

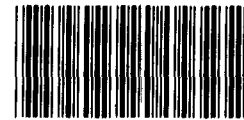
GAO

Report to the Chairman, Special
Committee on Aging, U.S. Senate

February 1993

PRESCRIPTION DRUG PRICES

Analysis of Canada's Patented Medicine Prices Review Board



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February 17, 1993

The Honorable David Pryor
Chairman, Special Committee on Aging
United States Senate

Dear Mr. Chairman:

As public concern about health care costs intensifies, the escalation in prescription drug costs—borne by consumers, insurers, and other third-party payers—has spurred congressional interest in ways to curb the growth of prescription drug prices. The 102nd Congress introduced at least 11 bills to constrain drug prices, yet none of these was enacted. To monitor prescription drug pricing, some of these bills would have created a federal board, modelled after Canada's Patented Medicine Prices Review Board. In a recent study, we found that manufacturers charge less for many drugs in Canada than in the United States and that the Canadian approach to regulating drug prices contributes to this price differential.¹

You asked that we (1) describe the purpose and structure of Canada's Patented Medicine Prices Review Board as well as its guidelines and procedures, especially those used to determine if a drug price is excessive, and (2) summarize the evidence about the effects of the Board's actions in Canada on the prices of new drugs, on price increases for existing drugs, and on pharmaceutical research and development (R&D).

Background

In 1987, the Patented Medicine Prices Review Board was established by the Canadian government to complement and counter a change in Canadian law that strengthened patent protection on pharmaceutical products and increased the monopoly power of drug companies. This change in patent law stemmed from concern that Canada's use of compulsory licensing² discouraged investment in pharmaceutical R&D in Canada.

¹Prescription Drugs: Companies Typically Charge More in the United States Than in Canada (GAO/HRD-92-110, Sept. 30, 1992).

²Compulsory licenses with respect to pharmaceuticals have been defined as the "right to use a patented invention in the production of a medicine without risk of successfully being sued for patent infringement." Compulsory licenses confer on the licensee the right to produce a patented invention or product in return for a royalty paid by the generic manufacturer to the licensee. See Janet Apse and Tom Brogan, *The Users' Guide to the Patented Medicine Prices Review Board*, unpublished manuscript (1990).

Between 1969 and 1987, the monopoly protection on pharmaceuticals previously afforded by Canadian patent laws was diluted by adoption of compulsory licensing, which fostered increased competition and lower drug prices by encouraging the development of generic copies of patented drugs. Under compulsory licensing, a generic manufacturer could obtain a license from the Commissioner of Patents to permit it to use the patented process to manufacture the drug. The manufacturer could then produce a generic version of the drug, even though the drug's patent was still nominally in force. By stimulating competition between generic drugs and their brand-name patented counterparts, compulsory licensing was supposed to make lower-priced versions of patented drugs available.³

By 1987, however, compulsory licensing was seen by Canadian government officials and representatives of the pharmaceutical industry as negating patent protection, and thereby discouraging pharmaceutical R&D in Canada.⁴ Subsequently, the Canadian government proposed restrictions on compulsory licensing to reinvigorate the Canadian pharmaceutical industry.⁵ The 1987 revisions to Canadian patent law were intended to reduce generic drug competition by introducing a 7- or 10-year waiting period during which generic copies of patented products would be prohibited from entering the Canadian market.⁶

In response to public concern that the revamped law, while stimulating pharmaceutical R&D, would permit manufacturers of patented products to charge excessive prices, Canada's Parliament included establishment of the Patented Medicine Prices Review Board in the 1987 patent law revisions. Some government officials had suggested that a balancing mechanism be devised to compensate for the proposed lengthening of the

³The patent law was not the only instrument used to restrain prescription drug prices in Canada. Specifically, provincial governments in Canada—each of which offers drug benefits to some or all of its population—often were able to obtain low prices from drug manufacturers. These prices sometimes extended to the private-pay market as well.

⁴Spending on pharmaceutical R&D was less than 5 percent of sales in 1987, compared with 15.8 percent in the United States.

⁵In return, Canadian pharmaceutical firms pledged to double the ratio of pharmaceutical R&D spending to sales in Canada within 10 years.

⁶A generic drug manufacturer must wait 7 years from the date the original patented drug was approved by Health and Welfare Canada (the Canadian equivalent of the U.S. Food and Drug Administration) to market a generic copy, if the active ingredient is manufactured in Canada. A generic manufacturer must wait 10 years from the date Health and Welfare Canada approved the drug, if the drug's active ingredient is imported (if it is not manufactured in Canada). If a medicine has been invented and developed in Canada, a generic manufacturer must generally wait until the patent has expired before making a generic copy.

period of market exclusivity.⁷ Responding to this concern, Canada's Parliament established the Board to review drug prices set by manufacturers and to remove market exclusivity or order a price reduction for products with excessive prices.

Scope and Methodology

To learn how the Patented Medicine Prices Review Board operates and to evaluate its effectiveness, we interviewed the Board's chairman and staff members; provincial government officials; representatives of research-based drug companies; and experts in the Canadian pharmaceutical market. We also reviewed Board publications, including its annual reports and guidelines; publications and commentary by consumer groups, provincial governments, and generic drug manufacturers; and academic and legal articles on drug price regulation, the Board, and Canadian patent law. To see whether the Board has affected drug prices in Canada, independent of other factors, we used an econometric analysis that we developed as part of a related study⁸ to determine how the Board's regulations affect the differences in individual drug prices in Canada and the United States.

We limited the scope of this study to examining the Canadian experience with drug price regulation. We did not evaluate whether the United States should adopt a drug price review board, nor did we examine how a board modelled after the Patented Medicine Prices Review Board would function or what its likely effects, if any, would be on pharmaceutical research and development in the United States.

We conducted our review from December 1991 through December 1992 in accordance with generally accepted government auditing standards.

Results in Brief

Canadian federal strategy for limiting prescription drug prices relies largely on the Patented Medicine Prices Review Board to determine when the price of a patented drug is excessive and to apply sanctions, when necessary, against drug manufacturers. The Board constitutes part of a three-pronged approach for controlling Canadian drug prices, which also includes federal policies that promote the sale of generic equivalents of brand-name drug products and provincial reliance on the bargaining power of provincial drug benefit plans.

⁷The period of market exclusivity is the period established by law in which the holder of a patent for a medicine is given the sole right to sell that medicine in Canada.

⁸Prescription Drugs (GAO/HRD-92-110, Sept. 30, 1992), pp. 29-35.

The Board has the power, following a public hearing, to order the removal of market exclusivity or a price reduction if it finds a price to be excessive. The Board induces manufacturers' compliance with its guidelines through the threat of negative publicity associated with a public hearing. The Board's powers are limited, however, in two important ways: first, its mandate is to keep prices from being excessive, not to keep them low; and second, its regulations apply only to patented drug products, not to generic products or drugs no longer under patent.

Canadian experience shows that a drug price review board can restrain prescription drug prices. Specifically, the Canadian Board has restrained price increases on existing patented drugs, though evidence of the Board's effect on introductory prices of new patented drugs is less definitive. Prices of existing patented drugs within the Board's purview rose more slowly than prices of nonpatented drugs outside its review authority. Moreover, our statistical analyses suggest that, relative to U.S. drug prices, the Canadian prices of some drugs, subject to Board review, were on average one-third lower than had there been no Board. As to introductory prices of new patented drugs, Canadian opinion is split on whether the Board is effective. Data are not available to easily resolve this issue. Our statistical analysis suggests that, at least for the small number of new patented drugs in our sample, the Board caused introductory prices to be lower than they would have been without the Board, but this finding may not hold for all new drugs.

While the Board has had some effect on drug prices and spending, its effect on Canadian pharmaceutical research and development is in dispute. Restraint of drug prices reduces the incentive for manufacturers to undertake innovative pharmaceutical research and development, but how manufacturers actually respond to this reduced incentive cannot be inferred from the Canadian experience with price review. In the Board's first 4 years, pharmaceutical firms' R&D expenditures increased relative to drug sales. However, at the same time that Canada introduced drug price review, two other factors came into play with the opposite, potentially favorable effect on R&D. The first factor was patent law changes and the second, a voluntary commitment by the Canadian pharmaceutical industry to the federal government that the industry would increase R&D. As a result, the effect of price review alone on pharmaceutical R&D cannot be isolated.

Principal Findings

Responsibility and Powers of the Patented Medicine Prices Review Board

The Patented Medicine Prices Review Board is the federal body responsible for restraining prescription drug prices in Canada. The five member Board is an independent, quasi-judicial body that is charged with ensuring that manufacturers' prices of patented medicines are not excessive. In fiscal year 1992-93, the Board was authorized a full-time-equivalent staff of 35 employees. The Board's jurisdiction applies only to patented drugs, and does not extend to off-patent or generic drugs. In addition to these responsibilities, the Board is required to report annually to Parliament on its activities, pricing trends in the pharmaceutical industry, and the ratios of pharmaceutical R&D expenditures to drug sales for individual patentees and for the patented pharmaceutical industry as a whole.

Board Uses Patent Laws to Induce Compliance With Its Guidelines

The Board periodically publishes guidelines that it uses to determine if a manufacturer's introductory price on a new drug or price increase on an older patented drug is excessive. The Board generally considers an introductory price to be excessive if the product's cost per day or per treatment exceeds the maximum cost per day or per treatment for therapeutically comparable medicines. If there are no therapeutically comparable medicines; that is, if the drug is a breakthrough product or judged to be a substantial improvement over existing therapies, the introductory price is excessive if it is higher than the median price charged for the product in seven other industrialized countries.⁹ The price of an existing patented drug is excessive if its cumulative price increase—either since its introduction or since the Board's inception, whichever is more recent—exceeds the growth in Canada's consumer price index (CPI) for the same period. (The Board's guidelines are discussed in more detail in appendix I.)¹⁰

If a manufacturer sets a price considered to be excessive, the Board can order the manufacturer to lower the drug's price, but has no authority to enforce that order. It can also take away a drug's market exclusivity, after a public hearing. When removing market exclusivity, the Board can choose to do so for the drug in question, another drug produced by the same

⁹France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States.

¹⁰The Board has recently proposed two changes to its guidelines. The first would restrict drug price increases to the annual change in the Canadian CPI rather than the cumulative change. The second limits the introductory price of most new medicines to the median of each drug's international price.

manufacturer, or both drugs. In enforcing compliance with its guidelines, the Board and its staff have three roles: investigatory, in that the staff investigates whether a drug manufacturer violated Board pricing guidelines; prosecutorial, in that the Board's staff brings evidence of violation before the Board; and judicial, in that the Board decides whether the product's price violates the Patent Act and the Board's guidelines.

Compliance With the Board's Guidelines

The majority of drug prices within the Board's jurisdiction are in compliance with the Board's guidelines. Of the 142 new drugs introduced in Canada in 1991 and through mid-November 1992 that had their prices reviewed by the Board, about 70 percent had initial prices that were within the Board's guidelines. Of the new drugs for which prices were initially judged to be outside the guidelines, prices subsequently have come into compliance with the guidelines in over three-fourths of the cases. (See table 1.) In some of these cases, the manufacturer achieved compliance by voluntarily lowering the drug's price or by limiting a subsequent price increase.

Table 1: Compliance of New Drug Products, 1991 and 1992 (as of January 1993)

| | Year drug was introduced | |
|--|--------------------------|------|
| | 1991 | 1992 |
| New drugs introduced | 98 | 61 |
| New drugs with prices reviewed by Board ^a | 98 | 44 |
| New drugs reviewed with introductory prices outside Board guidelines | 29 | 13 |
| New cases resolved | 27 | 5 |
| New cases still outstanding | 2 | 8 |

^aThe Board staff try to review new drug prices and bring them into compliance within 90 days of the drug's introduction.

Source: Patented Medicine Prices Review Board.

About 85 percent of price increases on existing drugs from 1991 through the first 6 months of 1992 were initially within the guidelines. Of the drugs initially found to be outside the guidelines, virtually all fell within the guidelines by the next pricing period. Of those drugs identified as priority cases—drugs for which the Board's staff considers the price to be significantly outside the guidelines—all but one has been resolved.¹¹ (See table 2.) Those drugs not identified as priority cases usually exceed the

¹¹The outstanding case is the subject of the Board's first public hearing. The hearing has been stayed by the Canadian courts pending resolution of a jurisdictional issue raised by the patentee.

guidelines by only a small amount—sometimes only a fraction of a penny—and generally fall into compliance by the next pricing period.

Table 2: Compliance of Existing Drug Products, 1991 and 1992 (as of January 1993)

| | Pricing Period ^a | | |
|--|-----------------------------|-------------------------------|----------------|
| | Jan.- June 1991 | Jan.-Dec. & July-Dec. 1991 | Jan.-June 1992 |
| Drugs with prices reviewed by the Board | 206 | 594 | 217 |
| Drugs reviewed with price increases outside Board guidelines | 35 | 86 | 31 |
| Drug cases identified for priority review ^b | 8 | 24 | 11 |
| Priority review cases resolved | 7 | 23 | 11 |
| Priority review cases still outstanding | 1 | 1 | 0 |

^aSome pharmaceutical manufacturers price their products using a 6-month pricing cycle while others follow a 12-month pricing cycle. The second column under 1991 gives compliance data for the second half of 1991 and, for those drugs that follow a 12-month pricing cycle, compliance data for all of 1991.

^bThe Board establishes priorities for further investigation based on several criteria including the amount by which a price exceeds the guidelines, the value of excess revenue, and a history of pricing above the guidelines. These criteria, which are subject to periodic change, assure that cases involving almost all of the excess revenue attributed to pricing above the guidelines are investigated and resolved.

Source: Patented Medicine Prices Review Board.

To date, the Board has largely been able to get drug manufacturers to comply with its guidelines without taking punitive actions, despite manufacturers' incentive to delay compliance. This incentive exists because manufacturers can retain excess revenues—revenues above what the manufacturer would have received had a drug's price complied with the Board's guidelines.¹² Nonetheless, the penalties associated with Board action—loss of market exclusivity as well as the possible adverse publicity and release of proprietary market data that may accompany a hearing—generally bring drug prices in line with Board guidelines. (Not all cases of noncompliance involve deliberate violation of the guidelines. In some cases, noncompliance may result from differences in interpreting the guidelines. In some such situations, the patentee's interpretation has prevailed.) Since the beginning of 1992, compliance with the guidelines for new drug prices—historically, the hardest to achieve—has usually been achieved within 90 days of product introduction. Compliance for drug price increases has been almost universal.

¹²According to the Board's 1991 annual report, excess revenues for new drugs were roughly 2 percent of total drug revenues in 1991.

**The Board Appears to
Restrain Drug Price
Increases; Effects on
Introductory Drug Prices
Are Less Clear**

**Board's Effect on Price
Increases on Existing Drugs**

Consistent with its record on compliance, the Board's actions appear to have held down price increases on patented drugs. Prices on patented drug products have risen slower since 1987 than both the Canadian CPI and prices on nonpatented drug products. (See fig. 1.)

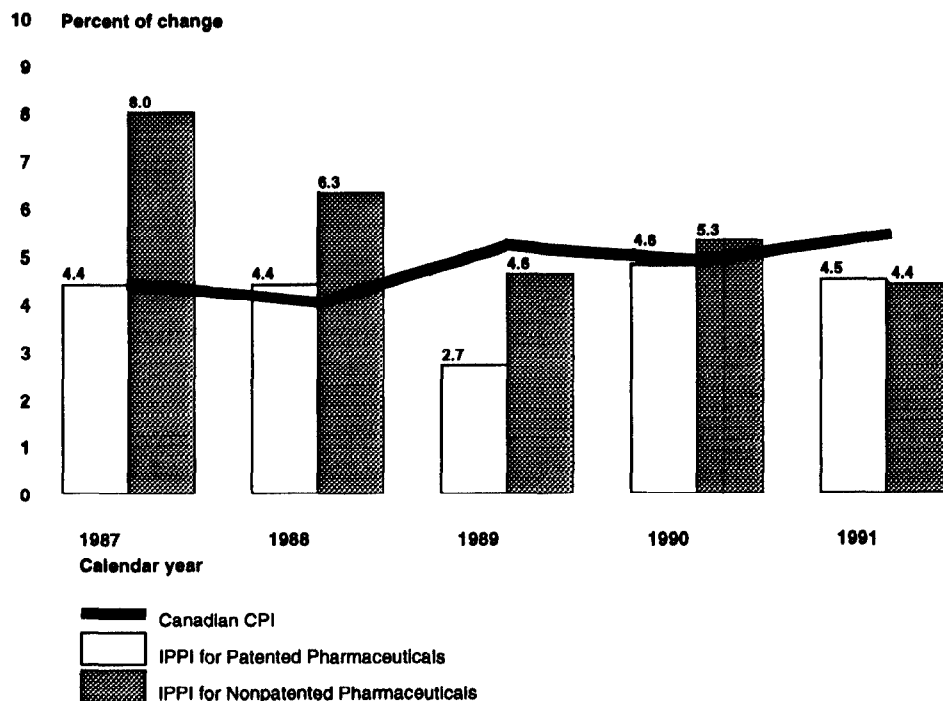
According to the Board's 1991 annual report, the ex-factory prices¹³ of existing patented drug products for the period 1987 through 1991 increased at an annual average rate of 2.9 percent, compared with the 4.7 percent annual rate allowed under the drug pricing guidelines.

Neither the Board nor pharmaceutical experts in Canada have analyzed what the prices of existing patented medicines would have been without Board controls. Nonetheless, drug industry experts in Canada believe that the Board's actions contributed to price restraint. In addition, a statistical analysis that we performed on factors that contribute to ex-factory drug price differences between the United States and Canada supports the experts' views. Our analysis suggests that holding other factors constant, U.S.-Canadian drug price differences for drugs in our survey are, on average, one-third higher for drugs subject to the Board's guidelines on price increases than for those outside its purview.¹⁴ (See app. II.)

¹³The ex-factory price is the price at which pharmaceutical companies sell their products to wholesalers and distributors.

¹⁴This analysis is based on May 1, 1991 prices for 120 of the top 200 drugs prescribed in the United States in 1990. (Seventy-nine drugs were excluded from our analysis because they were not sold in Canada, were not sold in the same dose and form as in the United States, were generic products manufactured by a company that had no affiliate marketing them in Canada, or were sold over-the-counter in Canada. An additional drug was excluded because we lacked data necessary for including it in the statistical analysis.) See Prescription Drugs (GAO/HRD-92-110, Sept. 30, 1992).

Figure 1: Growth in the Canadian CPI Compared to Growth in the Ex-Factory Price of Drugs Controlled and Not Controlled by the Board



Note: The IPPI (industrial products price index) measures the ex-factory price of goods and is comparable to the American producer price index.

As the Board only monitors the ex-factory prices of patented drugs, the IPPI for patented pharmaceuticals shows changes in the prices of drugs under the Board's control.

Board's Effects on Introductory Prices for New Drugs

In contrast to their consensus on the Board's effectiveness at restraining drug price increases, opinions among Canadian drug industry experts diverge on whether the Board has restrained introductory prices of new drugs. Our statistical analysis of U.S. and Canadian drug price differences suggests that, at least for the small number of new patented drugs in our sample, introductory prices of drugs are lower in Canada due to the Board's regulations.¹⁵ We do not have evidence on how well these results can be extrapolated to drugs outside our sample or to drugs reviewed by the Board after May 1991.

Informed observers of the Board expressed conflicting views on the efficacy of the new price guidelines. Some provincial officials and

¹⁵Of the 120 drugs in our survey, 7 were introduced after the Board issued its guidelines on introductory prices (see app. II).

Canadian drug industry experts suggested that the Board may have had little effect on new drug prices. But Board staff and at least one industry expert, while noting that the guidelines allow higher prices than those in some other industrialized countries, cited evidence that suggests the Board's actions kept prices lower than they would have been otherwise.¹⁶

Industry and Its Critics Split on Whether Board Is Too Generous to Manufacturers

Pharmaceutical company representatives with whom we spoke said the Board's guidelines are too stringent and that linking price increases to the CPI is arbitrary. Such guidelines, they said, do not reflect changes in production costs.¹⁷ Furthermore, they said that the Board guidelines for making distinctions among new products are imprecise. These guidelines allow greater leeway for pricing breakthrough drugs than for drugs that are line extensions of existing products, such as a sustained release form of a drug. (See appendix I.) These industry representatives asserted that the Board's guidelines do not adequately recognize the contribution of drugs that offer moderate improvements over existing products, and that drug manufacturers should be given greater flexibility in setting introductory prices for these types of drugs.

By contrast, generic manufacturers and some provincial authorities said that the Board's guidelines are too lenient. In particular, they assert that the benchmark price of a drug—either its 1987 price or the introductory price approved by the Board—is too high and that the Board continues to approve high introductory drug prices. In addition, consumer and generic drug advocates criticize the Board's lack of authority to recoup excess revenues. On this issue, the Board's chairman told us that drug manufacturers might delay their compliance—potentially until the Board threatens to remove market exclusivity—thereby collecting excess revenues for as long as they can. (The Canadian Parliament was scheduled in January 1993 to consider legislation to give the Board authority to collect these excess revenues.)

Criticism of the Board is not universal, however, and some individuals—including officials of provincial drug benefit plans—believe the Board guidelines are both reasonable and effective. Indeed, some

¹⁶For example, the Board has found the prices of 30 percent of new drugs to exceed its guidelines and has brought prices in line through application of its compliance policy. Most reductions have not been reported publicly, but the Board has published information regarding undertakings by Bristol-Myers Squibb to reduce the prices of Capoten and Desyrel. In 1992, Glaxo Canada, Inc., announced that it had lowered the price of Imitrex, a medicine for the treatment of migraines, by 12.5 percent to assure that it would comply with the Board's guidelines.

¹⁷These manufacturers added that many of their ingredients come from other countries, so that input costs are affected more by changes in foreign exchange rates than in the Canadian CPI.

provincial officials have incorporated the Board's guidelines into their own drug reimbursement plans. These provincial officials believe that drug prices might be even higher without Board controls. They note that the Board is not supposed to keep drug prices low or to guarantee a low return to pharmaceutical companies. Rather, the Board's goal is to keep prices from being excessive.

Regulations Restrained Some Drug Prices While Drug Spending Continued to Rise

By restraining drug prices, the Board slowed the growth in drug spending to some extent. However, it is important to recognize that spending on drugs is determined by their price and their volume (number of prescriptions). By its restraint of the prices on existing drugs, the Board is likely to have reduced the average price of all drugs. With respect to the volume component of spending, the Board's restraint of prices is unlikely to have induced physicians to write more prescriptions. As a result, it is reasonable to assume that overall spending increases were smaller than they would have been without the Board. Nonetheless, drug spending in Canada has continued to grow. For the years 1987 to 1990, inflation-adjusted spending per person on outpatient drugs rose at an estimated average annual rate of about 6 percent.

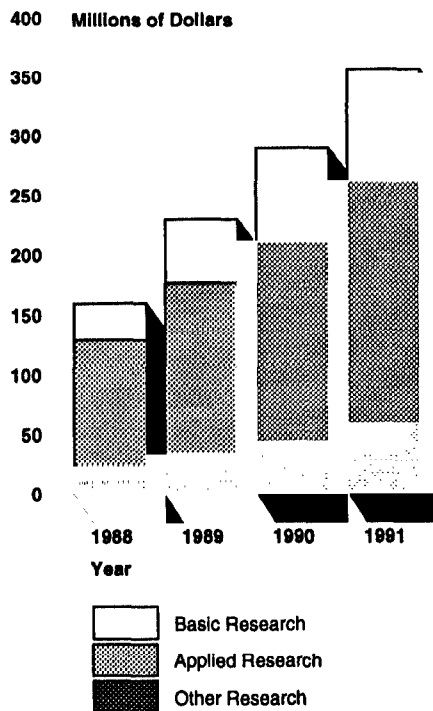
The coexistence in Canada of drug price restraint with continued growth in drug spending points to the importance of factors affecting spending growth that are outside the Board's control. Factors beyond the reach of the Board or any price control body include the number of prescriptions written and the mix of prescriptions written for newer, more expensive drugs and for older, less expensive products. With respect to increased prescription volume, the number of prescriptions per person in Quebec rose by an average of 7.4 percent per year between 1986 and 1991. With respect to mix, about one-third of the medicines prescribed in 1991 were not on the market in 1987. Moreover, if prescriptions in 1991 contained the same drugs in the same quantities as in 1987, the prices of these prescriptions would have risen at a rate well below inflation in Canada.

In addition, the Board does not have authority to influence prices on nonpatented products. Consequently, the Board has no direct effect, and presumably little indirect effect, on prices of products that are off patent or have never been patented. Finally, the Board only influences prices charged by manufacturers to wholesalers and does not control pharmacists' dispensing fees, which affect the retail price paid by consumers.

Canadian R&D on Drugs Has Increased but Board's Impact Unclear

Although drug R&D in Canada relative to sales is low compared to other industrialized countries, it has nonetheless increased since the establishment of the Board. In fact, the ratio of drug R&D investment to sales in Canada nearly doubled from 1988 through 1991. (See fig. 2.) However, the likely source of this increase is the increase in patent protection enacted by the federal government at the same time as it established the Board. The Board has no responsibility with respect to drug R&D other than to monitor and report on levels of R&D spending.

Figure 2: Canadian R&D Spending, by Type 1988-91



Note: Basic research consists of scientific investigations for which no immediate practical applications are envisioned.

Applied research is directed toward some practical application (for example, clinical or preclinical trials).

Much of the recent increase in Canadian research and development seems to have been in applied research, such as drug testing. Few innovative

drugs are being developed in Canada because multinational pharmaceutical firms tend to centralize their basic research activities in their home countries or in major market locations. Furthermore, drug company representatives told us that their firms were reluctant to undertake basic research (that is, new drug development) given their uncertainty about whether Canada's limits on compulsory licensing would be made permanent.¹⁸ Board staff and other pharmaceutical experts believe that the statistics on the expenditures on all drug research undertaken in Canada are accurate. However, one drug industry expert in Canada suggested that measured increases in basic research may be overstated because the companies may be classifying increased clinical testing as basic rather than applied research.¹⁹

Changes in Board Guidelines and Sanctions

As of January 1993, the Board's pricing and enforcement policies were undergoing revision in Canada. In particular, the Board proposed to modify its pricing guidelines. This proposal would restrict drug price increases to the annual change in the Canadian CPI rather than to the cumulative change (as is now allowed) and, for most new medicines, would limit the introductory prices to the median international price. The Board believes that these changes would enhance consumer protection against excessive drug prices.

In addition to these changes in the Board's guidelines, Canada recently enacted legislation that alters the enforcement sanctions available to the Board. The legislation abolishes compulsory licensing, thereby eliminating the Board's power to remove a drug's market exclusivity.²⁰ However, the legislation enhances the Board's powers in several ways. It (1) gives the Board authority it currently lacks to order price reductions or penalties that could compensate for past excessive prices, (2) provides for fines and imprisonment for failure to comply with the Board's price reduction orders, and (3) gives the Board's orders the same force and effect as an order of the Canadian Federal Court. In addition, the Board's jurisdiction will be extended for up to 3 years after the dedication to the public domain

¹⁸The legislation that created the Board and limited the use of compulsory licensing called for a formal Parliamentary review of these provisions in 1996.

¹⁹The Board has no audit power for verifying firms' reports of R&D activities.

²⁰This abolition is required by the North American Free Trade Agreement and proposed changes to the General Agreement on Trade and Tariffs, both of which bar the use of compulsory licensing in signatory countries.

or expiration of a patent. Currently, the Board loses jurisdiction when the patent is no longer in force.²¹

Conclusions

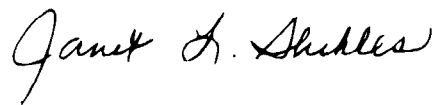
The Patented Medicine Prices Review Board has been effective at restraining prices of patented drugs, particularly price increases on existing drugs. However, its relatively narrow scope of responsibilities has limited its effectiveness in restraining overall drug prices. In this regard, the Board has authority to influence prices of drug products for which the patent has not expired, but lacks authority over products that are unpatented or for which the patent has expired. Consequently, the Board has little or no effect on prices of drug products that never were patented or now are off patent. As a result, the Board's effect on the average price of all drugs is less than it would be if its jurisdiction covered unpatented as well as patented products.

In addition, while the Board did help to slow drug spending growth, its actions were not sufficient to prevent a substantial increase in drug spending. Between 1987 and 1990, real spending on outpatient drugs per person in Canada rose at an average annual rate of roughly 6 percent. As sources of spending growth, drug prices are important but so are other factors for which the price review board has no jurisdiction: the number of prescriptions written and the mix of new, costly products versus older, less costly drugs. A body that only reviews drug prices can help slow spending growth, but it cannot control the impact of these nonprice factors of drug spending.

²¹Patent dedication refers to a patent holder abandoning its proprietary interest in the patent before the patent's expiration, and dedicating the patent's interest to the Canadian public. Once a patent is dedicated, the manufacturer is subject to competition from generic competitors without the need for the generic manufacturer to seek a compulsory license or pay a royalty.

As agreed with your office, unless you publicly announce its contents earlier, we plan no further distribution of this report until 30 days after its issue date. At that time, we will send copies to interested congressional committees; the Director, Office of Management and Budget; and make copies available to others upon request. If you or your staff have any questions about this report, please contact me on (202) 512-7119.

Sincerely yours,



Janet L. Shikles
Director, Health Financing
and Policy Issues

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Abbreviations

| | |
|------|----------------------------------|
| CPI | consumer price index |
| IPPI | industrial products price index |
| ODB | Ontario Drug Benefit Plan |
| PPI | producer price index |
| R&D | research and development |
| VPA | voluntary price adjustment |
| VCU | voluntary compliance undertaking |

Drug Pricing Guidelines of the Patented Medicine Prices Review Board (as of December 1992)

The 1987 patent law amendments that established the Board lists four factors the Board must consider in determining if a price is excessive. These factors are: (1) the prices at which the patentee has sold the medicine in the previous 5 years; (2) the prices of other medicines in the therapeutic class; (3) the prices of the medicine in other countries; and (4) the Canadian consumer price index.

On the basis of these factors, the Board has periodically issued guidelines that it uses on a case-by-case basis to determine when prices of patented drugs are excessive. These guidelines set criteria both for introductory prices of new drugs and for price increases of existing drugs.

The Board bases its price evaluation on sales and price data that patentees are required to submit to the Board semiannually. If the price of a patented medicine exceeds the price resulting from the application of guidelines, the Board will presume that this price is excessive unless there is significant evidence to the contrary.

Guidelines on New Drug Products

In setting pricing guidelines, the Board classifies all new drug products into categories that denote the level of therapeutic improvement provided by each product. These classifications are based on the recommendations of a permanent scientific advisory panel that evaluates information submitted by each patentee of a new drug.¹

The three categories used by the Board are:

Category i: Line extensions—new drugs of an existing or comparable dosage form of an existing drug product.

The price of a category i product is presumed to be excessive if the average introductory sales price per kilogram of the new drug product does not bear a reasonable relationship² to the price per kilogram of other drug products of the same medicine in the same or comparable dosage

¹The Board has two separate advisory panels—one for human drugs and one for veterinary drugs—consisting of three members each. These panels may also seek advice from other scientists and clinicians as needed.

²The Board applies a four part test in determining what constitutes a reasonable relationship. First, it compares the price per kilogram of a new strength with the prices per kilogram of other strengths of the same dosage form of the same medicine. Second, it compares the price of a new strength with the relationship of prices among different strengths of other medicines in the same therapeutic class. Third, it compares the price of a new strength with the relationship of prices among different strengths of other medicines in other therapeutic classes. Fourth, it conducts a therapeutic class price comparison using the price per day of comparable medicines to determine excessive price.

forms sold by the patentee. Where this methodology is not adequate or appropriate, the price may be compared to the prices of other drug products in the same therapeutic class.

Category ii: Substantial improvements—provide significant improvements in therapeutic effects (improved efficacy or reduction in side effects) or significant savings to the Canadian health care system. Includes breakthrough drug products, which are the first drugs sold in Canada that are clinically effective in the treatment of a particular illness or medical indication.

The price of a category ii drug is presumed to be excessive if its introductory price exceeds the prices of all other drug products in the therapeutic class and the median international price of the medicine.³

Category iii: Other new drug products, such as new chemical entities or new drug products of a different dosage form of an existing medicine that provides modest, little or no therapeutic advantage over other drug products in the same therapeutic class.

A category iii drug product is presumed to be excessive if its price exceeds the prices of other drug products in the same therapeutic class in Canada. The Board has recently proposed to amend this guideline to the lower of prices in the class and the median international price.

Guidelines of Price Increases for Existing Drug Products

Allowable price increases for existing drug products are evaluated against a base price—formally known as the benchmark price—that is determined for each product. The particular benchmark price used for each drug is based on when the drug was introduced:

Drugs patented and marketed before the Board's inception: For these drugs, the benchmark price is the price that prevailed on December 7, 1987 (the date of the Board's inception).

Patented drugs first marketed after the Board's inception: For these drugs, the benchmark price is the actual introductory price, if it is not excessive, or the maximum nonexcessive price calculated according to the Board's guidelines.

³The countries used to compute the median international price are France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States.

**Appendix I
Drug Pricing Guidelines of the Patented
Medicine Prices Review Board (as of
December 1992)**

Once the benchmark price is established, subsequent price changes are evaluated against the cumulative increase in Canada's CPI since the date of introduction (or since December 7, 1987, whichever is later), yielding a CPI-adjusted price.⁴ Where the current price is greater than the CPI-adjusted price, the current price is presumed to be excessive. Where the current price is less than the CPI-adjusted price, the current price is presumed to be not excessive.

⁴By evaluating price increases cumulatively, a manufacturer can raise a price faster than the rate of inflation in any single year, so long as the total increase (since the date the benchmark price was set) does not exceed the total increase in the CPI since that date. For example, if the CPI rose by 10 percent between 1991 and 1992, a manufacturer of a drug introduced in 1990—who did not raise prices in 1991—could raise the drug's price by 10 percent in 1992, even if the 1992 inflation rate was substantially less than 10 percent. In October 1992, the Board proposed to remove the cumulative feature of this test to limit actual increases to the annual change in the CPI.

GAO Estimate of the Patented Medicine Prices Review Board's Effect on U.S.-Canadian Prescription Drug Price Differentials

Our estimates of the Board's effect on prescription drug prices in Canada emerge from the results of a previous GAO study of U.S. and Canadian prescription drug price differentials.¹ In that study, we ran a multiple regression model to identify factors that affected the size of the price differential for 120 widely prescribed drugs that are sold in both the United States and Canada.² The study suggested that the Board's regulations were one of the factors that accounted for variations in the U.S.-Canadian price differential among drugs in the population. While these results are not necessarily generalizable to all drugs regulated by the Board (because the drugs in the study were not randomly selected), they can be used to quantitatively estimate the Board's effects on the drugs that were studied and may be suggestive of the Board's potential effects on other drug prices.

Data

The variables used in our multiple regression model, along with their mean values, are listed in table II.1. The dependent variable, LFRAC, was the natural logarithm of the ratio of a drug's factory price per package in the United States and Canada on May 1, 1991. The independent variables were dummy variables defined to capture the affects of various factors that could explain variations in price differentials.

Table II.1: Definitions of Variables Used in Multiple Regression Model

| Variable | Definition | Mean ^a |
|----------|--|--------------------|
| LFRAC | Natural logarithm of the ratio between the price per package (in U.S. dollars) of a prescription drug in the United States and Canada. | 0.406 ^b |
| PRE-C22 | Dummy variable for patented drugs subject to Board regulations on price increases but not subject to Board review on introductory prices. These drugs were patented before passage of the C-22 legislation that established the Board. Equal to 1 for patented drugs introduced before 1988, otherwise equal to 0. | 0.333 |
| D88/89 | Dummy variable equal to 1 for patented drugs introduced in 1988 or 1989, otherwise equal to 0. | 0.066 |

(continued)

¹Prescription Drugs: Companies Typically Charge More in the United States Than in Canada (GAO/HRD-92-110, Sept. 30, 1992).

²These drugs are among the 200 most frequently dispensed drugs in the United States in 1990, as listed by American Druggist. Of these 200 drugs, 79 were excluded from the study for one or more of the following reasons: the manufacturer did not sell the drug in Canada in the same strength or dosage form as in the United States; the drugs was sold by prescription in one country and over the counter in the other; the drug sold in the United States was a generic product that was manufactured by a company that had no affiliate marketing it in Canada; or the manufacturer selling the drug in the United States did not sell the drug in Canada.

**Appendix II
GAO Estimate of the Patented Medicine
Prices Review Board's Effect on
U.S.-Canadian Prescription Drug Price
Differentials**

| Variable | Definition | Mean^a |
|-----------------|---|-------------------------|
| POST89 | Dummy variable equal to 1 for patented drugs introduced after 1989, otherwise equal to 0. | 0.058 |
| ODB | Dummy variable equal to 1 if drug is listed on the ODB formulary, otherwise equal to 0. | 0.835 |
| GENERIC-US | Dummy variable equal to 1 if generic substitutes for the drug are available in the United States but not in Canada, otherwise equal to 0. | 0.107 |
| GENERIC-CAN | Dummy variable equal to 1 if generic substitutes for the drug are available in Canada but not in the United States, otherwise equal to 0. | 0.190 |
| GENERIC-BOTH | Dummy variable equal to 1 if generic substitutes for the drug are available in both countries, otherwise equal to 0. | 0.372 |
| ANTI-INFLAM | Dummy variable equal to 1 for anti-inflammatory drugs, otherwise equal to 0. | 0.174 |
| CARDIO | Dummy variable equal to 1 for cardiovascular drugs, otherwise equal to 0. | 0.190 |
| NERVSYS | Dummy variable equal to 1 for central nervous system drugs, otherwise equal to 0. | 0.207 |
| HORMONES | Dummy variable equal to 1 for hormones and synthetic substitutes, otherwise equal to 0. | 0.107 |
| USMFTR | Dummy variable equal to 1 if drug is produced by a U.S.-based manufacturer, otherwise equal to 0. | 0.603 |
| POST84 | Dummy variable equal to 1 if drug was first approved in the United States after 1984, otherwise equal to 0. | 0.333 |

^aWith the exception of LFRAC, all mean values denote the percent of total observations in each category. For instance, 33.3 percent of the observations are PRE-C22 drugs, 6.6 percent are D88/89, and 5.8 percent are POST89 drugs.

^bThe standard deviation for LFRAC is 0.52.

Of the 120 drugs in the population, 55 were subject to the Board's regulations. Of those 55 drugs,

- 40 (those for which the variable PRE-C22 equals 1) were patented and sold before the effective date of the 1987 legislation (known as C-22) that established the Board. Prices on these drugs have been subject only to Board regulations that affect price increases.
- 8 drugs (those for which the value of the variable D88/89 equals 1) were patented and introduced in 1988 and 1989. These drugs were subject to Board regulation on both introductory prices and price increases. However, the introductory prices may have been set before the 1990

Appendix II
GAO Estimate of the Patented Medicine
Prices Review Board's Effect on
U.S.-Canadian Prescription Drug Price
Differentials

publication of the Board guidelines on setting introductory prices (these guidelines were applied retroactively).

- 7 drugs (those for which the value of POST89 equals 1) were issued after 1989; we assume that the introductory prices of these drugs were set with knowledge of the Board guidelines. We also assume that many of these drugs may not have been on the market long enough to have been subject to Board regulations on price increases at the time we collected our data.

The regression results are listed in table II.2. Of the coefficients relating to Board regulations, those on PRE-C22 and POST89 are both positive and statistically significant. This result is consistent with the effectiveness of both the Board's CPI guidelines and its new drug price guidelines. The coefficient on D88/89, which represents drugs subject to retroactive new price guidelines, is not statistically significant from zero.

Table II.2: Estimate of the Regression Equation

| Dependent variable: LFRAC | | |
|---------------------------|---------------------|----------------|
| Variable | Coefficient | Standard Error |
| Intercept | -0.188 | 0.18 |
| PRE-C22 | 0.288 ^a | 0.10 |
| D88/89 | 0.206 | 0.19 |
| POST89 | 0.420 ^a | 0.24 |
| ODB | 0.265 ^a | 0.15 |
| GENERIC-US | 0.247 | 0.16 |
| GENERIC-CAN | 0.123 | 0.13 |
| GENERIC-BOTH | 0.389 ^b | 0.12 |
| USMFTR | 0.092 | 0.09 |
| ANTI-INFLAM | -0.110 | 0.13 |
| CARDIO | -0.039 | 0.13 |
| NERVSYS | 0.294 ^b | 0.12 |
| HORMONES | 0.278 ^c | 0.16 |
| POST84 | -0.182 ^c | 0.10 |

^aSignificant at the .05 confidence level (one-tailed test).

^bSignificant at the .05 confidence level (two-tailed test).

^cSignificant at the .10 confidence level (two-tailed test).

R-squared 0.3005

Adjusted R-squared 0.2147

Observations ● 120

F-Statistic 3.5020

Estimates of the Board's Impact on Drug Price Differentials

The regression results can be used to estimate the Board's impact on Canadian drug prices relative to U.S. drug prices. This estimate emerges by comparing the predicted price differential of drugs regulated by the Board to the prediction of what the price differential would be if drug prices were unregulated. These predictions, in turn, emerge directly from the regression coefficients.

Effect of the Board's Guidelines on Drug Price Increases

We estimated the effect of the Board's regulations on price increases by evaluating the size of the coefficient on PRE-C22. (PRE-C22 denotes products that have only been subject to the Board's guidelines on drug price increases.) According to the regression equation, the natural logarithm of the predicted U.S.-Canadian price differential for the i^{th} drug for which PRE-C22=1, PREDICT1, is equal to:

$$(1) \ln \text{PREDICT1}_i = -0.188 + 0.288 + (0.265 * \text{ODB}_i) + (0.247 * \text{GENERIC-US}_i) + (0.123 * \text{GENERIC-CAN}_i) + (0.389 * \text{GENERIC-BOTH}_i) + (0.092 * \text{USMFTR}_i) - (0.110 * \text{ANTI-INFLAM}_i) - (0.039 * \text{CARDIO}_i) + (0.294 * \text{NERVSYS}_i) + (0.278 * \text{HORMONES}_i) - (0.182 * \text{POST84}_i)$$

Note that the value of PRE-C22 is assumed to be 1. This means that the drug was marketed and patented before 1988; by definition, the values of D88/89 and POST89 must be zero. The prediction of the U.S.-Canadian price differential for the drug if it were not subject to the Board's regulation, PREDICT2, is the same as it would be if PRE-C22 were equal to zero, or:

$$(2) \ln \text{PREDICT2} = \ln \text{PREDICT1} - 0.288$$

The difference between predictions of the price differential in the Board's absence and the price differential under the Board's regulations can be found by restating equation (2) as:

$$\text{PREDICT2} = \text{PREDICT1} / e^{0.288}$$

or,

$$\text{PREDICT1/PREDICT2} = 1.33$$

This result suggests that the price differential on the 40 drugs for which PRE-C22=1 is, on average, one-third higher than it would have been in the Board's absence.

Effect of the Board's Guidelines on Restraining Introductory Drug Prices

The statistically significant coefficient on POST89 is consistent with the Board's effectiveness at restraining introductory prices for drugs issued after the Board's guidelines were published (that is, after 1989). Similarly to equation (1), the natural logarithm of the predicted U.S.-Canadian price differential for the i^{th} drug marketed and patented after 1989, PREDICT3, is equal to:

$$(2) \ln \text{PREDICT3}_i = -0.188 + 0.420 + (0.265 * \text{ODB}_i) + (0.247 * \text{GENERIC-US}_i) + (0.123 * \text{GENERIC-CAN}_i) + (0.389 * \text{GENERIC-BOTH}_i) + (0.092 * \text{USMFTR}_i) - (0.110 * \text{ANTI-INFLAM}_i) - (0.039 * \text{CARDIO}_i) + (0.294 * \text{NERVSYS}_i) + (0.278 * \text{HORMONES}_i) - (0.182 * \text{POST84}_i)$$

where 0.420 is the coefficient on POST89 in Table II.2. The U.S.-Canadian predicted price differential if these drugs were not subject to the Board's regulation, PREDICT4, is the same as it would be if POST89 were equal to zero, or:

$$\text{PREDICT4} = \text{PREDICT3} / e^{0.420}$$

The difference between predictions of the price differential in the Board's absence and the price differential under the Board's regulations is:

$$\text{PREDICT3/PREDICT4} = 1.52$$

This result suggests that the price differential on the 7 drugs for which POST89=1 is, on average, more than 50 percent higher than it would have been in the Board's absence.

Major Contributors to This Report

**Human Resources
Division,
Washington, D.C.**

**Jonathan Ratner, Assistant Director, (202) 512-7123
David J. Gross, Evaluator-in-Charge
Julie C. Cantor, Evaluator**

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