

**Global Impact of Regulatory
Policies on Pharmaceutical
Distribution and Innovation:
*Canadian Prescriptions for
American Patients***

Mr. John R. Graham
Director
Health and Pharmaceutical Policy Research
The Fraser Institute

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Introduction

Currently, US law makes it illegal for anyone but the manufacturer or his appointed agent to import a prescription drug into the United States. Nevertheless, the growing price difference for prescription drugs between Canada and the United States has created an opportunity for Canadian entrepreneurs to export prescription drugs from Canada to the United States. Canadian mail-order pharmacies currently enjoy reported sales of about \$650 million (US), a trivial amount of the US market for prescription drugs (Harris 2003).

Shipping medicines across the border is against American law, unless carried out by the manufacturer or his agent, and the US Food and Drug Administration (FDA) considers this cross-border trade to be illegal.

However, a number of American politicians would like to legalize it. There is also political support for this business in Manitoba, home to about half of Canada's mail order pharmacies (Baglolle 2002).

Canadian Prescription Drug Prices

Canadian cross-border mail order pharmacies exist because prices of many patented prescription drugs are lower in Canada than the United States. This invites two questions: "By how much?" and "Why?"

Many measures indicate that average Canadian drug prices are lower than those in the United States. The Patented Medicine Prices Review Board (PMPRB) is Canada's national agency that regulates manufacturers' prices of patented drugs. Manufacturers are required to report international price data to the PMPRB, which estimated that the Canadian discount to the United States for patented medicines was 40 percent in 2002 (PMPRB 2003: 23).

Using 2000 prices, a colleague and I compared American and Canadian wholesale and retail drug prices for the top sixty drugs ranked by prescriptions written in the US. We found that only forty-five drugs were comparable, but that price differences for those drugs ranged from a Canadian discount of 98 percent to a Canadian premium of 350 percent at the wholesale level, and a 95 percent discount to a 238 percent premium at the retail level. Two drugs were more expensive in Canada at the wholesale level and seven at the retail level. All these drugs were generics. The average retail price for generics was found to be higher in Canada than the US, whereas branded drugs were significantly discounted in Canada. We estimated that the volume-weighted average Canadian wholesale discount to US prices was 45 percent for patented drugs,

and for retail prices the discount was 35 percent. At the time, the PMPRB measured the discount at 38 percent (Graham and Robson 2000; PMPRB 2001: 21).

There are two reasons why prescription drug prices vary across borders: national regulation and relative incomes. It has never really been possible to fully disentangle these two causes of price differentiation.

Countries with higher incomes will pay higher prices for prescription drugs, as well as other goods and services, as long as markets can be segmented, that is, as long as vendors can prevent customers who enjoy lower prices from re-selling their goods to customers who pay higher prices (Schweitzer 1997: 138-141). A previous article has shown that changes in relative overall price levels (for all goods and services) in six European countries and Canada explain 91 percent of changes in relative prices for patented medicines in those countries (Graham 2002). Canadians have become significantly poorer than Americans over the last decade or more, and this is reflected in relative prices. Canadians started paying less than Americans for virtually all goods and services around 1990 (Baldwin and Yan 2003).

Two previous papers have analyzed the economic causes of the growing Canadian discount for patented medicines (Graham 2000, 2002). In 1987, US Gross Domestic Product (GDP) per capita was 20 percent greater than Canada's, but it widened to 55 percent in 2001, while the Canadian dollar collapsed. Therefore, goods and services overall have become more expensive in the United States relative to Canada. It is important to recognize this macroeconomic factor because it implies that even if the American and Canadian pharmaceutical markets were free markets, price differences would exist.

However, there is also government intervention in prices in Canada's prescription drug market. The PMPRB is the national quasi-judicial body that regulates manufacturers' prices of patented drugs, but it does not purchase drugs.¹ Governments are also bigger buyers of prescription drugs in Canada than in the US. Although private insurance and out-of-pocket payments by patients make up the slight majority of prescription expenditures, government drug benefit plans (primarily financed and managed by the provinces) pay for 45 percent of Canada's prescription drugs for outpatients (CIHI 2003: 66). Proportionally, this is about twice as much as in the US (CMS 2003: Table 3).

Free Trade versus Parallel Trade

The shipment of prescription drugs from Canada to the United States is an example of “parallel trade”. “Parallel trade occurs when differences in national economic, social, legal or regulatory regimes result in different prices among countries, creating opportunities for arbitrage” (Barfield and Groombridge 1999: 185).

The key difference between parallel trade and free trade is that free trade occurs with the voluntary participation of all parties. Parallel trade, on the other hand, opposes the interests and wishes of the affected manufacturers.

Parallel trade can only take place if governments prevent manufacturers from negotiating vertical restraints with distributors, that is, asking them to conform to limits on their reselling. Some governments, such as the European Union (EU), favour parallel trade, because they believe that using vertical restraints to maintain price differences is negative for social welfare. Anti-trust law often prevents manufacturers from imposing vertical restraints on distributors. For example, the doctrine of “first sale” prevents patent (or copyright) owners from stopping secondary sales (Barfield and Groombridge 1999: 196-199).

However, American law has traditionally restricted parallel imports. In a 1997 decision, the US Supreme Court decided on a “rule of reason” standard for judging vertical restrictions by manufacturers over distributors, reflecting economic thinking that recognized the value of voluntarily negotiated restraints for efficiency (reviewed in Graham 2003: 25-27).

Perhaps the most important thing to understand about trade in patented medicines is that usually only a small share of the sales price is accounted for by marginal costs of manufacturing and distribution. Because patents prevent competitors from making exact copies, the original manufacturer can charge what appears to be a high price. However, the extra profit goes to pay a return on the R&D. If this were not permitted, investors would not be interested in financing expensive R&D. However, it also means that manufacturers will be happy to sell their products at lower prices to customers who cannot pay the standard price, as long as the low-priced sales earn a little more than they cost to manufacture and distribute. However, the manufacturer must have a means to keep the two buyers separate, because the high-income buyers would also like to pay a lower price (Danzon 1997).

Problems of Parallel Trade in North America

The first problem of parallel trade from Canada to the United States is that it violates patent laws in both countries. Patent laws are national, and patents for many drugs expire on different dates in Canada than they do in the US. As well, the mechanism for introducing generic competition against branded medicines is different in Canada than the United States. For example, in the United States, if the patent-holder thinks that a generic manufacturer's products will violate his patents, he can generally stop the introduction of a generic competitor for 30 months. In Canada, a similar regulation provides for a delay of only 24 months. Furthermore, the United States provides for six months of exclusivity for the first generic manufacturer to successfully challenge a patent. This was a feature of the Hatch-Waxman Act of 1984 that was meant to give an incentive to the first generic competitor to successfully challenge an innovator's patents. Nothing similar exists in Canada. As well, the United States extends exclusivity for patented products in certain circumstances, especially if the drug is a so-called "orphan" (that is, has a small potential market), or is tested specially for use on children ("pediatric exclusivity"). As well, the US restores the terms of patents devalued by the time that the FDA takes to approve a medicine for safety and efficacy. The patent term is restored by the time it takes for the FDA to approve a medicine, by up to five years, for a total of no more than 14 years from the time the FDA approves until the patents expire (NIHCM Foundation 2000: 4). Canada has no similar provision to protect intellectual property from regulatory encroachment.

Another problem with parallel importing is that it can only thrive with government intervention that prevents drug makers from imposing certain conditions of sale on wholesalers and pharmacies. Because this intervention devalues the assets of foreign investors in Canada, it invites scrutiny under the international trade agreements to which Canada is a signatory, the most important being the North American Free Trade Agreement (NAFTA). It seems possible that the Canadian and Manitoban governments' support of parallel importing is a violation of certain NAFTA provisions.

Article 1110 states that: "No Party may directly or indirectly nationalize or expropriate an investment of an investor of another Party in its territory or take a measure tantamount to nationalization or expropriation of such an investment..." The actions of the Canadian and Manitoban Industry Ministers plausibly fall into this category. One of the achievements of Canada's strengthened patent law, which was firmed up in order to be in accordance with international trade agreements, was a significant increase in capital investment by multinational, including American, research-based drug makers. Prior to 1987, Canada had poor patent protection for pharmaceuticals and

pharmaceutical R&D in Canada was \$106 million (Cdn). As early as 1993, investment had increased to \$504 million (Cdn), and it has continued to grow to over \$1 billion (Cdn) in 2002 (McArthur 1999: 96; Pazderka 1999; PMPRB 2003: 30). The government's allowing parallel trade for the benefit of local intermediaries certainly appears "tantamount" to expropriation.

Article 1105 states that: "Each Party shall accord to investments of investors of another Party treatment in accordance with international law, including fair and equitable treatment and full protection and security." Through encouraging parallel trade, the governments of Canada and Manitoba are certainly not giving foreign-owned manufacturers "fair and equitable treatment and full protection and security", rather, they are destroying the value of their investments in Canada.

However, the pharmaceutical parallel trade between Canada and the US is also likely unsustainable in a practical sense, because those who manufacture the medicines will not tolerate its growth. The current level of pharmaceutical parallel trade from Canada to the US is a trivial share of the US market. The ultimate consequences of parallel trade depend upon how much this grows, how the drug makers respond to it, and how governments react in turn.

Table 1 shows different countries' projected share of the world pharmaceutical market in 2002.

Table 1: World Pharmaceutical Market 2002 (Projected)		
Region	\$ billions (US)	Share
United States	\$158	37%
Major Europe*	\$64	15%
Canada	\$8	2%
Rest of World	\$200	46%
Total	\$430	100%
Source: Graham 2003:17. *UK, Germany, France, Italy, Spain.		

The United States is by far the world's largest individual pharmaceutical market. Of the total projected \$158 billion in 2002, about \$145 billion (US) were brand-name medicines, the rest generic. For Canada, about \$7 billion (US) was brand name, less than 5 percent of US brand-name sales.²

If all the prescriptions going to the US from Canada were for patients who are not able to buy their medicines at US prices, parallel importing would be a win-

win scenario. Patients would get their drugs and manufacturers would gain some revenue that they would not otherwise have earned. However, this is not the case. By its very nature, parallel importation means that the drug makers have no idea who is buying their products; and millions of medically uninsured Americans are high-income earners (Irvine and Zelder 2002).

The willingness of the research-based drug makers to cut off supplies to Canada is conditioned by a couple of factors. Firstly, their ability to police and manage their supply chains to prevent the parallel trading. Secondly, the risk that the Canadian government would allow generic manufacturers to make copycat versions of patented drugs under compulsory licenses (which is permitted for emergencies) if the research-based drug makers stop supplying Canada. The more confidence they have that Canadian law will support the integrity of their distribution into Canada, the less likely they will be to restrict supplies.

Nevertheless, another approach might not create an “emergency” that would allow Canada to impose compulsory licencing without running afoul of international trade law. This would be for the drug makers to raise prices in Canada to the US level. This cannot be done easily with drugs already sold in Canada, because the PMPRB does not generally allow price increases greater than the annual change in the Consumer Price Index (CPI). However, Canadian prices of patented medicines have usually risen less than the change in the CPI. Last year, they even went down (PMPRB 2003). We should not expect this to continue.

For newly introduced breakthrough drugs, Canadian prices are set with regard to those in the United Kingdom, France, Germany, Sweden, Switzerland, and Italy, as well as the United States. We should expect the drug makers to raise prices of medicines in those first six countries to US levels, so that Canadian prices can be set similarly high. Indeed, as a general rule, we should expect one, global price to evolve for each patented medicine – a price similar to the one currently in the US – in response to broadening the scope for parallel trade from foreign countries into the US.

Because of both foreign and domestic pressure, it is then likely that the United States would adopt explicit price controls on prescription drugs. Foreign governments, whose people do not have as high incomes as Americans do, would be unable to pay US prices for the volume of drugs they need. They would put pressure on the US to implement explicit price controls in the United States, in order to reduce their own prices again (Calfee 2002).

The Effect of Canadian Prices on R&D

There is a well-established relationship between pharmaceutical companies' prospective earnings and their investments in R&D (Graham 2003: 25-29). Imposing Canadian prescription drug prices on the much larger US market would have consequences on companies' willingness to invest in R&D.

Table 2 breaks down the US patented pharmaceutical market of \$145 billion dollars in 2002 into four sub markets.

	Uninsured	Privately insured	Government insured	FSS/VA
\$ billions (US)	\$33	\$80	\$30	\$2
Price Index	118	100	100	59

Source: Graham 2003: 21

Tables 3, 4, and 5 describe the negative consequences to R&D of three different scenarios (as developed in Graham 2003: 20-22). Within each scenario, the insured population increases its use of prescriptions by 10 percent when US law forces prices down to Canadian levels. However, the uninsured increase their number of prescriptions by 20 percent, 40 percent, or 60 percent in each scenario. As well, the tables show what happens when the government forces Canadian prices on only the insured; when it forces Canadian prices on the uninsured plus those insured by government programs; and, finally, when it forces Canadian prices on all US sales. Each cell shows the estimated immediate reduction in new R&D dollars invested, plus the percentage drop from the world's actual pharmaceutical R&D investment in 2002 of \$32 billion (PhRMA 2003: 10).

Table 3 shows the "best case", assuming gross margins on US sales before price controls of 80 percent, and 10 percent of cash flow invested in R&D. In this case, global investment in pharmaceutical R&D drops by 3 percent if the government forces Canadian prices on only the uninsured, and by 15 percent if it forces Canadian prices generally on the US. Table 4, the "middle-of-the-road" scenario, assumes gross margins on US sales before price controls of 70 percent, and 20 percent of cash flow invested in R&D. In this case, R&D investment drops by 30 percent if the government imposes Canadian prices throughout the US. Table 5, the "worst case", assumes gross margins on US sales before price controls of 60 percent, and 30 percent of cash flow invested in R&D. In this case, global R&D drops by almost a half if the government legislates Canadian prices for the whole US population.

Table 3: Reduction in R&D from Canadian pharmaceutical prices in United States, 2002, \$ billion, (share of actual world R&D)

	<i>Increase in prescriptions for uninsured</i>		
Canadian prices applied to:	20%	40%	60%
Uninsured only	\$1 (4%)	\$1 (3%)	\$1 (3%)
Uninsured + Government insured	\$3 (8%)	\$2 (7%)	\$2 (6%)
Total US market	\$5 (15%)	\$5 (15%)	\$4 (14%)

NB: No. of prescriptions for insured increase 10%, Gross margins 80%, new R&D investments equal 10% of cash flow

Table 4: Reduction in R&D from Canadian pharmaceutical prices in United States, 2002, \$ billion, (share of actual world R&D)

	<i>Increase in prescriptions for uninsured</i>		
Canadian prices applied to:	20%	40%	60%
Uninsured only	\$3 (9%)	\$2 (8%)	\$2 (7%)
Uninsured + Government insured	\$5 (16%)	\$5 (15%)	\$4 (14%)
Total US market	\$10 (31%)	\$10 (30%)	\$9 (29%)

NB: No. of prescriptions for insured increase 10%, Gross margins 70%, new R&D investments equal 20% of cash flow

Table 5: Reduction in R&D from Canadian pharmaceutical prices in United States, 2002, \$ billion, (share of actual world R&D)			
	<i>Increase in prescriptions for uninsured</i>		
Canadian prices applied to:	20%	40%	60%
Uninsured only	\$4 (14%)	\$4 (13%)	\$4 (11%)
Uninsured + Government insured	\$8 (25%)	\$8 (24%)	\$7 (23%)
Total US market	\$15 (47%)	\$15 (46%)	\$14 (45%)
NB: No. of prescriptions for insured increase 10%, Gross margins 60%, new R&D investments equal 30% of cash flow			

Conclusions

Parallel trade in prescription drugs from Canada to the United States, or Canadian price controls in the US, are not solutions to the challenges that a small but significant number of Americans have in paying for prescriptions.

Imposing Canadian prices on the United States through price controls threatens to have a catastrophic impact on pharmaceutical R&D, by reducing it by 5 percent to 47 percent of annual global investment.

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¹ A previous paper has argued that the PMPRB cannot be a cause of low Canadian drug prices, but that it may cause prices to be rigid downward (Graham 2000: 12-14).

² For 2001, 8.4 percent of US sales were for generic drugs (GphA 2003). Assume the share stays the same for 2002.