

IMPORTATION OF PRESCRIPTION DRUGS AND RISKS TO PATIENT SAFETY

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ABSTRACT

Access to affordable prescription drug products is a serious challenge faced by millions of Americans. More than 40% of Americans take one or more prescription drugs; and a small, but increasing, number rely on drug importation to lower costs. Although some imported drugs are legal, a far greater number are unregulated within the U.S. drug distribution system and cannot be confirmed as safe and effective. Whether purchased online, from a storefront pharmacy, or during travel to another country, foreign prescription drugs pose risks to patient safety. The most serious risks include counterfeit potential, quality assurance concerns, presence of untested ingredients, and issues related to risk management and unsupervised use, labeling, language, and lack of information. Import blitz exams confirm that a wide variety of drug types entering the United States lack integrity in manufacturing, packaging, labeling, storage, or distribution. The FDA-initiated “Looks Can Be Deceiving” public information campaign educates American consumers about the dangers of buying unapproved foreign drugs, and current efforts to find and implement alternatives to such drugs seem promising. The FDA has been active in helping to accelerate access to generic drugs and exploring ways to lower drug development and manufacturing costs. Furthermore, the new Medicare prescription drug benefit will likely assist seniors in purchasing affordable and safe medications. The policies and regulations of the current, relatively “closed” U.S. drug distribution system maximize the safety and effectiveness of the domestic drug supply and serve as the model for systems around the world. Changes to the sys-

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tem, such as a legal commercial importation program, are not without costs and would require careful scrutiny before implementation. A personal importation system would likely result in an increased risk to American drug consumers.

INTRODUCTION

Access to affordable prescription drug products is a serious challenge faced by millions of Americans. The increased use of such products by an aging population and rising list prices over the past several years have translated into increased spending by American consumers. More than 40% of Americans take one or more prescription drugs;¹ and a small, but increasing, number rely on drug importation to lower costs.² Although some imported drugs are legal and pose little risk to patient safety, a far greater number are unregulated within the U.S. drug distribution system and cannot be confirmed as safe and effective.³

This essay presents a brief history of drug oversight in the United States, addresses the nature and scope of drug importation, and focuses on the serious risks to patient health and well-being posed by the importation of unapproved drugs. A discussion of alternatives to imported drugs and the recent findings of the Health and Human Services (HHS) Task Force on Prescription Drug Importation is also presented.⁴

A BRIEF HISTORY OF DRUG OVERSIGHT IN THE UNITED STATES

The policies and regulations of the current, relatively “closed” U.S. drug distribution system maximize the safety and effectiveness of the domestic drug supply. These policies and regulations also serve as the model for systems around the world.

The discovery of penicillin in the 1930s signaled the start of the modern era of drug research and development.⁵ As more new drugs

1. Victoria Arocho, *More Than 40% of Americans Using Prescription Drugs*, USA TODAY, Dec. 3, 2004, available at http://www.usatoday.com/news/health/2004-12-02-medicated-america_x.htm; U.S. DEP'T OF HEALTH & HUMAN SERVS., HHS TASK FORCE ON DRUG IMPORTATION, REPORT ON PRESCRIPTION DRUG IMPORTATION 37-38 (2004), available at <http://www.hhs.gov/importtaskforce/Report1220.pdf> [hereinafter HHS TASK FORCE].

2. HHS TASK FORCE, *supra* note 1.

3. *Id.*

4. *Id.*

5. *Id.*

emerged, Congress recognized the need for an oversight program to ensure proper testing and manufacturing practices. As such, Congress passed the Federal Food, Drug, and Cosmetic (FD&C) Act in 1938.⁶ The FD&C Act and its amendments in 1962 require that the U.S. Food and Drug Administration (FDA) approve all new drugs for safety and efficacy before marketing⁷ and limit the types of drugs that can be imported into the United States.⁸

In 1987, Congress passed the Prescription Drug Marketing Act (PDMA) to address concerns that counterfeit, substandard, and ineffective drugs were making their way into the U.S. drug distribution system.⁹ Importantly, PDMA also added the “American Goods Returned” provision to the FD&C Act, which prohibits drug reimportation into the United States by any entity other than the manufacturer of the drug.¹⁰

Passed by Congress in 2003, the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) provides the first-ever prescription drug benefit for seniors and individuals with disabilities. Provisions in MMA also allow the importation of certain FDA-approved prescription drug products into the United States from Canada, contingent upon certification from the Secretary of HHS that implementation of the new policy poses no added risk to public health and safety and results in a significant reduction in the cost of drugs to the American consumer.¹¹

Additionally, MMA mandated the Secretary of HHS to conduct a comprehensive study of issues related to drug importation. In February 2004, Secretary Tommy G. Thompson appointed Richard H. Carmona, Surgeon General of the U.S. Public Health Service, to lead a task force to conduct the requisite study, the findings of which were published in December 2004.

6. See, e.g., John P. Swann, *History of the FDA*, in THE HISTORICAL GUIDE TO AMERICAN GOVERNMENT (George Kurian ed., Oxford Univ. Press 1998), available at <http://www.fda.gov/oc/history/historyoffda/fulltext.html>.

7. *Id.*

8. *Id.*; HHS TASK FORCE, *supra* note 1; FDA, IMPORTATION OF PRESCRIPTION MEDICINES/DRUGS, http://www.fda.gov/ora/import/traveler_alert.htm (last visited Aug. 17, 2005).

9. HHS TASK FORCE, *supra* note 1.

10. *Id.*; *Joint Hearing of the Subcomm. on Health Care & Subcomm. on Int'l Trade of the Comm. on Fin.*, 108th Cong. (2004) [hereinafter *Joint Hearings*] (statement of William K. Hubbard, Associate Comm'r for Policy & Planning, FDA), available at <http://www.fda.gov/ola/2004/importeddrugs0427.html>.

11. HHS TASK FORCE, *supra* note 1.

SCOPE AND NATURE OF THE DRUG IMPORTATION PROBLEM

Although difficult to quantify, the number of prescription drug products entering the United States each year is large and has increased over time. Data from Intercontinental Marketing Services Health (IMS) suggests that about "\$1.1 billion in pharmaceuticals were imported into the United States in 2003."¹² Most imported drugs (e.g., inhalants, capsules, tablets, injectables, biologics, and controlled substances) are not approved by the FDA for quality, safety, and efficacy, and may not meet the standards of products available in American pharmacies.

At the present time, two categories of imported drugs are considered legal: those that are manufactured in an FDA-inspected facility and adhere to FDA standards, and those that are manufactured in the United States, sent abroad, and subsequently reimported to the United States by the manufacturer under standards set forth in the FD&C Act.¹³ The quality, safety, and efficacy of two other categories of imported drugs cannot be verified: those produced in a foreign facility that also produces the U.S.-approved version, and those produced in a foreign facility that have not been inspected by the FDA.¹⁴ The latter category poses the greatest risk to consumers because adherence to good manufacturing practices and the integrity of drug packaging, labeling, storage, and distribution cannot be verified.

Prescription drug products enter the United States through international mail facilities, private courier hubs, ports, and express consignment facilities, and pedestrian traffic across borders.¹⁵ "Storefront pharmacies," walk-in businesses that serve as the middlemen between foreign (primarily Canadian) drugstores and consumers, surfaced in early 2004.¹⁶ The Internet has further facilitated long-distance drug selling and purchasing.

12. Press Release, FDA, FDA Partners with States to Warn Consumers that "Looks Can Be Deceiving" (Apr. 13, 2004), available at <http://www.fda.gov/bbs/topics/news/2004/NEW01053.html>.

13. HHS TASK FORCE, *supra* note 1.

14. *Id.*

15. *Id.*

16. *Id.*

Pedestrian Traffic

In 2003, about twelve million prescriptions were sold by Canadian pharmacies to American consumers; cross-border prescription drug sales totaled \$695 million.¹⁷ Organized travel to Canada—most commonly, bus trips by senior citizen groups—has seemingly increased since 2000, and some of the trips have been organized by high-profile political figures (e.g., members of Congress and governors) to draw attention to the difference in price between U.S. and Canadian drugs.¹⁸ Although studies have not documented the types of drugs being imported in this manner, it is believed that most of the drugs are those used for chronic conditions, such as diabetes, high cholesterol, hypertension, and arthritis.¹⁹

In 2000, the FDA's Southwest Import District and other agencies conducted a survey at eight points of entry along the Mexican border to study the types of drugs being brought into the United States by pedestrians. After interviewing more than 600 individuals during a four-hour period at border entry points in Texas, Arizona, and California, the data showed that most of the drugs were pain relievers or antibiotics. Only 63% of the pedestrians had prescriptions. Of the pedestrians with prescriptions, 59% were U.S. prescriptions and 41% were Mexican prescriptions. Although many of the products were foreign versions of FDA-approved drugs, some of the products "bore no resemblance whatsoever to any FDA-approved product in the United States."²⁰

The findings of a second four-hour survey conducted by several U.S. government agencies at seven entry points along the United States and Mexico border in 2001 showed that 586 individuals transported 1120 drug products across the border.²¹ Only 56% of individuals had a prescription for the purchased drugs; 61% of which were U.S. prescriptions and 39% of which were Mexican prescriptions.²² As in the 2000 survey, many of the products were foreign versions of FDA-approved drugs, and others were not approved for American sale.

17. *Id.*

18. *Id.*

19. *Id.*

20. *Id.* at 16.

21. *Id.* at 37-38.

22. *Id.*

Storefront Pharmacies

Storefront pharmacies in the United States enable consumers to receive drugs from foreign drugstores without traveling to the source country. The illegal procedure is easily executed:²³ an individual “walks in” to a storefront pharmacy, presents a prescription, and pays the price specified for the drug. The prescription is then faxed to the foreign pharmacy. The unapproved drug product is mailed directly to the consumer, and the two “businesses” split the profits from the sale.

Many states have taken legal action against storefront pharmacies for violating laws prohibiting drug sales without proper licensing. In a major case against Rx Depot, a storefront pharmacy operating in various locations throughout the United States, a judge ruled that “drugs sold in this manner were both illegal and potentially unsafe.”²⁴ Nonetheless, many such establishments continue to offer their services to consumers seeking less expensive drug products.

The Internet

According to studies conducted in 2000 by the FDA Office of Criminal Investigations and the General Accounting Office, about 300 to 400 Internet sites—50% of which are located outside of the United States—sell prescription drug products directly to consumers.²⁵ In the United States, state boards of pharmacy have the primary responsibility of regulating online pharmacies, and agencies such as the FDA and Drug Enforcement Administration provide federal oversight.²⁶ The same regulations that apply to traditional pharmacies usually apply to online pharmacies. An online pharmacy can also voluntarily apply for Verified Internet Pharmacy Practice Sites (VIPPS) certification, a program established in 1999 by the National Association of Boards of Pharmacy to address legitimacy concerns.²⁷

Many properly licensed and certified online pharmacies provide notable advantages to consumers, including the convenience of ordering and receiving products without leaving home, the ease of compari-

23. *Id.*

24. *Id.* at 16.

25. *Id.*

26. See NAT'L ASS'N OF BOARDS OF PHARMACY, VIPPS CRITERIA: LICENSURE AND POLICY MAINTENANCE (2005), available at <http://www.nabp.net/vipps/consumer/criteria.asp> [hereinafter VIPPS CRITERIA].

27. *Id.*; Michelle Meadows, *Imported Drugs Raise Safety Concerns*, FDA CONSUMER, Sept.-Oct. 2002, available at http://www.fda.gov/fdac/features/2002/502_import.html.

son shopping, and increased privacy.²⁸ Yet others, both domestic and foreign, sell unapproved drug products based solely on an online questionnaire or without offering the services of a pharmacist.²⁹ Furthermore, some online pharmacies provide no contact information, such as a phone number or physical address; thus a consumer has no way of determining the source or quality of the product being purchased.³⁰ Of note is the fact that Canadian pharmacy Internet sites “are often not located in Canada or even regulated by the Canadian government” and evidence shows that “Americans are not always getting the same drugs as Canadian citizens when purchasing drugs from Canadian Internet sites or sites purporting to be Canadian.”³¹

RISKS TO PATIENT SAFETY

Whether purchased online, from a storefront pharmacy, or during travel to another country, foreign prescription drugs pose risks to patient safety; the most serious of which include counterfeit potential, quality assurance concerns, presence of untested ingredients, and issues related to risk management and unsupervised use, labeling, language, and lack of information.³² Products considered particularly risky for importation include injectable drugs, biological products, controlled substances, drugs inhaled during surgery, drugs with specific post marketing risk monitoring guidelines, drugs that require refrigeration or that must be kept frozen, and drugs with a high potential for counterfeiting on a global scale.³³

Some imported drugs may be counterfeit versions of the genuine product and contain unsafe (highly potent) or ineffective (subpotent or expired) substances. Highly potent drugs have the potential to induce adverse events, some of which could be life threatening. Subpotent or outdated drugs would likely not produce the desired benefit, yet a patient would be unaware that the source of treatment failure was the drug itself. Furthermore, because counterfeit drugs often bear the

28. VIPPS CRITERIA, *supra* note 26.

29. *Id.*

30. *Id.*

31. HHS TASK FORCE, *supra* note 1, at 17.

32. See Meadows, *supra* note 27; FDA, *FDA Crackdown on Illegal Products*, FDA CONSUMER, Mar.-Apr. 2004, available at <http://www.fda.gov/fdac/features/2004/204illegal.html> [hereinafter *FDA Crackdown*]; CTR. FOR DRUG EVALUATION & RESEARCH, FDA, LOOKS CAN BE DECEIVING: DON'T RISK YOUR HEALTH (2004), available at <http://www.fda.gov/cder/consumerinfo/border.htm> [hereinafter LOOKS CAN BE DECEIVING]

33. HHS TASK FORCE, *supra* note 1.

name of an FDA-approved product, consumers may be tricked into believing that a drug has been manufactured and regulated by U.S. standards.

The quality assurance procedures of drugs produced in foreign countries cannot be verified; thus consumers of such products have no guarantees that good manufacturing practices have been met or that packaging, handling, storage, and distribution procedures have been adequate to avoid deterioration, contamination, or degradation. Imported drugs could contain ingredients that have not been tested and confirmed safe and effective by U.S. standards, even though such ingredients may be legitimate and legal in the country of production. Furthermore, if problems arise with an imported product, consumers have little recourse with foreign operators.

Drugs purchased from foreign sources may be labeled in a language other than English, thereby making critical information about dosage and adverse effects inaccessible. Instructions may be lacking as to how to deal with emergent situations or false claims may be made about the drug's safety and efficacy or its intended or specific use. Consumers purchasing imported products may not have access to physician supervision, even though regular check-ups and follow-up examinations are important risk management measures while taking certain drugs.

IMPORT BLITZ EXAMS HELP TO QUANTIFY THE DRUG IMPORTATION PROBLEM

Import blitz exams (i.e., snap inspections) conducted by the FDA and U.S. Customs and Border Protection in July and August 2003 showed that 88% of the 1153 packages examined at four international mail facilities contained unapproved drugs.³⁴ The blitzes were conducted over a three-day period in Miami, New York (JFK airport), San Francisco, and Carson, California. The drugs entered the United States from all over the world, including 16% from Canada, 14% from India, 14% from Thailand, and 8% from the Philippines.³⁵

A second series of import blitz exams performed by the same agencies in November 2003 at international mail facilities in Chicago, Dallas, Buffalo, and Seattle, and private courier hubs in Memphis and Cincinnati revealed that 69% of the 3375 packages examined con-

34. *Joint Hearing, supra* note 10.

35. *Id.*

tained unapproved products, including recalled drugs, drugs requiring special storage, and drugs containing controlled substances.³⁶ Eighty percent of the packages entered the United States from Canada, 16% were from Mexico, and the remaining packages came from the United Kingdom, the Netherlands, Japan, Taiwan, and Thailand.³⁷

The following list includes examples of the types of products found during the blitz exams:³⁸

- Drugs improperly packaged in envelopes, sandwich bags, and tissue paper. Some drugs were “broken” or “crushed;”
- More than twenty-five different controlled substances (e.g., anabolic steroids, diazepam, codeine, alprazolam, lorazepam, and clonazepam), which were referred to the Drug Enforcement Administration;
- Drugs with the potential for harmful interactions with other drugs, including unapproved versions of sildenafil (Viagra) from the United Kingdom, Philippines, India, and Japan, as well as unapproved versions of simvastatin (Zocor) from Canada;
- Animal drugs not approved for use in humans, including clenbuterol, a drug used to treat airway diseases in horses. Of note is that this drug is known to be abused by body-builders and is banned by the International Olympic Committee;
- Drugs inadequately labeled for safe use or labeled in a language other than English;
- Drugs requiring risk management (screening and monitoring) programs, such as unapproved versions of the cholesterol drugs atorvastatin (Lipitor) from the Philippines, United Kingdom, Canada, Ireland, Thailand, Japan, Argentina, New Zealand, and Brazil, and pravastatin (Pravachol) from Canada;
- Drugs requiring careful dosing, including unapproved versions of phenytoin (Dilantin) from the Philippines, levothyroxine (Synthroid) from Canada, and metformin (Glucophage) from the Philippines and Canada;
- Drugs withdrawn from the market, including the unapproved Mexican drug Buscapina, which seemed to be

36. *Id.*

37. *Id.*

38. *Id.*; *FDA Crackdown*, *supra* note 32.

dipyrene (Dimethone), a fever and pain medication removed from the U.S. market in 1977;

- Unapproved drugs like human growth hormone and the immunosuppressant anti-azathioprine;
- Unapproved versions of FDA-approved drugs, such as Roaccutane, an unapproved version of the acne drug isotretinoin (Accutane) from Thailand, and taro-warfarin, an unapproved version of the anticlotting agent warfarin from Canada;
- Potentially recalled drugs—for example, the asthma treatment drugs Serevent Diskus and Flovent Diskus from Canada.

ALTERNATIVES TO THE IMPORTATION OF PRESCRIPTION DRUG PRODUCTS

The current relatively closed system of legal prescription drug distribution provides the American consumer with several layers of protection against receiving unsafe, ineffective, and poor quality drugs. Revamping the system to include legalized drug importation would likely result in an increased risk of substandard and counterfeit products entering the distribution chain. The implementation of a commercial importation program might be possible, but “new legal authorities, substantial additional resources, and significant restrictions on the type of drugs that could be imported” would be required.³⁹ In the end, such measures might increase, not decrease, the cost of drugs. A personal importation program would create “numerous vulnerabilities in the drug distribution system” and put American consumers at risk.⁴⁰

Current efforts to find and implement alternatives to imported drugs seem promising. The FDA has been active in helping to accelerate access to generic drugs and to educate consumers on their use. U.S. generics—which account for about one-half of all prescriptions—generally cost 50% to 70% less than their brand name counterparts.⁴¹ Of interest, a study conducted in 2002 shows that six of seven widely used U.S. generic drugs were less expensive than their brand

39. HHS TASK FORCE, *supra* note 1, at 23.

40. *Id.* at 58.

41. OFFICE OF PLANNING, FDA, FDA WHITE PAPER: GENERIC DRUG PRICES IN THE U.S. ARE LOWER THAN DRUG PRICES IN CANADA (2003), available at <http://www.fda.gov/oc/whitepapers/drugprices.html>.

name counterparts in Canada and five of the U.S. generics were less expensive than Canadian generics.⁴²

The FDA recently initiated the “Looks Can Be Deceiving” public information campaign to educate American consumers about the dangers of buying unapproved foreign drugs.⁴³ Educational materials, such as posters, tabletop displays in pharmacies, and prescription bag inserts, use straightforward language to caution customers that imported drugs may be of substandard quality, outdated, or counterfeit.⁴⁴ To more effectively distribute these materials, the FDA has begun partnering with state pharmacist associations and drugstore chains.⁴⁵ The FDA also continues to explore ways to lower drug development and manufacturing costs and anticipates that the new Medicare prescription drug benefit will further assist seniors in purchasing affordable and safe medications.⁴⁶

CONCLUSIONS

The standards of the FD&C Act regulate the way in which prescription drugs are manufactured, packaged, labeled, stored, and shipped. However, the safety and efficacy of products imported to the United States cannot be ensured because of noncompliance with the FD&C standards. The position of the author of this essay, that imported prescription drugs pose serious risks to patient safety and that a legal importation program would be difficult and costly to implement, is supported by the following key findings of the HHS Task Force on Prescription Drug Importation:⁴⁷

- The current system of drug regulation in the United States has been very effective in protecting public safety and should be modified only with great care;
- Significant risks are associated with the current manner of drug importation;
- Safety hazards from “individual” importation are difficult to address and prevent;

42. *Id.*

43. LOOKS CAN BE DECEIVING, *supra* note 32.

44. *Id.*

45. *Id.*

46. *See Joint Hearing, supra* note 10; LOOKS CAN BE DECEIVING, *supra* note 32.

47. HHS TASK FORCE, *supra* note 1.

- The overall national savings from legalized commercial importation would be a small percentage of total drug spending. Furthermore, developing such a program would be costly;
- The belief that most imported drugs are less expensive than American drugs is not generally true;
- Legalized importation would likely result in lowered research and development incentives;
- Legalized importation would likely result in numerous constitutional issues regarding intellectual property rights; and
- Legalized importation would likely result in liability concerns for consumers, manufacturers, distributors, pharmacies, and other entities.