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Senate Committee on Health, Children, Families, Aging and Long Term Care

(SC-HCFALTC)

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Record of Comm. Proceedings ... RCP

- 03hrAC-EdR_RCP_pt01a
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- 03hrAC-EdR_RCP_pt02

- *Appointments* ... *Appt*
- **

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Prescription Drug Prices in Canada and the United States—Part 4

Canadian Prescriptions for American Patients Are Not the Solution

John R. Graham

Contents

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Executive Summary

In the last couple of years, a grey market has risen between Canada and the United States: the illegal diversion of prescription drugs meant for Canadian patients to medically uninsured Americans who want prescriptions at Canadian prices, which are often much lower than those in the United States. Although sales are currently only about US$650 million, a drop in the bucket of America's huge prescription-drug market, this growing business has drawn criticism from physicians, pharmacists, community pharmacies, and research-based drug manufacturers, and attention from legislators and regulators. On the other hand, a growing number of American patients are taking advantage of Canadian cross-border mail-order pharmacies to save money on their life-saving prescriptions.

This paper looks at the cross-border mail-order pharmaceutical trade and determines that it suffers serious flaws:

- it exists because governments in the United States have made it very difficult for uninsured, low-income patients to get prescription drugs at low prices;
- it can only grow with government support;
- it violates the principles of free trade, and possibly the North American Free Trade Agreement (NAFTA);
- it is a less safe method of distributing prescription drugs than a free market that operates with the cooperation of research-based drug makers;
- it poses a serious risk that research-based drug makers will stop supplying Canada with their products, which would force the Canadian government to make difficult decisions about its commitment to patent law; and
- importing Canadian prices generally into the United States would reduce the profits of research-based drug makers to such a degree that they would reduce annual investment in research and development (R&D) by US$5 billion to US$15 billion, the latter estimate being almost half of global pharmaceutical R&D for 2002.

Therefore, the Canadian government must take steps to discourage and eliminate this illegal business. Furthermore, the American government must reduce government intervention that limits uninsured, low-income patients' access to prescription drugs. Both countries must undertake reforms that will allow patients and drug makers, not governments, to determine appropriate prices for prescription medicines.

Introduction

Current 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 difference between the price for prescription drugs in Canada and that in 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 US$650 million, a trivial portion of the American market for prescription drugs (Harris 2003), but the business has grown quickly and has attracted the support of a number of American politicians who want all Americans to enjoy lower Canadian prescription prices. For example, US Representative Gil Gutknecht, a Republican Congressman from Minnesota, and a number of colleagues have introduced the so-called Pharmaceutical Market Access Act. This Act would allow mail-order pharmacies from 25 countries to sell into the United States, despite the fact that those sales would violate the distribution contracts between manufacturers and wholesalers. As one of his co-sponsors, Congresswoman Anne Northrup (Republican, Kentucky), stated: "Americans should be allowed to purchase prescriptions at the same price these drugs are sold in Canada" (Gutknecht 2003).

Politically, this position seems to be a winner. A recent poll indicates that only 44% of Americans think that price controls would reduce investment in research and development (R&D) of pharmaceutical drugs (Pallarito 2003b). On the other hand, this cross-border trade has drawn the ire of research-based drug makers and community pharmacies as well as the condemnation of the National Association of Boards of Pharmacy and the American Pharmacists Association in the United States; and the National Association of Pharmacy Regulatory Authorities and the Canadian Pharmacists Association in Canada (CPhA 2003; NACDS 2003; NAPRA 2003; PhRMA 2003a). Until recently, Americans who wanted Canadian prescriptions had to drive across the border to get them. In the 2000 national election in the United States, many politicians, hungry for seniors' votes, sponsored bus trips to Canada to show how much seniors could save if only the drug makers would not "gouge" them. The point of these trips, of course, was not to promote the business of Canadian pharmacies but to validate the idea that government intervention would lower prescription drug prices in the United States.

Obviously, Canadian mail-order pharmacies tap a much larger potential market than bus trips do. Furthermore, they are marketing aggressively, by setting up partnerships with American street pharmacies (their natural competitors) to maintain kiosks that solicit customers to divert their prescriptions to Canada. Although at least three research-based drug makers, GlaxoSmithKline, AstraZeneca, and Pfizer, announced earlier this year that they would cut off supplies to these businesses, it appears that the Canadian mail-order operations are able to stock their inventories from Canadian street pharmacies. Shipping medicines across the border is against American law, unless carried out by the manufacturer or his agent, but the US Food and Drug Administration (FDA) has traditionally allowed individuals to bring in 90-days worth of medicines for personal use.[1] This is the loophole exploited by the cross-border mail-order pharmacies. In March, however, following a meeting between Canadian and American regulators, the FDA announced that it would enforce the law. Nevertheless, the kiosks and mail-order pharmacies continued to thrive, with no perceptible reduction of business until recently (Associated Press 2003; Baglole 2003a, b, c; Cusack and Stinson 2003; Friscolanti 2003; Pallarito 2003a). By the end of August 2003, drug makers had had some success in cutting off supplies to the cross-border pharmacies (Cohen 2003).

Nevertheless, a change of political opinion in the United States could quickly make the business legal. In 2000, President Clinton signed the Medicine Equity and Drug Safety Act, which permits this cross-border trade

if the Secretary of Health and Human Services certifies that it is safe (Graham 2001a). Neither President Clinton's nor President Bush's Health Secretary has done so but all it would take is a signature. Federal and state legislators too numerous to count have proposed further legislation similar to that of Congressman Gutknecht and colleagues.

There is also political support for this business in Manitoba, home to about half of Canada's mail-order pharmacies (Baglole 2002). When GlaxoSmithKline announced that it would cut off supplies to Canadian pharmacies that ship to the United States, Manitoba's Industry Minister, MaryAnn Mihychuck, prompted her federal counterpart, Allan Rock, to ask the national Competition Bureau to investigate GlaxoSmithKline's behaviour (Canadian Press 2003). The Competition Bureau declined to do so.

In May, the Canadian Health Ministry's Health Products and Food Branch Inspectorate released a *Guidance Document on the Commercial Importation of Drugs in Dosage Form under the Food and Drugs Act* that explains the conditions regulating traders importing and exporting medicines. The *Washington Post* interviewed senior officials of the US FDA who interpreted this as Canada's guaranteeing the safety of medicines shipped to the United States, because the Guidance Document confirmed that those medicines were subject to the same safety regulations as if they were sold in Canada. This prompted an official from Health Canada to write a letter to the newspaper, denying the Canadian government's responsibility for the safety of American patients who fill prescriptions via Canadian mail-order pharmacies (Gorman 2003; Health Products and Food Branch Inspectorate 2003a, b; Kaufman 2003a, b).

So, the regulatory environment on both sides of the border is confused and volatile, undoubtedly reflecting deep political divisions with respect to the value of this enterprise. The goal of this paper is to examine the consequences to American patients, to the supply of prescription drugs in Canada, and to the research and development of new medicines in the future, of this growing grey market for prescription drugs. It concludes that these cross-border mail-order pharmacies are harmful, that they will likely cause prices to rise in Canada and other countries, and that this will probably lead to increased pressure for explicit price controls in the United States, which would seriously reduce global investment in medical R&D.[2] It also suggests other options to serve the needs of the small number of American patients who cannot afford their prescription medicines.

Notes

1 One policy analyst interprets the exemption to be valid only for medicines that are not approved in the United States (Matthews 2003).

2 This analysis focuses solely on wholesalers and cross-border mail-order pharmacies that sell prescription drugs in violation of terms of sale negotiated with drug makers, not domestic mail order pharmacies that operate in good faith with drug makers, the latter being a valuable innovation in the distribution of medicines.

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?"

Comparing international differences in pharmaceutical prices is a challenging task. Professor Patricia M. Danzon and colleagues have demonstrated those challenges in a series of measurements (Danzon 1996, 1997a; Danzon and Kim 1998; Danzon and Chao 2000). Firstly, not all countries have the same drugs. Secondly, when the same drug is sold in different countries, it can be sold in different doses. Thirdly, patients in different countries consume different quantities of the same drugs, so the price differences will vary depending on whether the prices are weighted using Canadian or American quantities. For example, using American levels of consumption and comparing drugs with the same molecular composition (rather than brand name), and by standard dosage unit (rather than gram of active ingredient), the price index for Canadian drugs was 3% higher than in the United States! At the other extreme, using Canadian levels of consumption while still comparing molecular composition and standard unit, the Canadian price index was only 45% of the American level. For those interested in the challenges in comparing international price differences for pharmaceuticals, the work of Danzon and colleagues is highly recommended. Regrettably, this work uses data from 1992, so the results are not applicable to a timely analysis of the policy implications of parallel importing from Canada to the United States today.

Even if we cannot say exactly how much more expensive American drugs are than Canadian drugs, many measures indicate that Canadian drug prices are generally 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% in 2002 (PMPRB 2003: 23).

Using 2000 prices, a colleague and I compared American and Canadian wholesale and retail drug prices for the top 60 drugs ranked by prescriptions written in the United States. We found that only 45 drugs were comparable, but that price differences for those drugs ranged from a Canadian discount of 98% to a Canadian premium of 350% at the wholesale level, and a 95% discount to a 238% 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 United States, whereas branded drugs were significantly discounted in Canada. We estimated that the volume-weighted average Canadian wholesale discount to American prices was 45% for patented drugs; the retail discount was 35%. At the time, the PMPRB measured the discount at 38% (Graham and Robson 2000; PMPRB 2001: 21).

A subsequent paper showed the savings that could be obtained by a shopper who moved from the surveyed pharmacy with the highest price to the one with the lowest price in his home area. As well, it showed the maximum and minimum savings from cross-border shopping by an American patient who went to the adjacent Canadian area. For example, British Columbia is the Canadian province that neighbours the state of Washington. The American shopper from the pharmacy with the highest priced *Celebrex*® (celecoxib) in the Washington area who traveled to the British Columbian pharmacy with the lowest priced *Celebrex*®, saved US$62.77. However, the American customer who already shopped at the pharmacy with the cheapest *Celebrex*® in Washington and who traveled to the most expensive British Columbian pharmacy would save only US$36.62 (Graham 2001b).

Despite uncertainly about how much difference there is between the prices for prescription drugs in the two

countries, the growth of the cross-border trade indicates that there are significant price differences for a number of widely used medicines. There are two reasons why prescription drug prices vary across borders: national regulation and relative incomes. It has never been possible to disentangle these two causes of price differentiation fully. 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% of changes in relative prices for patented medicines in those countries (Graham 2002a). 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, 2002a). In 1987, US Gross Domestic Product (GDP) per capita was 20% greater than Canada's but the difference widened to 55% in 2001, while the Canadian dollar collapsed. Therefore, goods and services overall have become more expensive in the United States than in Canada. Automobiles, for example, cost 16% more in the United States than in Canada in 1999. This has created a grey market for cross-border shipments of cars: Ford Motor Company has reportedly fined its Canadian dealers up to $1 million for selling new vehicles to American buyers. When it launched the new MINI in Canada, BMW insisted that buyers undertake not to export their cars to the United States for a "windfall profit." Chrysler stated that it would stop honouring warranties in the United States on vehicles originally sold in Canada as of the 2003 model year. The struggle between automobile manufacturers and automobile exporters, broadly similar to that in the pharmaceutical trade, resulted in the exporters' launching an anti-trust lawsuit against the manufacturers in the United States in February 2003 (Graham 2002a and references; Keenan 2003). It is important to recognize this macroeconomic factor because there are no price controls in Canada's automobile market, which implies that, even if the American and Canadian pharmaceutical markets were free markets, price differences would exist.

There is, however, 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 does not purchase drugs.[1] Governments are also bigger buyers of prescription drugs in Canada than in the United States. 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% of Canada's prescription drugs for outpatients (CIHI 2003: 66). Proportionally, this is about twice as much as in the United States (CMS 2003: Table 3).

Note

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).

American Prescription Drug Prices

By most measurements (notwithstanding Professor Danzon's cautions about comparing international price differences), American prescription drug prices are much higher than prices in other countries and this difference cannot be explained simply by different national incomes (Graham 2002a). One explanation for this is that, because the American market is the largest in the world, other countries' governments can "free ride" on American investment in pharmaceutical R&D by regulating lower prices than would prevail in a free market. Public and quasi-public agencies are usually the largest buyers of prescription medicines in developed democracies outside the United States, so they have a big incentive to pass laws and regulations that allow them to take a "free ride." Because marginal costs of manufacturing and distributing prescription drugs are a relatively small share of their total costs, free riders can get medicines cheaply without contributing to the sunk costs of R&D and be confident that manufacturers will supply them nonetheless, because they can still earn a small marginal profit by doing so (Danzon 1997a: 93, b: 306; Schweitzer 1997: 150).

However, the United States also has domestic policies that keep prices higher than they would be in a free market. One reason for the high costs of American patented medicines is the uniquely high cost of American health care overall. In 2000, the United States spent 83% more per capita on health care than Canada did. However, it only spent 44% more on medicines than Canada did (Anderson et al. 2003: 91–94).[1] Canadian prices for health-related goods and services in general are even lower relative to those in the United States than prices for patented drugs are, despite explicit price controls on prescription drugs in Canada (Graham 2002a).

Of course, no American lobbies his government for access to Canadian hospitals or doctors! Unlike the Canadian market for prescription drugs, where there is still significant private payment, provincial government insurers that function as monopolist insurers dominate the market for hospitals and physicians. This is the cause of Canada's lengthy queues for diagnostic and surgical services, which now create a median wait of 16.5 weeks from the time a general practitioner refers a patient to a specialist until the specialist is able to provide the required treatment (Esmail and Walker 2002: 23). As well, the high cost and risk of product liability litigation in the United States has long been recognized as a factor increasing American pharmaceutical prices (Manning 1997).

The design of American health insurance has been one cause of the political debate over pharmaceutical prices in the United States, because patients who pay cash directly from their own pockets pay more than insurers do. This goes back to the 1950s, when insurers covered prescription drugs to a lesser degree than they do today (Frank 2001: 117). Starting in the Second World War, the US government allowed employers to offer health insurance to workers as a non-taxable benefit. This distorted the market so that individuals without company-benefits have limited access to health insurance and, therefore, the buying power of large health insurers.

Today, large buyers such as Health Maintenance Organizations (HMOs) and Preferred Purchaser Organizations (PPOs) get breaks on prices because they can move market share to drug makers who favour them with discounts. They also have an advantage in that they can often distribute medicines more efficiently through proprietary systems than traditional, community pharmacies can. For example, Pharmacy Benefit Managers (PBMs, to whom insurers such as HMOs contract out the management of prescription benefits) use mail order to deliver prescriptions from central warehouses. This efficiency gives them the leverage to negotiate discounts from both manufacturers and pharmacies. Individuals buying drugs for cash have traditionally used pharmacies that are too small to direct large volumes of prescriptions and, therefore, do not have enough market power to negotiate for substantial discounts from drug makers (Frank 2001: 122; Scherer 1997; US DHHS 2000: 103).

Nevertheless, because private insurers in the United States operate in a pseudo-competitive environment, they sometimes fail to negotiate big discounts if drug makers balk at cutting prices and patients demand a drug loudly. For example, *Claritin*® (loratidine) was launched in 1996 and the giant HMO Kaiser Permanente initially refused to list it on its formulary because the manufacturer refused to give Kaiser the discounts it wanted. However, Kaiser's clients demanded the drug and this pressure motivated Kaiser to list it without major discounting by the manufacturer (Kolassa 1997: 52–53).

However, the uninsured also suffer because the US government currently forces drug makers to raise prices artificially. The American market for prescription drugs became seriously distorted when government agencies started demanding discounts in the early 1990s, as enshrined by the Omnibus Budget Reconciliation Act in 1990. The fact that legal force rather than negotiation created these discounts had significant negative consequences for pharmaceutical prices because it made it illegal to give anyone else bigger discounts than the government enjoyed. Because government programs in the United States make up over one fifth of the prescription market, drug makers had to keep in mind the effect on prices to government agencies when they negotiated with private purchasers. Discounts to hospitals and private insurers shrank in the 1990s because of the government's reimbursement rules and HMOs saw their discounts fall from 24% in the first quarter of 1991 to 14% two years later (US GAO 1997, 2000). Furthermore, prices of generic drugs increased, probably because the government intervention reduced competition in the branded market (Scott Morton 1997a: 271).[2]

The impact on uninsured patients is serious, because it limits the discounts that research-based drug makers can offer on their proprietary discount cards, which they issue to low-income patients who apply for them. In 2002, GlaxoSmithKline and Bristol-Myers Squibb reduced discounts on a private discount card until the US government gave them relief on a technicality (Petersen 2002). Coincidentally and equally sadly, this legal inhibition of discounting also occurs in American hospitals, which are prevented from discounting services to uninsured people (Pryor and Seifert 2003; Wielawski 2000).

Another way that the US government artificially raises pharmaceutical prices is through the regulatory burden of the FDA. A number of authors, including Ronald Hansen of the University of Rochester, Henry I. Miller of the Hoover Institution, and Alex Tabarrok of the Independent Institute (Hansen 2000, Miller 2000, Tabarrok 2000), have analyzed how costs of the FDA's regulations have negatively influenced the pharmaceutical market.

The government formulary in the United States most deeply discounted is that of the Veterans Health Administration (VA). The VA manages prescription drugs on the Federal Supply Schedule (FSS), the lowest priced formulary in the land. Furthermore, the VA has negotiated prices even lower than those on the FSS for the "Big Four," itself and three other US government agencies, the Department of Defense, the Coast Guard, and the Public Health/Indian Health Service. Because of the VA's low drug prices, it is tempting to hold it up as a model for how the US government should manage a Medicare or even universal prescription drug benefit: use Uncle Sam's muscle to wring dirt-cheap drug prices for every American!

However, thinking that the US government could replicate for the whole country the special deals negotiated for the FSS or the VA is unrealistic for a number of reasons. Firstly, the VA serves a clearly defined population of 3.8 million veterans and is, therefore, similar to a private retiree benefit. The beneficiaries of the other agencies in the Big Four are also limited to a small share of the federal government's employees or retirees and the whole group that paid FSS prices only spent US$1.5 billion in 1999. Secondly, US law demands that manufacturers list their medicines on the FSS if they want to supply Medicaid, the socialized health plan for the poor. Medicaid accounts for a significant share of American spending on prescription drugs and pays just a tick less than private insurers do. It is important for drug makers to be on Medicaid, so they will list on the FSS despite its low prices, because those prices do not apply to Medicaid (US GAO 2000: 10; CMS 2003: table 3). Thirdly, over half the physicians living in the United States have worked within the VA. If their prescribing behaviour persists after leaving the VA, it makes sense for drug makers to list on the FSS, even at extremely low prices, so that those doctors are familiar with their products (PMPRB 1999: 4).

Another reason that the VA formulary cannot be used for the entire country is that the VA manages a closed formulary, which restricts its beneficiaries' choice of medicines. This is because the VA's negotiations have not resulted only in generally lower prices from drug makers. Rather, manufacturers who reduced prices increased sales and those that did not were left out of the closed therapeutic classes. For example, after the class of proton pump inhibitors was closed in 1997, *Prilosec®* (omeprazole, the "purple pill"), dropped from almost 100% of market share to almost nil, in favour of *Prevacid®* (lansoprazole), because *Prilosec®*'s maker would not reduce prices to the VA's satisfaction. Prices for drugs that were listed on the formulary dropped by 13% to 36% from what they had been before the formulary was closed for those classes. The closing of the formulary affected the medicines that patients used, which invites the question of whether they are using appropriate ones, but there has not been specific research on the health outcomes of the closed VA formulary (Huskamp et al. 2003: 153–56). This limited selection of drugs is becoming common for government plans that demand deep discounts but is not usual for private health plans, which indicates that the broader American population will resist such an approach.

Indeed, one reason that manufacturers do not launch new, patented drugs at deep discounts to market leaders is because such an approach has not succeeded in capturing enough market share to validate the discounting strategy. For example, *Prevacid®* entered the American market in June 1995 at a 10% discount on the price of *Prilosec®* but captured less than 4% of the market by 1997. It appears to have required government intervention to move patients away from *Prilosec®*. *Univasc®* (moexipril HCL) entered the crowded market of ACE inhibitors (for hypertension) in June 1995 at half the price of market leader *Vasotec®* (enalapril) but had captured less than 1% of the market by 1997 (Kolassa 1997: 4).

Finally, the patients who are really having trouble filling their prescriptions are not primarily the elderly. According to a recent survey, elderly Medicare beneficiaries were found to be less than half as likely as working-age people with employer coverage to report that they paid a lot out of pocket for prescriptions or dental services (Davis et al. 2002: W317). In another survey, 29% of America's uninsured and 26% of Medicaid beneficiaries (non-elderly poor) reported that they did not obtain a drug due to cost; only 8% of Medicare beneficiaries said the same (Cunningham 2002: 2). Using the Medicare Current Beneficiary Survey for 1996 through 1999, another analysis found that less than 3% of American seniors reported not getting the medicines that they were prescribed and some of these chose not to fill their prescriptions because they did not want the medicines that their physicians prescribed, not because they could not afford them (Craig et al. 2003).[3] Therefore, the problem of the affordability of prescription drugs is less widespread than is often believed and domestic laws and regulators are responsible for some of it.

Note

1 This includes both prescription and over-the-counter drugs.

2 Scott Morton did not conclude that patented drug prices increased as a result of the most-favoured-customer rule. However, she did not have price data for HMOs or Pharmacy Benefit Managers and was looking only at the pre-rebate Average Wholesale Price, which is a list price not a transaction price (Scott Morton 1997a: 271–72, 278; US DHHS 2000: 98).

3 Another survey published last year reported a higher proportion of seniors, 22%, not filling prescriptions due to costs (Safran et al. 2002: W263). However, Safran and colleagues over-sampled low-income subjects and had are response rate of 55%, whereas Craig and colleagues had a response rate of 94%.

Free Trade versus Parallel Trade

The illegal shipment of prescription drugs from Canada to the United States is an example of "parallel trade," the subject of a useful economic and legal literature (see Appendix A, page 25). "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). When a country's exchange rate appreciates, so do parallel imports (Barfield and Groombridge 1999: 245 and references). The long-term depreciation of the Canadian dollar is certainly one cause of the pressure to allow pharmaceutical parallel trade with the United States today.

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. For this reason, it is defined as a "grey market" (Ruff 1992: 120). This is important to understand because some proponents of pharmaceutical parallel trade incorrectly criticize efforts to stop it as anti-competitive. If GlaxoSmithKline, a company with its headquarters in Britain, were lobbying to prevent an American drug maker, such as Pfizer or Eli Lilly, from selling its products in the United Kingdom, that would violate the principles of free trade; efforts by GlaxoSmithKline to secure its own distribution do not.

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. Laws and regulations regarding parallel importing have become increasingly complicated and technical (Rothnie 1993: 471). Some governments, such as the European Union (EU), favour parallel trade because they believe (incorrectly) 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 the owners of patents (or copyrights) from stopping secondary sales (Barfield and Groombridge 1999: 196–99).

However, analysis going back to the 1960s shows that many vertical restraints favour competition and a small literature on the benefits of price differentiation and discouraging parallel trade has been written in the last 20 years (see Appendix A, page 25). This has influenced American law, which has traditionally restricted parallel imports, although parallel trade for trademarked goods (such as luxury-branded handbags) increased significantly during the 1980s. 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 for efficiency of voluntarily negotiated restraints (Barfield and Groombridge 1999: 196–99; Malueg and Schwartz 1994: 168; Ruff 1992: 121).

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 1997a).

The technical term that describes the reach of patent-holders' rights after the first sale of their protected products is "exhaustion." Under national exhaustion, a patentee can prevent parallel importation of his product from a foreign country. Under international exhaustion, the patentee loses the right to control further trade in his

product after he has first sold it abroad, and this facilitates parallel importing. Regional exhaustion is a middle ground between the two. For example, the European Union has regional exhaustion and American politicians who support the cross-border trade in prescription drugs from Canada but no other country implicitly support regional exhaustion (Fink 1999: 173–74).

The North American Free Trade Agreement (NAFTA) and the World Trade Organization's Agreement on Trade Related Intellectual Property Rights (TRIPS) are silent on the question of whether countries should enforce national or international exhaustion of patent rights. Although some American judges have favoured arguments supporting parallel importing, the United States has traditionally respected national exhaustion. It was American negotiators who succeeded in putting the "right of importation" into the TRIPS Agreement, which lets countries give patentees the right to stop parallel importing (Barfield and Groombridge 1999: 190–99; Fink 1999: 175; Rothnie 1993: 170–85). This makes President Clinton's Medicine Equity and Drug Safety Act of 2000 and similar proposed legislation quite remarkable. They completely reverse the United States' position on the question of exhaustion. As we shall see, this has considerable consequences for the validity of US patents.

Failure of Parallel Trade in Europe

The European Union (in its previous incarnation as the European Economic Community) has allowed parallel trade within its borders since the early 1970s. At the time, the then-patented *Valium*® (diazepam) was supplied by Roche (UK) for $1.60 while Roche (Holland) sold the same medicine for $1.98, a 24% differential. A Dutch wholesaler bought *Valium*® from the United Kingdom and sold it in Holland. The EU approved of the trade and parallel importing took flight. In a European parallel-trading lawsuit from 1981, the research-based drug-makers' lobby reported a German price for *Moduretic*® (amiloride) that was more than twice the British price. Like everywhere else, income per capita explains some of the price differences for prescription drugs between European countries. Because Britain's economy was performing poorly in those days before Prime Minister Thatcher, it had lower prices than its neighbours and was a parallel exporter. During the 1980s, British prices for prescription drugs rose relative to other European prices and Britain now parallel imports about 20% of its pharmaceutical sales (Fink 1999: 175; Reekie 1996: 11; Rothnie 1993: 475–76; Ruff 1992: 125–27; Towse 1998: 272; West and Mahon 2003: 62).

The accession to the European Union of countries such as Spain and Greece, which had very low prices, increased the opportunities for parallel trade. Also, the harmonization of therapeutic approval by the European Medicines and Evaluation Agency (similar to Health Canada's Therapeutic Products Directorate and the United States' FDA) has reduced the cost of repackaging by parallel importers (Danzon 1998: 294).

Parallel trading in Europe has failed to contain growth in pharmaceutical costs and likely contributed to reducing the European Union's capacity to research and develop new medicines. Furthermore, the negative consequences of parallel trade for Europe are probably minor relative to what they would be in North America, because of important differences between the markets on the two continents.

In Europe, a manufacturer cannot choose into which markets it will sell and into which it will not; EU law requires that the entire Union be supplied. Even if a manufacturer could select which countries to supply, it would be unlikely to cut off the Spanish market, for example, in order to preserve its margins in France. The differences in size among European markets are not nearly as large as the difference between the Canadian and American markets. Europe is too large in the global market to cut off entirely, because its largest five countries alone make up 15% of the world's market, but it does not dominate the global market as the United States does (IMS Health 2003). As long as parallel importing is contained within Europe, there is a welfare loss but it is not as huge as it would be if there were parallel trading between Canada and the United States, or between Europe and the United States.

In addition, parallel importing in Europe is limited by a number of factors. Firstly, European national markets are traditionally heterogeneous: prescription drugs that are widely used in one country are not necessarily popular in other countries, although this is less true of newer products (Rothnie 1993: 485, 493). More importantly, European prices are not generally set by patients or private insurers but by national policies, so parallel trading has not resulted in one European price. Instead, parallel trade simply transfers one country's regulated prices to its neighbours (Pollard 2003). Because some EU countries use European averages to set prices, it is in drug makers' interests to keep prices as high as they can in countries that allow it. Also, a manufacturer's lowering a price in one country may simply create another source of supply to neighbours who have higher prices (West and Mahon 2003: 68). For example, GlaxoSmithKline's predecessor delayed launching *Imigran*® (sumatriptan) for several years in France because of a low price offered in that country. Some companies have reported that they have delayed launching products in Europe until they can achieve one, continent-wide price (Danzon 1998: 300).

However, European nations have not equalized their prices generally because they have conflicting objectives. They are forced to make a trade off between prices and encouraging a research-based pharmaceutical industry within their borders. Governments that value pharmaceutical investment in their countries will accept higher prices (but not at American levels).[1] Furthermore, socialized health systems have a bias towards buying from domestic manufacturers; so local products tend to enjoy relatively higher prices. Although a EU directive was meant to minimize this tit-for-tat behaviour (in order to rationalize local production distortions), different national health systems have nevertheless valued innovation differently (Barfield and Groombridge 1999: 260; Healy 1996: 163; Jacobzone 2000; Rothnie 1993: 488; Towse 1998: 273).

Also, because national health systems decentralize pharmaceutical budgets to different degrees, control by national governments varies (Huttin 1999). For example, a committee appointed by the country's doctors and health-insurance industry initially negotiated Germany's reference prices for prescription drugs. The federal government took over in 2001, as a consequence of a legal decision that found the committee anticompetitive (Kanavos and Reinhart 2003: 18–19).

As well, Europe's pharmacists are not as highly motivated to engage in parallel importing as one would expect, because public payers either reimburse them less for parallel-traded medicines, or claw back some of the pharmacists' profits (West and Mahon 2003: 4).

Besides parallel importing, EU countries introduced various price controls beginning in the 1980s. Combined, these measures have had a negative impact on pharmaceutical investment in the European Union. Between 1988 and 1998, US-based manufacturers increased their share of the top fifty drugs worldwide from 19 to 33. By 1999, they sold eight of the top ten. Germany had 16% of the world's new drug patents in the years 1980 to 1985 but that share dropped to 8% in the years 1986 to 1990 (Schweitzer 1997: 121–22). There is no reason to expect the trend to have changed since then. As well, firms based in Europe are now moving most of their operations to the United States (Calfee 2002).

It has also been recognized for at least a decade that controlling drug prices does not restrain ballooning health-care budgets (Rothnie 1993: 507–08). During the 1980s, a decade in which European prescription drug prices shrank relative to those in the United States, volumes of prescription drugs consumed, per capita, in Europe grew from about 40% more than in the United States to over two and a half times more (Danzon 1997b: 40). This means that controlling drug prices is not even guaranteed to limit growth in pharmaceutical spending. France, which has had low pharmaceutical prices for a developed country, has traditionally had very high drug spending as a share of total health spending (Schweitzer 1997: 148–49).

Parallel trade in Europe takes a serious bite out of the research-based drug makers, about 18% of sales, but even the most optimistic estimate of Europe's parallel trade shows trivial savings to purchasers. A survey commissioned by the trade association that represents Europe's parallel traders concluded that savings were €635 million in 2002, about US$600 million at the average market exchange rate for that year, less than 1% of the value of the five largest European countries' total prescription expenditures (IMS Health 2003; Pollard 2003: 18; West and Mahon 2003).

Neither patients nor governments really benefit from Europe's parallel trade: only the parallel traders do.

Note

1 This is not a universal rule. Australia and Canada, countries with small pharmaceutical industries, have higher prices than European countries with larger industries (Productivity Commission 2001: 73; Graham 2002a).

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. The inventor of a patented good is meant to be free from competition from equivalent, identical products (Barfield and Groombridge 1999: 233).

Patent laws are national, and patents for many drugs expire on different dates in Canada than they do in the United States. As well, the mechanism for introducing generic competition against branded medicines is different in Canada than it is in 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 guarantees six months of exclusivity to the first generic manufacturer to challenge a patent successfully. This was a feature of the Hatch-Waxman Act of 1984 that was meant to give an incentive to the first generic competitor to challenge an innovator's patents successfully. 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 United States restores the terms of patents devalued by the time that the FDA takes to approve a medicine for safety and efficacy; terms are restored 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.

Regulations governing the introduction of competing generic products are changing in the United States. Similarly, Canadian legislators are reviewing Canada's patent regulations for prescription drugs. If US legislators allow parallel importing, they will import Canadian patent policy. Legislatures should not shake the confidence of inventors by changing patent laws in such a bizarre fashion and any legislative decisions with respect to parallel trade should be made explicitly and deliberately, with full regard to all consequences.

For example, Hillary Clinton demanded lower American drug prices during her 2000 Senate campaign and presented a list of six drugs patented in the United States and their prices in Canada. One of those drugs was *Nolvadex®* (tamoxifen), for which she reported a price of US$390, compared to Canadian tamoxifen at US$50 (Clinton 2000). However, there had been no patent on the drug for many years in Canada.[1] The fact that she compared a drug patented in the United States to a generic version in Canada magnified the savings. Obviously, importing a generic drug into a country where a patent is in force violates the patent but Mrs Clinton did not explain why she thought that American patents on *Nolvadex®* should be repealed. This indicates that, if the other five drugs on her list had not been patented in Canada, she would have compared Canadian generic prices to US patented ones for those drugs as well.

Patents on the following five, widely used prescription medicines illustrate that there will often be times when parallel trade between Canada and the United States will violate patent law in one or the other country. *Prilosec®* (omeprazole, named *Losec®* in Canada), is currently subject to generic competition in the United States. This is a drug that has been surrounded by many patents. Nevertheless, a number of generic competitors applied to the US FDA to sell generic versions of it, claiming that some of the longer running patents were invalid. In December 2001, the brand-name manufacturer, AstraZeneca, claiming that the challenged patents were valid, commenced legal action to stop the generic drug makers from selling copy-cat omeprazole. In October 2002, a US court decided that two of the patents on *Prilosec®*, which lasted until 2007, were valid. Initially, this prevented three of the generic competitors from making the drug. However, the judge determined

that a fourth generic manufacturer, Schwartz, would not violate the patents if it sold omeprazole manufactured according to its own process. Schwartz was not the generic manufacturer that had the six-month exclusivity for the first generic substitute. The FDA had already granted that right to two of the generic drug makers that lost the case, Andrx and Genpharm. Therefore, the generic manufacturers negotiated a deal in November 2002 whereby Andrx and Genpharm would give up their exclusive rights and allow Schwartz to speed its drug to market (Andrx 2002; AstraZeneca 2002; Biotech Week 2002; Freudenheim 2002a, b). Although the litigants are continuing their legal action, generic omeprazole is currently for sale in the United States. In Canada, generic competitors have launched a number of challenges to the patents protecting *Losec*®, none of which have yet succeeded. Therefore, only patented *Losec*® is legally available in Canada.

Because there are currently only a few generic competitors manufacturing it in the United States, generic omeprazole sells for about one fifth less than branded *Prilosec*®, a smaller discount than usual for generic drugs.[2] However, given the complexities of this case, it is possible that more generic competitors could enter the US market while *Losec*® is still patented in Canada, driving the US price below the Canadian price. (This would be the reverse of the situation for *Nolvadex*®, described above.) In such a situation, would the Canadian Industry Minister or the Canadian government allow parallel importing of generic omeprazole in violation of Canadian patents?

Nexium® (esomeprazole, a recent successor to omeprazole), lists patents expiring in February 2016 in Canada and in May 2020 in the United States: a difference of over four years in favour of American patent protection. *Lipitor*® (atorvastatin) is the prescription drug with the largest sales volume in Canada (IMS Health Canada 2002). According to Health Canada's Patent Register, its patent protection lasts until July 2016. According to the FDA's Orange Book, it is protected in the United States until January 2017: a difference of almost six months in favour of the US patent. However, for *Altace*® (ramipril), the second biggest seller in Canada, Health Canada's Patent Register lists a patent expiring in March 2018 whereas the Orange Book shows it protected only until October 2008: a difference of over nine years in favour of the Canadian patent. Similarly, *Norvasc*® (amlodipine), another medicine among the ten best sellers, is protected in Canada until August 2010 but only until September 2007 in the United States: a difference of almost three years in favour of the Canadian patent.

American drug makers make both *Altace*® and *Norvasc*®. When it comes to pass that generic versions of these medicines are sold in the United States, will American politicians be happy for those generic versions to be sold to Canadians via parallel importing in violation of Canadian patents held by those US-based companies?

Another problem with parallel importing is that it can only thrive with government intervention that prevents drug makers from negotiating certain conditions of sale with 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: "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 strengthening of its patent law 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 CDN$106 million. As early as 1993, investment had increased to CDN$504 million and it has continued to grow, until it was over CDN$1 billion in 2002 (McArthur 1999: 96; Pazderka 1999; PMPRB 2003: 30). The governments' bushwhacking these companies, by allowing parallel trade for the benefit of local intermediaries certainly appears "tantamount" to expropriation.

Article 1105 of NAFTA states: "Each Party shall accord to investments of investors of another Party treat-

ment 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.

This weakening of intellectual property rights also means that inventors can neither prevent parallel traders from debasing the quality of their products nor deter counterfeiting. Strong intellectual property rights give innovators and distributors an incentive to invest in marketing, service, and quality guarantees (Maskus 2000: 155). Therefore, parallel importing is less safe than free-market distribution of prescription drugs because it threatens to prejudice manufacturers' interests in the safety of their medicines as well as their ability to provide safety. Furthermore, parallel trade is actually more expensive than free trade, because it adds unnecessary costs of transportation and administration (Danzon 1998: 299). There is no natural competitive advantage for Canadian warehouses in distributing mail-order prescriptions to American patients. If a free market solution can be implemented to solve the problem of American patients who cannot afford their prescriptions, it will be safer and more efficient than illegal shipments from Canada.

As well, generic drugs are often cheaper in the United States than in Canada (Graham and Robson 2000: 13; Palmer D'Angelo 2002). This situation makes no sense and addressing it does not even pose the challenges of parallel trade, because each market is dominated by domestic suppliers. Why does there not appear to be free trade in generic medicines between Canada and the United States? Some home-country bias may be explained by the sales strategies of generic manufacturers but surely provincial drug-benefit plans and Canadian private insurers should be looking to save money through purchasing the lowest-priced generics wherever they can.

As well, although this is an ethical rather than a legal problem with parallel trade, there is an astonishing hypocrisy on the part of Canadian politicians who support the practice. If the entrepreneurs launching cross-border mail-order pharmacies tried to open clinics or hospitals to serve Canadian patients, many provincial governments would forbid them from doing so because they only allow publicly funded hospitals to operate. So, parallel trade allows an inefficient misdirection of entrepreneurial energy away from solving the problems in Canada's own health-care system.

The preceding examples make it clear that politicians on both sides of the border who promote parallel trade in pharmaceutical drugs have not begun to think through the consequences of allowing this misallocation of resources and infringement of national sovereignty. However, the pharmaceutical parallel trade between Canada and the United States 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 United States is a trivial share of the American 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. The United States is by far the world's largest individual pharmaceutical market. Of the total projected $158 billion in 2002, about US$145 billion was brand-name medicines, the rest generic. For Canada, about US$7 billion was brand name, less than 5% of US brand-name sales.[3] If the average US price is $100, the marginal costs of manufacturing and distributing the medicines account for $30 (discussed below). This implies a gross margin of 70% of US$145 billion, or US$101.5 billion. If the average Canadian price is US$60, that is, 40% less than in the United States, and the marginal costs are the same as in the

Table 1: World Pharmaceutical Market 2002 (Projected)

	US$ billions	Share
United States	$158	37%
Major Europe*	$64	15%
Canada	$8	2%
Rest of World	$200	46%
Total	$430	100%

Source: IMS Health 2003; author's calculations.
Note *: Major Europe includes the United Kingdom, Germany, France, Italy, and Spain.

United States, the average gross margin on a Canadian sale is US$30, or 50% of the price. When applied to total Canadian sales volume of US$7 billion, this implies a gross margin of US$3.5 billion, which is about 3% of the American figure of US$101.5. The difference in prices implies that the actual volume of Canadian prescriptions is about 8% of US prescriptions (ignoring Professor Danzon and colleagues' evidence that the two countries have different portfolios of medicines available).

If all the prescriptions going to the United States 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).

Let's assume an extreme case where the supply of prescription drugs to Canada is fixed and that American customers who had previously filled their prescriptions at home purchased all of Canada's brand-name drugs, leaving no medicines for Canadians' use. The loss to the manufacturers would be about $5.8 billion ($2.3 eroded from American profits, plus $3.5 billion from lost Canadian profits) or about 8% of total Canadian and American gross profits of $105 billion. However, if the drug makers simply stop supplying Canada, the loss is only $3.5 billion, which is clearly a better case for the manufacturer.

The analysis above assumes that the entire Canadian supply of drugs is sold in the United States via parallel exportation. It gets more complicated if we assume that the drug makers continue to supply Canada, and that the new supply keeps getting drawn into the United States. This depends on the capacity of the parallel traders to supply the American market, which is unknown. Obviously, the more capacity they have to export to the United States, the bigger the problem for the manufacturers.

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 copy-cat 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. Unfortunately, the recent actions of the Manitoban and Canadian Industry Ministers, as well as Health Canada's guidelines, give no confidence in this regard. The real question then becomes the degree to which research-based drug makers will risk Canada's returning to a regime of compulsory licensing, which depends upon whether the American government would then allow Canadian generic medicines to be parallel traded into the United States, thereby completely abolishing American patents. Despite Senator Clinton's apparent willingness to do so, it is this author's opinion that such a drastic step by the American government would be unlikely. Therefore, it is very real possibility that research-based drug makers will close up shop in Canada if this parallel trade is not stopped.

Nevertheless, there is another approach that might not create an "emergency" that would allow Canada to impose compulsory licensing without running afoul of international trade law. Drug makers could raise prices in Canada to the American 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 the levels in the United States, 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 current price in the United States—in response to broadening the scope for parallel trade from foreign countries into the United States.

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 incomes as high as those of Americans, would be unable to pay American prices for the volume of drugs they need. They would put pressure on the US government to implement explicit price controls in the United States, in order to reduce their own prices again (Calfee 2002).

Domestically, some American politicians who support parallel trade only do so because the law and the White House currently oppose it. They would prefer to have explicit price controls in the United States, in order to show their voters that they are stopping the drug makers' "gouging." As well, they can get other politicians who support open markets on the bandwagon because they confuse parallel trade with free trade. Because it is not free trade, it will fail. This will increase the influence of those who advocate explicit price controls. The next section looks at what would happen to pharmaceutical R&D if American price controls forced American prices to Canadian levels.

Notes

1 *Nolvadex®* (tamoxifen) was patented in the United States until February 2003 and generic competition started there in March.

2 Author's search of CostCo online pharmacy, June 11, 2003.

3 For 2001, 8.4% of sales in the United States were for generic drugs (GPhA 2003). Assume the share stays the same for 2002.

The Effect of Canadian Prices on R&D

The proportion of sales allocated to R&D in the brand-name pharmaceutical industry has increased over the last almost four decades from about 10% in the 1960s to 18.2% in 2002, while production costs went down as a share of sales (Schweitzer 1997: 25–26; PhRMA 2003b: 10). Of course, this has increased the incentives for parallel trade, because it can only thrive in industries with high sunk costs and low marginal costs of production.

There is a well-established relationship between pharmaceutical companies' prospective earnings and their investments in R&D. The effects of President Clinton's proposed health plan of 1993 is exemplary of the consequences of government intervention in prices. His plan would have given the US government the ability to set prices of breakthrough drugs so that American prices would be the lowest of 22 designated countries. From 1981 through 1993, average annual increases in spending on R&D by brand name drug makers had been 11% in real (inflation-adjusted) dollars. In 1994, when President Clinton's health plan seemed likely to pass, spending on R&D dropped to 3% and, in 1995, to 4%. However, President Clinton's health plan failed and, in the late 1990s, R&D investments returned to the previous level of about 11% (Calfee 2000: 46; Danzon 1998: 297). Furthermore, stock prices of the large, research-based pharmaceutical manufacturers dropped by 54% after the Clintons proposed their health-care plan (Ellison and Mullin 2001).[1]

If the loss of $3.5 billion dollars through cutting off the supply of brand-name drugs to Canada effects a loss of cash flow of a similar amount and 20% of cash flow is reinvested in R&D, this results in a loss of R&D investment of about $700 million. Given global pharmaceutical R&D spending of $32 billion in 2002, this would hardly amount to a catastrophic reduction (PhRMA 2003b: 10). However, imposing Canadian prescription drug prices on the much larger American market would have much more serious consequences. In this section, I estimate the effect such controls would have on short-term R&D spending.

Table 2 breaks down the American market for patented pharmaceuticals ($145 billion dollars in 2002) into four submarkets and shows the relative prices in each. For example, uninsured patients pay about 18% more than those who are insured.

Tables 3, 4, and 5 describe the negative consequences to R&D of three different scenarios (as developed in Appendix B). Within each scenario, the insured population increases its use of prescriptions by 10% when US law forces prices down to Canadian levels but the uninsured increase their number of prescriptions by either 20%, 40%, or 60%. 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 2003b: 10).

Table 3 shows the "best case," assuming gross margins on US sales before price controls of 80%, and 10% of cash flow invested in R&D. In this case, global investment in pharmaceutical R&D drops by 3% if the government forces Canadian prices on only the uninsured, and by 15% 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%, and 20% of cash flow invested in R&D. In this case, R&D investment drops by 30% 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%, and 30% 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 American population. Although this is a very simple model, the results are broadly similar to Professor John A. Vernon's simulations described in Appendix A (Vernon 2002/2003, 2003).

Table 2: US Patented Prescription Drug Market, 2002 (total US$145 billion)

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

Various sources, author's calculations at Appendix B.

Table 3: Best-case reduction in R&D from levels in 2002 if Canadian pharmaceutical prices were enforced in the United States—US$ billion (share of actual world R&D)

Canadian prices applied to:	Uninsured increase number of prescriptions they purchase by:		
	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: Number of prescriptions for insured increase 10%, gross margins 80%, new R&D investments equal 10% of cash flow.

Table 4: Middle-of-the-road reduction in R&D from levels in 2002 if Canadian pharmaceutical prices were enforced in the United States—US$ billion (share of actual world R&D)

Canadian prices applied to:	Uninsured increase number of prescriptions they purchase by:		
	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: Number of prescriptions for insured increase 10%, gross margins 70%, new R&D investments equal 20% of cash flow.

Table 5: Worst-case reduction in R&D from levels in 2002 if Canadian pharmaceutical prices were enforced in the United States—US$ billion (share of actual world R&D)

Canadian prices applied to:	Uninsured increase number of prescriptions they purchase by:		
	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: Number of prescriptions for insured increase 10%, gross margins 60%, new R&D investments equal 30% of cash flow.

Note

1 Ellison and Mullin (2001) measured changes in stock prices specifically attributable to the Clintons' plan from the time Governor Clinton issued a white paper on health care in January 1992 until Mrs. Clinton testified to Congress about the final proposal in October 1993. Then, military crises in Somalia and Haiti, allegations of inappropriate behaviour by the Clintons with respect to the Whitewater land development, and accusations by Arkansas state troopers that Mr. Clinton had engaged in extramarital affairs while Governor, drove health-care reform off the agenda (Ellison and Mullin 2001: 106). Ellison and Mullin also observed that stock prices of generic drug makers declined similarly to those of research-based drug makers, which suggests to them that the Clintons' health plan may not have had negative consequences for pharmaceutical R&D (Ellison and Mullin 2001: 118). However, they appreciate that generic drug makers may not be an appropriate portfolio for comparison.

Conclusion

Parallel trade in prescription drugs from Canada to the United States or imposing Canadian prices on the United States through price controls are not solutions to the challenges that a small but significant number of Americans have in paying for prescriptions. They distract policy-makers and citizens from the real causes of the lack of access that some Americans have to prescription drugs, which are largely a function of the following government interventions:

- the reimbursement rules that forbid drug makers from giving bigger discounts to the uninsured than they do to the government;
- the expensive regulatory burden of the FDA; and
- an inefficient system of health insurance that exposes a small number of patients to high drug prices.

Furthermore, parallel trade is illegal because:

- it violates the patent laws of both countries; and
- it may put Canada in violation of certain articles of NAFTA.

As well as being illegal, parallel trade has little to recommend it:

- it is a less safe method of getting prescriptions to patients than the free market;
- parallel trade in Europe has mostly transferred money from drug makers to parallel traders, with little benefit to patients or taxpayers;
- manufacturers will not allow parallel trade to grow in North America but are likely to restrict or eliminate their supplies to Canada or raise their Canadian prices, if their products flow unimpeded across the border to the United States; and
- for both foreign and domestic reasons, the employment and subsequent failure of parallel trade will increase the risk of explicit price controls on prescription drugs in the United States.

Finally, imposing Canadian prices on the United States through price controls threatens to have a catastrophic impact on investment in pharmaceutical R&D, which is primarily funded by American patients.

Unfortunately, the incentives for politicians to go in the wrong direction when it comes to prescription drug prices are very large because they can get a quick political pay-off by artificially lowering drug prices for seniors and not worry about the long-term consequences to R&D.

Policy Choices—from Parallel Trade to Free Trade

The Canadian government's priority should be to secure the supply of prescription drugs in Canada by stopping parallel trade and re-establishing free trade in prescription drugs between Canada and the United States. Canadian law must enforce contracts into which pharmaceutical wholesalers, pharmacies, and drug makers enter for the purpose of supplying Canada. Needless to say, the Canadian government must rewrite Health Canada's recent Guidelines to remove any comfort from parallel traders that they are operating under the protection of the Canadian government.

Furthermore, if the United States does allow wholesale parallel importing, Canadian law has remedies. The *Food and Drugs Act* permits drugs packaged with "Export" overprinted on the label to be shipped out of Canada with a certificate from Health Canada that the product conforms to Canadian Good Manufacturing Practices. This certificate is not required by Health Canada. It is provided as a service to facilitate other countries' acceptance of the product. Health Canada should not issue export certificates for shipments improperly destined for the United States. Furthermore, Canadian customs agents should monitor wholesale shipments at the border, stripping export certificates off misdirected stocks.

A perhaps stronger measure is described in the Import Permits Act. This authorizes the government to establish an "Export Control List, including therein any article the export of which the Governor in Council deems it necessary to control ... to ensure that there is an adequate supply and distribution of the article in Canada for defence or other needs." Putting parallel-traded prescription drugs on such a list would give drug makers the confidence to continue supplying Canada.

In the longer term, Canada must also address the valid criticism that it is free-riding on R&D primarily paid for by American patients. We do not know how much of Canada's pharmaceutical discount is due to government intervention and how much is due to Canada's low income relative to that of the United States but we do know that the only way to discover the right prices is to let markets work. Two reforms will achieve this:

- abolishing the Patented Medicine Prices Review Board; and
- reforming provincial drug benefit plans and, ultimately, the entire health system to incorporate more private choice.

The United States must resist the temptation to destroy the free trade in prescription drugs in favour of parallel trade. To do this, it will have to address the needs of uninsured patients who struggle to pay for prescriptions. This paper cannot describe all the reforms to the American health-care system necessary to achieve that. However, rather than more government intervention, which has already had detrimental effects on costs and access in the United States, it would better to reduce government intervention in order to allow private discount cards to grow and to reform US health insurance to reduce the risks of people falling through the cracks. One plan that points in this direction is the Prescription Drug Security Plan developed by Joseph R. Antos of the American Enterprise Institute and Grace-Marie Turner of the Galen Institute (Antos and Turner 2002).

Politicians, however, face strong incentives to intervene in the market in prescription drugs: they can buy votes from seniors cheaply by offering to lower drug prices but do not themselves suffer the unintended consequences of their interference. To improve patients' ability to get the prescription they need while ensuring that investors will continue to be willing to risk their savings on pharmaceutical R&D, Canadians and Americans must demand responsible reform from their governments. We hope that this paper will help them do so.

Appendix A: Annotated Bibliography of Relevant Models of Price Differentiation, Price Controls, and Parallel Importing

In the 1960s and 1970s, the Chicago School of economists developed arguments showing that vertical restraints such as exclusive dealing favoured competition (reviewed by Barfield and Groombridge 1999: 224–27). However, exclusive dealing in these cases generally refers to manufacturers of differentiated products selecting exclusive dealers within one geographic area and forbidding them from stocking competing products rather than the parallel importing addressed here (Mathewson and Winter 1990: 130–36).

Hausman and MacKie-Mason (1988)

Professors Hausman and MacKie-Mason demonstrate that price discrimination is beneficial to static efficiency alone because it allow manufacturers to sell to markets into which they would not if uniform pricing were in effect. Their model focuses on markets for patented goods because they are more likely to have the exclusivity required to permit price differentiation. As well, their model emphasizes the result for two markets only. However, improvements in static efficiency need not necessarily occur if manufacturers already supply both markets under uniform pricing, in which case subsequent price discrimination may either decrease or increase overall welfare. Furthermore, they note that if the manufacturing process has economies of scale, marginal costs will be reduced if new markets are added through price discrimination, which increases the benefits of price differentiation. They use the fibre *Kevlar*® (aramid) as an example.

Malueg and Schwartz (1994)

Professor Malueg and Mr. Schwartz developed a general model to demonstrate the superiority for social welfare of price discrimination instead of uniform pricing for an environment of more than two markets, for both trademarked and patented goods. Their model identifies price discrimination, driven by income differences, as well as free riding, as the cause of most parallel importing, while noting that those two causes are not exclusive. Therefore it is empirically difficult to determine which of the two is causing parallel imports. Generally, parallel imports surge as a country's currency appreciates. (Although the Canadian dollar has appreciated against the US dollar for much of 2003, the long-term historical trend is of depreciation.) If parallel importing causes manufacturers to withdraw from one or more markets, overall welfare decreases. However, if uniform pricing does not cause manufacturers to exclude a market, overall welfare is increased. This leads them to their conclusion that parallel importing is beneficial across markets where demand functions are similar, and detrimental where they are not. However, as with Hausman and Mackie-Mason, Malueg and Schwartz do not consider the effect of parallel importing on R&D, just on static welfare.

Elzinga and Mills (1997)

In a valuable contribution, Professors Elzinga and Mills point out that in the United States, drug makers do not segment their market into those with high elasticity of demand and those with low elasticity. The price elasticity of demand of the patients themselves is irrelevant. Rather, it is the buying power of the managed care organization that segments its members from others. Elzinga and Mills argue that patients left out of managed care do not pay more than they would have in the absence of that market structure, simply that the insured get better prices because of the power of the managed care organization. They also argue that this may be beneficial to the uninsured because the managed care organizations segregate patients with low-demand-elasticity (presumably defined as such because they are employed and likely to have higher incomes than many of the uninsured), thus solving the drug makers' marketing challenge of segregating those who are unwilling or unable to pay high prices.

Unfortunately, this analysis is limited by not recognizing the situation where the insurer employs a most-favoured customer clause (as the US government does), which prevents the drug maker from selling at low prices to buyers whose high-demand-elasticity implies that they would buy only at prices even lower than those enjoyed by insurers.

Danzon (1997b)

Professor Danzon broadens the analysis of the models above by analyzing the dynamic welfare effects of price discrimination on R&D. She addresses the fact that R&D expenditures in the prescription drug industry are global joint costs, that is, there is no obvious way to allocate the sunk costs of R&D to individual purchasers (all of whom rationally want to avoid paying those costs), and shows that price differentiation is a benevolent way to allocate the costs of R&D, because the rich pay more. She does this by developing a model of Ramsay pricing, which was originally developed to price the outputs of regulated industries with large joint costs, such as utilities. She also recognized that this beneficial price differentiation will occur in the absence of government interference as long as manufacturers can prevent arbitrage and included a case where many countries have single, government agents as buyers.

Scott Morton (1997a, b)

Professor Scott Morton shows mathematically that a supplier facing a most-favoured-customer clause, whereby the "lowest price" is defined as a fixed dollar price, will raise its lowest price when the most-favoured-clause takes effect. If the newly defined price to the most-favoured-customer is defined as a percentage discount from an average price, the solution is more complicated. However, when the discount is well below a quantity-weighted average price, as was the case with US Medicaid after 1990, the firm will likely raise prices. The relative size of Medicaid and the elasticity of demand of non-Medicaid users will influence the magnitude of the price increase. However, Scott Morton's view of price differentiation is very different than Danzon's. She argues that products facing the closest substitutes, generic and branded off-patent drugs, will have greater price differentiation than patented drugs (Scott Morton 1997b: 164).

She supports this with empirical research that is, unfortunately, limited by using only invoiced prices, rather than prices after rebates (Scott Morton 1997a: 278; 1997b: 158–59). As well, Scott Morton observes a different type of price differentiation of dispersion than this paper addresses. One way that drug manufacturers differentiate prices is through the different doses or packages that they sell. For example, convenient packages like "accudose" packs that mark daily doses are more expensive than ordinary packages (Scott Morton 1997b: 159). She examines the dispersion of prices for these portfolios of the same medicine, rather than price dispersion of each dose and package.

Sager and Socolar (2000)

Professor Sager and Ms Socolar's proposal is extremely reckless and is only mentioned here because Professor Sager is a health-policy advisor to the Commomwealth of Massachusetts, implying that he has some influence in state government. Sager and Socolar calculated that the United States would have saved $35.3 billion in 2000 if all US prices were forcibly reduced to those on the Federal Supply Schedule (FSS). They demonstrate no intellectual acquaintance with the benefits of differential pricing, as developed above. Despite published, empirical, academic research indicating that the demand elasticity for prescription drugs in the United States is less than unity (see below), they use estimates from Wall Street financial analysts who claim that demand is elastic and that reductions in prices would increase volumes to such a degree that revenues would be the same or greater. The obvious problem with this idea is that, if it were true, the drug makers would lower prices on their own initiative. Perhaps cognizant of this flaw in their proposal, they propose that governments guarantee stable revenues to the drug makers in return for lowering all American prices to the FSS level. In an era when the increasing investment in lobbying by drug makers is a concern to many, it is hard to imagine a more destructive proposal than this one. This would make not only patients, but also the research-based pharmaceutical industry, completely dependent on the state. Instead of investing in therapies that patients value, the industry would focus its efforts on satisfying the whims of its political masters.

Pecorino (2002)

Professor Pecorino concluded that parallel imports from Canada would increase profits to firms in the United States. The fact that research-based drug makers uniformly oppose parallel importing immediately challenges this argument. Professor Pecorino errs in stating that price differences for patented medicines between Canada and the United States are not due to price differentiation but to the "single payer" system under which Canada sets prices for prescription drugs. As explained above, classical price differentiation by income is a feature of international drug prices but Professor Pecorino mistakenly claims that Canada and the United States have similar income levels (Graham 2000, 2002a). This is a major weakness because his model assumes that manufacturers simply make up for parallel importing by raising Canadian prices without losing sales. It also measures only gains to the American consumers from effective parallel importing but not the lost surplus to Canadian patients from higher prices. Nor does he estimate the dynamic welfare effects through changes in R&D investment.

Furthermore, his model deviates from the real world because there is no Canadian single payer but ten different provincial pharmaceutical benefit plans plus a handful of small federal plans, all of which make up only 45% of the Canadian market.

Vernon (2002/2003, 2003)

Building on previous research that quantifies the relationship between profitability and R&D investment, Professor Vernon found that there is a high negative correlation between a firm's profit margins and the proportion of its sales sold in non-US markets, which makes sense because non-US markets have lower prices (Vernon 2002/2003). Analyzing the period from 1988 to 1999, he predicted that if prescription drug prices in the United States were reduced to the average level in the rest of the world, the intensity of global research and development expenditures would drop by between 36% and 48%. His model does not use prices directly but goes straight to profit margins from financial statements to analyze the impact on R&D.

In a subsequent paper, he uses computer simulations to determine the effect of profit regulation on R&D and new drug introductions (Vernon 2003). Pharmaceutical innovation is a lottery, with a small number of new medicines earning most of the profits. Even for medicines that successfully get launched, only 30% earn positive after-tax returns, and the top 10% earn twice as much as the second 10%, according to research on drugs introduced in the 1980s (Grabowski and Vernon 1996: 196–200). Vernon's simulations do not control rates of return for drugs already on the market, only those launched after implementation of price controls. Nevertheless, in his worst-case scenario, the government reduces the returns to the top 30% of newly launched drugs (the only ones that make a profit) to break even. This results in a reduction of R&D such that the cumulative number of new drugs introduced over the next 50 years drops by over one third from 728 to 461. In his best-case scenario, where the government reduces the rate of return of only the top 10% of new drugs by 10%, the cumulative number of new drugs drops by about 6% to 688.

Perhaps most important aspect of Vernon's model, given the current political pressures, is that reduced R&D investment does not start to flatten relative to the baseline case (no rate regulation) for five years and does not start collapsing until after about ten years. The level of new product introductions does not collapse until after about 20 years. This shows why politicians cannot be allowed to set prices: they will not be around to suffer the long-term consequences of their actions.

Appendix B: Estimating the Effect of Canadian Prices on Pharmaceutical R&D in the United States

It has long been known that pharmaceutical manufacturers' investments in R&D depend on how profitable they are. I use a number of sources to build a financial model in tables 3, 4, and 5 that describes the prescription drug market in the United States and attempts to answer what the effect on R&D would be if Canadian prices were imposed in the United States by explicit price controls. This model is sensitive to a number of things:

1. the size of various sub-markets in the United States: the privately insured, uninsured, beneficiaries of government insurance (e.g. Medicaid), and government agencies on the FSS;
2. the prices and volumes in those sub-markets;
3. the share of prices that covers marginal costs of production and distribution;
4. the price elasticity of demand of American pharmaceutical buyers; and
5. the amount of marginal cash flow that manufacturers invest in R&D.

Table 2 was developed from a number of sources. CMS (2003: table 3) reports prescription drug spending in the United States from cash, private insurance, federal government, and state governments for 2001 at $141 billion. Cash spending includes co-payments and deductibles from insured customers. Thomas et al. (2002: W411) discuss a large sample of the privately insured and report that their out-of-pocket spending was 17% in addition to what their insurers spent. Therefore, I calculated 17% of the amount that CMS reported from insurers, carved that amount out of the cash segment and added it to the insured segment. US GAO (2000) reports the size of the VA and FSS markets for 1999. I scaled this up to estimate a figure for 2001, and carved FSS spending out of federal spending as reported by CMS. Although the VA negotiates better prices than other FSS customers, I generously allocated VA prices to all FSS customers for simplicity's sake.

IMS Health (2003) reports audited US sales for 2002 and an estimate of global sales derived from a proprietary model. From this, I interpolate projected pharmaceutical sales of $158 billion for 2002 in the United States. GPhA (2003) reports that 8.4% of sales in 2001 were generic. Assuming the same proportion for 2002, projected brand-name drug sales for 2002 were $145 billion. My calculations use the sub-market shares developed for 2001 but scale them up to 2002 linearly (i.e., multiplying by 145/141) to estimate dollar amounts.

US DHHS (2000: 98) reports pharmaceutical prices for cash buyers, private insurers, Medicaid, and the FSS. US GAO (2000: 15) claims that the VA receives an average 33% discount off FSS for 308 drugs. Assuming that these make up 50% of VA prescriptions, I estimate that the VA's average price is 59% of the price to those insured privately or through Medicaid, versus 71% for the FSS. However, I assign VA prices to the entire FSS submarket. I assign the private insurer/Medicaid price to federal drug-benefit plans that do not enjoy the FSS. As per the PMPRB (2003: 23), I assign the average Canadian price to be 60% of the average price in the United States. With prices and sub-market shares known, I developed an index of volumes of prescriptions for each sub-market by solving simultaneous equations.

Because of limits to published financial statements, it is not possible to identify exactly which are costs are marginal and which are fixed, because accumulation and depreciation periods are not transparent (Clarkson 1996: 240). Mr. Jacobzone reports that distribution costs may account for half the expenditure on some products, when retailing and wholesaling margins are included, and that these costs may vary up to 10% from country to country (Jacobzone 2000: 19). He reports that, for 1989, manufacturing costs accounted for about 25%

of sales, marketing about 24%, R&D about 12%, 28% operating profit, and the balance other expenses, but this does not differentiate between fixed and marginal costs (Jacobzone 2000: 91). Danzon estimates the same figures for marketing and manufacturing, arguing that marginal costs could be as low as 25% of the US brand-name price (Danzon 1997a: 305; 1997b: 4, 1998: 297). According to Merck & Co., materials and production for its pharmaceuticals business alone were 18% of sales (Merck & Co. 2003: 28). My calculations estimate marginal costs as 20%, 30%, or 40% of the average US price before price controls.

It is difficult to estimate the amount by which American volumes of prescriptions consumed would increase if the government forced prices down. Most research on consumers' price elasticity of demand for prescription drugs addresses relatively modest changes in co-payments or deductibles. In this small interval, it appears that demand is inelastic, with a 1% increase in price leading to a reduction in prescriptions of less than 1% (Graham 2002b: 9 and references). In one recent analysis, multiple tiers of co-payments were sometimes associated with higher spending. However, it is not obvious how to interpret the difference between an insurance policy with a flat co-payment of $10 for each prescription versus another that has two tiers, one for which patients pay $5 and the other $10 (Thomas et al. 2002). This author is not aware of research that measures the response of uninsured consumers to price changes, which is the important question in parallel importing. The famous RAND health insurance experiment in 1991 did observe large changes in volumes of prescriptions consumed, from $82 for patients who received prescriptions for free, to $46 for those who had to pay 95% of the price of their prescriptions. However, the RAND observations were for patients who faced different payments for all medical services. Those who faced higher co-payments visited their physicians less frequently and this explains why they did not receive as many prescriptions as those who paid less. The authors conclude that demand for drugs, independent of this effect, is quite inelastic (Newhouse and the Insurance Experiment Group 1993: 166–71, 365–66). For this reason, using the implied elasticity from the RAND experiment for legislated controls of prescription drug prices in the United States, without other reforms to the system (i.e. how doctors are paid), is questionable. Sager and Socolar (2000) noted literature that showed demand elasticity for prescription drugs ranging from −0.10 to −0.64, that is, a 1% reduction in price would result in an increase in volumes of prescriptions of between one tenth of a percent and about two thirds of a percent. My calculations assume that the marginal elasticity of demand for insured patients is always 10%, and describe three elasticities for the uninsured population, 20%, 40%, and 60%.

Pharmaceutical manufacturers fund their R&D almost entirely out of cash flow, of which about one third goes into R&D (Vernon 2003: 59). Grabowski and Vernon (2000) determined that both changes in cash flow, the current productivity of R&D, and pre-tax profit margins were good predictors of R&D. For example, a $100 increase in cash flow explains an increase in R&D of between $12 and $31, depending on the specification of the model. My calculations assume that changes in revenue equal changes in cash flow and describe scenarios where 10%, 20%, or 30% of cash flow is reinvested into R&D.

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