Patent Act applies only to the pharmaceutical industry and permits the issuance of compulsory licenses to import. This is the chief focus of concern for the patent-holding firms and the repeal of this legislation has been their main objective. They are also critical of provincial policies requiring the substitution of generic products for brand-name products. But for practical and precedent reasons it has been to their advantage to attack federal regulation since it is the main body of policy making.

Specifically, Section 41 of the Patent Act deals with chemical processes intended for food or medicine, and for the purpose of this paper contains two major provisions: the protection of products only by way of their patented processes of manufacture, and compulsory licenses for the manufacture, import, use or sale of patented inven-

tions capable of being used in the preparation of production of medicine.[1] The section also provides for payment of royalties to the patent holder, which have been set by the Commissioner of Patents, Foods and Medicine as mentioned at "....4% of the net selling price of the drug in its final dosage form or forms to purchasers at arms length."[2]

Prior to the 1969 amendments, few applicants for compulsory licenses were made. The Economic Council of Canada reported that during the period between 1935 and June 27, 1969, 49 applications were made; of these, only 22 resulted in the granting of a licence, 4 were refused, and 23 were abandoned or withdrawn for reasons including the timeliness of licence issuance no longer being profitable to market the drug. Subsequent to the amendment, 559 licenses to import and sell have been applied for; of these, 306 have been granted, 15 have been refused or terminated, 96 have been abandoned or withdrawn, and 142 were still pending as of January 31, 1985.[3]

The amendment resulted in the licensing of brand name products by firms, often referred to as "generic" firms, which could then produce and offer for sale their own brand of the basic generic drug, and the making available for sale of more than one of many of the commonly prescribed prescription drugs in direct competition to the patent holding firms.

More recently, the federal government has assessed the effects of Section 41(4) on the pharmaceutical industry and engaged in discussions of possible changes in the Patent Act with interested parties, such as industry associations, consumer groups, professional organiz-

ations, and various levels of government. This is partly due to the continued lobby by both consumer interest groups and drug manufacturers and because of the recent emergence of biotechnology as a major area seen for future medical advances. This has led to concern for the current applicability of Section 41 to discoveries in this field and poses the question of whether new determinants have entered into or will become relevant to the evaluation of these effects?

All the above has contributed to the erosion of the patent holding firms competitive advantage in the drug industry. This position has specific reference to key variables of market performance such as R and D, profits and sales.

The pharmaceutical industry in Canada is intensive in research in comparison to other sectors of Canadian manufacturing industry, but not to the world-wide pharmaceutical industry. This relative research intensity is reflected in the fact that, in 1982, the pharmaceutical industry, with only 0.8 per cent of all employees in manufacturing, employed 3.5 per cent of that sector's scientists and other research personnel. The pharmaceutical industry expended 2.8 per cent of the funds spent on research in manufacturing. Furthermore, a survey of 55 of the largest firms indicated that 41 had funded their entire research and development expenditures from internal sources and their foreign parent which accounted for approximately 84 per cent of the total research of the 55 firms. Government support for such research amounted to approximately 12 per cent of the total spent, which was approximately equal to the average for all manufacturing industries in 1981. However, government contribution to research exceeds that

identified above, because it provides very substantial tax incentives for research by allowing deductions from income by more than the sums expended for that purpose. These tax incentives are amongst the most generous in the world. Their adequacy in the judgement of the industry is reflected in the recommendations of the P.M.A.C. that the current system of grants and tax incentives for research be continued.

This study is devoted to exploring the issue through the formation of econometric models in which R and D efforts in the pharmaceutical industry are explained. The question to be answered is whether the amendments to the Patent Act in 1969 have had adverse effects upon R and D, and as such, have reduced the level of spending by pharmaceutical firms in this area.

1.1 BACKGROUND INFORMATION

Compulsory licensing is not new to Canada, in fact, it was first introduced to Canadian Legislation in 1923.[4] However, this additional provision to the Patent Act was of little concern to Canadians for many years. It was not until the 1950's and 1960's that growing public awareness of climbing prices for ethical drugs (prescribed, over-the-counter, and veterinary medicine) prompted investigations into the industry by the Canadian government.

From 1958 to 1968, the pharmaceutical industry was under close observation. Public concern over rising ethical drug prices prompted the Canadian government to launch full inquiries into the practices governing the pharmaceutical industry and its setting of prices. This critical attitude proliferated from the Kefauver inquiry in the United States which was unsuccessful in gaining economic-oriented changes and shifted its focus to safety issues. It is helpful in understanding the findings of these investigations by studying the efforts made by main groups commissioned to undertake these studies.

In 1960, the Ilsley Commission, concerned about rising costs of health-care, recommended that "pharmaceutical companies be permitted to patent product claims to pharmaceuticals while at the same time being subjected to compulsory licensing.[5] In 1963, the Restrictive Trade Practices Commission concluded that the continuance of monopoly pricing for drugs would create harmful effects that would outweigh any likely benefits to Canada and recommended the complete abolition of patents for pharmaceuticals.[6] In 1964, the Hall Report recommended "retaining pharmaceutical patents with a streamlined pro-

cedure, standard royalty, and expansion to permit licensing of imports."[7]

From 1965 to 1967, a special parliamentary committee, known as the Harley Committee, was appointed to study the high prices once again. As part of its study, the commission held public hearings across Canada to help determine the nature of drug prices.

The Harley Committee, along with its counterparts, agreed that "drug prices in Canada were among the highest in any industrialized nation in the world."[8] The Committee recommended the introduction of compulsory licensing to import drug products, as a means of implementing more competitive market forces to curb the rising price levels. It was these recommendations that saw the introduction of bill C-102, and the ensuing changes to the Patent Act in 1969. By accepting the suggestions made by the Harley Committee, the principle of patent protection was to be maintained, with the hope that competition would be stimulated via compulsory licenses to import, thereby encouraging lower ethical drug prices.[9] It was conceivable that this might affect profits and research expenditures as well. This brief account of the history of concern about high prices charged by the Canadian pharmaceutical industry leading to the Patent Act amendments in 1969, will help to explain the context of R and D expenditures in Canada.

1.1.1 Foreign Ownership

Canada, among industrialized nations, has an unusually high level of foreign ownership in many of its industries. This fact is apparent within the pharmaceutical industry. Specifically, U.S. owned firms

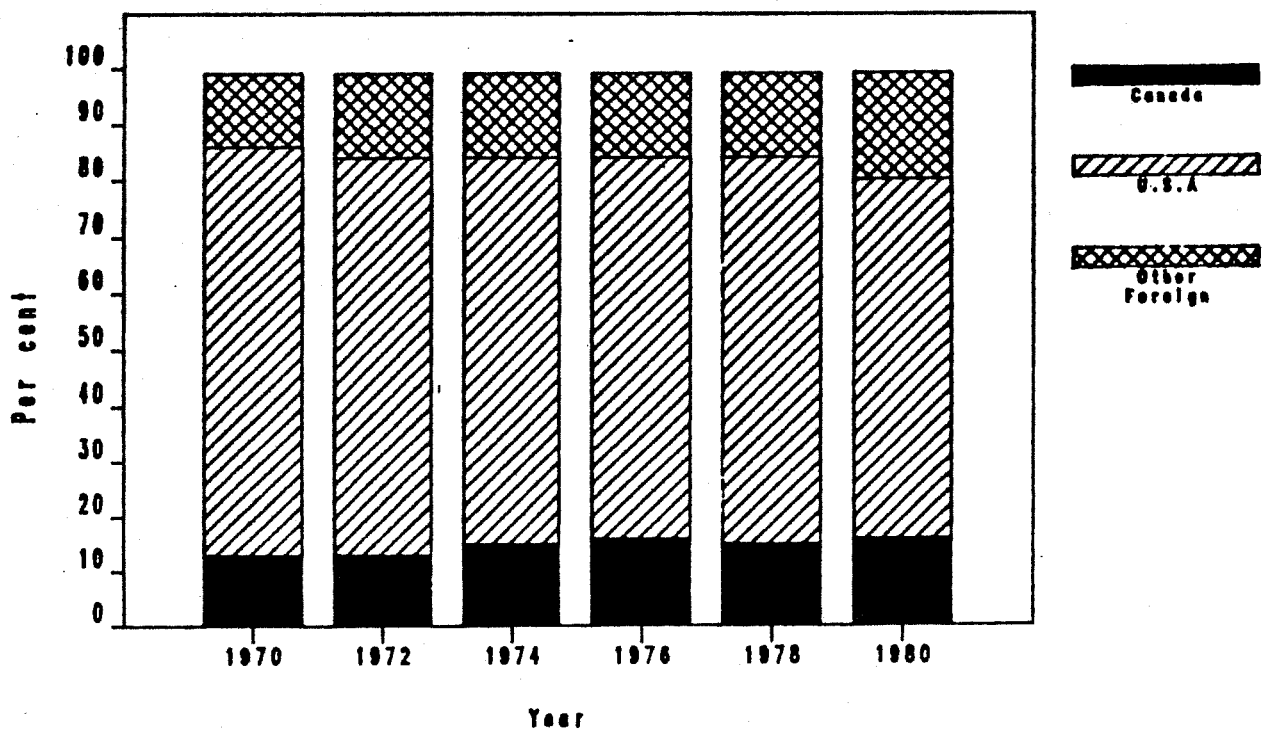
play a substantial role in the Canadian pharmaceutical market, as do firms from Switzerland, the United Kingdom, West Germany, France and Sweden. From 1970 to 1980, some 60 per cent of all enterprises in the pharmaceutical industry were Canadian owned. However, these Canadian-owned firms accounted for less than 20 per cent of overall employment in the industry and produced less than 16 per cent of the value of factory shipments. On the other hand, there appears to be small growth in the relevant share of value of shipments by Canadian firms.[10]

Over the period 1967 to 1982, total expenditures on intramural R and D (defined as the sum of current intramural plus capital expenditures on R and D) by the pharmaceutical industry in Canada has been in the range of 3.5 to 4.8 percent of world sales.[11] For other comparable industrialized nations, this ratio is moderately higher than that for Canada. For example, in the U.S. it is 7-8 percent, in West Germany it is close to 12 percent, in Japan it is 8 percent, in Switzerland 9-10 percent and in Italy, 6-7 percent.[12] See Appendix A for data figures on Canadian R and D expenditures.

In attempting to explain the relatively minor amount of R and D performed in Canada, one can examine the level of foreign ownership present. Although the degree to which pharmaceutical firms allocate resources to R and D differs from country to country, it is clear that these expenditures are higher for those countries that host the headquarters for these firms. For example, of the largest 20 companies operating in Canada, all are foreign-owned, none have headquarters in this country, yet they control more than two-thirds of

the total domestic market and do relatively little R and D, of which most falls into the category of clinical testing and packaging.[13] Thus, Canadian pharmaceutical production, which accounts for 1.5 to 2 percent of world sales, is dominated by multi-national firms, which supply 85 percent of the drugs purchased in Canada.[14] The following chart as determined by Statistics Canada through an examination of the distribution of voting shares of companies depicts the above impact on the proportion of the value of factory shipments between Canada and other countries.

Proportion of value of Factory Shipments in the Pharmaceutical Industry by Ownership of Enterprise: Canada, 1970-80



Sources: Statistics Canada, Domestic and Foreign Control: Manufacturing Industries (Catalogue 31-401).

Canada constitutes a negligible force in basic research in the world-wide pharmaceutical industry. United States firms dominate the Canadian market, and do 85 percent of their research in the United States, while most of the rest is done in the United Kingdom, West Germany and France.[15] The level of foreign ownership provides one important explanation for the low level of R and D performed, while other factors could include: tax incentives, level of subsidies and grants provided, government and market tolerance of high prices, and support of relevant science in universities and institutes.[16] Finally, as long as the foreign firms could operate in Canada with a strong patent position, there has been little incentive, by these firms, to establish manufacturing plants or to do more R and D in Canada.

1.1.2 Transfer Pricing

As was outlined earlier, high prices for ethical drugs charged to consumers prompted the investigations into the industry. Transfer pricing provides one explanation to why prices for ethical drugs are so high. Since world-scale firms supply their subsidiary plants, payments are made between any subsidiary and its parent. These inter-firm payments or transfer pricing will pass through to countries that offer the company lower tax rates or complete exemptions. This provides the incentive for firms to inflate prices charged to subsidiaries. It also gives a legitimate account of pricing needed for drug formularies in each province. Transfer pricing is in no way as simple an operation as described above. Although two of the major criteria we mentioned (branches in at least two jurisdic-

tions and differences in tax rates between at least two jurisdictions) are essential, the multinational firm must consider a number of other factors before determining whether or not transfer price manipulation pays. They include: revenue recognition rules, provincial or local taxes, rates of customs duties, foreign tax credit arrangements, tax treaty provisions, legal limitations on transfer pricing, special incentives such as tax exemptions for new plants, currency controls or similar restrictions on profit repatriation, and rules concerning charges for management fees and R and D services. Trade statistics indicate that an increasing proportion of Canada's drug imports come from other jurisdictions. Thus, whatever factors from the above criteria come into play, we can affirm that in some cases it pays multinationals to lower transfer prices and in others to raise transfer prices in order to shift profits in or out of Canada. Even so, it is not certain how much Canada will lose in tax revenues from such practices as compared to the gain in consumer surplus from our present policies on price sensitivity. Since the decision is so complicated it is by no means clear that a small increase in incentives, however provided, will be sufficient to bring about any great increase in the volume of drug manufacturing in Canada.[17] Nevertheless, a sample of 14 major drugs in Canada revealed that transfer prices were more than three times higher than prices paid for the same drugs in the open market.[18] This affects the way in which profits are reported in Canada and makes it more difficult to employ statistical series based on Canadian data.

1.2 COMPULSORY LICENSING

R and D expenditure levels in Canada, along with Compulsory Licensing as incorporated in the Patent Act, are the main subject of analysis in this paper. The Canadian Patent Act of 1969 provided innovators with a patent term of 17 years exclusivity on their discoveries. The patent applied strictly to the process for manufacturing the active drug ingredient in the product and were not granted on the finished product, the material content or purpose itself. Without going into an analysis of government objectives or general purpose of patents, it is sufficient to say that this type of protection is considered not to be exclusive enough. One reason is that it does not restrict others from making the product by another process thereby deterring the patent holder from excluding potential competition from his market to an extent unwarranted by public interest. This policy has been criticized for encouraging inventing around existing process patents producing 'me-too' drugs of no better quality or usefulness as originally intended by the legislation. It is argued that this accomplishes nothing other than a waste of resources in the effort to extinguish as many processes to a drug as possible while trying to corner a particular product market. There is evidence in countries such as Poland, Argentina, Mexico and India, that this form of patent protection has encouraged the development and growth of local firms. Although Canada is a country which provides for special patent treatment for food and pharmaceutical products like that described above, process patents were later mixed with compulsory licenses as an intrinsic part of a structure of patent protection designed to induce

the appropriate amount of innovation while protecting consumer interests in the market place. Unfortunately, this excludes most industrialized nations of the world. Countries which provide a longer patent period and more specific product protection for the chemical compound itself include the United States, the United Kingdom, France, Switzerland, Italy and Spain.[19]

In 1969, the Patent Act was amended to provide for the compulsory issue of licenses that would permit copies of the patent holder's active drug or finished product to be imported and marketed in Canada. The license allows generic firms to produce copies of patented drugs without incurring the cost of any research themselves. Significantly, the legislation did not specify when a license could be granted, so there was no guaranteed period of monopoly pricing for the patent holder. However, a 4% royalty is payable to the patent holder to help recoup this cost.

The drugs are then sold in Canada with the provision that a royalty fee be paid to the patent holder. Some countries have special conditions for the pharmaceutical industry, such as price controls, profit limits, or else special provisions which exclude pharmaceutical products from patent coverage; but Canada is said to be the only country in the industrialized world to use such a licensing system.

It should be noted that this royalty fee has, in practice, always been set by the Commissioner of Patents at the four percent level, without any explanation as to why this level was chosen. Four percent is near to the portion of sales traditionally spent on R and D by these firms, so that this might be the explanation. Perhaps, it may

have been selected because it is the rate often agreed upon voluntarily by firms for non-compulsory licenses.[20]

The foreign firms operating in Canada have argued that since the Patent Act changes were made in 1969, the Canadian government has created a hostile environment for them and is in fact discouraging R and D spending in this country. It is claimed that a 4 percent royalty fee is quite inadequate to justify the huge expenses incurred in discovering, developing and bringing a new drug product to the market. This is not easy to resolve because Canada constitutes, on average, about 2 percent of the world market implying that a 'fair' royalty rate might be based on that. In any case, the firms are not arguing for a higher royalty rate, but for an extended period of patent monopoly. On a normative point of fairness, the compulsory licensing approach has resulted in the argument that Canada is less than eager to welcome investment in the pharmaceutical industry.

However, Canada's approach does not prohibit multinational firms from using the 'generic' subsidiaries they control (mainly in the U.S. where they account for the bulk of generic sales) from entering Canada by means of taking out compulsory licenses on brand name products sold by competitors. The 1969 law, therefore, seems to be neutral in that it does not discriminate against foreign investment. There are also no restrictions against the use of market tactics to delay the application for a license by which time it might not be as profitable for a generic firm to follow through and market the drug. Here the Act provides rules by which the license may be revoked if the Commissioner of licenses feels that a Licensee has had adequate

time, usually around 3 years, to produce and market the drug.

The Pharmaceutical Manufacturers Association of Canada (PMAC) in its submission to the inquiry on the pharmaceutical industry contended that "under the present negative patent climate in Canada, they are unable to compete with the licensed imports and still justify large investment in R and D."[21] Additionally, PMAC feels that the 1969 changes to the Patent Act are an "attack on the fundamental rights of scientific researchers" and that this is a "clear case of discrimination....."[22] Other interest groups have claimed that the real purpose of this claim is to remove Canada's functioning example of a practical policy for this industry before it becomes a precedent for other countries to copy. For example, the Consumers Association of Canada argued on a number of occasions that the investment argument was part of a vigorous lobbying effort by the firms. The Association states: "multinationals are mounting an incredibly heavy lobby to get rid of Section 41 of the Patent Act" and that "it's the most superbly orchestrated lobby campaign....., they've hired consultants, gone to the provinces, universities...., anyone they could possibly use to make it look like the sky is falling in."[23]

In 1984, the Federal government appointed Dr. Harry Eastman to head a commission of inquiry into the pharmaceutical industry.[24] After careful study on the industry, Eastman concluded that "aggregated data for the pharmaceutical industry in Canada does not show adverse effects from the introduction of compulsory licensing to import in 1969."[25] He also concluded that "compulsory licensing has had no visible effect on the profitability of the pharmaceutical

industry in Canada."[26]

The PMAC, which represents the major foreign firms operating in Canada, still feels that the changes made to the Patent Act have encouraged negative effects on the level of investment performed in this country. However, Eastman concluded that the present Patent Act has not had a substantial negative effect on the profitability of Canadian innovation because such research activities are undertaken to develop new products for sale on the world market and not simply in Canada. More specifically, Eastman argues:

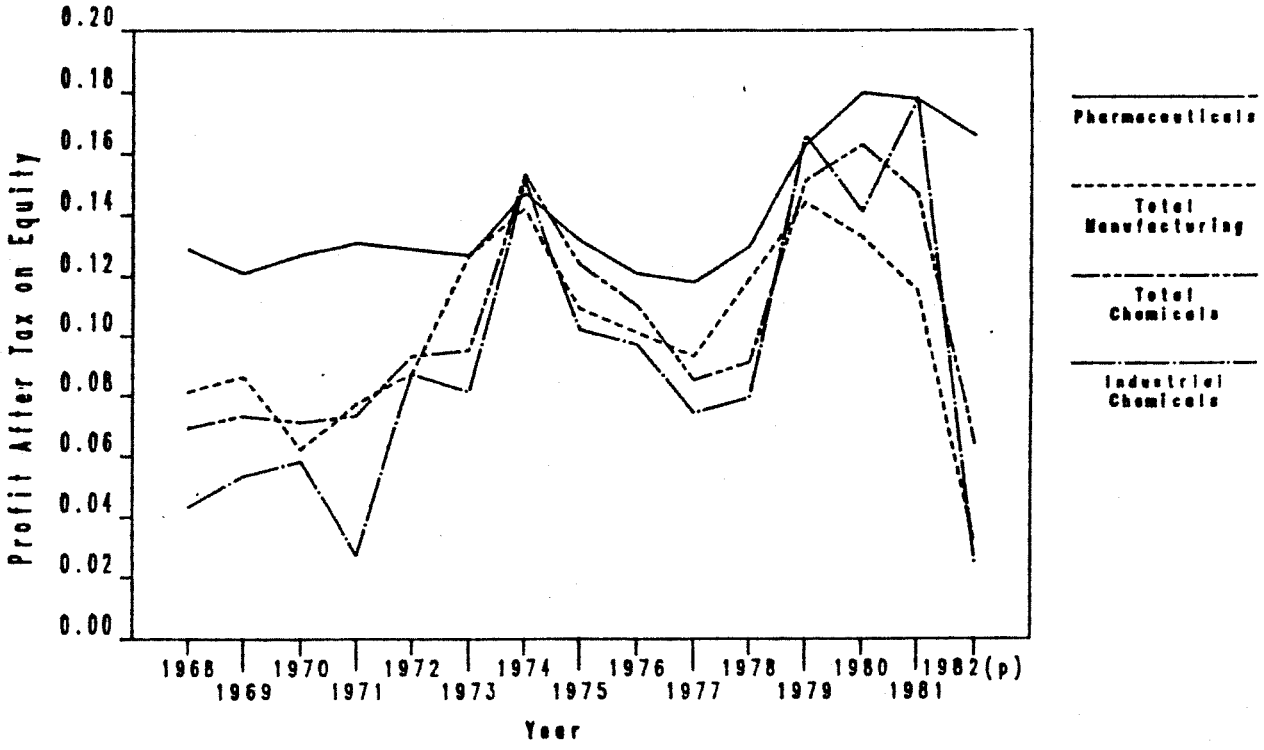
> New drug discovery is a risky enterprise for a multinational firm, but investing in Canada is not. The multinational firm sells in Canada drugs that have been developed for the world market. The costs of research and the profit from discovery are recovered in the transfer price, the royalty, or the charges for research paid by the Canadian subsidiary to the parent firm. The profits of the Canadian subsidiary itself reflect only a return on manufacturing the final dosage form and on a selling function which is not especially risky and does not justify exceptionally high profits.[27]

In determining profit rates for the pharmaceutical industry in Canada, several measures can be employed. For our purposes it is useful to look at after-tax profits on equity. By examining the following chart based on Statistics Canada catalogue 61-207 on profits for the years 1968 to 1982, the trend appears to have been maintained at a consistent level. The actual profit rates are within the 12 to 18 percent range. This trend seems to indicate that profitability in the pharmaceutical industry was high and relatively stable over the entire period from 1968 to 1982.[28]

Compared to other industries, the profitability of pharmaceuticals clearly exceeds that of other manufacturing industries who are

in the more fluctuating neighbourhood of 2 to 14 percent.[29] Consideration of the available evidence does not permit the conclusion that profits were harmed by the 1969 Patent Act amendments.

Profit After Tax on Equity, Comparison of Pharmaceutical Industry to Selected Other Industries: Canada, 1968-82



Source: Statistics Canada, Corporations Financial Statistics (Catalogue 61-207).

Without making a hasty inference about the 1969 amendments, profits are the result of a wide variety of complex factors. Hypothetically, a negative relationship between profits and compulsory licensing to import might well have been expected had not a number of offsetting positive influences on profits not occurred. For example, the steady growth in the coverage of the population by third-party (private and government) pharmicare insurance, or the steady growth of the portion of the population aged 65 or more, who are known to have disproportionately high levels of consumption of pharmaceutical products. Since the changes to the Patent Act were specific to the Pharmaceutical industry, any major impact on profitability associated with these changes should be indicated (ceteris paribus) by the comparison of profitability in pharmaceuticals to those in the other industries. Accordingly, without a comprehensive analysis of all the factors that influence profitability, it is not possible to infer from the information on comparative levels of profit that the 1969 amendments resulted in lower relative profits for manufacturers of pharmaceuticals and medicines.

However, the Eastman Commission was asked to recommend ways of increasing R and D expenditures in Canada, whether or not the 1969 Patent Act was inhibiting. Thus, the Commission recommended an adaptation of the existing policy by legislating a period of exclusivity of four years and increasing royalties to provide a pool of funds to reward firms doing research in Canada. The proposal was suggested as a means of trying to encourage more R and D in this country.[30]

2.0 HYPOTHESIS

The main thrust of this report is to investigate the validity of the claim made by the pharmaceutical firms operating in Canada, that the introduction of the Patent Act in 1969 has been a deterrent to the amount of research and development they perform within Canada. In fact, any evaluation of the patent act amendments would be incomplete if no attention was paid to its effect on such indicators of industry performance as research and development, prices, profits, or even advertising. Not only was the Harley Committee, as discussed earlier, concerned about some of these impacts, but the patentees, through their trade association, the PMAC, have made presentations to government alleging that section 41(4) and concomitant policies described in the Patent Act, have had adverse affects on industry performance. An assessment of these effects is thus necessary in order to make any judgement as to the overall impact of the 1969 changes.

One can already see from the material presented so far that a lively debate has been and is continuing in Canada over the subject of research and development. Tantamount with this are issues concerning the influence of foreign ownership, the 'low' level of R and D, government incentive policies, and the level of industry profits. All of the above have been discussed and possess many related aspects to the Patent Act and are for this reason suitable for measuring the impact of the 1969 amendments. However, when one pursues the endeavor more closely one finds that some are more appropriate for analysis than others for reasons already mentioned and to be discussed below.

The drug industry is generally recognized as one of the most

research intensive of all manufacturing industries. Hence, if the 1969 changes have adversely affected the level of research and development, then this is likely to show up in the determinants of the level of R and D. One such variable is profits. Since, it is plausible that profits may be the result of successful R and D. Conversely, if profits are high more funds may then be available for R and D.

Profits serve as one of the principle indicators of market performance. This is true both at the level of the individual firm as well as for the industry. For the firm, profits relative to the industry average are probably the best indicator of the performance of that firm and its employees. If profits are consistently high, it is usually possible to attribute them to performance and planning rather than to chance. However, profits are usually influenced by a wide variety of factors not necessarily under the control of firms. Excessively high or low profit levels may be more indicative of the failure or success of government policies than of the collective success of individual firms. Similarly, high or low profits may reflect short-run market conditions as opposed to long-run conditions and thus will not trigger the otherwise expected entry or exit of firms from the industry. High or low profits may reflect relatively high or low degrees of risk within a industry, demand side factors, or the degree of protection and/or subsidies that are afforded firms as a result of what are usually complex and comprehensive government policies within which an industry must operate. Accordingly, some of these variables, such as various market conditions, are extremely difficult to quantify as determinants for profits.

The relationship between profits and R and D, however, is more direct. The only complexities encountered here is the lack of precise information on the profits of pharmaceutical firms related directly to the sale of ethical products in contrast to profits related to proprietary drugs and the wide variety of other commodities produced by these firms such as toiletries, personal care goods, chemicals, and so on. Related to the first problem, is the shifting number of firms that are said to be manufacturers of pharmaceuticals and medicines. In allocating firms to a particular industry class, Statistics Canada follows the criterion of allocating a firm to the industry according to which products account for the largest percentage of a firm's sales in a particular year. Though Statistics Canada attempts to avoid rapid shifts in classification from one year to the next, it is possible that some technical shifts have occurred. Accordingly, the annual estimates of profit do not in every year apply to a consistent set of firms. As a result of the above ambiguities, and due to the specific allegations by the PMAC for more favourable legislation in order to stimulate, not 'profits' directly, but more investment and research, the 1969 amendments are likely to have a more significant effect on R and D than any other determinant variable. Specifically, the PMAC argues on behalf of the industry, that since its introduction in 1969, the Patent Act has significantly reduced the amount of dollars spent by them on R and D. They feel that "companies operating in Canada have retrenched the growth of their research" and "some have decided to import their finished products instead of manufacturing."[31]

Attention is now confined specifically to the influence of compulsory licensing as incorporated in the 1969 Patent Act amendments on R and D activity in Canada. Clearly, compulsory licensing is not an incentive to conduct R and D. Studies for countries with major R and D programmes suggest that if patent protection were seriously eroded, R and D would fall significantly.[32] Several reports suggest that compulsory licensing is a disadvantage when the Canadian subsidiary is competing for investment funds from the parent firm and has led to reduced R and D in Canada. For example, the OECD (1977, p.218) commented that section 41(4) "...may well be significant...," while a federal Department of Industry, Trade and Commerce (1979b, p.19) study on R and D in the health care products sector commented "...there is some evidence that it has contributed to the decline in international drug companies' R & D in Canada..." This latter study also notes that regulatory requirements in Canada "...constitute a substantial impediment to more R & D being carried out in Canada." In neither case, however, is hard evidence cited to substantiate the view that compulsory licensing to import has led to a decline in R and D.

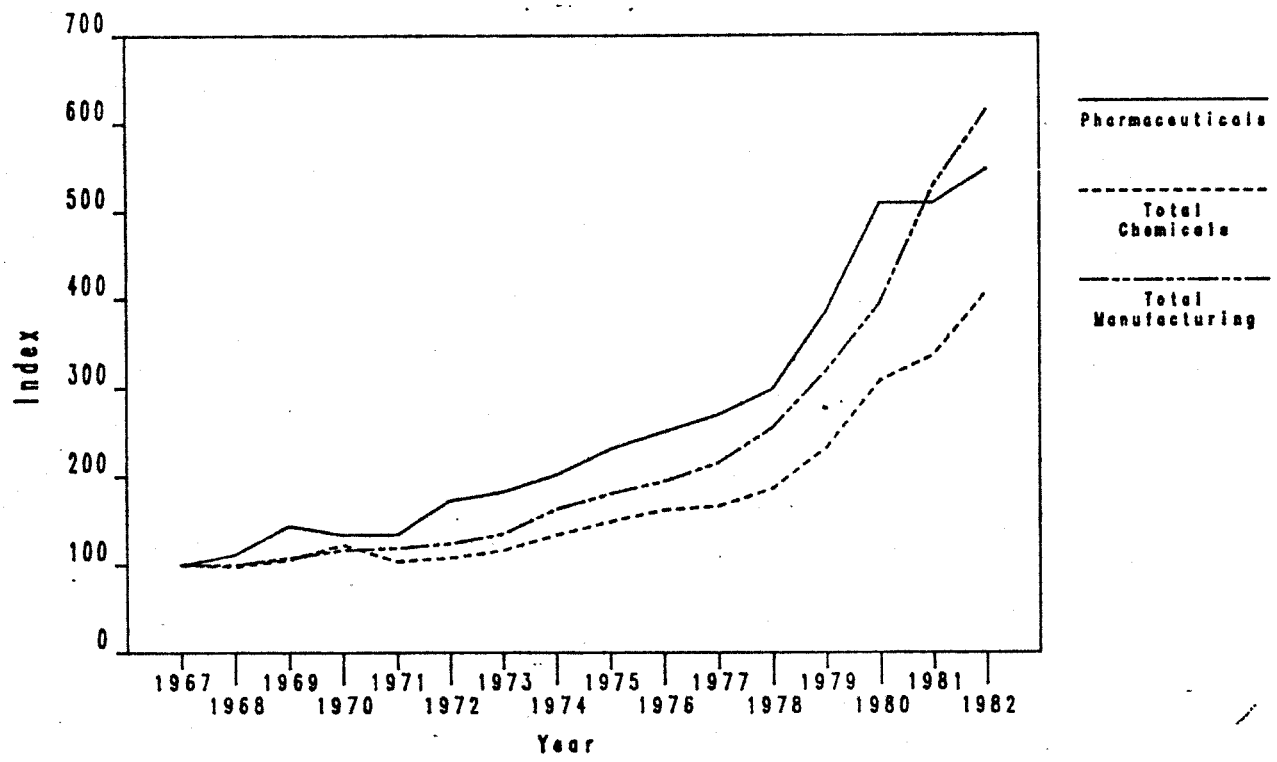
Comparing R and D levels in Canada to that in the U.S. provides an alternative framework for considering the 'reasonableness' of R and D levels in the pharmaceutical industry in Canada. In particular, differences in the trends of these levels can likely be more directly related to Canada's 1969 change in the Patent Act rather than to either broad changes in the economy or to the market for pharmaceuticals. Though a detailed comparison of the nature of the market

between the U.S. and Canada has not been attempted, there are similarities and differences to contend with. In both countries we find the number of persons aged 65 and over to be steadily growing. However, the returns to R and D investment fell dramatically in the U.S. during the mid and late 1960's and 1970's compared to alternative investments and the rates of return experienced in the early 60's.[33] This fall in the rate of return was also caused by similar and separate factors; the stringent regulatory requirements imposed on new drugs because of the 1962 amendments to the Food, Drug and Cosmetic Act, incited by the Kefauver commission we mentioned earlier, and the depletion of research opportunities, a worldwide phenomenon.[34] As a result, U.S. multinational firms, in response to the above factors, have substantially increased R and D expenditures abroad since the early 1970's.[35] One would not expect Canada to capture a significant share of this R and D investment for two main reasons. First, one of the major factors causing the change in location of U.S. investment was the 1962 amendments regarding drug safety and efficacy. Canada has a system very similar if not more stringent than that in the U.S.[36] Second, it seems that much of the R and D investment abroad by U.S. firms is in setting up a second major research center. As discussed previously, these have not been sited in Canada but in countries with more favourable tax incentives such as the United Kingdom, which also have less stringent, though not necessarily less adequate, regulatory systems for screening new drugs. The above discussion of the factors, both general and those relating to compulsory licensing as incorporated in the Patent Act amendments, influencing

the level of R and D expenditures in Canada leads to the inference that such expenditures may well have declined due in part, to the 1969 changes, but also due to the regulatory procedures for establishing the safety and efficacy of new drugs.

There are however, comparisons of the level of R and D between the pharmaceutical and other industries in Canada. A look at the following chart provides an alternative to evaluating the level of R and D levels in the pharmaceutical industry. Specifically, we find that from 1967 to 1982, the level of total intramural R and D (defined as the sum of current intramural plus capital expenditures on research and development) by pharmaceuticals was consistently higher than that for total chemicals or total manufacturing industries. From the information presented in the chart, it is difficult to detect a major change in the trend that could be associated with the date of any impact of changes in compulsory licensing. The trend for pharmaceuticals is clearly similar to that for all chemicals and all manufacturing. These are strictly level comparisons and do not represent any further knowledge into the explanation for these levels or the relationship between the 1969 amendments and R and D levels.

Index of Total Intramural Research and Development Expenditures in the Pharmaceutical Industry and Selected other Industries: Canada, 1967-82
(1967=100)



Source: Statistics Canada, Industrial Research and Development Statistics of Science and Technology Statistics Division., 1985 (Catalogue 88-202).

A survey of the available data explaining R and D expenditure in Canada was made from the period 1959 to 1984. Four econometric models were formulated to determine the impact of the Patent Act on the level of this type of investment performed in this country by the pharmaceutical industry. The models are of the following form:

(1) R AND D = BO + B1[SALES + SALES(-1)] + B2[PROFIT + PROFIT(-1)] + B3[D]

(2) RDS = BO + B1[SALES + SALES(-1)] + B2[PROFIT + PROFIT(-1)] + +B3[D] + B4[CFM] + B5[POPN] +B6[POPSC]

(3) R AND D = BO + B1[SALES + SALES(-1)] + B2[PROFIT + PROFIT(-1)] + B3[D] + B4[R AND D(-1)]

(4) R AND D = BO + B1[SALES + SALES(-1)] + B2[PROFIT + PROFIT(-1)] + B3[D]

where:

R AND D, is the dependent variable research and development.
R AND D(-1), is research and development from the previous year.
B0, B1, B2, and B3, are the parameter coefficients.
SALE, is aggregate sales of pharmacies.
SALE(-1), is lagged sales of one year.
PROFIT, is net profit of pharmaceuticals.
PROFIT(-1), is lagged net profit of one year.
D, is the dummy variable to incorporate govt. legislation.
CFM, is the Cash Flow Margin defined in section 2.1.
POPN, is annual population figures for Canada as a whole.
POPSC, is the population of senior citizens aged 65 and over.

Note: model (4) remained the same as model (1) at the estimation stage, but the D variable was suppressed at the simulation stage.

The above models were formulated to test the hypothesis of whether or not the Patent Act amendments of 1969 imposed negative effects upon the level of R and D expenditure, as claimed by the pharmaceutical firms operating in this country. Models (2), (3) and (4) were slightly modified from model (1) to allow for other effects to be tested and incorporated into the analysis, such as, past R and D expenditure levels and population growth to be discussed

in the following section.

Other plausible explanatory variables could have included: past R and D success in so called "breakthrough" drugs in which investment becomes concentrated around "molecule manipulation" of highly promotable compounds. This obviously weakens the purpose of patents on these drugs which allow for this sort of chemical alteration and ultimate loss of long-run profitability used to finance investment in this type of innovation. As a measure to embrace the above phenomenon of questionable health payoff in "me-too" products and to check the rising costs of drugs, compulsory licenses have also claimed and received extensive study as to their affect on R and D. Specifically, as mentioned earlier, the acquisition of these licenses by less research intensive companies and the reimbursement of inadequately low royalties as claimed by the patent holders should theoretically lower the amount of R and D pursued in subsequent years. Another commonly used indicator of R and D expenditure is the number of qualified scientists and engineers engaged in R and D as a percentage of total employment. Obviously, if this ratio rises it is suspected that R and D is on the increase. Firm diversification level, and government legislation, such as allowances for taxes and incentives or more stringent testing regulations which deters innovation by increasing the cost to develop and market drugs are other possible variables. Although many of these may play a role, they are extremely difficult to model due to the unavailability of accurate and comprehensive data. The following is a more comprehensive analysis of the variables chosen.

2.1 ANALYSIS OF DATA

2.1.1 RD (Research and Development)

The data used in the formulation of R and D over the period 1959 to 1984 were obtained from Statistics Canada catalogue numbers 13-203, 13-401, 13-516, 13-520, 88-001 88-202, and 88-509. Statistics Canada has collected data on R and D for Canadian industries since the early 1950's. The data reported are generally by the company or enterprise, in this case, drugs and medicine outlets.

One problem with a study of this type is to ensure that the quality and accuracy of the data used is satisfactory so as to render the survey meaningful. One cannot expect that all firms engaging in R and D activities will be surveyed or that they will report accurately. As such, the survey cannot be complete. Another problem deals with the classification of R and D data by industry. Since a company can only be assigned to one industry there may be leakages and overall misallocations of the relevant information if the companies have establishments or subsidiaries in several related industries. Because industrial R and D is highly confidential, the use of the company/enterprise as the main reporting unit also means that classification cannot be very detailed in order to preserve classified company data. Also, R and D is a term that is subject to individual interpretation and is, therefore, difficult to define. For example, what the federal government classifies as R and D regarding a contract to industry may not be reported as such by the contractors and subcontractors as drugs are passed on to other stages before they reach final dosage form. Section 37, of Regulation 2900 of the Income

Tax Act specifically excludes some activities as R and D, which represents another area of concern. With specific regard to the practices of some pharmaceuticals mentioned earlier, R and D does not include (i) market research, sales promotion, (ii) quality control or routine analysis and testing of materials, devices or products destined for market. The technical definition of R and D used by Statistics Canada is a "systematic investigation carried out in the natural and engineering sciences by means of experiment or analysis to achieve a scientific or commercial advance..., which is not known in advance on the basis of current knowledge or experience but can include technical improvements to a product or process on the same grounds as above."[37] As discussed earlier, Canada has been rather lenient in enforcing this latter definition resulting in much R and D activity falling under the former categories above. Although other definitions are not exactly the same, resulting in the manipulative practices discussed above, those used by Revenue Canada or other countries are very similar in terms of the scope and spirit they try to embrace. With this in mind the R and D data reported is Total Intramural R and D expenditure by industry in millions of constant dollars. Intramural R and D encompasses all expenditures for R and D work performed within the reporting company, regardless of the source of funds. This type of data was the most readily available and consistent. In the period 1972 to 1976, of total current R and D expenditures by firms classified to industry 374, 79 to 81 percent were classified as intramural. In addition, intramural expenditures are most accurate in capturing trend activity.

Finally, the data collected were yearly, in millions of constant dollars from the years 1959 to 1984. It is not difficult to understand the importance of using constant data figures in the evaluation of R and D activities and for the determination of appropriate economic policy towards technological change. However, using R and D deflators such as the GDP or GNE would lead to the problem of over or under-estimating the percentage increase in real R and D expenditures across industries. For example, using the GNE deflator, real total industrial R and D expenditures from 1963 to 1980 increased by 193%; but using R and D deflators, the percentage increase was 97% or one half the magnitude calculated by the GNE deflator. This is because the GNE deflator is a price index for output reflecting the rate of increase in input prices, the cost shares of inputs, productivity growth and scale economies, while the R and D deflator is an index for single inputs whose price increase represents only a fraction of the total cost. There is also the need to measure real R and D as an index other than mere price inflation since the result of R and D activities accumulates over years and forms a stock of knowledge or R and D capital.[38] Eight types of R and D expenditures were used: wages and salaries, current and total costs, land and building costs, equipment costs and total capital costs. After multiplying each group by its share out of total R and D expenditures or the appropriate Paasche price index the sum of these weighted input indexes yield the Paasche R and D expenditure price index, which was then used to deflate raw total R and D figures into constant dollars. In this way we can determine that either R and D activities are expanding or that

the same level of activity merely costs more to undertake. There also exists preliminary estimates for R and D to 1989, but these values have not been revised and were not used for this reason.

2.1.2 SALES

Sales figures were obtained from Statistics Canada, catalogue number 63-005. The statistics collected were monthly Total Net Sales of Pharmacies, Drugs, Patent Medicines and or Cosmetic stores from the years 1959 to December 1984. Total net sales include sales of merchandise and receipts from related services, such as any commissions earned from sales of goods. Given the worldwide nature of the markets for pharmaceutical products and in particular the reliance of firms on the sales of a fairly small number of products, it is perhaps to be expected that the industry is characterized by a relatively high level of sales promotion activities. As is profit a good indicator of industry performance, sales are in the same fashion related to R and D. However, although a given increase in sales might imply an increase in R and D, this inference must be qualified by the various decisions firms must consider, such as manpower allocated to sales, marketing, advertising and other promotional activities.

Finally, sales data were the only series listed monthly while all other series used were reported yearly. As such, the monthly sales data were summed into yearly figures, in order to ensure that all series were consistent.

2.1.3 PROFITS

Data used to obtain profit figures came from Statistics Canada catalogue numbers 61-207, 61-003, and from the department of National

Revenue Taxation Statistics, catalogue RV68 T17. Data obtained were from Corporation Financial Statistics from the years 1959 to 1984, for Pharmaceuticals in millions of constant dollars. The data came from financial statements of corporations filed with T-2 corporation income tax returns.

Net profit figures were used, defined to be the amount of income remaining after all expenses and provisions, including income taxes, had been deducted. This does not include subsidiary profits or losses or the interest expense of income debentures.

There is some evidence (usually discovered through audits) that this industry is exceptional in its use of transfer pricing in order to have income declared by affiliated subsidiaries or parent companies which are located in jurisdictions that have low tax rates.[39] If this activity is wide spread, the series which reports Canadian profits may be less reliable. Statistical analysis usually makes use of changes (especially deviations from averages) and, while the effects of mis-reporting is by no means certain, regression analysis may still be able to capture the effects we wish to examine. On the face of it, the incentive to use transfer prices (in an industry which has been profitable throughout) should be independent of the change in the law which took place in 1969. Based on the above and on the previous section profits may, therefore, still be a useful variable, certainly more useful than a statistical analysis which had to make sure that the level of profits reported were very accurate.

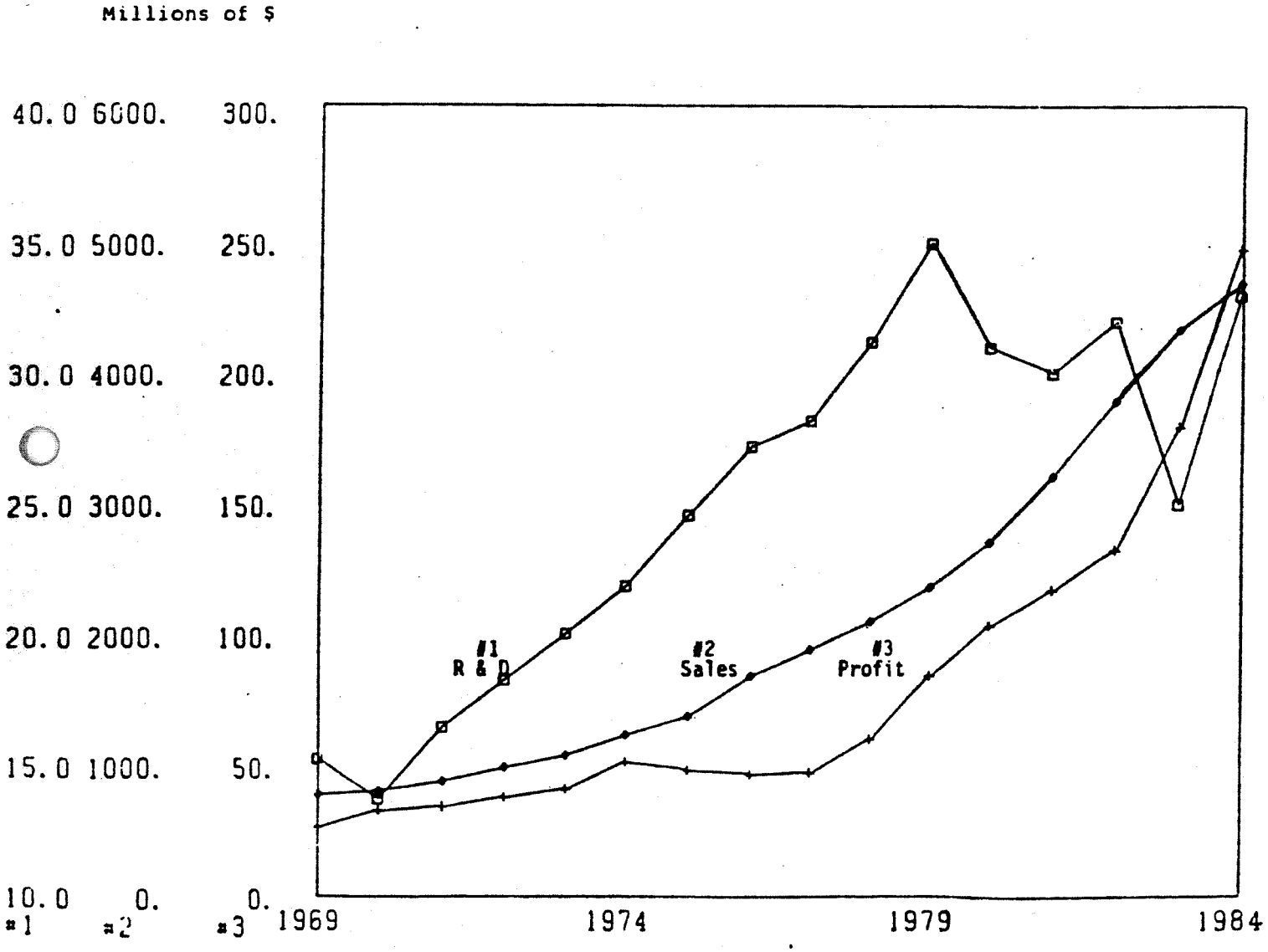
To view the graphical representation of these series, see Figure 1.

2.1.4 DUMMY VARIABLE

Indicator or Dummy variables are often used in the modelling of unmeasurable or qualitative factors. In the context of this analysis, government policy, such as the changes made to the Patent Act in 1969, fall under the heading of qualitative variable. In order to capture the full effects of the changes, a dummy variable, D, was introduced. Formation of the model with D equal to 0 prior 1969, and D equal to 1 in 1969 and after offers an appropriate solution.

Figure 1

Plot of R and D, Sales, Profit



2.1.5 CFM (Cash Flow Margin)

This variable was employed in model (2) and is of the following form:

$$CFM = \frac{PROFIT(-1) + DEP(-1)}{SALES(-1)}$$

where DEP are depreciation figures from the years 1959 to 1984. This variable includes current amounts charged as depreciation on pharmaceuticals income statements. Data were obtained from Statistics Canada Catalogues NR-20T38, 61-207 and 61-003, as well as from catalogue RV68 T17 of the National Revenue Taxation Statistics. The variables PROFIT and SALES remained as above.

2.1.6 POPN (Population)

This variable was also used in model (2) and represents annual population figures of all age groups in Canada from the period 1959 to 1984. Data was cross checked for most accurate figures from the World Bank Tables 1976, 1983, the Canada Year Book 1985, Historical Statistics of Canada 1983, and Statistics Canada catalogue 91-210 on Quarterly Estimates of Population for Canada and the Provinces.

2.1.7 POPSC (Population over age 65)

This variable was used in model (2) and covers data for the years 1959 to 1984. Data were obtained from Statistics Canada Catalogue 91-203. This age group represents disproportionately high levels of consumption of pharmaceutical products thus being highly sensitive to rising drug prices. With their numbers rising at a faster rate as a proportion of total population, this group will have an ever increasing effect on the drug industry in the future. Not only on the demand for ethical drugs but also on their influence in public policy concerning drug prices.

3.0 BUILDING THE MODELS AND ANALYSIS OF RESULTS

3.1 Model 1

Model (1) incorporated sales, profits and government legislation explaining the performance of the R and D sector in the pharmaceutical industry. As stated it is very difficult to isolate the main elements that affect R and D in pharmaceuticals, since there are so many possible factors to consider. The study has, therefore, only explored the most plausible factors, which may have then restricted the analysis to those explanations for which evidence is most readily available.

The explanatory variables that have been included are present and lagged sales, present and lagged profits and a dummy variable to capture the effect of the Patent Act Legislation of 1969. As discussed earlier, the body of knowledge associated with research accumulates over time so that any contribution to present R and D is likely to have been built up from previous time frames. Similarly, the decision to contribute to R and D is likely to be highly related to the performance of both previous, rather than future, sales and profit levels. Historically, R and D has always been measured as a percentage of sales implying a lag on sales would be more significant in capturing the positive relationship to R and D. This ratio is a basis for reference of R and D relative to other industries or countries since R and D could not be judged in a vacuum. However, any relation to R and D might also be influenced by previous profit levels. This might be qualified depending on long run profit stra-

tegies, or on the decision to manipulate transfer prices and so on. Although it is difficult to differentiate between the spill overs, a time lag of one year on profits and sales is sufficient to reveal any such influence. This type of a model makes use of moving averages, and is of the following form:

R AND D =B0 + B1[SALE + SALE(-1)] + B2[PROFIT + PROFIT(-1)] + B3[D]

where: R AND D is the dependent variable research and development
B0, B1, B2 and B3, are the parameter coefficients
SALE is aggregate sales of drugstores and pharmacies
SALE(-1) is lagged sales of one year
PROFIT is net profit of pharmaceuticals
PROFIT(-1) is lagged net profit of one year
D is the dummy variable to incorporate govt. legislation.

The model was estimated using ordinary least squares (OLS), which is the equivalent of looking for parameter estimates which minimize the sum of the squares of the residuals.

Table 1 summarizes the relevant figures derived from the results of our regression analysis:

Table 1
Regression Results for Model 1

Regressors	Coefficients	Standard Errors	T-Statistics
B0 (Intercept)	4.16873	1.4	2.9
B1 (Sales)	0.00613	0.0015	4.0
B2 (Profits)	-0.09513	0.0348	-2.73
B3 (1969 law)	10.63020	1.855	5.71

R-SQ=0.89 ADJ R-SQ=0.87 SSR=263.086 DW=1.409 COND=20.1

The above are the most important and significant results obtained from the research, and they are quite satisfactory by usual statistical standards. However, by observing the results more closely, the value for the Durbin-Watson coefficient DW suggests the presence of

autocorrelation and that it is of some significance. This issue will be addressed shortly with a discussion of the Cochrane-Orcutt transformation for autocorrelation.

In the above statistical exercise, results yield a coefficient on sales, B1, as a positive, small number with a highly significant t-statistic within the five percent level. As discussed, it might be expected that R and D expenditures would increase as sales increased, and this result is validated by the positive sign on B1.

The profit coefficient, B2, is negative indicating that as profits increased, R and D expenditures decreased. Theoretically, holding the profit strategy decisions mentioned above constant, the opposite results were expected with a strong positive relationship. To complicate this matter, the t-statistic is also significant at the five percent level. From our discussion earlier, the most plausible explanation for this result may be at least partially explained by the existence of transfer pricing or the low quality of the profit data reported by firms. Even if firms followed a rule relating R and D to sales or if they merely did clinical testing in Canada (to satisfy our health and in some cases R and D standards) the sign and t-statistic are perplexing.

Finally, and most important, the value obtained for B3, the dummy variable, was a significant, positive number. The dummy variable was introduced to explain whether significant detrimental effects were imposed upon R and D as a result of the new more stringent requirements of the patent act. This result suggested that B3 played a valuable role in the explanation of R and D but that the 1969 law, did

not decrease the level of R and D spending in Canada. Rather, since the 1969 patent act was introduced, R and D has increased.

Due to the moderately low value of the Durbin-Watson[40] statistic of 1.409, the Cochrane-Orcutt (C-O) procedure was used to correct for the presence of autocorrelation. The following are the transformed results:

Table 2
Regression Results for C-O Transformation

Regressors	Coefficients	Standard Errors	T-Statistics
B0 (Intercept)	49.6661	26.1329	1.9
B1 (Sales)	-0.0024	0.0023	-1.03
B2 (Profit)	0.0448	0.0334	1.34
B3 (1969 law)	2.5763	2.9916	0.86

R-SQ=0.92 ADJ R-SQ=0.91 SSR=163.2 DW=2.29 COND=4.88

The presence of autocorrelation was corrected through the Cochrane-Orcutt procedure. This procedure involves a series of iterations, each of which produced an improved estimate of the value of p (rho) used in the calculation of the DW value, than the previous one. It uses the notion that p is a correlation coefficient associated with errors of adjacent time periods. These revised parameter estimates are then substituted into the original equation, and new regression residuals are obtained. Standard procedure is to stop the iterations when the new estimates of p differ from the old ones by less than .01 or .005.

The prime difficulty with this method is that there is no guarantee that the final estimate of p will be the optimal one, in the sense of minimizing the sum of squared residuals. This may be the

case since the iterations may lead to a local rather than a global minimum.

Once the C-O transformation was applied, the value of the DW increased to 2.29. Exact interpretation of the DW statistic is difficult because the sequence of error terms depends not only on the sequence of error's but also on the sequence of all the X values. For this reason, tables are provided to indicate the possible range that the DW statistic can take. Using Pindyck and Rubinfeld's table for the Durbin-Watson test statistic we obtain an equivalent value for the DW of 1.71. This is a significant improvement since the value had moved from the inconclusive range to the rejection range.

In addition to decreasing the level of autocorrelation, the transformation improved other results as well. Associated with the improvement was a higher value of R-SQ of 0.92 where 1.0 indicates a perfect fit, lower sum of squares of residuals of 163.248 and less multicollinearity, indicated by the COND (condition number used in the Eigensystem analysis of correlation coefficients) value of 4.88. On the other hand, standard errors increased and t-statistics declined in significance, as outlined in Table 2.

The goodness of fit of a regression line to the actual data points is indicated by the R-SQ statistic. As a rule, a 'good' equation is one which helps to explain a large proportion of the variance of the dependent variable (in this case, R AND D). By definition, the R-SQ statistic must lie between the value of 0 and 1, with a value closer to 1 being the more desirable. This would indicate that a large proportion of the variance of R AND D was being explained by

the model. Model 1 has an R-SQ of 0.89, indicating good statistical results. However, the R-SQ statistic could also be increased by adding more explanatory variables to the model or by increasing their range if possible. This will not necessarily improve the performance of the model since other important statistics discussed above may have worsened. Because statistical operations are related and interact simultaneously care must be taken to review all explanatory statistics together when evaluating the results. Only in this way will changes yield the optimal model. On the whole, the transformed results proved to be better, on average, as compared to model 1 of Table 1, since in particular the level of autocorrelation had been reduced.

With respect to correlation among the explanatory variables, a high degree was present. For example, correlation between B1 and B2 was 96 percent. This result was anticipated simply because the variables chosen were somewhat related and dependent upon each other. The model can still be used with all its variables if sufficient care is given to interpretating the regression results.

Multicollinearity exists when two or more explanatory variables are highly (but not perfectly) correlated with each other. The Eigensystem analysis uses characteristic roots or eigenvalues of X'X or correlation coefficients between the regressors. One or more small eigenvalues imply that there are near linear dependencies among the independent variables. The COND or condition number is just a measure of the spread in the eigenvalues spectrum of X'X. Multicollinearity is indicated by the initial COND value. As a general rule,

multicollinearity is said to be a problem if the COND value exceeds 100. In our case, 20.146 is not large, suggesting that this potential problem is not important in this analysis. Although we may have predicted a more severe positive relationship between sales and profits, it appears that our earlier problem of transfer pricing and mis-reported data on both sales and profits seems to have caused a significant enough divergence in the figures between the two variables so as not to present a greater problem.

3.1.1 Forecasting with Model 1

The single equation regression models used in this study, were formulated with forecasting in mind. Specifically, the models were used to evaluate present values of R and D, as well as to predict future levels. The exogenous data were extrapolated beyond the period over which they were estimated, so that the information contained in them could be used to make forecasts about future events related to R and D. It is useful to distinguish between two types of forecasting: ex-post and ex-ante. Both forecasts predict values of the dependent variable, R AND D, beyond the time period in which the model is estimated (in this case, 1984).

Actual data values ended in 1984 with the result that values to 1999 were extrapolated in order to be able to forecast to the end of that period. Extrapolation calculates the average growth rate, in the sample data, and applies this same growth rate to the future, with the result that ex-ante R and D values take on a smooth growth rate pattern. The extrapolated exogenous data are listed in appendix B.

In an ex-post forecast the forecast period is such that observations on all variables are known with certainty. Ex-post forecasts can be checked against existing data and provides a means of evaluating the model. Ex-ante forecasts predict values of the dependent variable beyond the estimation period, using explanatory variables which may or may not be known with certainty.[41]

In examining the ex-post forecast simulation output for the period 1969 to 1984, it is important to the investigation that forecast values track the actual values fairly closely. That is, one would expect the results of the historical simulation to match the behavior of the real world rather closely. It is therefore desirable to have some quantitative measure of how closely individual variables track their corresponding data series. The measure that is most often used is called the Root Mean Squared (RMS) forecast error is a very important statistic in the evaluation of model performance. The RMS forecast error provides a measure of the ability of the model to forecast well. A model designed for forecasting purposes should have as small a forecast error as possible. In this case, the RMS forecast error is 3.24 indicating good model performance.

When a model has been designed for forecasting purposes, then the ex-post forecast error is another very important criterion for model performance. In an ex-post forecast, the forecast results are compared to recent data. The forecast error, or the simulation error computed over the forecast range, provides a measure of the ability of the model to forecast well. This is Theil's inequality coefficient or the Theil U statistic and is a useful simulation statistic that

can be applied to ex-post forecasts. Scaling of the Theil U dictates that its values should ideally fall between 0 and 1. If U is equal to 0, this indicates a perfect fit between the actual and simulated values. Conversely, if U is equal to 1, the predictive performance of the model is not very reassuring since simulated values do not follow the actual data values very closely.

In this case, the Theil U is equal to 0.98, which indicates that the model does not demonstrate the best predictive ability according to the scaling of the Theil U. A no change forecast corresponds to a Theil U=1. This indicates, therefore, that this forecast is almost equivalent to a no change, on average.

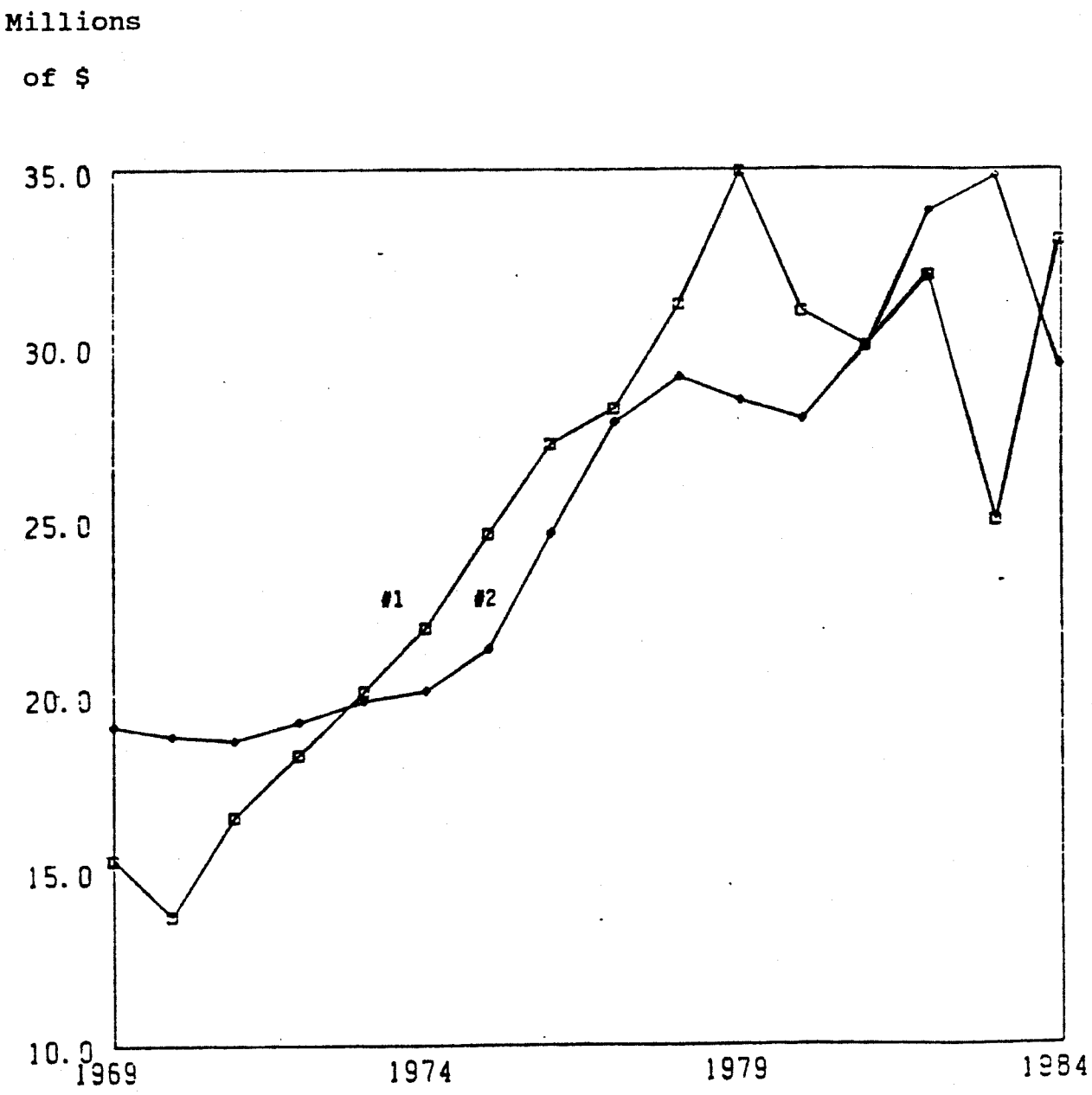
The ex-ante simulation period takes place between 1985 and 1999. For a model such as this one, a useful measure of model performance could include the standard error of forecast and a corresponding confidence interval. For this period, the Theil U statistic cannot be calculated because extrapolated data is used.

By inspecting Figure 2, one can clearly see considerable fluctuation between forecasted and actual values of R and D. The intertwining levels present a confusing picture as to the impact of the 1969 amendments on R and D. Prior to 1973 and between 1981 and 1983, forecasted values are greater than actual values meaning the 1969 changes did not adversely affect R and D. Between 1973 and 1981, the opposite results are deduced. This may be associated with the inherent practices of the pharmaceutical industry, such as long run profit strategy or transfer pricing, as reflected in the data. It may also be due to technical problems with the model itself. Such as the stipulation

of the parameters or with the indices applied to R and D figures. Nevertheless, both levels of R and D show a rising trend above that of 1969, which does not permit the claim made by the P.M.A.C that the 1969 Patent Act changes have reduced the level of R and D investment.

Figure 2

Actual to Forecasted R and D (Model 1)



#1 Actual R and D

#2 Forecasted R and D

3.2 Grabowski and Vernon, 1983

In surveying the available literature on this topic, the study of the U.S. pharmaceutical industry by Grabowski and Vernon (1983) was employed for comparative purposes due to the global nature of the industry.[42] In their study, Grabowski and Vernon formulated an econometric model for the U.S. market as a measure of R and D performance.

The model is of the following form:

$$RDSit = f\{ NRit, DVRi, CFMit, PCit \}$$

where:

RDSit, is research and development expenditures divided by sales for the ith firm in year t.
NRit, is an index of past R and D success for the ith firm in year t. More precisely, it equals sales of firms new products during the first three years of the product's commercial life divided by R and D expenditure in year t-2.
CFMit, is the cash flow margin for the ith firm in year t, in particular, lagged profits after taxes plus depreciation divided by sales.
DVRi, is a Herfindhal-type index of the ith firms level of diversification that equals 1-E(sj) where Sj is the fraction of firms ethical drug sales in the jth class.
PCit, is the percentage of ith firms total sales accounted for by ethical drug sales in year t.[43]

The ultimate purpose of this comparison is to see if the economic variables explaining the behaviour of U.S. firms turned out to be the variables which explain industry behaviour in an economy such as Canada's which consists largely of branch plants of these same firms.

In the situation of a country such as Canada, it is often assumed that much of the economy, and in particular its industries, operate and are affected in the same manner as its counterparts in the United States. This seems to be the case due to the close proximity and similarities between the two countries resulting in the great deal of

interaction that takes place between them. In devising an appropriate model for the Canadian industry, many of the above U.S. variables did not apply. For example, the NR variable takes into account new product sales as an index of past R and D success. However, since many of these products would first be introduced in the home country, and since the Canadian market is only about two percent of the world market, such data is neither readily available or meaningful. Also, the variable DVR did not play a large role since the firms diversification level would again not apply to Canada due to the nature of our 'branch plant' industry. Although the above factors accounted for some of the inability to use the Grabowski-Vernon model, it was the unavailability of comparable Canadian data which proved to be the chief inhibiting factor.

3.2.1 MODEL 2

Thus, the above version of the Grabowski-Vernon model was not employed for this study, with the result that model 2 was created incorporating two of the variables, RDS and CFM. Both of these variables were appropriate for Canada's industry and data were readily available. The model is of the following form:

$$RDS = B0 + B1[SALE + SALE(-1)] + B2[PROFIT + PROFIT(-1)] + B3[D] + B4[CFM] + B5[POPN] + B6[POPSC]$$

where RDS, is the ratio of R and D expenditures to sales.
SALE, is aggregate sales of drugstores and pharmacies.
SALE(-1), is lagged sales of one year.
PROFIT, is net profit of pharmaceuticals.
PROFIT(-1) is lagged net profit of one year.
D, is the dummy variable for patent act legislation.
CFM, is the Cash Flow Margin defined in section 2.1.
POPN, is annual population figures for Canada as a whole.
POPSC, is the population of senior citizens over age 65.

Primarily for comparative purposes the dependent variable, RDS, as well as the explanatory variable CFM, remained comparable to the variables in the Grabowski-Vernon model. The ratio RDS was also justified due to its influence on the overall level of competition in the pharmaceutical industry being a function of competition for market share through new product innovation and the sales promotion of new and existing products rather than through price competition on existing products. Since the ratio of expenditure to sales promotion is disproportionately larger than that to R and D, and since R and D activities are generally larger in the pharmaceutical divisions, overall ratios of R and D expenditures to sales serve to reduce the estimate of the relative size of R and D. This is particularly useful in evaluating whether expenditures on R and D are directed principally towards the maintenance of market shares or towards the discovery of new drugs. It is also a useful figure when looking at the degree to which pharmaceutical firms allocate resources to R and D differs from one country to another according to sales. These figures were presented in section 1.1.1. However, the similarity between the two models ended at this point, since other variables were added to model (2) to capture a better fit of the unique Canadian market.

The above variables are relatively simple and straight forward.

However, the inclusion of POPSC should be explained further. This variable is important to the understanding of medicine sales in Canada's drug industry. As a percentage of the total population Canada's population over the age of 65 was roughly 10 percent representing a disproportionately large share that was rapidly growing at a rate of 17.9 percent between 1976-81. Studies have shown that in the future this group will continue to increase at a rate over twice that of the population as a whole, out-pacing all other age groups. As a result of the declining growth rates of all other age groups, senior citizens will produce significant effects upon the pharmaceutical industry due to their larger intake of prescribed ethical drugs, thereby justifying the inclusion of POPSC.

The following were the most significant standard regression results obtained for model 2:

Table 3
Regression Results for Model 2

Regressors	Coefficients	Standard Errors	T-Statistics
B0 (Intercept)	-44.732	20.567	-2.16
B1 (Sales)	-0.009	0.003	-0.29
B2 (Profit)	-0.027	0.046	-0.57
B3 (Dummy)	4.377	3.199	1.36
B4 (CFM)	-117.482	188.821	-0.62
B5 (POPN)	0.875	1.786	0.49
B6 (POPSC)	27.956	14.380	1.94

R-SQ = 0.94 ADJ R-SQ = 0.91 DW = 1.9 COND = 209.697

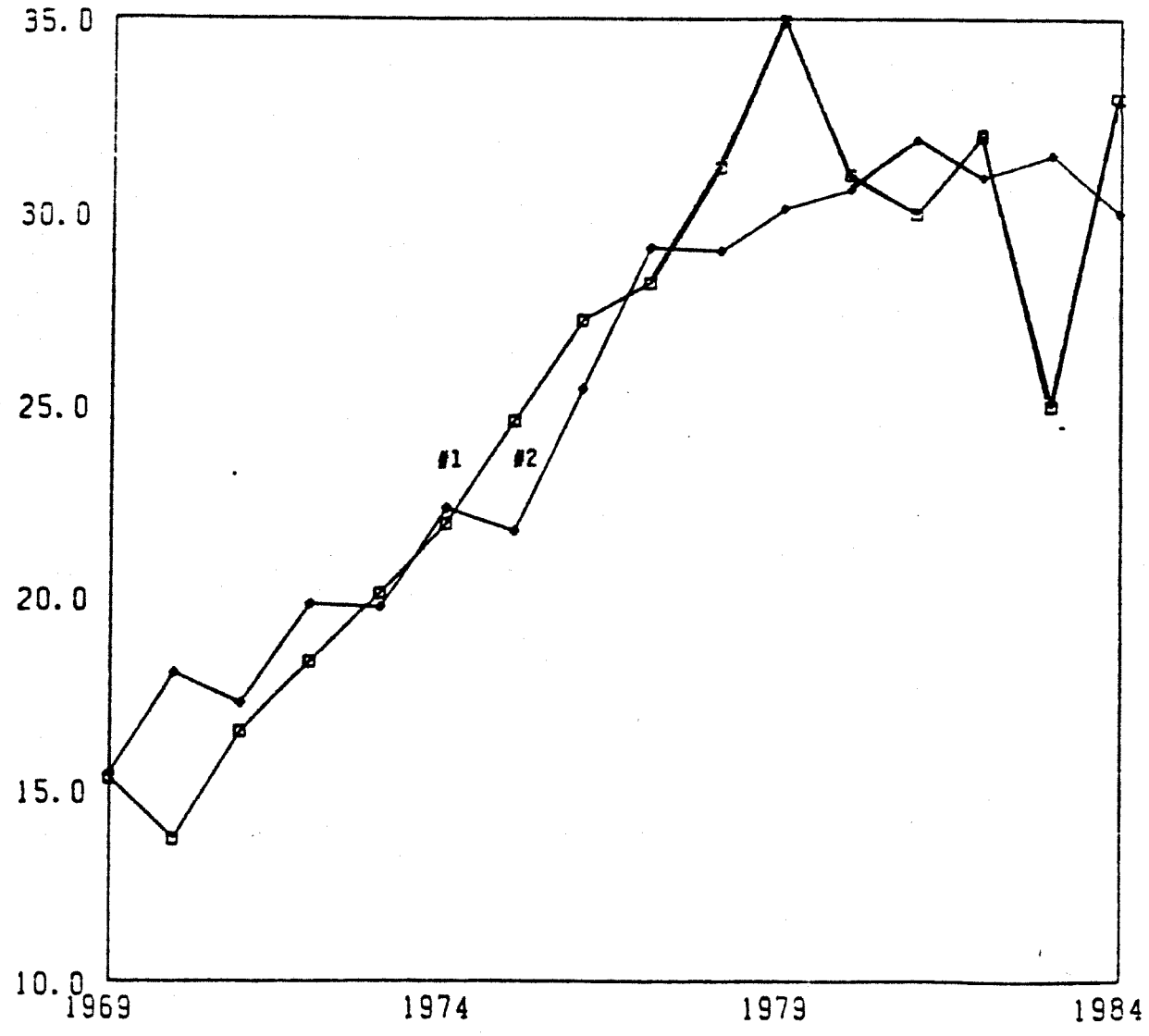
Inspection of the signs on the coefficients B1, B2 and B4 yield results that are perverse, in that they should have ideally been positive. In addition, corresponding t-statistics are not significant

at the five percent level, indicating that B1=B2=B4=0. That is, we cannot reject the null hypothesis of a zero slope implying virtually no explanatory power. The other coefficients, B3, B5 and B6, were all consistent with respect to signs, however, t-statistics for B3 and B5 were insignificant at the five percent level. On the whole, these results did not prove to be encouraging. The R-SQ of 0.94 and Durbin-Watson of 1.9 are satisfactory by the usual statistical standards, while the COND value of 209.697 indicated the presence of moderate multicollinearity in the variables. See Figure 3 for a graphical view of Model 2.

The standard regression treatment of the above model, as well as manipulations in various other versions, gave results which were, on the whole, statistically meaningless. After careful inspection and analysis of the above variables it was concluded that this model was inappropriate for the explanation of R and D within the Canadian pharmaceutical industry. For this reason model 1 remained the primary model for this study.

Figure 3

Actual to Forecasted R and D (Model 2)



#1 Actual R and D

#2 Forecasted R and D

3.3 MODEL 3

Model 3 was introduced adding to model 1 a one period lag of the dependent variable, R AND D, thereby taking into account previous R and D expenditures which would affect the way funds were allocated for the present year's R and D expenditures. This is theoretically plausible since R and D efforts are sometimes started and finished at later dates resulting in spillovers into the present time span talked about previously. Also, the nature of innovation in this industry is such that research in one field or drug often overlap into breakthroughs in other areas. So that any research spent is never wasted research since the information gained adds to a ever increasing body of medical knowledge and not a 'win/lose' lottery of failed and successful R and D as claimed by the industry. As was mentioned earlier, Canada's level of expenditure on R and D has always been around 5 percent of world sales. The above may be a further explanation as to why it has remained at this level. The following are the results:

Table 4
Regression Results of Lagged Dependent Variable

Regressors	Coefficients	Standard Errors	T-Statistics
B0 (Intercept)	2.1208	1.22507	1.73
B1 (Sales)	-0.0005	0.00212	-0.24
B2 (Profits)	0.0182	0.04053	0.45
B3 (Dummy)	3.1991	2.44342	1.30
B4 [RANDD(-1)]	0.8052	0.212969	3.78

R-SQ=0.93 ADJ R-SQ=0.92 SSR=153.42 DW=2.29 COND=40.27

Briefly, the R-SQ, DW and COND values are statistically satisfactory, while the t-statistic, with the exception of B4, are all

insignificant at the five percent level. It should be noted that use of the DW statistic to determine the presence of autocorrelation is not appropriate in this case because of the lag in the dependent variable. The presence of the lagged variable exerts bias towards 2 even when errors are serially correlated. Hence, the alternative test provided by Durbin is the Durbin h statistic.[44] The Durbin h is 3.55, and when tested at the five percent level, indicates the presence of positive autocorrelation. Coefficient estimates of the parameters are all acceptable, with B1 being in question due to its perverse sign. The Theil U statistic is 0.98, which is very close to the original value. This model proved to be a useful mechanism in concluding that past expenditures on R and D may well influence future spending. See Figure 4 for the illustration of Model 3.

The Durbin h value of 3.55 indicated the presence of autocorrelation, therefore, the Cochrane-Orcutt transformation was applied in an attempt to correct for this. The following were the results:

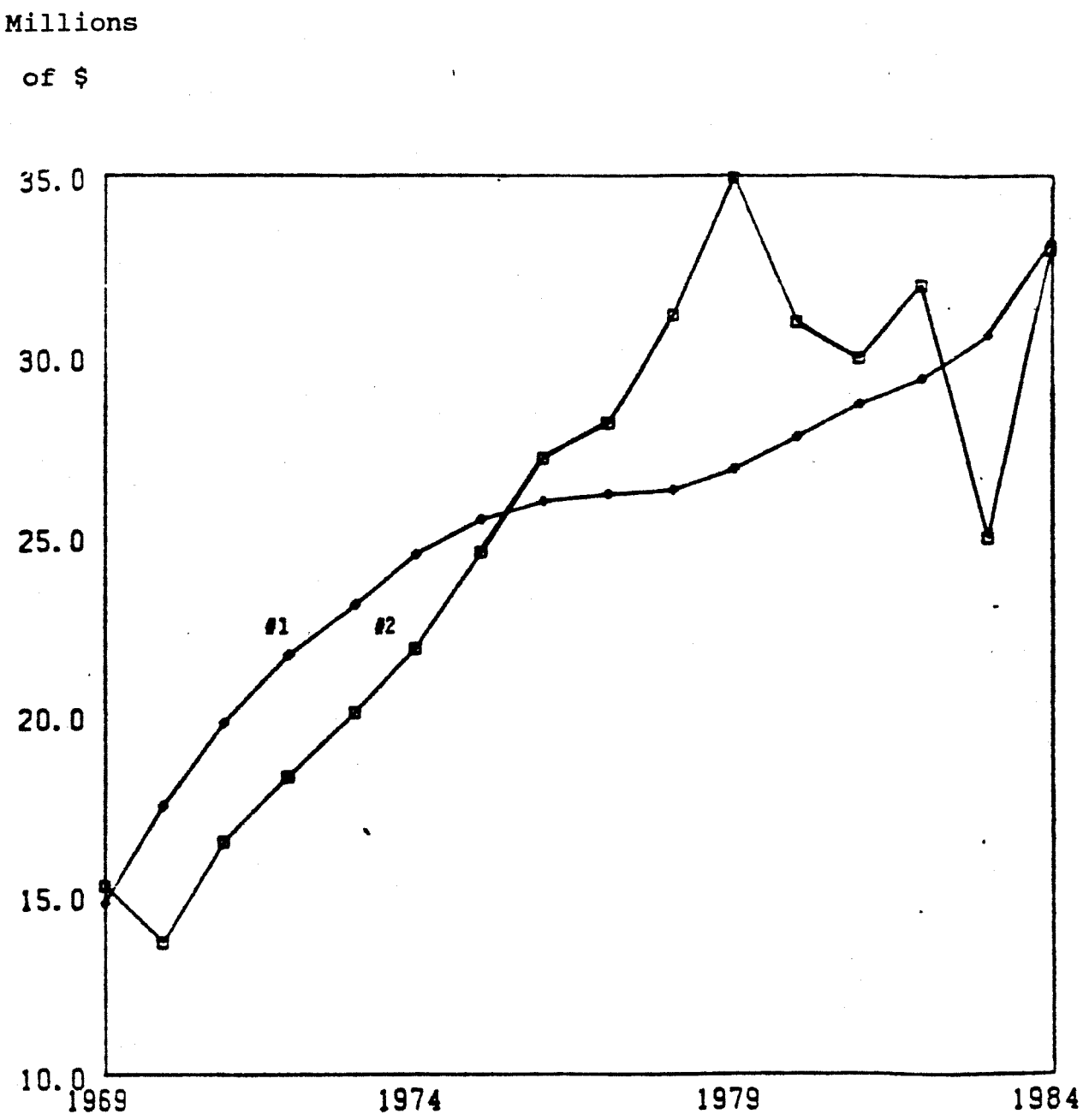
Table 5
Regression Results of Lagged Model 3 with C-O Transformation

Regressors	Coefficients	Standard Errors	T-Statistics
B0 (Intercept)	1.14302	0.6886	1.65
B1 (Sales)	-2.611	0.0014	-0.02
B2 (Profit)	-0.0064	0.0287	-0.22
B3 (Dummy)	2.1102	1.5984	1.33
B4 [RANDD(-1)]	0.9538	0.139	6.85

R-SQ=0.94 ADJ R-SQ=0.92 DW=1.97 SSR=125.071 COND=48.8

Figure 4

Actual to Forecasted R and D (Model 3)



#1 Actual R and D

#2 Forecasted R and D

By inspecting the above results, it is clear that in comparison to the original model 3, the coefficient estimates worsened, in general, with respect to signs. T-statistics declined in significance at the five percent level for B0, B1 and B2, while they improved slightly for B3 and B4. All standard errors declined in magnitude. The R-SQ remained relatively unchanged, while the DW value approached 2, indicating a fall in autocorrelation. On the whole, these transformed results did not prove to be superior to model 3 without the transformation.

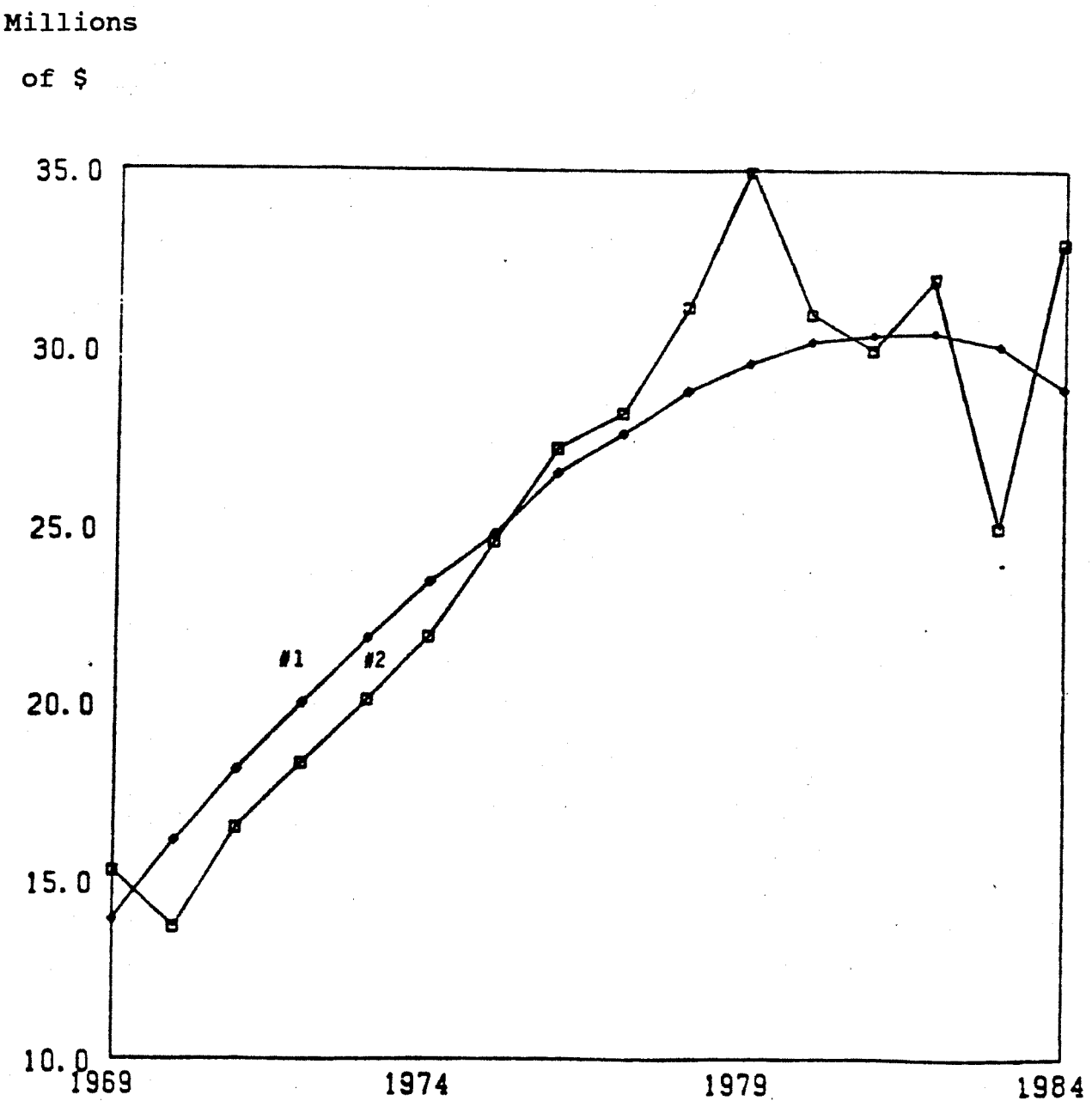
As a final note, the Theil U statistic improved to 0.69 from 0.98, indicating that this revised version possessed superior predictive ability. See Figure 5 for a graph of this version.

3.4 MODEL 4

When modelling for forecasting purposes, one must attempt to explore as many different facets of the problem as is possible. For this reason, Model 1 was re-simulated with the dummy variable D suppressed at the simulation stage (Model 4). In other words, the original coefficient estimates and related statistics would remain unchanged, while the dummy was amended. The model is estimated on preamendment data (1959-1969) and then employed to forecast what the levels of R and D would have been in the post-1969 period in the absence of regulation. The effects of the 1969 amendments are computed as the residual difference between actual and forecasted levels of R and D. By examining the evidence, this model concludes that less R and D would have been performed had the 1969 changes never been implemented. See Figure 6 for the results of Model 4.

Figure 5

Actual to Forecasted R and D (Model 3)

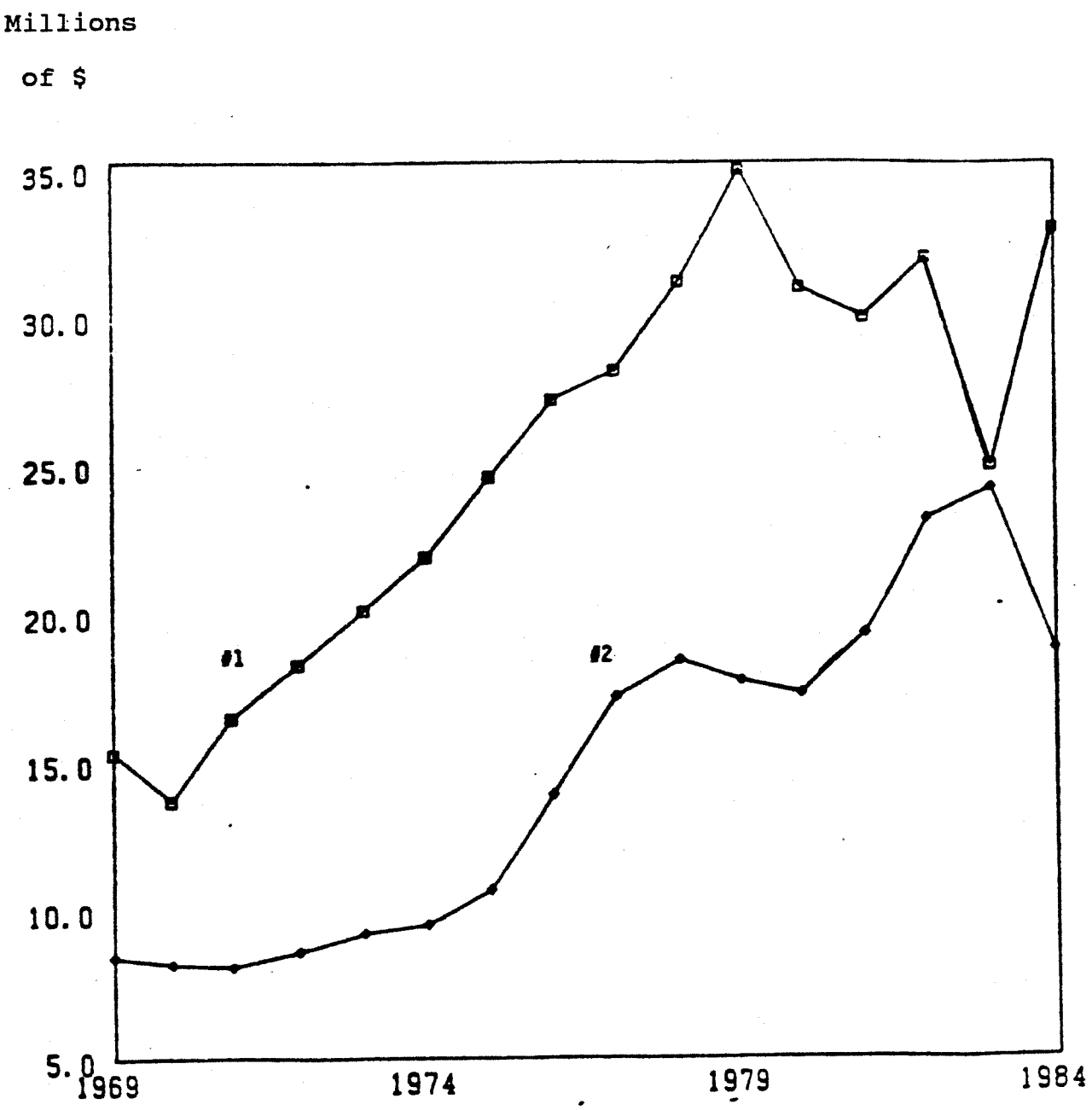


#1 Forecasted R and D (with C-O transformation)

#2 Actual R and D

Figure 6

Actual to Forecasted R and D (Model 4)



#1 Actual R and D

#2 Forecasted R and D

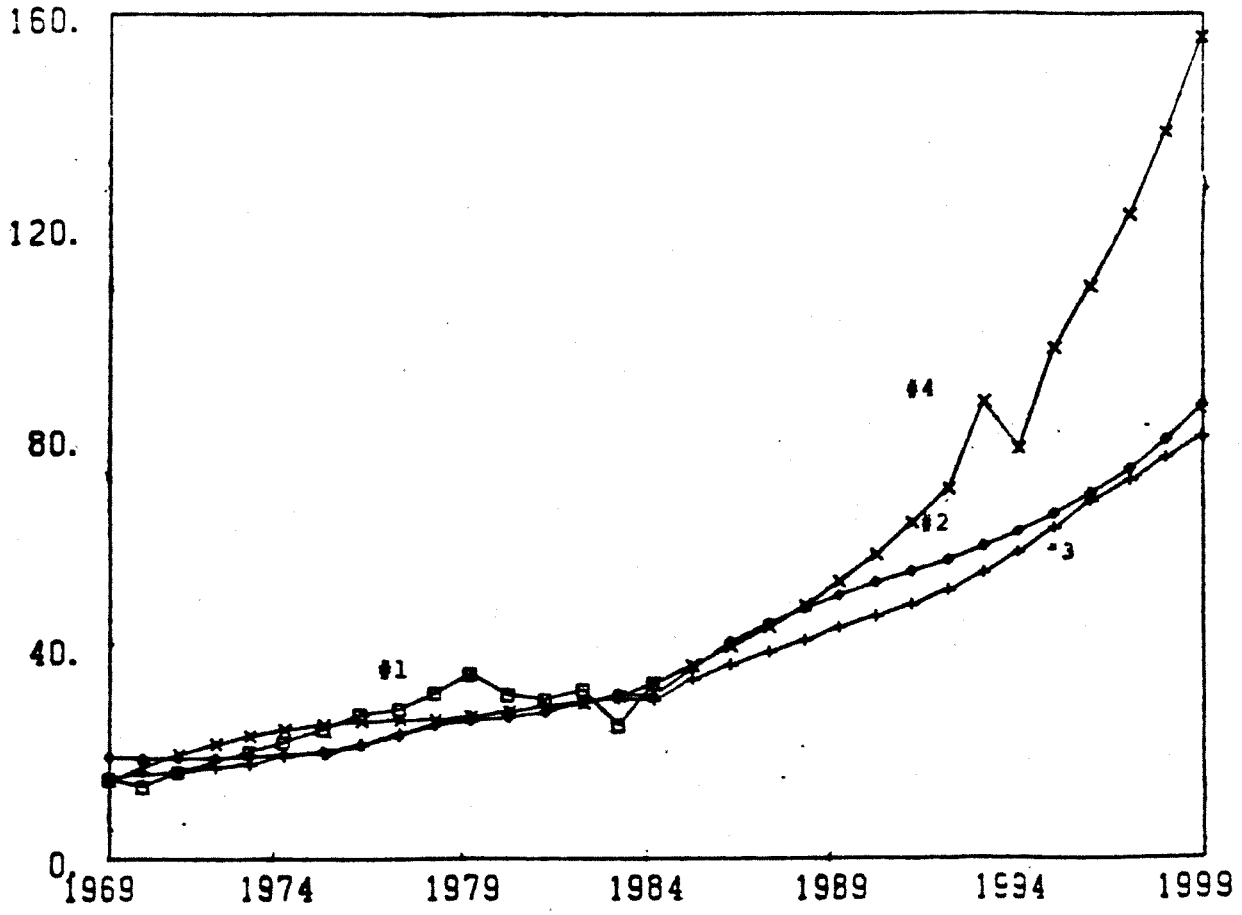
In an overall examination of the four models used and the subsequent results achieved, it was concluded that all four contributed to the explanation of R and D expenditures within the pharmaceutical industry. In general, results obtained from the Cochrane-Orcutt transformations of Models 1 and 3 proved to be the most satisfactory by the usual statistical standards. However, the transformed Model 3 provided the best Theil U statistic indicating superior predictive ability. Simulation results for each model proved to be consistent with the conclusion that R and D expenditures did not decrease after the 1969 amendments to the Patent Act. Figure 7 reveals the ex-ante simulations of R and D for each model. It strengthens the above conclusion by the rising trend of constant R and D expenditures in each model above that of the 1969 levels. Although these predicted values are based on the explanatory variables we evaluated in our models, it is not known with certainty whether these variables will prove to be good indicators of R and D performance, as depicted in the models, for the future. As the phenomenon in the pharmaceutical industry changes; such as the world wide reduction of research opportunities or the report and classification of industry data, it can be expected that other variables may enter into the models as better indicators of R and D performance. Nevertheless, to make the inferences illustrated in Figure 7, one is not likely to deviate substantially from the arguments presented here. Although one should be careful in doing so without the thoughtful qualification of new events that may put different perspectives on interpretating old conclusions.

Figure 7

Simulations to 1999

Millions

of $



#1 Actual R and D
#2 Forecasted R and D (Model 1)
#3 Forecasted R and D (Model 2)
#4 Forecasted R and D (Model 3)

4.0 CONCLUSIONS

The above models were formulated and the analysis undertaken in order to test the hypothesis of whether the introduction of the Patent Act in 1969 had been detrimental to the level of R and D expenditures within the Canadian pharmaceutical industry.

The 1969 changes to the Patent Act reduced the size of monopoly profits to be earned on products for which the country granted a patent. It made use of Compulsory Licenses and royalties to inject a measure of price competition into the market place. This governmental response obliged the multi-national patent holders to accommodate in good faith the generic drug companies to compete in the multi-million dollar market. This basic change has led sellers of brand name products to put intense pressure on the federal government to amend the Patent Act in favor of encouraging more R and D.

The government undertook the 1969 legislative changes in an attempt to curb the relatively high prices being charged for ethical drugs to the Canadian consumer. Canadians have indeed been paying lower prices in the 1970's and 1980's as a result of the 1969 changes. For example, for 42 licensed drugs sold in Canada in 1983, the price of the generic product was, on average, half the price of the same product sold by the large pharmaceutical firms.[45]

This very success is 'rational' economic reason for the multinational firms to oppose the provisions. The 1969 changes provide an example which might be followed in other countries where these multinationals operate. In fact, H. Eastman's major enquiry which reported

in 1985 concluded the fact "that Canadian policy is currently all but unique among industrially advanced countries does not make it wrong. Indeed, it can be thought of as a mechanism to provide socially optimal patent protection in the pharmaceutical industry that other countries might well emulate."[46]

This result indicated that the changes to the Patent Act had served their initial purpose. On the other hand, the large drug firms claimed that the Patent Act and various other legislation had turned Canada into an inhospitable environment in which to undertake any further R and D.[47]

In 1986, in response to intense pressure from the U.S. multi-national drug lobby, the Canadian government announced major concessions. Bill C-22 was introduced with the intention of extending the patent protection period, with the hope of encouraging further research in Canada. More precisely, the extension took the following form in section 41.14 (1) of the act:

> Notwithstanding anything in section 41 or in any license granted under that section, where the notice of compliance that is first issued in respect of a medicine is issued after June 27, 1986, no person shall, under a license granted under that section in respect of a patent for an invention pertaining to the medicine, have or exercise any right, (a) where the invention is a process, to use the invention for the preparation or production of medicine, or (b) where the invention is other than a process, to make or use the invention for medicine or for the preparation or production of medicine for sale for consumption in Canada, until the expiration of seven years after the date of that notice of compliance.[48]

In return for this greater protection, the multi-nationals have proposed increases in the amount of R and D and manufacturing they do in Canada. The agreement is worded in such a way that 10 percent of

sales would be invested in R and D as opposed to 5 percent currently being invested, although this is a promise rather than a requirement of the proposed legislation.[49] However, the whole issue of more research in Canada obscures the underlying nature of the industry in that Canada, representing only 2 percent of the world market, does not significantly affect the 'world payoff' from more pharmaceutical research. Hence, if we assume that the manufacturers are perfectly rational, R and D will be situated wherever profits will be maximized, since this relates to the ultimate survival of the firm. Whether or not this is beneficial to public interest in terms of products that contribute to therapeutic gain or products which do not add anything of value other than excessive prices is very much a normative issue to be decided by government regulatory boards and the market place.

Subsequently, doubts still exist as to whether or not these new concessions to pharmaceutical firms will, in fact, yield substantial R and D gains. The investment question discussed in this paper is only one of two key issues at stake, the other being the cost of price impacts allowed to the Canadian consumer.

From the models that have been formulated with the available statistical techniques, the evidence yields results which indicate that the introduction of the Patent Act amendments in 1969 have not had detrimental effects on research and development in Canada during the post 1969 period. This conclusion is clearly illustrated by the graphical representations of actual to forecasted research and development (Figures 2 to 6). In fact, the results show that the

firms are actually doing more R and D in Canada after 1969.

The results found here are not inconsistent with those of the Eastman Commission. Eastman states that R and D

> levels found in Canada are similar to those found in several other countries that are roughly similar in size and have roughly similar standards of living but whose economies do not include activities by home-based pharmaceutical firms. There are of course yet other countries with substantial markets for pharmaceuticals and medicines in which there is less R and D than is currently carried out in Canada.[50]

In fact, compared to the leading countries of Japan, England, West Germany, Switzerland, Italy and the U.S., the ratio of 5 percent in Canada, although lower, indicates that the pharmaceutical industry in Canada has relatively high allocations of resources to R and D considering its market share in the world.

However, reasons for caution still remain in the interpretation of these results. As usual, there are a number of problems inherent in the models formed such as lack of data or simplicity. Although models which explain behaviour in the U.S. economy were tried and did not explain behaviour in Canada, there is in any statistical investigation, a probability that some unforeseen explanatory variable has been omitted. This indicates that the reader should exercise normal caution and interpret the results accordingly.

Since bill C-22 was passed in 1987 it would be interesting to employ statistics at a later date when there is adequate data available to examine whether or not the multi-national firms have increased there level of R and D spending in Canada. Attempts were made to model the effects to 1989; but with the data used being preliminary and not revised, as well as the years surrounding the 1986

Patent Act amendments being controversial in interim, the results proved to be undesirable by the usual statistical standards of evaluation. Also, this important examination will, unhappily, not be possible unless provisions exist to make sure that expenses claimed as R and D are classified on a consistent basis. Otherwise, after an effective PMAC lobbying effort to recognize more overall spending on R and D, clinical testing and other overlapping expenses, which represent a substantially greater expenditure than R and D, may be considered as part of the R and D costs inherent in developing a new drug. This will make it extremely difficult to use statistical tests to see if R and D promises have been kept.

It can be reported that the totality of the evidence to date in Canada is compelling. The Eastman commission reported in 1985 that "the present Patent Act does not present a financial barrier to research or to collaboration between small research-intensive firms and multi-national pharmaceutical firms."[51] Paul Gorecki's widely respected 1981 study for the Economic Council of Canada reviews the data on a number of influences, concluding that "..... when related to industry sales, again contrary to either a priori expectations and the general trend in the economy, which saw R and D expenditures as a percentage of GNP decline from 1.28 in 1967 to 0.92 in 1977, there is no decline in pharmaceutical R and D except for a small decrease in 1978 of 0.5 of a percentage point for current intramural R and D expenditure."[52]

In this paper, the evidence before and after 1969 has been examined with forecasting techniques. This investigation is in accord

with the earlier work: that the 1969 law had no detrimental impact on investment. Finally, models of the type developed in this study should be useful in the future for examining R and D investments in Canada in the pharmaceutical industry.

APPENDICES

Appendix A

Data Bases Used for Modelling (1959-1984)

YEAR	R & D	Sales	Profit	CFM	POPN	POPSC
1959	2.0	404.27	15.7	0.039	17.48	1.31
1960	2.3	408.65	14.1	0.049	17.87	1.34
1961	2.8	418.49	12.1	0.045	18.24	1.39
1962	3.2	426.00	10.8	0.040	18.58	1.42
1963	5.8	456.51	15.2	0.034	18.93	1.45
1964	8.8	477.00	15.3	0.042	19.29	1.48
1965	9.3	563.14	15.8	0.041	19.64	1.51
1966	9.8	614.73	17.0	0.035	20.01	1.54
1967	10.4	696.01	19.1	0.034	20.38	1.57
1968	11.6	718.85	24.3	0.041	20.70	1.61
1969	15.3	775.07	27.0	0.041	21.00	1.65
1970	13.7	812.49	33.2	0.041	21.30	1.70
1971	16.5	882.36	34.8	0.048	21.60	1.74
1972	18.3	979.51	38.4	0.048	21.80	1.79
1973	20.1	1080.21	41.3	0.049	22.04	1.84
1974	21.9	1236.98	51.8	0.048	22.36	1.88
1975	24.6	1382.42	48.6	0.051	22.70	1.94
1976	27.2	1697.53	47.0	0.044	23.00	2.00
1977	28.2	1894.81	47.7	0.036	23.27	2.07
1978	31.2	2110.24	60.5	0.032	23.52	2.13
1979	35.0	2372.51	85.3	0.036	23.75	2.20
1980	31.0	2713.47	104.5	0.043	24.04	2.28
1981	30.0	3209.63	117.9	0.045	24.34	2.36
1982	32.0	3782.92	132.9	0.044	24.58	2.43
1983	25.0	4334.93	180.0	0.041	24.79	2.49
1984	33.0	4688.18	248.2	0.048	25.00	2.55

R & D: Total Intramural R & D (millions of constant dollars).
Sales: Millions of dollars.
Profit: Net Profit after taxes (millions of dollars).
CFM: Cash Flow Margin.
POPN: Annual Population Figures (millions).
POPSC: Annual Population over the age of sixty five (millions).

Appendix B

Extrapolated Data

Year	Sales	Profit	CFM	POPN	POPSC
1985	5317.18	282.80	0.060	25.4	2.6
1986	5870.77	322.23	0.062	25.7	2.7
1987	6482.01	367.15	0.063	26.0	2.7
1988	7156.89	418.34	0.065	26.4	2.8
1989	7902.03	476.66	0.067	26.8	2.9
1990	8724.75	543.12	0.068	27.2	3.0
1991	9633.13	618.84	0.070	27.5	3.1
1992	10636.10	705.12	0.072	27.9	3.2
1993	11743.50	803.42	0.074	28.3	3.3
1994	12966.10	915.44	0.075	28.7	3.3
1995	14316.10	1043.07	0.077	29.2	3.4
1996	15806.60	1188.49	0.079	29.6	3.5
1997	17452.40	1354.19	0.081	30.0	3.6
1998	19269.40	1542.98	0.083	30.4	3.7
1999	21275.70	1758.10	0.085	30.9	3.8

1. Patent Act, R.S.C., c. P-4, S. 41(1), 41(4).

2. Frank W. Horner v. Hoffmann-La Roche Ltd. (1970), 61 C.P.R. 243, p. 262.

3. Economic Council of Canada, Report on Intellectual Property (Ottawa: Information Canada, 1971), p. 70.

4. Eastman, p. XXXIV.

5. Canada. Royal Commission on Patents, Copyright and Industrial Design, Report on Patents of Invention (Ottawa: Queen's Printer, 1960), p. 92-97.

6. Canada. Department of Justice, R.T.P.C., Report Concerning the Manufacture, Distribution and Sale of Drugs (Ottawa: Queen's Printer, 1963), p. 516-24.

7. Canada. Royal Commission on Health Services, Report of the Royal Commission on Health Services (Ottawa: Queen's Printer, 1964), Volume 1, p. 701-9.

8. Canada. Royal Commission on Health Services, Report, Volume 1, p. 641.

9. Brief to the Commission of Inquiry on the Pharmaceutical Industry. Consumer's Association of Canada, Ottawa, Aug. 1984, p.24.

10. Eastman, p. 54.

11. Eastman, p. 62.

12. Ibid., p. 233.

13. Compulsory Licensing of Pharmaceuticals., p. 8.

14. Ibid., p. 7.

15. Eastman, p. 423.

16. Ibid., p. 422.

17. G. David Quirin., Transfer Pricing of Drugs and Pharmaceutical Intermediate Products, 1985, p. 6, 29.

18. Compulsory Licensing of Pharmaceuticals, p. 3.

19. Eastman, p. 3.

20. Ibid., p. XX.

21. Submission to the Commission of Inquiry on the Pharmaceutical Industry, P.M.A.C., p. V.

22. Ibid., p. V.

23. Brief to the Commission of Inquiry on the Pharmaceutical Industry., p. 11-12.

24. Eastman, p. xi.

25. Ibid., p. xviii.

26. Ibid., p. xviii.

27. Ibid., p. 347.

28. Statistics Canada, Catalogue No. 61-207.

29. Eastman, p. 259. Other industries include Total Manufacturing, Total Chemicals, and Industrial Chemicals.

30. Ibid., p. xxi.

31. P.M.A.C., p. V.

32. See Taylor and Silberston (1973, pp. 231-266) for the results of a survey evaluating the effects of patent protection for the U.K. drug industry.

33. Schwartzman and Clymer, 1976, pp. 136-161.

34. Grabowski, et al. 1978.

35. Ibid, 1976, pp. 44-48.

36. Scrip and Canada, Department of Industry, Trade and Commerce, 1979b, p. 19.

37. Bernstein, Price Indices for Canadian Industrial Research and Development Expenditures. Statistics Canada (Catalogue 88-509), Ministry of Supply and Services Canada 1986, p. 5.

38. Ibid., pp. 8-26.

39. Compulsory Licensing of Pharmaceuticals., p. 16.

40. Pindyck and Rubinfeld., Econometric Models and Economic Forecasts, 1981, p. 159.

41. Ibid., p. 204.

42. Grabowski and Vernon, The Regulation of Pharmaceuticals, 1983, p. 12.

43. Ibid., p. 19.

44. For the definition and example of how the Durbin h test was obtained, see Pindyck and Rubinfeld., 1981, p. 194.

45. Crane, D. New Debate Over Generic Drugs Looms, p. A18.

46. Eastman, p. 348.

47. Gordon and Fowler, p. 86.

48. Patent Act 1987, ch. 41, 35-36 Eliz. II, p. 1182.

49. Crane, p. A18.

50. Eastman, p. 233.

51. Eastman, pp. 425-426.

52. Gorecki, pp. 35-36.

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