Innovation and Drug Reimportation: Cost, Value, and Tradeoffs – Economic, Legal, and Public Policy Implications

Based on the proceedings of a University of Michigan Center for Medication Use, Policy and Economics symposium, April 18–20, 2004, Washington, D.C.

HIGHLIGHTS

• Legislation and Pharmaceutical Reimportation
• Price Regulation and Innovation
• Price Differentials Between Canada and the United States
• Reimportation and the European Experience: What the United States Can Expect

PANEL DISCUSSIONS

• Implications of Research for Public Policy

Supported by an educational grant from AstraZeneca Pharmaceuticals LP
Pharmaceutical Innovation
In the Face of Drug Reimportation

The conference from which this supplement is derived is one of a series organized by the University of Michigan Center for Medication Use, Policy and Economics that is intended to shed light on the debates relative to drug reimportation.

Pharmaceutical innovation vulnerability is an overlooked risk. The articles within will serve to assist noneconomists in understanding why the pharmaceutical business sector relies more on the integrity of intellectual property and the ability to entice significant investment than do other business sectors. Setting aside questions of counterfeiting and medication safety, the material in this supplement comes from a unique forum that focused on the potential impact of pharmaceutical reimportation on medical innovations. Internationally renowned academic economists with significant work in pharmaceutical policy research were selected to participate. Each came to share original research, in-depth observations, and insightful speculations on the reversible and nonreversible effects of experimentation on policy that are having a measurable impact on the U.S. pharmaceutical research infrastructure.

Due to the complexity and political sensitivity of this dimension of the reimportation debate, selected experts also agreed to participate in question-and-answer sessions to address pressing issues from the audience. Highlights of those sessions are included here. The experts represented have a commitment to translating the economic and policy subtleties related to reimportation. Several faculty members specialize in research on innovation, intellectual property, and pricing theory. These scientists have a passion for innovation and a keen awareness of the risks of large-scale policy experimentation. The publication of these edited transcripts provides readers with a significant opportunity to come to the forefront of the reimportation debates.
Innovation and Drug Reimportation: Cost, Value, and Tradeoffs – Economic, Legal, and Public Policy Implications
Based on the proceedings of a University of Michigan Center for Medication Use, Policy and Economics symposium, April 18–20

WELCOME MESSAGE
Pharmaceutical Innovation in the Face of Drug Reimportation ............... Opposite
PATRICK L. MCKERCHER, PhD
Director, Center for Medication Use, Policy and Economics, University of Michigan, Ann Arbor

FEATURE PRESENTATIONS
Status of Legislation on Pharmaceutical Reimportation................................. 3
FRANCIS B. PALUMBO, PhD, JD
Professor and Director, Center on Drugs and Public Policy
University of Maryland School of Pharmacy, Baltimore

The Economic Fundamentals of the U.S. Pharmaceutical Market....................... 7
KRISTINA M. LYBECKER, PhD
Assistant Professor of Economics, Drexel University, Philadelphia

The Economics of Price Regulation and Innovation......................................... 10
ROBERT B. HELMS, PhD
Resident Scholar, American Enterprise Institute, Washington

QUESTION-AND-ANSWER SESSION
PANELISTS AND PARTICIPANTS ........................................................................... 12

FEATURE PRESENTATIONS
Explaining Price Differentials Between Canada and the United States .............. 14
JOHN R. GRAHAM, MBA
Adjunct Scholar, The Fraser Institute, Vancouver, British Columbia

This supplement is supported by an educational grant from AstraZeneca Pharmaceuticals LP. The material in this supplement has been independently peer reviewed. The sponsor played no role in reviewer selection.

Opinions are those of the authors and do not necessarily reflect those of the institutions that employ the authors, AstraZeneca, MediMedia USA, or the publisher, editor, or editorial board.

Clinical judgment must guide each clinician in weighing the benefits of treatment against the risk of toxicity. Dosages, indications, and methods of use for products referred to in this supplement may reflect the clinical experience of the authors or may reflect the professional literature or other clinical sources and may not be the same as indicated on the approved package insert. Please consult the complete prescribing information on any products mentioned in this publication. MediMedia USA assumes no liability for the information published herein.
Long-Term Ramifications of Reimportation for the Health Care System ..........17
TOMAS J. PHILIPSON, PhD
Professor, Irving B. Harris Graduate School of Public Policy Studies, University of Chicago

QUESTION-AND-ANSWER SESSION
PANELISTS AND PARTICIPANTS ..................................................................................18

FEATURE PRESENTATIONS
The Relevance of Intellectual Property Laws to Reimportation ...............................20
WENDY J. WAGNER, JD, MA
Associate, Advocacy Department, International Trade Law
Gowling Lafleur Henderson LLP, Ottawa, Ontario

The Relationship Between Market-Based Pricing and Biopharmaceutical Innovation .........................................................23
ROGER A. EDWARDS, ScD
Director, Life Sciences, TIAX LLC, Cambridge, Mass.

Pharmaceutical Reimportation: The European Experience – What the United States Can Expect ...............................................26
JOSEPH H. GOLEC, PhD, MA
Associate Professor of Finance and Healthcare Management
University of Connecticut, Storrs, Conn.
JOHN A. VERNON, PhD, PhD
Assistant Professor of Finance and Healthcare Management
University of Connecticut, Storrs, Conn.

The Impact of Reducing U.S. Revenues on Research and Development Assessment ............................................................30
THOMAS A. ABBOTT III, PhD
Abbott Consulting LLC, North Wales, Pa.

QUESTION-AND-ANSWER SESSION
PANELISTS AND PARTICIPANTS ..................................................................................33

FEATURE PRESENTATIONS
European Parallel Trade: Lessons for Reimportation ............................................35
NANCY MATTISON, PhD

Innovation and Drug Importation: Perspectives from an Industry Public Policy Executive .........................................................38
ROBERT A. FREEMAN, PhD
Executive Director, Public Policy, AstraZeneca Pharmaceuticals LP, Wilmington, Del.

QUESTION-AND-ANSWER SESSION
PANELISTS AND PARTICIPANTS ..................................................................................40

PANEL DISCUSSION
What Are the Implications of the Research for Reimportation Policy? ..............41
MICHAEL DICKSON, PhD; PATRICK L. MCKERCHER, PhD; DAVID P. NAU, RPH, PhD;
STEPHANIE TAYLOR, PhD, Moderators

COMMENTARY
Reimportation and Health Care Covenants ...........................................................43
GLENNA CROOKS, PhD
Few issues are more inflammatory than that of drug reimportation. Driven by cost concerns and an energized populace, U.S. legislators are considering a number of strategies to handle the demand for less expensive medicines. There is a sense among some that purchasing medicines outside the United States offers a cost-effective solution. This article addresses the legal trends relative to drug reimportation and governmental responses to the issues that it raises. The dynamic nature of these issues presents a danger relative to this discussion, however, as new initiatives are continually emerging. Certainly, several factors that show no signs of abating drive the increased interest in drug reimportation: higher drug utilization, the aging population, and increasing drug prices.

Access and price
Access to needed medicines is a key and emotional concern underlying the reimportation debate. By 2005, there will be approximately 4 billion prescriptions filled in the United States on an outpatient basis (Time 2004). Certainly we are seeing increasing incidence of chronic illness. Added to this mix, according to the recent Institute of Medicine study, is the fact that more than 43 million U.S. residents under age 65 lack basic health coverage, not necessarily drug coverage alone.

The price differential between Canada and the United States, real and perceived, drives much reimportation activity; many drugs can be purchased from Canada at 40 percent less than in the United States.

Counterfeiting and ensuring quality
Patients, pharmacists, the pharmaceutical industry, governments, and managed care organizations have a profound interest in reimportation. The counterfeiters, however, are major stakeholders who are profiting substantially from this situation and have much to lose.

Relative to counterfeiting, the quality of the product received at the pharmacy level is a major concern. A larger question is whether reimportation is causing the occurrence of counterfeiting or at least facilitating it.

We want to be able to ensure that high standards are maintained in manufacturing and distribution. A pedigree is a document (paper or electronic) verifying the origin and path of sale of a drug. According to the 1992 Prescription Drug Amendments to the Prescription Drug Marketing Act (PDMA), unauthorized wholesale distributors must provide purchasers with a statement identifying each prior sale of the drug. Nevertheless, this issue is not clear cut. In 1999, the U.S. Food and Drug Administration issued final regulations on pedigrees. Yet, after several delays, implementation has been stayed pending examination of other, nonpaper, pedigree methodologies. Regardless of their official nature, these documents are essential in identifying where a product has been in the chain of distribution.

Prescription Drug Marketing Act
The federal government has been quite active in the reimportation arena, attempting initiatives that are geared to governing reimportation distribution channels and protecting the quality of drug products that are received from outside the country. These efforts often have met with difficulties with respect to required documentation. The PDMA addresses several issues: sampling, diversion, licensing of wholesale distributors, and reimportation.

The PDMA was passed to tackle some serious problems in the United States concerning drug diversion through wholesalers, hospitals, retailers, and others.

The PDMA states that only the manufacturer could reimport a medication, or if the medication was approved by the Secretary of the Department of Health and Human Services (HHS), others could reimport in emergency situations. It also required state licensing of wholesale distributors of prescription drugs — a huge task, given the approximately 26,000 registered wholesale distributors in the United States.

Medicine Equity and Drug Safety Act of 2000
The Medicine Equity and Drug Safety Act of 2000 (MEDSA 2000) added pharmacists and wholesalers as potential reimporters. MEDSA 2000 also stated that to become effective, the HHS secretary would have to
demonstrate that reimportation would pose no additional risk to consumers and would result in a significant reduction in prices that consumers paid for effective products. Neither of the past two secretaries felt that they could certify to either of those elements in a way that would satisfy the requirements of Congress, however. So, in effect, although MEDSA 2000 was enacted, it has never been implemented, leaving us for all intents and purposes under the PDMA.

**Personal use exemption**

Reimportation implies that a drug was produced in the United States, exported, and then brought back into the country. Much of what we categorize as reimportation, even with respect to Canada, is importation; the medicines are produced elsewhere and then brought into the United States.

Much of this occurs under personal use exemption — the FDA’s guidelines. Personal use exemption is neither

<table>
<thead>
<tr>
<th>TABLE 1 Reimportation and new Medicare legislation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Element</strong></td>
</tr>
</tbody>
</table>
| **Subtitle C** | • Pharmacists and wholesalers as potential importers  
• Similar to the Medicine Equity and Drug Safety Act (MEDSA) 2000  
• Health and Human Services Secretary must certify (similar to MEDSA), issue report on reimportation, promulgate regulations  
• Pharmacists/wholesalers must provide:  
  ◦ Name/quantity of active ingredients  
  ◦ Description of dosage form  
  ◦ Date prescription drug is shipped  
  ◦ Drug quantity  
  ◦ Point of origin and destination  
  ◦ Price paid by importer  
  ◦ Documentation from foreign seller specifying original source and quantity of each lot originally received by the seller from that source  
  ◦ Lot or control number assigned by the manufacturer  
  ◦ Contact information for the importer  
  ◦ Certification that the drug is approved for U.S. marketing, is not adulterated or misbranded, and meets all labeling requirements  
  ◦ Laboratory records from a qualifying laboratory showing that the drug meets established specifications  
  ◦ Indication that the testing was conducted in a qualifying laboratory  
• Manufacturer  
  ◦ Provide an importer with written authorization to use, at no cost, the approved labeling for the prescription drug |
| **Individual** | • The U.S. Food and Drug Administration should:  
  ◦ Focus enforcement on cases in which the importation by an individual poses a significant threat to public health, and  
  ◦ Exercise discretion to permit individual importation where it is clearly for personal use and it does not appear to present unreasonable risk to the individual |
| **Waivers** | • Waivers may be granted to individuals:  
  ◦ By regulation or  
  ◦ On a case-by-case basis (the HHS Secretary will publish and update guidance on this issue)  
  ◦ With a waiver of the prohibition of importation of a prescription drug … under such conditions as the HHS secretary determines to be appropriate  
• Waivers on drugs imported from Canada may be granted when the medications are:  
  ◦ Imported from a licensed pharmacy, for personal use, not for resale, and no more than a 90-day supply  
  ◦ Accompanied by a copy of a valid prescription  
  ◦ Imported from a seller recognized by the HHS secretary  
  ◦ A prescription drug approved by the HHS Secretary under chapter V of the Food, Drug, and Cosmetic Act (FDCA)  
  ◦ In the form of a final finished dosage, manufactured in an establishment registered under section 510 of the FDCA  
  ◦ Imported under such other conditions as the HHS secretary determines |
a law nor a regulation; it is a policy, which means it is legally unenforceable. The policy states that FDA personnel can use their discretion to detain a product at the border or to refuse to allow its entry. There are several scenarios through which a product may be personally imported. In one scenario, its intended use must be appropriately identified, it may not be indicated for a serious condition, and it may not be known to represent a significant health risk. In a second scenario, the product’s intended use is unapproved in the United States, is for a serious condition for which effective treatment may not be available domestically, and is not commercialized or promoted to persons in the United States by those involved in the product’s distribution.

In addition to these potential scenarios, the product may not be considered to represent an unreasonable risk (which is difficult to certify). The individual seeking to import the drug must affirm in writing that the product is for the patient’s own use and that the prescription length does not exceed three months. The patient also must provide the names and addresses of the treating U.S. physician(s) or provide evidence that the drug is for continuation of therapy that had been initiated in another country.

While the policy sets out specific guidelines, it is also important to understand what the guidelines do not state. The policy does not permit one to simply go outside the United States or to use the Internet to bring drugs into the United States for chronic conditions necessitating ongoing therapy. Yet, that often has been how the policy has been interpreted.

State and local activity
As a consequence of these factors, there is significant activity at both the state and federal levels. To save money, states are forming buying groups, expanding Medicaid programs, and examining supplemental rebates and pharmacy discounts. States that are attempting to address drug costs are approaching reimportation as both a

**TABLE 2  Current and upcoming federal legislation**

<table>
<thead>
<tr>
<th>Legislation</th>
<th>Highlights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gutknecht bill (HR2427)</td>
<td>• Status: Passed House of Representatives, stalled in the Senate</td>
</tr>
<tr>
<td></td>
<td>• Provisions</td>
</tr>
<tr>
<td></td>
<td>◦ Allow pharmacists, wholesalers, and &quot;qualified individuals&quot; to reimport prescription drugs from a number of industrialized countries</td>
</tr>
<tr>
<td></td>
<td>◦ Define a qualified individual as someone who is not a pharmacist or wholesaler</td>
</tr>
<tr>
<td>Remedies Act of 2004 (S2307)</td>
<td>• Introduced by Sen. Charles Grassley on April 8, 2004</td>
</tr>
<tr>
<td></td>
<td>• Provisions</td>
</tr>
<tr>
<td></td>
<td>◦ Legalize reimportation from exporters approved by the U.S. Food and Drug Administration</td>
</tr>
<tr>
<td></td>
<td>◦ Require the U.S. Food and Drug Administration to provide proper labeling for imported drugs</td>
</tr>
<tr>
<td></td>
<td>◦ Charge a user fee to registered exporters</td>
</tr>
<tr>
<td></td>
<td>◦ Require pedigrees from the manufacturer to the dispensing pharmacist</td>
</tr>
<tr>
<td></td>
<td>◦ Permit a 20 percent increase in R&amp;D tax credits for manufacturers that do not attempt to limit or prevent importation</td>
</tr>
<tr>
<td></td>
<td>◦ Allow for a loss of business expense deduction for advertising expenses for manufacturers that do attempt to limit importation</td>
</tr>
<tr>
<td></td>
<td>◦ Require FDA to submit final regulations within 90 days of enactment</td>
</tr>
<tr>
<td></td>
<td>• Provisions</td>
</tr>
<tr>
<td></td>
<td>◦ Amends pedigree requirements of the Food, Drug, and Cosmetic Act (FDCA)</td>
</tr>
<tr>
<td></td>
<td>◦ Requires manufacturers to implement chain of custody procedures</td>
</tr>
<tr>
<td></td>
<td>◦ Establishes prescription drug monitoring programs</td>
</tr>
<tr>
<td></td>
<td>◦ Requires internet pharmacy inspections</td>
</tr>
<tr>
<td></td>
<td>◦ Restricts the personal use exemption for importing a controlled substance</td>
</tr>
<tr>
<td>Dorgan bill (S2137)</td>
<td>• Provisions</td>
</tr>
<tr>
<td></td>
<td>◦ Allows importation of drugs from 25 countries if the drugs and facilities are approved by the FDA</td>
</tr>
<tr>
<td></td>
<td>◦ Allows importation of the drug if shipped utilizing counterfeit-resistant technologies</td>
</tr>
<tr>
<td>Kennedy amendment</td>
<td>• Amends the FDCA</td>
</tr>
<tr>
<td></td>
<td>◦ Permits pharmacists and wholesalers to import Health Canada-approved prescription drugs from Canada (alone) via Canadian exporters</td>
</tr>
</tbody>
</table>
political issue and a business decision. The key is that states are covering a variety of constituents: state employees, Medicaid programs, prison systems, and hospitals. This makes the states large purchasers (in addition to being political entities), and they are taking measures to alleviate their problems. Individual localities, pressed by escalating drug costs, also are pursuing solutions.

As of March 2004, at least 22 states have filed 47 bills or resolutions addressing importation. Certain municipalities, such as Springfield, Mass.; Burlington, Vt.; and Montgomery, Ala., lead a growing number of cities that are purchasing or facilitating the purchase of medicines from Canada.

Confusion reigns

In the absence of clear direction from the federal government, individual states and cities are going their own way. Their confusion is understandable. We find ourselves stuck in a quagmire relative to importation. The PDMA is still the law. We have MEDSA 2000 and a new Medicare law (Table 1, page 4) that seek to change it. We have a personal importation guideline that the FDA has put forth, which is now being changed into a law through the new Medicare act but still does not amend the Food, Drug, and Cosmetic Act. In addition, we have a number of proposals to amend the FDCA. (Table 2, on page 5, provides a summary of recent activity.)

Where is this activity going? How will the safety and integrity of the drug supply be protected? Regardless of a medicine's price, if one cannot feel confident that a product at the pharmacy level is a product of integrity, then we will have taken major steps backward.

Reference
In examining the economic fundamentals of the pharmaceutical industry, this article focuses on the competitive forces in the global marketplace and on the importance of intellectual property rights protection. Both elements are critical to an industry that increasingly is characterized by costly innovation and significant uncertainty. Although estimating the cost of drug development is controversial, it is clear that pharmaceutical research and development is an expensive undertaking. According to a recent estimate by the Tufts Center for the Study of Drug Development, the cost of R&D is now close to $900 million (Tufts 2003). Given the high cost of R&D and the competitive nature of the industry, it is not surprising that patent protection is disproportionately more important in the pharmaceutical industry than in perhaps any other sector for ensuring that the researcher appropriates the returns to R&D.

In the beginning

In 1897, Felix Hoffmann created a new industry. He engineered a method for adding a cluster of two extra carbon and five extra hydrogen atoms to a material extracted from willow bark. The resulting substance is known to chemists as acetylsalicylic acid and, more commonly, as aspirin. This innovation transformed Bayer, the dyemaker for whom Hoffmann worked, into the world’s first modern drug company. For years following Hoffmann’s innovation, the process of drug discovery was an unpredictable one. This uncertainty stemmed primarily from scientists’ limited understanding of the workings of the human body. Only recently has the innovative process been refined. This has become possible largely through a heightened understanding of genetics combined with such technological advances as combinatorial chemistry, high-throughput screening, and laboratories-on-a-chip.

Nevertheless, the process of drug discovery is still long, complex, risky, and expensive. As such, the industry’s reliance on patent protection is not surprising.

- **Long.** Currently, to bring a drug from the laboratory through the entire R&D process to approval by the U.S. Food and Drug Administration takes 10 to 15 years (IFPMA 2004).
- **Complex.** New technologies and growing emphasis on targeting specific conditions and genetic diseases make the process of drug discovery increasingly difficult.
- **Risky.** From an initial pool that comprised between 5,000 and 10,000 compounds, only 250 will make it to preclinical testing. Of those 250, only 5 will continue on clinical testing, and of the 5, only 1 will be approved by the FDA (Tufts 2003).
- **Expensive.** According to the Tufts Center for the Study of Drug Development, the average cost per new molecular entity is $802 million. This figure rises to $897 million if the costs of postapproval R&D are also considered (Tufts 2003).

Advancing through drug discovery — from the chemistry to the preclinical testing to the phase 1 through 3 trials, and finally, to approval and marketing — is a lengthy process, which frequently, as described previously, takes more than a decade. The research pipeline is also extremely leaky, as the process narrows the number of compounds at every stage. These factors combine to make the process of drug discovery a highly expensive one and a challenge that the pharmaceutical industry has met with growing investments in R&D. In 2003, Pharmaceutical Research and Manufacturers of America (PhRMA) member companies invested an estimated $33.2 billion in R&D (PhRMA 2003c). This amounts to...
17.7 percent of domestic sales on R&D—a higher R&D-to-sales ratio than any other U.S. industry. Moreover, the development component (costly large-scale, multistep clinical trials) of the R&D process consumes more than 70 percent of the R&D budget (IFPMA 2004).

Patents and other forms of intellectual property rights protection safeguard the industry’s ongoing investment in R&D. The absence of price controls and other government regulation in the United States clearly has facilitated innovation; “The United States is the epicenter of prescription drug research for the planet, producing more new drugs than all other countries combined” (Turner 2003). This fact is illustrated in Figure 1, which depicts global pharmaceutical R&D spending (Ward Health Strategies 2003). Reimportation dilutes this investment and diminishes the industry’s ability to invest in R&D.

Are these investments paying off? Is the long, complex, risky, and expensive process worthwhile? Yes. The global pharmaceutical market is growing, and it reached approximately $492 billion in 2003. To put the global market into perspective, the North American market is undeniably the most lucrative and important to the industry, comprising 49 percent of sales. Figure 2 describes global sales by region (IMS Health 2003).

**Finding a balance**

The challenge for the pharmaceutical industry is finding a balance between providing for continued investment in innovation and assuring access to affordable medicines. On one hand, the industry has patent protection as set out in the U.S. Constitution, providing it with a limited period of market exclusivity. This allows the innovating company some control over price and provides for market segmentation through Ramsey pricing. Economic theory has established that Ramsey pricing is the most efficient mechanism for recovering shared (global) R&D costs by charging different consumers different prices based on their price sensitivity (price elasticity of demand). That is, consumers who are relatively insensitive to price changes will be charged a larger markup over marginal cost than consumers who are more price sensitive. The result is the set of prices that generates sufficient revenue to cover the shared development cost and generates the highest level of consumer welfare.

---

3 The U.S. Constitution gives Congress the power “to promote the progress of science and useful arts, by securing for a limited time to authors and inventors the exclusive right to the respective writings and discoveries.”
At the same time, 7 out of 10 branded medicines approved by the FDA do not generate sufficient sales to cover average R&D costs (PhRMA 2003b). There are a number of forces posing great challenges to the industry. As described, the process of drug discovery is both increasingly difficult and expensive. Combined with shorter effective patent lives, enhanced branded in-class competition, growing generic competition,4 and large drug purchasers negotiating for lower prices, the ability to capture the returns to R&D is ever more elusive. Evidence of this challenge is apparent in the number of patent expirations on the horizon. Of the 57 marketed blockbuster drugs in 2002, more than 30 are expected to lose patent protection between 2003 and 2008 (Reuters 2004). The total 2002 sales for these products exceeded $60 billion. To consider where reimportation enters the equation and how it will affect the economic fundamentals of the pharmaceutical industry, it is necessary to first examine the forces influencing and changing the industry. These forces can be broken down into demand-side factors and supply-side factors. They are broadly described by the list in Figure 3. Pharmaceutical reimportation is motivated by patient demand and will only be possible if facilitated by government regulation. The questions surrounding drug reimportation are drawn from these forces and influences. A thorough understanding of reimportation necessitates a closer examination of these factors and the impact it will have on innovation.

References

4 Between 1984 and 2000, generics’ share of the U.S. prescription market increased from 18.6 percent to 47 percent (PhRMA 2003a).
In the pharmaceutical sector, research, manufacturing, and sales often are executed in geographically separate regions, with different sets of economic factors informing decisions about the physical and regulatory environment in which each activity is conducted. Research and development activities increasingly are being moved into the United States, often near universities. Meanwhile, the nature of pharmaceutical products — materials with high value relative to their bulk — allows companies to scatter manufacturing activities around the world, situating them wherever economic and regulatory factors are most favorable. From there, finished products easily can be shipped to their distribution channels and ultimately to consumers.

**Defining the markets**

Economists define various kinds of markets based on how each works. In a price searcher’s market, a company has some latitude to search for the price that would maximize profits. In the real world, single pricing rarely is found outside agricultural commodities markets, in which sellers (price takers) must accept the price that is set by the market.

More commonly, sellers have an incentive to separate markets to maximize profits. The airline industry provides the classic example of market separation. Airlines can command higher prices from business customers — who often fly on short notice without paying the fare themselves — than from recreational customers, who have more time to shop for lower fares and are unwilling to pay high business prices. Rather than let seats go unfilled, airlines sell them at a discount. The marginal cost of flying an empty seat from one location to another, to the extent that it can be measured, ultimately serves as a floor to this type of pricing.

The keys to such multipart pricing (also known as multimarket or Ramsey pricing, and formerly, as price discrimination) are searching for prices within a market and keeping markets separate. In practice, multipart pricing is difficult to employ. First, the seller must identify each market. Second, entrepreneurial customers must be prevented from buying the product at the lower price and reselling it to the other market, thereby acquiring the profits that otherwise would go to the manufacturer.

In the United States, drug discounting is common, with manufacturers responding to the profit incentive by giving discounts to the Veterans Administration, pharmacy benefit managers, and health plans. Compared with selling a drug at a single list price, a company can maximize its profits by selling at discounts to various buyers. State and federal regulation of the distribution of prescription drugs greatly facilitates the seller’s ability to prevent reselling of its products from one market to another.

We often hear the argument that because most of the developed countries in Europe and Asia set prescription drug prices low, U.S. manufacturers must shift costs — by increasing prices charged to U.S. consumers — to pay for R&D. From this premise, it follows that U.S. trade negotiators should induce other countries to raise their prices to promote continued R&D. A related argument is that if the government, via Medicaid, drives down drug prices in one market, then the price must be raised for everyone else.

Cost shifting is logically possible but highly unlikely. The incentive to set prices in one market has nothing to do with the price charged to customers in a different market; the price searcher sets prices in each market so as to maximize profits in that market. The flaw in these arguments is revealed by asking: If companies could have acquired greater profits by raising their prices in the unregulated market, why didn’t they do so long ago?

The large unregulated U.S. market, within which numerous discounts are available, drives most of a company’s decisions about which drugs to develop, and how fast. In smaller countries with national health systems, the question is whether the company should sell the product at the price demanded by the country’s buying authority. The economics of the situation reveal that if the company can obtain a price that covers the marginal cost of producing and marketing the drug while satisfying regulatory policies, selling the drug in a given country makes more sense than not selling it. When markets are separate, a seller has a strong incentive to set prices...
so as to maximize profits from each market.

Cost-shifting and competition

This is not to say that sellers would not like to shift costs. In fact, many say that companies want to shift costs but that it usually does not work. Likewise, people who pay higher prices claim to be victims of cost-shifting. While cost-shifting arguments abound, they must be judged on their economic merits.

The U.S. pharmaceutical market dwarfs the Canadian market, with 2001 sales amounting to $131 billion and $3 billion, respectively. Reimportations from Canada were about $1 billion in 2003. Obviously, U.S. companies will not continue to send products to Canada that can be sent back to the United States at a lower price, because doing so only undercut their larger U.S. market.

Price is one way in which drug companies compete. They also compete to develop and market new drugs. Many large companies still conduct their own R&D, but the purchase or lease of products is an increasingly popular method for bringing new products to market. Companies also compete in managing the U.S. Food and Drug Administration approval process and in product promotion. Price competition gradually becomes more important in the later stages of a product’s life cycle. The life cycle of a new chemical entity typically is 20 to 25 years, starting with the idea that leads to its development. A hypothetical product life cycle, based on empirical studies by Grabowski, Vernon, and DiMasi, is illustrated in Figure 1. Before the product reaches the market, the company’s cash flow is negative, and the years of positive cash flow usually will be limited by entry into the therapeutic class of new branded or generic products. A financial analyst or a drug industry decision maker would look at this life cycle in terms of present value — discounting future revenue back to the present value. If the market rate of interest was 6 percent, the present value of a $20 million investment in year 5 would be $14.95 million — while the present value of $20 million in positive cash flow in year 15 would be only $8.35 million.

The act of making decisions looking into the future is driven by expectations about future revenue and costs. The longer the expected development time, the lower the present value, because of the longer period of negative cash flow. Likewise, the smaller the expected market or the greater the risk of failure, the lower the present value (Grabowski 2002).

In the context of these economic considerations that affect R&D, how would a pharmaceutical company respond to price controls (i.e., the legalization of reimportation, which would be tantamount to importing the Canadian price controls)? This is clearly illustrated in Fig-
The expected future revenue is assumed to be cut in half to only $10 million in year 15. The present value also has been cut in half to only $4.17 million, while nothing has happened to the present value of the investment that occurs prior to approval.

If a company expects to operate in an environment with price controls, standard economic theory predicts the company would reduce its R&D investment. Further, the company would concentrate on drugs with the largest markets instead of small-market products like vaccines. A company also would have an incentive to pursue short-term projects instead of longer-term projects. It is obvious that in a market that is expected to be limited, a company will reduce the risk profile of its projects.

Given the important role that the U.S. market plays in international markets, imposing price controls on the U.S. market would have a substantial effect on the expectations of R&D decision makers. This would not be the same as deciding to sell to a small country at a discounted price.

One historical example of how a research-intensive industry responded to price controls is given by the field market for natural gas. In the 1960s, when a Supreme Court decision led to much greater federal regulation of the natural gas production market, natural gas producers responded by cutting back on the search for new gas fields and by diverting gas into the unregulated intrastate market. The natural gas industry is analogous to the pharmaceutical industry in that investors are willing to incur high risk and up-front expenditures, provided there is the possibility of a large discovery and future revenues. The difference is that natural gas is a well-known product with well-defined characteristics, while new chemical entities are surrounded by uncertainty regarding safety and medical effectiveness. This provides an extra level of risk when compared to the search for new gas deposits.

As the pharmaceutical sector changes domestically and internationally, a major debate is occurring among securities analysts and economists regarding the viability of the blockbuster drug as the major motivating factor, and whether drug companies will reduce the risks they are willing to take in the face of smaller markets and lessened expectations. But there is no doubt that price controls in the United States would have a detrimental effect on what has been, up to now, an extremely productive industry.

**Reference**


**Additional reading**


**Question-and-Answer Session**

**PARTICIPATING FACULTY**

ROBERT B. HELMS, PhD
Resident Scholar
American Enterprise Institute

FRANCIS B. PALUMBO, PhD, JD
Professor and Director
Center on Drugs and Public Policy
University of Maryland School of Pharmacy

**QUESTION:** Dr. Palumbo, if reimported medications are allowed to be dispensed through in-state pharmacies, or if personal importation is allowed to persist in some manner, will there be any attempt to regulate the Canadian pharmacies that are exporting drugs?

**FRANCIS B. PALUMBO, PHD, JD:** If pharmacists are allowed to act as importers of drugs, it will have an impact on the state pharmacy practice acts. The acts will have to be rewritten to accommodate the fact that pharmacists would be doing more than dispensing medications and providing information and counsel to patients, but are actually involved in importing. The states may end up changing their regulations on registration of importers, wholesalers, and distributors and require pharmacists to register as such in addition to being licensed as a pharmacist. This is all speculation on my part, however.

With regard to Canadian pharmacies, they’re outside the reach of the states. A state’s board of pharmacy has no jurisdiction over any Canadian pharmacy or any Canadian pharmacist, or anybody outside that state. And the federal government, because it doesn’t license pharmacists or pharmacies, is not in that business at all.

**QUESTION:** Dr. Helms showed that a higher rate of return would promote research and new discoveries. Am I correct in assuming that consumers would benefit indirectly from that additional competition coming forth because of the higher rates of return?
ROBERT B. HELMS, PHD: Yes, you would have more market entry and more competition. You can argue that the one thing that would really benefit manufacturers and consumers would be to shorten the approval time. Basically, you would shift the supply curve to the right and put more downward pressure on all the prices. In terms of present value, a shorter approval time would let pharmaceutical companies get to a net positive cash flow position sooner, and it would be a benefit.

QUESTION: What we have with pharmaceuticals is directed consumption rather than free-choice consumption. A lot of patients consume medicines because they are basically directed to do so. It’s not technically a free choice in the same way that they may want to go out and buy a television or a car. Does this make a difference in terms of the overall economic theory?

HELMS: It makes a small difference, but it does not fundamentally change the laws of demand. It explains that this is a joint effort. There is a lot of evidence that consumers value pharmaceutical products, and they go to a great deal of effort to become informed about what is medically productive and what is not. What is affected in terms of the pure theory of demand is the role of insurance, which creates more of a moral hazard problem. In other words, the sense that somebody else is paying increases the quantity demanded by consumers, because they do not perceive that they are paying the full cost once it’s covered by insurance.
The primary reason that American patients and many government representatives are in pursuit of purchasing brand-name prescription drugs from Canada is the reduced prices associated with medications from north of the border. This article, while accepting that many patients find bargains in Canada, provides some context to this core tenet of reimportation. The issue of determining actual price differences between countries has been addressed by a number of analysts.

A colleague and I compared prices for drugs from the Ontario Drug Benefit formulary and Costco, the membership warehouse store, in the United States. While there were price differences for most drugs, the range of price differences was wide (Table 1). In other words, if policy implications of reimportation are being considered, there is no simple answer, such as “American cost multiplied by 0.6 provides the cost savings of reimportation.”

An aggressive and informed shopper in the United States can save significantly even shopping locally. In another survey, we found that patients in Seattle could have saved $17 on a 30-day supply of Celebrex if they had shopped around the region. If these consumers had gone from the most expensive pharmacy in Seattle to the least expensive pharmacy in neighboring British Columbia, there would have been a savings of $63; the differential between the least expensive pharmacy in Seattle and the most expensive pharmacy in Vancouver, however, was approximately $37.

The point here is not whether there are absolute savings but that the range of savings is a variable that is not well determined. Therefore, it is difficult to support policies claiming that buying drugs in Canada will result in a specific percentage of savings. When calculating savings, it is challenging to estimate on an aggregate basis what consumers would save if this business were normalized.

Patricia M. Danzon, PhD, and colleagues at the Wharton School of Business at the University of Pennsylvania have studied international price differences for medicines in a number of articles published in economics journals. They have concluded that there is no one satisfactory measurement of international price differences. Medicines are sold under different names, in various packaging, in a range of doses, and in varying forms, even in countries as similar as Canada and the United States.

Nevertheless, many U.S. patients apparently save money by filling their prescriptions in Canada. Supporters of reimportation attribute the savings to two causes: price controls and monopsony buying power by the national health system. Both causes are quite unlikely.

Price regulation in Canada

Drug prices are regulated in Canada via the Patented Medicine Prices Review Board (PMPRB), a federal quasijudicial agency established under the Patent Act in 1987. Prior to 1987, there was little patent protection for prescription drugs. When the Canadian government improved patents, some were concerned that patent protection would result in higher drug prices for Canadians. Therefore, the government instituted the PMPRB to regulate the prices of patented medicines (not, however, generics or branded off-patent medicines). The PMPRB does not buy medicines for Canadians, as it has no budget to do so; it simply approves prices at which manufacturers want to sell.

The PMPRB puts new medicines through an evaluative process that first asks: Is this medicine a “blockbuster,” a line extension, or a “me too?” In the case of a blockbuster, which would be categorized as a product for which there is no reasonably comparable drug available, the PMPRB takes the median price of seven other countries: the United States, United Kingdom, France, Germany, Sweden, Switzerland, and

| TABLE 1 | Price variations across borders, 2001 |
|---|---|---|
| | Celebrex | Lipitor | Paxil |
| Domestic (WA) | $17.59 | $23.59 | $16.71 |
| Cross-border maximum (WA/BC) | $62.77 | $76.90 | $54.52 |
| Cross-border minimum (WA/BC) | $36.62 | $37.35 | $28.36 |

BC=British Columbia, WA=Washington
SOURCE: GRAHAM 2001
Italy. That median price is the limit at which the manufacturer may sell its drug in Canada. In the case of line extensions or “me-too” drugs, prices must be in line with similar medicines already sold in Canada. Once marketed in Canada, a patented drug’s price generally cannot increase by more than the change in the Consumer Price Index.

**No Canadian drug benefit**

Many Americans hold the misconception that prescription drugs are covered by a Canadian national health system. Although necessary hospitalizations and physician visits are controlled by a provincial government monopoly (supported by transfers from the federal government), prescription medicines are purchased privately. Provincial government drug plans pay for somewhat less than one half of all spending; private insurance pays for about one third; and patients pay directly out-of-pocket for approximately one fifth (Table 2).

Although each of the 10 provinces has a prescription drug benefit, each province has its own formulary and coverage varies. Through the new “Common Drug Review,” provincial governments are trying to harmonize the process. Yet this will prove very challenging, however, as each province controls its own budget. It appears unlikely that, for example, British Columbia would allow reviewers selected outside the province to determine the makeup of the British Columbian formulary, with its attendant impact on the British Columbian provincial budget.

**TABLE 2  How drug prices are set in Canada**

**Patent Medicine Prices Review Board (PMPRB)**

- Only regulates patented medicines, not generic or branded off-patent
- Existing medicine prices can increase by Consumer Price Index
- Newly launched drugs in three categories:
  - Blockbusters — no greater than median of seven countries (U.S., U.K., France, Germany, Sweden, Switzerland, Italy)
  - Line extensions — similar to other drugs in the line
  - Me-too — similar to other drugs in class
- Effects of PMPRB unclear
  - Generic drugs often higher priced in Canada
  - Canadian discount for branded, off-patent drugs greater than for patented drugs

**FIGURE 1  Overview of Canadian health care**

Prescriptions’ share of total health spending in United States and Canada

- United States
- Canada

SOURCE: GRAHAM 2003
Drug spending vs. overall health budget

Interestingly, drug spending in Canada accounts for about 12 percent of the country’s overall health care spending vs. about 9 percent in the United States (Figure 1). Certainly, this may be telling us only that U.S. physician and hospital costs are high, whereas in Canada provincial governments artificially ration such care and create long waiting lists for treatment under their monopolies, thereby reducing monetary costs.

Reasons for the prescription drug pricing gap

Macroeconomics reveals the primary cause of the price differential relative to prescription drugs; almost everything is more expensive in the United States. Table 3 shows the premium that U.S. consumers pay. In fact, if all the Canadian regulations were eliminated, the Canadian health care system privatized, and the PMPRB drug prices removed, the United States and Canada still would not be equalized in drug pricing because they are not equalized in other areas. General price levels are different, because Canada is a less productive country than the United States and Canadians earn significantly less than Americans.

The importance of patents

A technical challenge to reimporting as a way to lower U.S. drug prices is that patents are national. A medicine may be patented in one country but not in another. When running for the U.S. Senate, Hillary Clinton held up tamoxifen as an example of a drug that was much cheaper in Canada. Yet, at that time, tamoxifen was patented in the United States and not in Canada. Is it appropriate to violate a U.S. patent simply because no patent exists in a foreign country? Obviously, the logical conclusion of this policy is the destruction of an effective U.S. patent system. When measuring price differences, comparing a patented medicine in the United States to a foreign generic leads to inappropriate results.

Table 3: Canadian price differences

<table>
<thead>
<tr>
<th>Product</th>
<th>CN price (U.S. $)</th>
<th>U.S. price ($)</th>
<th>U.S. premium (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quicken Basic</td>
<td>20.52</td>
<td>34.95</td>
<td>70</td>
</tr>
<tr>
<td>AOL Unlimited</td>
<td>15.72</td>
<td>21.95</td>
<td>40</td>
</tr>
<tr>
<td>No name acetylsalicylic acid</td>
<td>3.08</td>
<td>4.99</td>
<td>62</td>
</tr>
<tr>
<td>Bayer aspirin</td>
<td>3.99</td>
<td>4.99</td>
<td>25</td>
</tr>
</tbody>
</table>

References


The reimportation debate often centers on the short-term desire to purchase drugs at lower costs, and the associated attempt at lowering drug budgets of state and local governments as well as the out-of-pocket expenses of American consumers. This article will instead focus on the long-term implications of reimportation.

Defining the issue
There is a great sense of confusion concerning reimportation, with some framing it as a free trade issue. It is not, however, as a result of free trade that we exploit gains from trade across countries, because some countries have determined better ways to manufacture drugs than American companies. Clearly, the manufacturing and production of drugs by foreign companies are allowed in the United States, so that is not an issue.

Reimportation has to do with the policy that does not allow wholesalers to sell drugs back to the United States, as opposed to allowing manufacturers to do so. Reimportation may be thought of as a form of reference pricing, when the goal of reimportation proponents is for another country’s prices to prevail in the United States. It is a fairly expensive method of achieving reference pricing, in the sense that drugs are shipped back and forth across the U.S.-Canadian border to arrive at a de facto reference price as opposed to direct reference pricing.

The tradeoff of patents
The real tradeoff of reimportation appears to be an elasticity of research and development to profits. If this tradeoff did not exist, there may not even be an issue. (In fact, if R&D was not elastic to profits, there should simply be generic competition on the first day after a new product is introduced to the market.) Patents reward R&D innovation through monopoly market power. The system sacrifices competition to provide companies with incentives to undertake the fixed costs of R&D. The standard tradeoff of patents, which is what reimportation seems to be all about, is the fact that monopolies want to price their products above cost (as opposed to competition that usually is intended to bring prices down to cost). Therefore, there is a persistent loss that is created by some consumers who are willing to pay the price it takes to develop a medication but not the price manufacturers are charging.

It is still believed, however, that the positives of patents outweigh the negatives. The primary positive is that patents underwrite new technology, which outweighs the negative of restricted consumption while the patent is effective. Although it is difficult to measure the true impact of reduced profitability on R&D, there is considerable evidence that R&D is highly sensitive to profits. For instance, it is clear that potential market size drives R&D; the Orphan Drug Act, which made small markets more profitable, also resulted in R&D in categories for which little activity had existed previously.

So, although the typical reimportation tradeoff is presented as an inexpensive drug compared with an expensive drug, the real tradeoff is no drug compared with an initially expensive one.

Patent breadth
Reimportation, therefore, is essentially a discussion of how much patent breadth there should be. Economists distinguish between patent length — the number of years the product retains exclusivity — and patent breadth — how much profit per year a manufacturer can achieve on a given patent.

Reimportation, by essentially allowing arbitrage from low-cost consumers to high-cost consumers, makes price discrimination across countries more difficult. Nevertheless, this arbitrage opportunity also is driving down the breadth of the patent. Obviously, a manufacturer makes higher profits when allowed to discriminate regarding the price of the drug.

The actual long-term consequences or tradeoff are not public health versus financing, which is how the discussion has been framed. The real tradeoff is about reducing R&D; it is a question of cutting prices now versus cutting R&D spending for the future. Any lowering of the economic value of a patent will essentially lower prices today, but would raise the true prices for drugs to-
morrow through reduced innovation. It is an intergenerational tradeoff (a benefit for one generation today, but a potential problem for future generations), and the political process may or may not favor one generation or another; that is where the tradeoff appears to be, however.

In addition, the present value of an innovative return involves an initial investment period of negative cash flow, a break-even promotional period, and then a positive cash flow that hopefully finances that investment in the drug product. This is the current equation and one that might be in jeopardy should reimportation damage patent protection incentives.

Future scenarios
The Medicare Modernization Act has mandated that the Department of Health and Human Services publish a report that examines the impact of reimportation (assuming some form of legal reimportation). The relevant topics to be addressed by the report include the potential long- and short-term impact on drug prices and prices for consumers associated with importing drugs from Canada and other countries. In addition, the report will be assessing the effect on R&D and the associated effect on consumers and patients if importations were permitted.

The report is evaluating three potential reimportation scenarios: no impact, medium impact, and large impact. The no-impact scenario assumes that producer behavior and legislative regulations essentially will offset each other. The medium-impact scenario indicates that prices would gravitate to a level that is extremely close to current private prices because there would be price discrimination allowed across two countries. The common price between the Canadian and U.S. markets would be driven by the United States; Canadian sales are roughly 5 or 6 percent of U.S. sales. Additionally, it is a small market relative to the U.S. market, and presumably because it is not as wealthy a nation, it is more price sensitive.

In the medium-impact scenario, U.S. prices fall only slightly relative to the old pricing structure. The price for the Canadian population would rise dramatically, however, because it is a small part of the market and more elastic. One might expect to see an enormous impact on Canadian prices but a miniscule effect on U.S. prices.

The large-impact scenario assumes foreign prices prevail in the United States, an assumption made by governors and mayors when they advocate purchasing drugs from Canada. Nonetheless, it is unclear which incentives and regulations would be in effect. Yet, it is expected that new technology development (elastic to profits) will be curtailed.

The value
Ultimately, this issue revolves around the concept of value. As a society, we will be determining where the value lies, paying a higher cost for current drugs to fund new technology, or paying less for drugs now but foregoing some (potentially critical) R&D. The basic question that the HHS report will attempt to answer is: Is it true that patents are better or are welfare-enhancing in the pharmaceutical industry? The implications for the long-term could be dramatic.

Question-and-Answer Session

PARTICIPATING FACULTY:

JOHN R. GRAHAM, MBA
Adjunct Scholar
The Fraser Institute

DAVID P. NAU, RPH, PhD
Assistant Professor
Center for Medication Use, Policy and Economics
University of Michigan

FRANCIS B. PALUMBO, PhD, JD
Professor and Director
Center on Drugs & Public Policy
University of Maryland

TOMAS J. PHILIPSON, PhD
Professor
Irving B. Harris Graduate School of Public Policy Studies
University of Chicago

QUESTION: If patients are served by Medicare and get their prescriptions filled by whatever means in Canada, does that contribute toward the deductible or not?

FRANCIS B. PALUMBO, PHD, JD: I don’t think the law specifically addresses obtaining drugs from outside the country and how that would affect the deductible, but my strong sense is that you would not be able to apply to your deductible to any drug that you purchased from outside the country (assuming that it’s illegal to do so). So, presumably, you might never be able to use the benefit if you were going to be doing that.

QUESTION: You buy at the lowest cost, if you really search around, and the evidence is that you can save a lot if you do that in the United States. But, you wouldn’t be able to deduct the list price; you would have to use the actual market prices to calculate how much would apply to the deductible. This is going to change the dynamics of marketing drugs to Medicare beneficiaries very soon. Is this essentially going to make the reimportation issue less serious in terms of the public debate?

PALUMBO: I think it might have some effect on drugs from
other countries, but we still have this large group of nonelderly individuals in the United States who don’t have access to health care or access to drugs, who I think would continue to drive this movement toward importation. They’re also going to have access to all the price data on the Internet. They may not have the “card,” but many consumers in that category are already members of the preferred provider organizations and the managed care plans that are using the pharmacy benefit managers and the large group buying power anyway. It will generate a narrow range of prices.

DAVID P. NAU, RPH, PHD: Pharmacists are telling us that it’s not just older Medicare beneficiaries interested in importation; it’s customers of all ages who are looking for lower prices. So, even with the Medicare discount card, there are going to be a lot of people still looking for those lower prices from Canada or other places.

QUESTION: How might all of this influence the patient-provider interaction and decision making about appropriate therapies?

TOMAS J. PHILIPSON, PHD: This is essentially about “search costs,” and both theory and recent evidence suggest that price differences or price variance across manufacturers go down when search costs go down. The best evidence we have of this is in the life insurance markets. When they went on the Internet, you saw dramatic reduction in the variance of, for example, term policies.

PALUMBO: As far as the patient-provider relationship, I think doctors are quite interested in keeping costs down for their patients. I think it is a question of educating providers as to what they ought to advise or not advise their patients when they come into their office.

NAU: Just anecdotally, we are getting feedback from clinicians within the University of Michigan health system from office managers who are saying, all we care about is finding the cheapest source so that our patients can get their medications.

QUESTION: Has reimportation pushed down prices for drugs for patients without any insurance coverage whatsoever?

JOHN R. GRAHAM, MBA: These uninsured patients are paying more than anybody else. The problem is that OBRA [Omnibus Budget Reconciliation Act] stated that Medicare and Medicaid had to get the biggest discounts. Yet, if the drug company expands its patient assistance program too much for uninsured people, there will be complaints that everyone should be getting this price. The political dynamics that prevent price differentiation within the United States are a big problem.

QUESTION: Hasn’t the train already left the station on this one, in terms of politics? How are the politicians not going to support importation when the voters are so adamant about it?

PALUMBO: Because of the pedigree requirement having been stayed once again, we still have no confidence that the products coming into this country from outside the country are the ones we expect to be showing up. I think this is going to keep the train in the station for at least a little while longer. I think a lot of it does turn on what happens in the United States with counterfeiting activities. I believe that there is a lot that still bodes for not making any rash decisions on bringing drugs in from outside the country, even from Canada.

PHILIPSON: Without some drastic change in how we educate people about the importance of R&D and the tradeoff between cheaper drugs today and future technology, misperceptions will dictate policy.
International intellectual property rules and Canadian and U.S. intellectual property laws have implications for the cross-border pharmaceutical trade that are often overlooked in the context of the overall debate. Although the grey market in prescription drugs remains a grey area with respect to international intellectual property rights, the cross-border trade will frequently result in patent infringement in the United States and Canada. Proposed state and federal legislation to allow imports of Canadian drugs into the United States does not appear to address the rights of the holders of patents and trademarks on the drugs. In addition, by condoning the practice, the Canadian government exposes itself to a claim by the U.S. government or individual U.S. companies that Canada is failing to abide by its North American Free Trade Agreement (NAFTA) obligations.

Cross-border prescription drug trade creates the potential for intellectual property right violations because the trade is not free trade. The prescription drug trade represents a grey market that exists because it presents an opportunity for arbitrage. The primary difference between grey market or parallel trade and free trade is that free trade occurs with the voluntary participation of all parties, while parallel trade opposes the interests and wishes of the affected manufacturers (Graham 2003). Holders of patents and trademarks associated with prescription drugs oppose drug importation and are entitled to take action to enforce the rights that are being violated.

The ability of intellectual property holders to use their patent and trademark rights to restrict cross-border prescription drug trade depends on whether the importation results in a breach of international or national intellectual property rights in each circumstance. The international intellectual property agreements currently in place do not prevent the United States from allowing drugs to be imported from Canada. According to the doctrine of exhaustion, once the first sale of a patented product has occurred, the patent holder has received its just reward for the innovation behind the drug, and other parties can resell it without worrying about patent infringement. Simply put, if patent rights have been exhausted, the patent holder lacks recourse against importation or reimportation of a patented drug. Article 6 of the TRIPS agreement states that nothing in that agreement shall be used to address the issue of exhaustion, allowing each country to determine when the patent rights in its country are exhausted.

Countries can choose to apply the doctrine of exhaustion on a national, regional, or international level. The United States generally applies a rule of national exhaustion. This means that a first sale of the patented product by the U.S. patent holder in the United States generally exhausts the patent holder’s rights in the United States. If, however, the first sale occurs in a foreign country, the patent holder’s rights in the United States might not be exhausted and unauthorized importation of the drugs into the United States may infringe upon the U.S. patent. Judicial decisions by U.S. courts regarding the application of this principle are somewhat conflicting; however, it is likely that if a drug is manufactured in Canada pursuant to a Canadian patent and then is exported to the United States, exhaustion does not apply and the U.S. patent holder retains its right under

---

1 Jazz Photo v. ITC (CAFC) 264 F.3d 1094, which held that exhaustion does not occur if the first sale of the patented product occurs in a foreign country. The national exhaustion rule has not been consistently applied in this manner. See, for example, Holiday v. Mattheson, 24 F.185, 186 (CCSDNY 1885) and Kanita Hattori Seiko v. Refac Tech. Dev. Corp., 690 F. Supp. 1339, 1342–1343. (SDNY 1988 [Holding that a sale abroad by a party authorized to sell under the United States patent bars the U.S. patentee from preventing resale in the United States].)
its U.S. patent to restrict importation.2

Regional exhaustion characterizes the situation in the European Union. In the EU, the first sale of a patented drug exhausts the patent holder’s rights in all other EU countries, allowing parallel importation to occur communitywide.

International exhaustion describes the situation in Canada. If a product patented in Canada is sold anywhere in the world under either the Canadian patent or a foreign patent, that exhausts the patent holder’s rights under the Canadian patent.3 The patent holder in general cannot restrict importation into Canada, unless the patent holder structures the initial sale of the product in a manner to ensure that exhaustion does not happen (e.g., by negotiating express licenses with distributors that impose geographical restrictions on sale or segregating the ownership of its patent portfolio).

In the United States, patent infringement will likely result from importation of drugs from Canada in the following three situations:

1. The patented drugs were manufactured in the United States or Canada and the U.S. patent holder expressly restricted the sale to Canada (by an express license).4

2. The patented drugs were originally manufactured in Canada by a party with an exclusive license to manufacture in Canada and with no rights under the U.S. patent.5

3. The product imported is a generic copy of a U.S. patented product.

Imports of generic copies of patented products are particularly troubling. There is significant incentive to import generic copies of U.S. patented products from Canada, a practice that invariably results in infringement of rights under the U.S. patent. If a generic copy can be made in Canada but not in the United States, the Canadian generic is likely to be cheaper than the patented drug in the United States. This practice is occurring with more and more frequency as Canadian mail order and Internet pharmacies turn to third countries, such as India and Brazil, to import generic drugs that are still patented in the United States and Canada. Although it is difficult to verify, there is suspicion that these products are being imported into Canada for ultimate resale in the United States. In addition, Canadian patent rights are not exhausted and importation into Canada from third countries of drugs ultimately destined for consumption in the United States can occur if:

- The sale of the patented product was geographically restricted in the third country. (That is, if a patented drug is imported into Canada from Britain under circumstances in which the sale of the drug was restricted to Britain.)
- The patent on the prescription drug product is held by independent subsidiaries or licensees with exclusive manufacturing rights in the country from which the drugs are exported (i.e., Britain) and Canada.

As stated earlier, the WTO TRIPS agreement and NAFTA do not expressly restrict parallel importation. Because the cross-border trade gives rise to widespread patent and trademark infringement, the practice arguably is inconsistent with Canada’s obligations under NAFTA to provide adequate intellectual property rights protection to U.S. drug companies. Under NAFTA,
Canada is required to give “effective action” against patent infringement to U.S. and Mexican holders of Canadian patent rights (NAFTA Articles 1701 and 1714). It is also an open question whether Canada’s failure to prevent exports of Canadian drugs to the United States “nullifies or impairs” the benefits U.S. drug companies expected to enjoy under NAFTA. One reason that the United States negotiated NAFTA was to ensure that U.S. drug companies would enjoy greater intellectual property protection. The United States could argue that by condoning the cross-border trade, the Canadian government is turning a blind eye to widespread intellectual property rights violations and is failing to provide the level of protection that negotiation of NAFTA was expected to bring.

It is important to keep in mind that the above argument is available only to the U.S. government, and not to individual U.S. drug companies. Given that the U.S. political sentiment currently appears to favor reimportation, it is unlikely that the U.S. government will take action against Canada in this manner despite widespread infringement of patent rights.

U.S. drug companies are, however, entitled to bring a direct action against the Canadian government for failure to protect their investment in Canada under NAFTA Chapter 11. Canadian patents held by U.S. drug companies represent an investment in Canada. It is open to the companies to argue that the cross-border trade in prescription drugs reduces the value of these Canadian patents because a sale of the drug in Canada cannibalizes profits in the United States when the drugs are imported into the U.S. It remains to be answered whether Canada’s failure to stop the cross-border trade denies U.S. companies fair and equitable treatment and full protection and security of their investment (NAFTA Article 1105), and whether it is worth it for the U.S. pharmaceutical companies to pursue this argument in the current political environment.

An action for “nullification or impairment” of the expected benefits of NAFTA can be brought pursuant to NAFTA Annex 2004.

References


Economists understand that financial growth is tied to innovation — even if that message has failed to emerge as a campaign theme in this year’s presidential election. Measuring the direct value of innovation is difficult; however, 2 years ago I worked on a collaborative study examining the relationship between market-based pricing and biopharmaceutical innovation.1 Specifically, we looked at whether pharmaceutical innovation was affected by price regulation.

We examined four subpoints to determine the effect of price regulation on innovation and related health care, economic, and societal benefits:

• Effect of market-based pricing on industry returns
• Effect of market-based pricing on the pharmaceutical industry and research and development investment
• Effect of market-based pricing on the level of biopharmaceutical innovation in the United States
• Economic contributions derived from the pharmaceutical sector under market-based pricing

To determine the effects of price regulation in these four areas, we reviewed the literature, created economic investment models, and conducted interviews with economists, academic experts in the United States and abroad, members of advocacy groups and trade associations, buyers, providers, and a state government agency.

Industry returns

Using Jensen’s alpha to measure pharmaceutical sector returns,2 our analysis showed that pharmaceutical returns in the 1990s remained steady relative to returns from the 1980s (Figure 1, page 24) (Edwards 2003). The monthly return was less than 1 percent above the cost of capital. The data showed that pharmaceutical sector returns were well aligned with risk and remained consistent throughout a 20-year period. Our findings were consistent with data analyzed by the U.S. Office of Technology Assessment in 1993,3 when evaluating the relationship between cost of capital and rate of return (OTA 1993). Using Jensen’s alpha, we found that the rate of return in the pharmaceutical industry between 1980 and 1999 was similar, and in some cases lower, than in other industries.

Research and development

The major role that U.S. pharmaceutical companies play in funding worldwide R&D is often overlooked. U.S. pharmaceutical companies provided $20.3 billion, or 67 percent, of worldwide private pharmaceutical funding in 1998. In addition, U.S. companies provided $19.5 billion, or 57 percent, of worldwide public funding for health R&D that same year (WHO 2001). Public R&D efforts, which are largely basic research, would not lead to marketable products without private R&D capabilities and support. Expansion of price regulation into the U.S. market via reimportation would inhibit R&D by reducing private R&D capabilities. The creation of new pharmaceuticals would likely be delayed and the return on all public and private research would also be delayed.

Innovation

Between 1963 and 1999, major U.S. pharmaceutical companies contributed 62 percent more new chemical entities to the U.S. market than their European counterparts (Edwards 2003). The top 16 U.S. pharmaceutical companies had 243 new chemical entity approvals compared with 150 from European companies (DiMasi 1994; Edwards 2003). Additionally, the number of novel biotechnology product approvals in the United States was nearly double the number of those in Europe.

1 The study “Examining the relationship between market-based pricing and biopharmaceutical innovation” was made possible by Aventis; the John F. Kennedy School of Government at Harvard University; JP Morgan; the New York State Office of Science, Technology, and Academic Research; Pfizer; Pharmacia; Stanford University; and Wyeth.
2 Jensen’s alpha is used to assess whether total return reflects any differential return above the expected return based on the cost of capital as measured by the Capital Asset Pricing Model.
3 The 1993 U.S. Office of Technology Assessment study determined that the 1981–1990 rate of return was 2 to 3 percent above the cost of capital.
Biotechnology R&D exploded in the 1990s. Over a 10-year period (1990 to 2000), there was 370 percent growth in the number of drugs in development. In addition, during that period there was 920 percent growth in the number of drugs on the market, and 600 percent growth in revenues (Figure 2) (Gilpin 2002). Because of these increased investments, the generally favorable financial community, and a market-based pricing structure, the U.S. public benefited from a substantial rate of growth in the number of new treatments available.

**Economic contributions**

Using the IMPLAN model (a tool for economic analysis) to describe commodity flow from producers to intermediaries to final consumers, our study showed that in 1999, the U.S. pharmaceutical industry4 directly generated $101 billion in sales and $30.1 billion in labor income, and employed more than 211,000 people. An additional $57.8 billion in sales and $21.1 billion in labor income, and more than 313,000 employees in the United States in 1999 were indirectly supported by the pharmaceutical industry through its purchases from other industries. The induced demand, which reflects the purchases made from other supporting industries by pharmaceutical workers and owners, contributed an additional $69.9 billion in sales and $24.2 billion in labor income, as well as more than 557,000 employees. In total, the pharmaceutical sector contributed $229.2 billion in sales and $75.4 billion in labor income, and nearly 1.1 million employees to the U.S. economy (Edwards 2003).

**Value of innovation**

Innovation, as demonstrated in such Far East countries as Korea, Singapore, and several others, has a significant effect on economic growth. The recent experience of Korea in contrast

---

4 The pharmaceutical industry’s direct, indirect, and induced economic effects are estimated using IMPLAN’s multipliers for the drug industry (SIC Code 283), which includes four subgroups: medicinal, chemical, and botanical products; pharmaceutical preparations; in vitro and in vivo diagnostic substances; and biological products excluding diagnostic products. IMPLAN describes commodity flow from producers to intermediate and final consumers via an input-output model. More information on IMPLAN is available online at: «www.implan.com/what.html»

The U.S. revenue and employment numbers shown in the Pharmaceutical Research and Manufacturers of America annual membership survey are used as the proxy for output — usually the production output — of the pharmaceutical industry.
to Mexico is illustrative. The average real wage in Korea grew ninefold from 1960 to 1990, while real minimum wage in Mexico stayed almost the same during the same period. Between 1990 and 1998, Korea's real economic growth rate was eight times that of Mexico (Enriquez 2001). The short-term price of innovation can be significant, but the long-term economic benefits are substantial. As the United States continues to commit to supporting pharmaceutical R&D, extrapolation from our data clearly shows that biopharmaceutical innovation in the United States will continue to thrive under our market-based pricing system.

Putting an exact dollar figure on the cost savings of innovation is difficult because information changes rapidly and research findings are likely to be obsolete by the time of publication. Nevertheless, our data show that reimportation would have negative effects on the innovative creation process in the United States. Pharmaceutical innovation in the United States has significant economic and medical benefits, and I believe that market-based pricing is essential to this process. Price regulation hurts innovation, and reimportation is a form of price regulation because it unfairly brings other countries' regulations to the United States.

Reimportation favors those who have diseases with existing treatments and hurts those who have or will develop diseases without existing or better treatments. Patients have to ask themselves if they are willing to accept this standard of therapy and slow innovation in exchange for a short-term price benefit.

Introduction of a reimportation system into the United States would reduce the number of technologies that support pharmaceuticals, such as new drug deliveries and implantable systems. The standard of care outside the United States would consequently suffer, as the incentive to further innovation decreased.

References

Acknowledgements
Dr. Edwards would like to extend his gratitude to Haleh Armian-Hawley, MS; Kai Zhang, MD, and his colleagues at Aventis; the John F. Kennedy School of Government at Harvard University; JP Morgan; the New York State Office of Science, Technology, and Academic Research; Pfizer; Pharmacia; Stanford University; and Wyeth for their substantial contributions to this work.
To evaluate the economic impact of reimportation, costs must be weighed against the benefits, which would likely involve wealth redistribution from the pharmaceutical companies to reimporters and consumers who may pay less for high-priced drugs. Nevertheless, the likelihood is that only a few would benefit because most studies show that the elasticity of pharmaceutical demand is extremely low (Keeler 1988). This is particularly true for blockbuster drugs that are highly therapeutic and have few substitutes. Certainly, these are also drugs that necessitate and attract a large share of pharmaceutical research and development. Therefore, the costs of reimportation would translate into reduced R&D growth and, in turn, a reduction in new medications. This paper focuses on reimportation in economic terms and in terms of its effect in Europe where reimportation has been legal for many years.

**Framing the issue**

Reimporting drugs from Canada and Europe is equivalent to importing foreign price controls and can be expected to significantly diminish the incentives to invest in risky R&D. The result could be an exodus of resources from pharmaceutical and biotech R&D, which has already been seen in Europe where reimportation has been growing. Vernon (2003a, 2004) and Grabowski and Vernon (2000) have shown that expected profitability is the primary determinant of firm R&D investment in the pharmaceutical industry.

New pharmaceutical and biotech products are distinctive inventions: Companies spend more than 10 years and hundreds of millions of dollars to obtain information about a new chemical or biological structure (D’Masi 2003). The fixed costs of this research far exceed the typical production costs of the final product. This creates some unique problems in the market for pharmaceutical and biological inventive activity: once a new product is brought to market, the efficient utilization of the product requires that the price be set equal to the marginal manufacturing cost, which excludes the fixed cost of investing in the R&D needed to reach the market. When the most efficient utilization is achieved, however, the incentives to innovate are severely diminished. The creation of property rights (via the awarding of a patent) allows for pricing above marginal cost, and thus creates incentives for companies to undertake R&D. This, however, leads to the underutilization of the product once it has been brought to market—a fundamental tradeoff between static inefficiency costs (underutilization once a product has been brought to market) and dynamic inefficiency costs (diminished incentives to innovate due to limited appropriability).

Unfortunately, in policy debates, dynamic inefficiency costs often take a “back seat” to static inefficiency costs. This is not entirely surprising, considering that short-run benefits and costs (a reduction in static inefficiency costs) are more tangible and immediately recognizable than long-run benefits and costs. Moreover, the costs of forgone innovation are less obvious. In addition, politi-
cians are reelected in the short-run, not in the long-run when dynamic inefficiency costs are incurred.

The European experience

Reimportation has been available in Europe since the Treaty of Rome established a common market in 1958, supporting free movement of goods across borders and prosecuting those who restrict it. Each European country regulates prices differently and pharmaceutical companies may choose to set prices according to income levels of different countries. Therefore, drugs can be sold at a wide range of prices. Although these pricing conditions seem ripe for reimportation, pharmaceutical companies have managed to forestall it through (1) different pricing systems (GlaxoWellcome) or discount systems (Organon Laboratories) for products sold domestically versus those meant for reimportation; (2) sales conditional on no reimportation (Sandoz); and (3) supply restrictions (Bayer). Furthermore, they have sought to stop reimporters’ unauthorized use of company trademarks. During the early to mid-1990s, each tactic was struck down by the European Commission or Trademark Directive. Consequently, although reimportation was minimal in 1990 at less than 2 percent of the market, it was estimated at more than 7 percent in 2001 and forecast to rise above 10 percent by 2006 (Reuters 2001).

According to the 2002 annual report of the European Federation of Pharmaceutical Industries and Associations, growth in reimportation is eroding the value of R&D conducted in Europe. European-based companies have responded by spending only 59 percent of their R&D budgets in Europe in 1999 compared with 73 percent in 1990. R&D has, therefore, been redeployed from Europe to the United States.

Also, R&D spending by new biotech companies shows Europeans far behind. In 2000, European biotech companies spent about $4.7 billion on R&D compared with U.S. biotech companies that spent about $11.5 billion (Ernst & Young 2002), partially because U.S. companies are generally larger. When small European companies expand, it appears that reimportation, in part, is responsible for their decision to move operations to the United States. For example, the following companies moved their research or operational headquarters to the United States: Aventis (1999), GlaxoSmithKline (2000), Boehringer Ingelheim (2003) (MedAd News 2003), and Novartis (2002).

Implications for the United States

Reimportation may impinge on the decision of U.S. companies to invest in R&D in two principal ways: an expected-profitability effect and a supply-of-funds effect. The latter assumes that capital market imperfections exist in the market for R&D finance, and thus impart a lower cost of capital to internal funds (cash flows) relative to external funds (equity and debt). Such imperfections may result from significant transactions, asymmetric information, and/or financial distress costs. Lichtenberg (2001) argues that the expected-profitability effect is the dominant factor. Vernon (2004) provides a detailed quasistructural decomposition of these two effects within the context of a robust empirical model of R&D investment. Scherer (2001) and Giacotto (2003) also observe that these two effects likely play a major role in a company’s decision to allocate resources to R&D.

Recent research conducted by Vernon (2003b, 2004) identifies a significant difference in pharmaceutical profit margins across U.S. and non-U.S. markets. In his most recent study, Vernon uses this fact to ask, “What would happen to firm R&D investment levels if U.S. pharmaceutical profit margins were driven down — through price regulation or reimportation legalization — to the same levels as those outside the U.S.?” His findings suggest that R&D investment would decline by 23.4 percent to 32.7 percent, ceteris paribus. Interestingly, this range is highly consistent with two other recent studies that employed strikingly different methodologies (Giacotto 2003; Vernon 2003c).

The present discounted value of all forgone R&D resulting from legalized reimportation is estimated. The simple Gordon growth model may be used to determine this figure, which gives the discounted value growing perpetuity. The model applied to R&D spending requires an estimate of current R&D spending, growth in spending, and cost of capital.

Recent research by Scherer (2001) estimated that R&D investment (by PhRMA member companies) grew at an average annual rate of 7.5 percent from the early 1960s through most of the 1990s. This in an inflation-adjusted rate and, therefore, it is assumed to be a reasonable approximation of the future growth rate in R&D investment. For current R&D expenditures, $33.2 billion (PhRMA 2004) will be used and for the cost of capital, 11 percent real cost (DiMasi 2003). If g is the growth rate, r is the cost of capital, and $RD_{t-1}$ is research and develop-


3 Internally generated funds always are cheaper than externally generated funds. Companies typically pay issuance costs from 3 to 10 percent of the value of the funds raised when they bring equity securities to market.

4 This is a smaller decline than he found in his 2003 study (Vernon 2003a), which considered a longer period and used a different model specification; thus, it may be reasonable to view this estimate as conservative, all caveats for his studies considered.

5 $33.2 billion is the 2003 estimate of R&D expenditures. Because the forthcoming results will be driven by this value, and because expenditures in 2004 — or whenever the policy is enacted — will almost certainly exceed this amount, this figure should be viewed as conservative. Moreover, it only reflects R&D expenditures by PhRMA member companies. For example, worldwide pharmaceutical R&D has been estimated at above $60 billion.
development spending at time t-1, the current value of all expected future R&D spending is:

**Present Value R&D**
(No Reimportation Policy):

\[
PV_t = \sum_{i=1}^{\infty} \frac{RD_{t+i}(1+g)^{i-1}}{(1+r)^i} = \frac{RD_{t+1}}{r - g}
\]

\[
= \frac{\$33.2B}{0.11 - 0.075} = \$948.6B
\]

Vernon’s (2004) range for a one-time decrease in R&D expenditure due to reimportation can be translated into a range for a decrease in R&D growth rates, which may correspond closer to the actual effects of reimportation. That is to say, a decline in R&D growth may be observed instead of an abrupt one-time drop in R&D.

For equivalent results, Vernon’s (2004) range of 23.4 to 32.7 percent translates into lowered growth from 7.5 percent to a range of 6.43 to 5.8 percent. A mid-range value is also added. A 28 percent one-time decrease in R&D spending is equivalent to a decrease in spending growth from 7.5 to 6.13 percent. Estimates of the loss in present value R&D investment from the legalization of pharmaceutical reimportation range from $222.0 to $310.2 billion (using this equation, the minimum drop would be from $948.6 billion to $726.6 billion; maximum drop, from $948.6 billion to $638.4 billion). The midrange value is $266 billion (with present value R&D falling from $948.6 billion to $682.4 billion).

The final task is to translate these declines in the present value of R&D into decreases in the number of new drugs in the future. For this, a present cost per new drug developed is needed. DiMasi (2003), a relatively neutral source, estimates this cost at about $800 million. This means that the low-, mid-, and high-end estimates of foregone new pharmaceuticals due to reimportation are 278, 333, and 388, respectively.

The implications of our study with respect to foregone new drugs under these different per-drug cost estimates can be conveniently gleaned from the figure. Clearly, the cost is substantial in almost every case. Furthermore, the lower the assumed cost of creating a new drug, the greater the number of lost innovations. The midrange of the figure, the number of foregone new drugs is between 300 and 400. Considering that the average annual number of new drugs over the past 10 years is 32, the long-run costs of reimportation are large indeed (PhRMA 2004).

**Conclusion**

Reimportation apparently has reduced growth in European R&D spending, which is not surprising, and U.S. reimportation will have a negative long-term impact on U.S. R&D spending as well. Conservatively, it is expected that the negative effects of reimportation, manifested over a long period, will be equivalent to 300 foregone new pharmaceuticals.

**References**


Lichtenberg FR. Probing the link between gross profitability and R&D spending. *Health Aff.* 2001;20: 221–222.


The reimportation debate frequently focuses on issues such as access, fairness, free trade, efficiency, or safety of the drug supply. Although these issues are all important, there is another important dimension to consider—the impact of allowing broad-based importation on the incentives for future product innovation. This is the focus of my efforts.

Risky business

To set the stage for any discussion concerning innovation, it is important to have a common understanding of critical background information. It is understood that the pharmaceutical industry is a high-risk business in which most products fail. As seen in Figure 1, it is getting more expensive every year to develop new products.

At the same time, one must look at the expected revenues. On average, the present value (PV) of the after-tax revenue at the time of launch are approximately $525 million (Figure 2). The PV of the after-tax cost of development at launch is $480 million. That means that at launch a pharmaceutical company expects to earn, on average, about $45 million in net present value (NPV) profits. This profit provides the incentives to invest in pharmaceutical R&D.

With the United States accounting for 51 percent of pharmaceutical revenues, as shown in Figure 3, it is clear that global industry profits are sensitive to U.S. market conditions. A significant reduction in U.S. revenues could threaten to turn this expected profit into a loss and would result in companies rationally choosing not to continue some development projects.

In my model, the maintained assumption is that pharmaceutical companies are for-profit enterprises that follow rational investment policies. Companies use basic research to develop a pool of compounds with potential clinical benefits and clinical research to establish their benefits in specific disease conditions. The critical phase, from a business perspective, is the step taken to decide whether or not to move a product forward into phase 1 clinical programs. After that decision has been made, the compound generally moves forward based on technical success at each phase of development.

The decision-making process and determination of value

A relatively simple NPV calculation may be used for understanding this decision-making process (Figure 4, page 32). The evaluation begins in phase 1 at which point the company can make the investment (call it C1 dollars) and one of two things can happen: Either the product fails (approximately 30 percent of the time) or the product moves on to phase 2 when the company has the option to invest an additional C2 dollars and continue the process. The product can again either fail or the company...
has the option of investing C3 dollars in phase 3 research. If the company is prudent as well as lucky, the compound will be successful in all three phases of development, and the company will earn revenues (SR). My model assumes that the company understands this basic process and has estimated the costs of development (C1, C2, C3) and potential revenues (SR) at the time of making the phase 1 Go/No Go decision. Furthermore, it is assumed that the company calculates the expected NPV of that decision and moves forward only if the expected NPV of development is positive.

Although the model appears simplistic, the option value associated with discontinuing a project due to technical failures is factored into the decision process. At the same time, the model does not factor in the option value of any knowledge gained from investigating a specific compound (and how that could be applied to other compounds).

Currently, a simulation model utilizing data from DiMasi (2003) (table) is being developed. It runs through a distribution of products based on the 1990s and asks the question: What would have happened in 1990 if importation of drugs from Canada (or other policies) were put in place that would decrease the revenue stream that companies could attain? As shown in Table 1, out-of-pocket costs for product development through phase 1 are on average $15.2 million and increase to $23.5 million in phase 2 and to more than $86 million in phase 3. And, at the end of this pipeline, the associated probability of success is about 1 in 5 for getting a product out to market. It is an expensive proposition. The continuing problem is that some products, even after an enormous investment in development, do continue to lose money; the costs of marketing and sales exceed the revenues from the product.

In fact, when this model is run under full information, it is found that 59.3 percent have a negative NPV—the return to investment for those products is negative even though the product was successful. This corresponds to the earlier finding by Grabowski that only 3 of 10

<table>
<thead>
<tr>
<th>TABLE</th>
<th>Cost data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean cost in millions (Std dev)</td>
</tr>
<tr>
<td>Phase 1</td>
<td>$15.2 (12.8)</td>
</tr>
<tr>
<td>Phase 2</td>
<td>$23.5 (22.1)</td>
</tr>
<tr>
<td>Phase 3</td>
<td>$86.3 (60.6)</td>
</tr>
</tbody>
</table>

SOURCE: DIMASI 2003
products cover the average cost of development. (My model does not include the cost of basic research because at the time of the phase 1 decision, these costs are sunk.) Clearly, if companies were able to predict the future perfectly, they would not rationally invest in these negative NPV projects. Thus, there is a need to calibrate the model based on how much information the company actually has at the time of the phase 1 decision. Using a rational expectations framework, it is apparent that companies actually possess only about 15 percent of the idiosyncratic information. Using this parameter, 95 percent of the products developed would have met the NPV threshold for development.

**Impact of reduced revenues**

Using this Expected NPV Model, the impact of price controls on R&D decisions can be assessed (Figure 5). These preliminary results demonstrate what happens at different levels of price controls. If expected U.S. revenues were reduced 10 percent, 86 percent of the products would have still met the NPV threshold and would have been developed. Conversely, 14 percent of the products actually brought to the market during the 1990s would not have been developed. If prices were cut...
more dramatically, and revenues were reduced by 40 percent (which some proponents of reimportation have claimed could happen), the impact of innovation would be much larger. My model suggests that nearly 7 of 10 products launched during the 1990s would have been rationally scrapped before starting even phase 1 testing because they would not have projected a positive NPV to the investment.

Conclusion

It can be concluded from this analysis that reduced revenue, whether it is directly through price controls or through importation, will reduce the investment in R&D. The impact of relatively small cuts, 5 or 10 percent, varies from a minimal decrease in the number of products developed to a decrease as high as 20 percent depending on which model of information is used (results not shown).

Yet, as just noted, if more dramatic price cuts are seen, such as the 40 percent suggested by some importation advocates, the industry will see a significant decrease, upwards of 70 percent, in phase 1 R&D activities. Further, fewer products entering phase 1 means that in the future fewer products make it to the market.

The model on which this work is based is in preliminary form and is being improved. One critical feature missing in the current form is the effects of demand stimulation from a price cut. The impact of demand elasticity will be incorporated in the next version. In addition, a key policy question raised when product development is curtailed is whether the me-too or innovative products are the ones discontinued. Yet, if importation results in a 70 percent reduction in the number of products developed, the answer does not really matter; because, with such a massive cut, there will be significant reductions across the board. Nevertheless, it is an important issue to address when looking at some of those lesser price cuts/product development reductions. The answer to that question could have a tremendous impact on public health.

References


IMS Health. Global pharmaceutical sales by region, 2001. IMS Health. IMS sets 4Q 2002 dividend. Available at:


PARTICIPATING FACULTY:

THOMAS A. ABBOTT III, PhD
Abbott Consulting LLC

WENDY J. WAGNER, JD, MA
Associate, Advocacy Department
International Trade Law
Gowling Lafleur Henderson LLP

QUESTION: The supply issue is a huge one. Given the dominance of the United States in the overall pharmaceutical market, I wonder how other countries think about us saying that we want to buy up all their lower-cost drugs?

WENDY J. WAGNER, JD, MA: I don’t think the Canadian government ever really considered reimportation to be something that would happen, that legislation would ever really be passed in the United States. And it’s only been in probably the past three to four months, when that has looked like such a realistic possibility that I think the Canadian government is getting very, very scared.

QUESTION: There is going to be a limited supply of imported or reimported drugs that would be available. So, how does a wholesaler or how do pharmacists determine which of their particular customers should receive those lower cost drugs? I think the limited supply issue has all sorts of ramifications once you get down to the operational issues that people haven’t talked about and haven’t addressed but could cause all sort of issues once it comes time to implement this — if it were to ever pass.

WAGNER: The Canadian Internet pharmacies have said that in the face of a shortage of supply they will supply Canadians first. The other really significant issue is the one of transshipment and procuring drugs from other countries, because there have been several Canadian Internet pharmacies or mail order pharmacies that have stated flat out, “We are sourcing from other countries.”
QUESTION: Given that retail pharmacies are also profit maximizers, whatever that arbitrage is may not be entirely passed on to the consumer.

THOMAS A. ABBOTT III, PHD: Absolutely. Economists are good at describing what equilibriums look like; they are not very good at describing the transition. The issues that we are raising have to do with the transition. The new equilibrium, at least in my view of the world, is that if this policy gets pushed to its logical extension, you basically get a collapse in the structure of pricing that exists today.

QUESTION: Isn’t this really a welfare issue fundamentally, not a price-of-drugs issue? I’m worried that if we don’t make the costs clear, we are never going to get anything approaching a social optimal.

ABBOTT: Fundamentally, I agree with you. There are a variety of issues that underpin all this. I wanted to develop a simulation model and some kind of quantitative analysis to help us understand and think rationally about whether price controls would have a small effect or a large effect. It is, however, a much broader social justice and welfare question and issue that stretch beyond reimportation. It’s just gotten all wrapped up into this one focus.

QUESTION: Have any of the models started to include biotech and the differential types of products that we see coming out in the future?

ABBOTT: The impact on the biotechnology companies could be greater than the effect we are finding for these large pharmaceutical companies. That is because many of these small biotech companies depend on venture capital and do not have cash flow. The extension to biotechs is a natural one, and it is one that we are moving toward.
As the debate about reimportation intensifies in the United States, proponents often point to parallel trade in Europe as proof that significant cost savings are possible. The relevance of the European experience, however, is limited by a number of key differences between parallel trade and reimportation as currently proposed or practiced.

**Parallel trade market characteristics**

A central goal of the European Union (EU) is the creation of a single European market within which goods, people, services, and capital move freely. Opportunities for parallel trade are produced by the “free movement” rules. Parallel trade occurs when a product is purchased in Country A and then resold in Country B, where it is more expensive, without the consent of the original manufacturer. In Country B, the imported product competes directly with the identical product sold by the original manufacturer or its local licensee. Under EU law, all goods may be parallel traded, not just prescription medicines. EU patent law, however, allows parallel traders to purchase products only within the EU and the European Economic Area (EEA).

Currently, most prescription medicines sold in parallel trade are purchased in France, Greece, Italy, or Spain and resold in Denmark, Germany, The Netherlands, Norway, Sweden, and the United Kingdom. The medicines most attractive to parallel traders are those with larger sales volumes and higher prices, usually newer and on-patent products.

Within the EU, approximately 70 to 100 specialized parallel distributors conduct virtually all parallel trade in prescription medicines. These companies buy from wholesalers in countries where the product is cheaper and then export to wholesalers or directly to pharmacies — but not patients — in countries where the same product is more expensive. They are subject to the same rules and regulations governing the import-export and sale of prescription medicines as are the original manufacturers, including, for example, licensing, pedigree tracking, lot sample retention, labeling, and patient package inserts. The safety of the supply of imported products in the EU has not been an issue because of these requirements and the effective prohibition of direct sale to patients.

Although parallel traded prescription medicines account for only about 4 to 5 percent of the total EU market (EFPIA 2004), the impact is far greater in some countries and for specific products or manufacturers. Figure 1 shows the percentage of total pharmaceutical sales accounted for by parallel trade in key EU markets. At 15 percent, the United Kingdom experiences the greatest in-
flux of parallel imports (EFPIA 2004). In 2003, the accounting company KPMG estimated that the pharmaceutical industry in the United Kingdom loses as a result some £1.7 billion (~$3 billion) in sales yearly (ABPI 2003). As an example of the impact on individual companies, a leading German pharmaceutical manufacturer estimated in 2003 that a third of its sales in the United Kingdom were being lost to parallel trade (Scrip 2003). For individual products, parallel trade may account for as much as 60 percent of sales on average; for the 12 most affected products, the average is 43 percent (EFPIA 2004).

**Incentives for parallel trade**

Parallel trade in prescription medicines has been encouraged by payers in the destination countries for two main reasons. First, it lowers procurement prices and, second, it theoretically creates a competition effect, encouraging the original manufacturer to reduce product price to discourage parallel imports. Pharmacy incentives, including both financial inducements and regulatory requirements, have been critical to realizing savings through lower procurement prices. In Germany, for example, 7 percent of a pharmacy’s yearly turnover must be dispensed in parallel imported products to avoid financial penalties. In The Netherlands and the United Kingdom, the payer “claws back” a portion of the discounts that the pharmacy is expected to have received from wholesalers as the result of parallel imports, and the pharmacy keeps a far greater share. Sweden requires that the lowest priced parallel import be dispensed and provides indirect incentives, through yearly pharmacy bonuses, to increase parallel import dispensing.

Incentives for patients to seek out parallel imports are minimal for two reasons. First, pharmacies may not pass on savings to patients, even when permissible and, second, patients in much of the EU pay very little out of pocket. Copayments are low compared to those in the United States — rarely more than the equivalent of $10 to $15 and usually a flat fee rather than a percent of the price. Moreover, the elderly are exempt from copayments in most of the EU; children under 18 and patients with certain life-threatening illnesses may be as well.2

**Assessment of parallel trade**

Estimates vary as to the impact of parallel trade on health care spending. Savings to health care budgets can be extremely difficult to quantify for several reasons. Reliable, sufficiently detailed data are not readily available in most countries, requiring researchers to make a number of often-debatable assumptions. In addition, frequent changes in cost containment measures aimed at prescription medicines can make the attribution of savings to any one factor questionable at best. These concerns and others have led to heated criticism of virtually all studies done to examine the benefits and costs of parallel trade, including a recent analysis that estimated savings from parallel trade in 2002 at a total of €631 million (~$750 million) across five countries, Denmark, Germany, The Netherlands, Sweden, and the United Kingdom (West 2003). Sponsored by the association of parallel distributors in Europe, the report did not attempt to estimate profits to that industry, which many observers believe substantially outweigh savings.

All governments in the EU either determine the market price of prescription medicines or impose strict controls on the reimbursement price, thus artificially constraining the market both within and across countries. Unable to adjust product prices sufficiently in importing countries or raise prices in exporting countries, pharmaceutical manufacturers have paid indirectly for the savings from parallel imports. Such country-level price controls also have meant that the expected competition effect has not occurred.

Although parallel trade is not the only consideration, concern about the future of the pharmaceutical industry in Europe has highlighted its effect on research-based companies. Countries that traditionally have been export sources have begun to adjust pricing policies for new products, granting somewhat higher prices — in part to help minimize the impact of parallel trade. Any losses in savings may be offset by other measures, but recognition of the deleterious effect of parallel trade on the pharmaceutical industry is clear. In addition, the treaty governing the expansion of the EU in May 2004 delays most parallel export of prescription medicines from the new members.

**Lessons for reimportation**

Despite the differences, the European experience with parallel trade offers several critical insights relative to the U.S. debates about reimportation. With respect to safety, risks to patients in Europe have been minimized by restricting the parallel trade process to tightly regulated distributors, wholesalers, and pharmacies; allowing direct sale to patients under reimportation may substantially increase risks. The tradeoff for greater safety, however, has been minimal direct savings for patients under parallel trade, despite clear reductions in procurement prices for payers. Parallel traders obviously profit; wholesalers and pharmacies may as well. Pharmaceutical companies invariably lose, a situation made worse by pricing restraints in the source or destination countries, which prohibit a flexible market response.

Reimportation potentially is a much greater threat to the pharmaceutical industry than parallel trade has been
to date. Not only are more products likely to be affected, but the size of the U.S. market also makes it far more critical to maintaining sales and earnings than the few importing countries in Europe. As other articles in this supplement suggest, the repercussions of the likely losses under reimportation would extend well beyond the industry itself and well beyond today.

References


A
ccess to affordable prescription drugs is the real issue facing the pharmaceutical industry. Enthusiasm for alternative sources of pharmaceuticals is forcing the industry to struggle with the challenge of importation. This article provides a perspective from one pharmaceutical company concerning the vexing issue of drug importation.

Forces driving cross-border trade

By and large, drug importation is a political solution to the problem of providing affordable prescription drugs to certain individuals in this country who currently do not have access to them. Importation is the solution intended to remedy this situation.

Importation is attractive to individuals who believe in a free market or free trade, although it does not truly represent free trade because the trade occurs without the consent of the patent holder. Importation also appeals to those who would advocate some degree of regulation in pharmaceutical prices and a reduction in expenditures. In effect, importation imposes price regulations from other countries. Importation particularly appeals to cash-paying consumers. They are a key source of the political demand for importation because they pay the highest prices for hospital care, physician care, and pharmaceuticals. These consumers, however, represent only an extremely small segment of pharmaceutical sales at the retail level — between 4 and 7 percent.

In reality, the United States, in terms of its economy, can afford prescription drugs and health care. The American economy is so vast that it can absorb the high rate of expenditures needed for prescription drugs. The problem is, however, that there are specific individuals, employers, and insurers who cannot afford the sharp increases in cost and the ultimately prohibitive level of spending. These circumstances affect those who are currently unemployed and who are retired. One of the most serious public health problems in the United States relates to the uninsured and underinsured and the sustainability of health care coverage.

Opposition to reimportation

Naturally, most major research pharmaceutical manufacturing companies oppose importation. Patent protection, safety concerns, and research and development ramifications are among the many reasons that they object to cross-border trade. In addition, wholesalers, chain drug stores, and independent community pharmacists generally oppose importation. (Although CVS and Walgreens previously objected to reimportation, they recently voiced support for reimportation through appropriate channels.) A central issue that does not get addressed frequently, but is an important driver of the opposition to importation, is exposure to tort liability when negative health care consequences occur due to this type of trade.

Commercial assessment

Price differentials between the United States and Canada are sufficiently large to make cross-border trade profitable. Expensive breakthrough medications generally need as little as an 8 percent price difference to be profitable, while others require a 16 to 17 percent difference. In reality, market arbitrage can occur whenever the price differential between two markets is sufficiently large to permit the trader to realize a profit. Thus, it remains to be seen if reimportation is really a commercial threat to the industry if price differentials shrink or consumers realize the true level of risk. The Canadian market is one-tenth the size of the U.S. market. In fact, compared with Canada, the United States has larger pharmacy benefit manager and managed care contracts, accounting for greater sales. The Canadian market is small and cannot adequately supply the United States. Yet, the Canadian market accounts for about $1.1 billion in reimportation trade (Saatsoglou 2004). Approximately 60 percent of this trade is transacted via the Internet and 40 percent via a longstanding practice of foot traffic — people who simply walk across the border to make purchases. These are historic trading patterns, involving a full range of goods and services.

Notably, prices in the United States may be much closer to Canadian prices than recognized. The price dif-
ferential is eliminated, to a large extent, based on relationships that pharmaceutical companies have with individual states, PBMs, and managed care organizations that negotiate rebates and discounts. Nevertheless, as mentioned previously, the remaining challenge is developing the means to accommodate the cash-paying consumers who are only beginning to benefit from these types of practices through manufacturers’ discount cards and the transitional Medicare prescription drug benefit.

**Legislative environment**

Some believed that the passage of the new Medicare law would diminish Congressional interest in legalizing reimportation. That has not been the case, however. It seems certain that a new importation law will be passed this year. In effect, the law currently exists, but the secretary of Health and Human Services and U.S. Food and Drug Administration commissioner have had difficulty certifying that specific reimported drugs are safe and that they produce cost savings.

Although the federal government has not acted as quickly as expected, states have taken decisive actions. Approximately 20 states that have some type of legislation to facilitate importation of drugs from Canada or to set either U.S. Federal Supply Schedule or Canadian prices.

**Areas of concern**

The drug supply situation in Canada could be a profound problem, and the supply of pharmacists is shrinking because they are moving away from community practice into mail order operations (Ward 2004).

Transshipments, the importation of pharmaceuticals from other countries for the purpose of sales to U.S. consumers, are another area of concern. It is known that transshipments are coming in through Canada from other countries, such as Bulgaria, Pakistan, China, and Argentina. Canadian sources are attractive, because the regulatory safeguards for Canadian citizens are comparable to U.S. Food and Drug Administration safeguards for U.S. citizens. Nevertheless, Health Canada does not certify pharmaceuticals for exportation to U.S. consumers. Consequently, pharmaceuticals from unregulated sources can be sold to U.S. citizens circumventing any regulation. This is going to be a significant problem. If U.S. manufacturers restrict supplies from legitimate sources using shipment quotas, then sourcing from illicit markets will increase.

Finally, there is a concern that reimportation may not produce meaningful cost savings for consumers. As in every business, some company has to profit from this type of trade and, in this case, it is most likely going to be the wholesaler and retailer. (Otherwise, there is no incentive for this practice to take place.) What occurs then, to a great extent, is a redistribution of profits from the pharmaceutical industry to the distributors.

**Impact on R&D**

Decisions made by a pharmaceutical company are driven by two factors: (1) new R&D leading to an approved drug and (2) the probability of commercial success. Given that a developed drug is proven safe and effective, is there sufficient unmet need and sufficient reimbursement to make this product profitable?

R&D is an extremely fragile process and adequate cash flows and operating margins need to be generated to sustain existing research as well as to undertake new research. With downward pressure on company profits, one may expect to see a greater degree of risk aversion — and a heightened inclination to let others take the risk. That is, let the start-up companies focusing on biotechnology or the specialty companies conduct the research using venture capital and equity funding. Then, the pharmaceutical company can enter into codevelopment and co-marketing deals with successful companies. Clearly, one can forego existing research plans if there are alternative sources.

**Predictions**

I predict that there will be some type of pharmaceutical importation legislation this year. It may involve importation from Canada exclusively, but with gradual expansion to the European Union, Australia, Japan, and New Zealand. In addition, increased activity at the state level and increased litigation can be expected.

Before responding to the question of reimportation, the industry needs to respond to other extremely difficult questions, for which there are few easy answers. First, given that the real issues are access and affordability, can a pharmaceutical company aggressively oppose importation? Opposition could foster potential political ramifications including draconian price controls; change in tax laws (e.g., losing credits for R&D and direct-to-consumer advertising); and impact on patent life or exclusivity. Furthermore, if something goes terribly wrong through the use of imported pharmaceuticals, what is the industry’s legal exposure? This scenario ties into larger tort-reform issues. The point is that our industry’s stance on this issue is not without serious implications that go beyond reductions in U.S. sales.

Lastly, it would be an oversight if the consumer was not appropriately placed at the center of this issue when forming an opinion. Does importation actually produce cost savings? If so, shouldn’t the entire cost savings go to the consumer? AstraZeneca’s position, for instance, is that when we participate in a discount-card program, 100 percent of the savings must go to the consumer.

A number of questions — from tort reform to the ability of the FDA to police a new policy — are legitimate. These questions, however, must be viewed in the context of access and affordability — with importation representing a short-term solution to a longer-term problem.
many to 15 percent in the United Kingdom. What is most profoundly affecting the income of the pharmaceutical industry and discouraging innovation is the constant ratcheting down of prices. In addition, the United States has become a more attractive place both to perform research and development and to market the result, which has stimulated a serious brain drain in Europe that has been great enough to seriously damage its science base.

**QUESTION:** Critics charge that a significant portion of R&D costs are borne by the American consumer, even though people from all over the world benefit from the drugs. Do you agree with this statement?

**FREEMAN:** Yes, although we also have to make some frank recognitions that the United States is a wealthy country. Also, an aspect of our social values is that we want access to innovation quickly, and we are willing to pay for it. Whereas in other countries, you do not see innovation valued as highly as it is here. Under the concept of Ramsey pricing, wealthier nations that are willing and able to pay more do so, not just for pharmaceuticals but for other goods and services. Ramsey pricing is the most efficient pricing model we have to maximize utility globally.

**QUESTION:** What is the position of the pharmacy industry on importation? I have seen presentations where they are shown as a stakeholder against reimportation, but then someone else says that the industry would be for it, if they could participate.

**FREEMAN:** My general observation is that if community pharmacists were convinced that importation was safe, their willingness to become importers would increase. I think the issue of safety and tort exposure is going to trump that, however.
PANEL DISCUSSION

What Are the Implications of the Research For Reimportation Policy?

PARTICIPATING FACULTY:

THOMAS A. ABBOTT III, PhD
Abbott Consulting LLC

MICHAEL DICKSON, PhD (MOTERATOR)
Professor of Pharmaceutical and
Health Outcome Sciences
University of South Carolina

ROBERT A. FREEMAN, PhD
Executive Director
Public Policy
AstraZeneca Pharmaceuticals LP

JOHN R. GRAHAM, MBA
Adjunct Scholar
The Fraser Institute

ROBERT HELMS, PhD
Resident Scholar
American Enterprise Institute

KRISTINA M. LYBECKER, PhD
Assistant Professor of Economics
Drexel University

NANCY MATTISON, PhD
President, The Mattison Group Inc.

PATRICK L. MCKERCHER, PhD (MOTERATOR)
Director
University of Michigan Center for Medication Use, Policy and Economics

DAVID P. NAU, RPh, PhD (MOTERATOR)
Assistant Professor
University of Michigan Center for Medication Use, Policy and Economics

FRANCIS B. PALUMBO, PhD, JD
Professor and Director
Center on Drugs and Public Policy
University of Maryland School of Pharmacy

STEPHANIE TAYLOR, PhD (MOTERATOR)
Assistant Professor
University of Michigan Center for Medication Use, Policy and Economics

PATRICK L. MCKERCHER, PhD: The question has been raised as to how pharmaceuticals might fit into some form of price control.

JOHN R. GRAHAM, MBA: I think to some degree the pharmaceutical industry was too enthusiastic about jumping onboard with this new pharmaceutical benefit under Medicare law. A few years down the line, you could have various U.S. government agencies becoming the largest buyers of prescription drugs in the world and all the perverse incentives that currently exist for public purchasers in other countries would affect the United States.

KRISTINA M. LYBECKER, PhD: The pharmaceutical industry, in addition to the chemical industry, more than any other sector of the U.S. economy, is reliant on patents and the protection they provide. It’s through the revenue received from the free market prices that these companies have been able to fund continued innovation. The pipeline that we have full of new medicines has been fed largely by the profitability of the U.S. market.

THOMAS A. ABBOTT III, PhD: Inherently, there is really no reason why price regulation couldn’t be imposed on the pharmaceutical industry. The question is what would be the impact on all the incentives around it and what kind of distortion would you get? There is nothing inherently inconsistent with regulated prices and innovation. One can look at the telecommunication industry, which was heavily regulated in the 1950s through the 1970s and yet produced tons of patents and Nobel laureates and tons of innovation. And if you look what has happened since deregulation you see that innovation has taken off even more.

McKERCHER: Given all this, where is the pharmaceutical industry going now?

NANCY MATTISON, PhD: The worldwide regulation of the pharmaceutical industry is shaping R&D decisions in undesirable ways. A new drug for a critical illness that also is extremely prevalent — heart disease, for example — concerns payers because of its potentially high volume or comparatively high price, which results in tight price controls, as it often does in Europe. Furthermore, incentives for research to further advance treatment for that disease will be dampened; companies understandably may fear that even breakthrough drugs in the same therapeutic category will be subject to such price restraints.

ROBERT B. HELMS, PhD: One of the most encouraging
developments from a policy perspective has been former FDA Commissioner Mark McClellan and Tomas Philipson looking at ways to improve regulatory efficiency. To bring this back to importation, many drugs that are moving through expedited reviews now will have two or more years of close postmarketing scrutiny. They may not have those types of approvals in other countries.

FRANCIS B. PALUMBO, PHD, JD: Regardless of federal government activity, I think that, in general, the states are for reimportation and will continue to be drivers. They are trying to pass laws to facilitate the state being able to get access to imported drugs, not necessarily reimportation, but importation. From what I’ve seen so far, however, the states that have enacted laws, West Virginia and Maryland, for example, have passed weak pieces of legislation. The Florida law is a bit more restrictive in terms of requiring pedigrees, but that is the biggest effect I’ve seen so far.

ROBERT A. FREEMAN, PHD: I think the U.S. Food and Drug Administration is going to play the definitive role in whether importation will become law. The FDA and U.S. Customs are going to have to write coordinated regulations to ensure the integrity of the U.S. supply chain. Although there have been many different approaches suggested, if they can solve the safety issues related to reimportation, then I think it is likely that the [Health and Human Services] secretary will propose it. I do not believe, however, that regulations will be 100 percent effective in assuring supply given the complexities of global supply chain issues.

MCKERCHER: There was a question whether or not the task force would actually make recommendations. Some feel that their charge does not require recommendations. What are your feelings?

FREEMAN: One way or another there need to be recommendations.

MCKERCHER: Why is there such a groundswell for this, given all the information we have that is fraught with danger?

GRAHAM: I think there was a bit of a misfire from the pharmaceutical industry and that it focused on the specific technical details of the anti-reimporting situation. So, some have confused reimportation with free trade.

LYBECKER: The answers that have been coming from this panel are primarily economically based answers. It comes largely out of theory. It’s much easier to pay attention to the side of the problem that you can put a face on, and that’s what they are paying attention to. The people who will be hurt in the future don’t yet have an identity.
Healers today face an impossible task. Increasingly, aging seniors, patient expectations, and scientific opportunities are clashing with American willingness to pay for care. Provider credibility has eroded. Tensions are reaching the blowing point in Congress and in court. Add to that the upcoming election, during which campaign rhetoric will no doubt blister those who provide for care, claiming prices are too high and quality too low. Can such conflicts be resolved? Or will health care melt down under the pressures to care for a population that is aging, demanding, obese, and chronically ill?

My talks last year with health care leaders produced increasingly worrisome results. Early in the year, physicians said they could not afford to accept new Medicare patients. By December, they would no longer take 60-year-old patients, because they would be on Medicare in five years. Employers said that they were looking for a way out of health coverage. State legislators said that they were looking for someone to blame. Old policy buddies in Washington had little to say; the town was driven by politics.

At one time, I believed that public policy debates would create viable solutions. I no longer believe that. Too many of our policy debates occur in political settings and politics, by its nature, is hard-wired for conflict — witness the current debate over importation of medicines. Conflict may well be a necessary part of politics, but it is not the best way to resolve the decisions of the day in an enterprise as important as healing.

I found a surprising answer to these challenges when I went looking for a solution. It was not a futuristic notion but a historical one, which held that the healer-patient encounter was a relationship held sacred by the healer, the patient, and the community. It was called a covenant — not a contract. There were two types of covenants that were applied to our healing systems and imbedded in health care oaths: covenants of grant, in which the patient needed do nothing to be healed, and covenants of obligation, in which patients and communities were participants and obligated to do their part. Hippocratic healers entered into covenants of obligation in the oath, but only with each other. To their patients, they granted health and healing. Centuries later, Maimonides crafted a new oath that called on patients to be obligated to participate in their healing by complying with clinical advice. It is unfortunate that most of us today do not heed his advice.

In our sophistication, we lost sight of covenants and layered them with contracts. The valuable notion of covenant was lost and, even worse, the Hippocratic foundation of western medicine never matured enough to support the complexities of modern health care. It is time to return to reconsider how patients and others should now be called into covenants of obligation to support healing. To do this, we need to step outside our politics, conflicts, and contracts and enter into covenants.

My prescription for doing this has three parts. First, all healers need to embrace covenants of caring. Clinicians already do. But today’s new healers should join them. Insurance company executives, health company staffs, legislators, regulators, Internet players, Madison Avenue advertisers, sales representatives, and evening news anchors are the modern extensions of the ancient healers. They do not treat patients directly, but they make equally important health care decisions. As societies became more complex and segmented, so too did providing care. If more of today’s players in health care ascribed to a covenant oath with patients, many of our problems would be more easily resolved.

Second, patients should be invited into these covenants of obligation and called on to be better managers of their health and should be held accountable for the failure to do so. Third, communities — including this nation as a whole — should be called into the covenant as well, by asking that they better support healing through funding and through better public policy choices for safe and healthy communities.

The time has come to acknowledge that while we may be required in our current health business climate to live with contracts, we must also return to the covenants — especially to covenants of obligation among healers, patients, and communities. It is time to end the political debate and begin a healing dialogue, to disarm our hair-triggered willingness to shoot at the enemy on the other side of the healing tables we share. If health care is to be healed, everyone involved in the healing enterprises of the
day — the healers, patients, and communities — must now consider the nature of the relationships they have with each other.

Within covenant relationships, the toughest questions must be addressed; we can no longer avoid them. These are questions of reciprocity and responsibility. If a patient can sue a managed care provider for failure to provide care, can managed care sue patients for failure to follow medical advice? If patients do not take their medicines or change their lifestyles, should payers be responsible for covering the cost of the more expensive diseases that will result? If employers cover the cost of a flu shot, should they also deny sick leave to unimmunized employees who get the flu? If the nation allows its citizens to carry guns, can insurers levy a surcharge for the likelihood of higher emergency room costs in areas of high gun ownership? In other areas of our lives we pay — financially — for the consequences of our choices. If we change an airline ticket, arrive late for a daycare pickup, check-out of hotels early, or fail to show up for restaurant reservations, we incur financial penalties. Should health care be different?

Today we are faced with the issue of pharmaceutical importation, and it has covenant implications. Those who know international pharmaceutical supply chain management caution us about the risks. Why do we ignore them? They are not just experts, they are healers.

If we proceed nonetheless, how should we engage in our healing encounters? Should patients who import drugs notify physicians so that product efficacy and safety can be tracked within clinical practices? If adverse events from adulterated medicines occur, should health care payers be required to cover the costs, or should patients bear the burden? Should companies and suppliers be exempt from litigation if patients are injured? Should surcharges be added to imported medicines for new tracking devices? If importation becomes widespread, should government end its product review and approval role and rely on foreign government regulatory approvals, saving billions of dollars on clinical trials and regulatory actions here? Or better yet, should the nation recognize the value of its medicines and provide those who cannot afford them with a drug benefit that meets their needs?