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VIA E-MAIL and FEDERAL EXPRESS

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rm. 1061
Rockville MD 20852

Re. Docket 2004N-0115: Prescription Drug Importation

Dear Sir or Madam:

Pfizer Inc. ("Pfizer") respectfully submits these comments to the docket recently opened by the Food and Drug Administration ("FDA" or "Agency") to address safety and cost-related issues associated with the importation of prescription drugs. Pfizer, one of America's leading pharmaceutical companies, is dedicated to improving the health and quality of life of people around the world. Pfizer supports safe drug distribution practices, and is committed to maintaining the integrity of the U.S. drug supply.

As explained herein, due to significant and widely documented safety concerns, Pfizer strongly opposes certification of the drug importation scheme established under the Medicare Prescription Drug, Improvement and Modernization Act of 2003 ("Medicare Modernization Act" or "MMA").¹ Drug importation outside of the current legal framework, regardless of the scheme employed, poses immediate and life-threatening risks to the American public. These risks have been documented, confirmed, and subsequently highlighted by leading American and Canadian health officials.

Irrefutable evidence confirms that American consumers would be subject to a wide range of risks, including the risk that unapproved, untraceable, counterfeit, adulterated, substandard, and tampered drugs would enter our drug supply. If we open our borders beyond the current legal framework, eviscerating our regulatory controls, unscrupulous individuals throughout the world would further target our open borders and inundate the American drug supply with dangerous, unapproved

¹ Pub. L. No. 108-173, 117 Stat. 2066 (2003).

products. Tragically, once our borders have been opened, no safeguards would be capable of reassuring the safety of our drug supply; moreover, the promised economic benefits would remain illusory due to the faulty premise of, and costs associated with, such a decision.

Despite documented health and safety risks, the MMA would permit importation of prescription drugs outside of the current legal framework if the Secretary of the Department of Health and Human Services (“HHS”) certifies to Congress that the MMA will: (1) pose no additional risk to the public’s health and safety; and (2) result in a significant reduction in the cost of covered products to the American consumer. Based upon the factual record - which is completely and irrefutably one-sided in confirming the safety risks associated with imported drugs – it would be arbitrary, capricious, and contrary to the mandate to protect public health, for the Secretary to certify the MMA importation scheme.

Regulators in the United States should be responsible for developing a system that protects American consumers from dangerous imported drugs. Rather than disabling our current safety system via implementation of the MMA importation scheme, Pfizer strongly believes that HHS and FDA should further strengthen our drug distribution system by securing and safeguarding our borders. As Congress and the FDA have long recognized, other countries are simply not in a position to monitor and regulate drugs exported to the United States, and are incapable of ensuring the safety of the U.S. drug supply. The health of American citizens should not be dependent upon the vagaries of other countries’ regulatory limitations, resource decisions and whims.

Indeed the State of Minnesota has recently acknowledged the safety issues associated with the importation of foreign drugs. Although now permitting, and indeed encouraging, its state employees and their dependents to purchase prescription drugs from Canada, the State has nonetheless disclaimed all legal liability to its citizens for the injuries or damages that they might suffer from the use of those drugs: “The State of Minnesota makes no warranty, express or implied, of merchantability and fitness for a particular purpose, and accepts no legal liability, with respect to any product offered, or pharmaceutical care provided, by the pharmacies listed on this Website.” Certainly such a liability disclaimer would be unnecessary if the State of Minnesota was confident that imported drugs posed no safety concerns or risks to their citizens.

In addition to the above-mentioned safety concerns, the notion that consumers would experience an economic benefit under importation is a chimera. Historic experience with other importation regimes demonstrates that wholesalers, retailers, and a new industry of middlemen would extract and capture a significant share of any existing price differential, leaving consumers with only a fractional share of any cost benefit. In effect, the net benefit of legalized importation would be to transfer resources from research and development (“R&D”) based pharmaceutical firms to the middlemen who will make the market in traded pharmaceuticals. Furthermore, the significant costs required to even attempt to monitor the safety of imported drugs would be substantial, and would come at significant taxpayer cost. It is estimated that such costs – which would include the costs of end-product testing at U.S. borders and increasing border staffing to inspect imported drug packages – could easily run into the billions of dollars if the volume of cross-border trade is assumed to be large. Moreover, these costs would be in addition to those resulting from the impact of reduced pharmaceutical research and development (“R&D”) on consumer health, limited consumer access to medications, and the loss of consumer confidence in the security of the public health system.

Importation, whether from Canada or from any other country, would in essence import price controls – with the attendant misallocation of resources, impact on R&D, and mandatory consumer rationing of health care. Such imported price controls – which would exist solely because of the policy decisions of foreign countries – would be subject to sudden change at the whim of foreign regulatory bodies. Assuming importation would cause a significant volume of current sales to be shifted to foreign sources, the impact on revenue would, by definition, reduce profits for innovator pharmaceutical companies. This would reduce the ability to raise capital (which would be particularly detrimental for early stage biotechnology and research-based companies), and would significantly reduce investment in early stage R&D projects.

Based upon the 10-15 year timeline for developing new drugs, the impact on consumer health would not be noticed for at least a decade. At that point, policy-makers would be impotent to reverse course and improve the existing pharmaceutical pipeline. It is estimated that the missing products a decade hence would be worth much more in terms of revolutionizing health care than the potential short-run savings generated by importing price-controls. This does not even factor in the critical human cost of diseases and conditions that may never be cured or ameliorated.

The sole rationale for enacting importation legislation is to exploit the price differences that exist between the United States and certain other markets. None of those price differences is the result of free market forces, such as efficiencies or economies of scale. Rather, all of the price differences result from the fact that the other countries engage in government price controls. The rationale supporting importation is premised upon such foreign governmental price fixing. Thus, the choice for U.S. policymakers could not be more stark: continue to support a successful market-driven healthcare system where innovation and access to safe and efficacious medicines advance the standard of care year after year or slowly import a centralized, cumbersome and highly-regulated healthcare system where research is delayed or eliminated, and treatment is rationed by ever-increasing wait lists and delayed access to important new therapies. In Europe, for example, where centralized health systems are common, it takes an average of two years from the time a drug first becomes available on the market until it is accessible by most European consumers. Such delays are largely a result of the process used by foreign nations to establish reimbursement rates and establish price controls for new drugs.

The proponents of importation propose a frightening role of the dice for healthcare in America. Given the declining standard of care and collapsing healthcare systems in so many foreign markets, we have to ask whether it is even remotely possible to import foreign medicines and foreign pricing systems without the negative consequences of increased counterfeits, loss of innovation and delayed access to important new treatment.

Pfizer appreciates the opportunity to provide these comments to the Agency.

Sincerely,



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I. Executive Summary

A. Certification Background

As noted, the importation provisions of the MMA may be implemented if, and only if, the Secretary of HHS certifies to Congress that the MMA will: (1) pose no additional risk to the public's health and safety; and (2) result in a significant reduction in the cost of covered products to the American consumer. The first prong does not include a risk/benefit assessment; rather, it requires the Secretary to conclude that the importation scheme does not pose any additional risks to the public's health and safety. The second prong requires the Secretary to conclude that American consumers would experience a significant reduction in the cost of covered products, taking into consideration all related costs passed on to consumers.

In the past four years, Secretaries of HHS have twice been asked to certify to the safety of drugs imported outside our current legal framework. Based upon the factual records, the Secretaries have emphatically refused to do so. Both former Secretary Donna Shalala, in 2000, and current Secretary Tommy G. Thompson, in 2001, concluded they could not certify under the Medicine Equity and Drug Safety ("MEDS") Act of 2000² because of significant, documented safety concerns. Nothing has changed to warrant altering these conclusions.

The significant safety concerns associated with drugs imported outside of the current legal framework have been further documented and confirmed since the above-mentioned refusals to certify. In light of the unambiguous and consistent factual record, and taking into consideration prior certification decisions, it would clearly be both arbitrary and capricious for the Secretary to certify the MMA importation scheme.

B. Importation Outside the Current Legal Framework Would Pose Significant and Incalculable Risks to Public Health and Safety

The current closed drug distribution system employed in the United States is structured to keep potentially dangerous drugs out of the U.S. stream of commerce. In 1987, Congress -- recognizing that it was impossible to assure the safety of imported drugs once these drugs were distributed outside the control of the drug manufacturer -- passed the Prescription Drug Marketing Act ("PDMA"). The Act strictly limited the reimportation of drugs into the United States in an effort to protect the integrity of the U.S. drug supply. Under our current closed drug distribution system, drugs on the market are subject to strict oversight by the FDA, are required to meet the FDA's rigorous safety and efficacy standards, and can only be distributed by highly regulated and monitored entities. Congress and the FDA wisely recognized that keeping the U.S. distribution system closed was the only way to ensure that counterfeit, adulterated, and diverted drugs are kept off the U.S. market.

In the seventeen years since the PDMA was passed, the HHS has never certified that importation of drugs could be done safely. Rather, HHS (along with the FDA and Congress) has recognized that the expansion of worldwide counterfeiting and the diversion of unapproved drugs into the United

² Pub. L. No. 106-387, 114 Stat. 1549 (2000).

States make it impossible to import drugs safely outside of our current legal framework. In fact, a recent FDA Task Force made extensive recommendations to strengthen the current closed drug distribution system in an effort to decrease the number of counterfeit drugs in the United States.

Given the FDA's own admission that extensive work is necessary to keep counterfeit medications out of the U.S. market even under the current closed system, opening our borders to allow importation would be dangerous and misguided. Doing so would be in direct conflict with the recommendations made by the FDA Task Force to strengthen the closed drug distribution system in the United States, and would weaken our drug distribution system - subjecting American consumers to substantial health and safety risks. The available evidence makes overwhelmingly clear that importation of drugs outside our closed system is inherently unsafe, and even our best efforts cannot create viable alternatives to offset the risks.

1. Specific Safety Risks Have Been Documented Extensively

Although the current U.S. drug distribution system is one of the best in the world, existing protections can still be breached. There is no question that U.S. consumers are currently exposed to unapproved, counterfeit, and adulterated drugs diverted from countries throughout the world into the United States. Even with our current safeguards, prescription drugs are already being imported into the United States in vast numbers at our land borders and through international mail facilities. FDA's own inspections have shown that a significant number of these drugs are unapproved and pose unacceptable safety hazards. Expanding the current system to allow importation would result in an even greater influx of imported drugs into the United States. As the number of drugs imported into the country climbs, the risk that unapproved, hazardous drugs would enter the U.S. drug supply would increase dramatically.

In the past few years alone, government officials have identified the following categories of dangerous drugs that have been imported into the United States:

- Counterfeit innovator and generic drugs;
- Drugs that appear to be from Canada, but in fact have been transshipped through Canada from other countries;
- Sub-potent drugs;
- Super-potent drugs;
- Drugs containing no active ingredients;
- Drugs containing unlisted ingredients, which may pose a danger of allergic reactions, adverse reactions with other medicines, and in fact be contraindicated with certain medical conditions;
- Drugs not manufactured, shipped, or transported under drug good manufacturing practices ("GMPs");
- Drugs banned in the United States;
- Drugs recalled in the United States;
- Drugs never approved in the United States;
- Drugs with no labeling, incorrect labeling, or foreign language labeling only;
- Drugs available over-the-counter ("OTC") in Canada but restricted to a prescription in the United States;
- Drugs inappropriately packaged;

- Animal drugs not approved for human use;
- Controlled substances;
- Drugs subject to risk management or restricted distribution programs in the United States, including drugs that may produce birth defects;
- Drugs requiring supervised use - such as initial screening, careful monitoring, and careful dosing by a health care professional - imported in the absence of a prescription and in the absence of physician monitoring;
- Unlicensed vaccines and biologics;
- Investigational products not authorized for use in the United States and not found to be safe;
- Foreign versions of FDA-approved drugs; and
- Drugs containing dangerous untested substances.

In addition to these documented risks, additional major risks posed by importation would include the risk that imported drugs would be subject to product tampering or be used to commit a terrorist act against our public health system. HHS and FDA should not discount the possibility that terrorists may seek to take advantage of any opening in the U.S. drug distribution system. In fact, FDA officials have publicly acknowledged the increased risk of terrorism that would exist if Canadian borders were legally opened to drug importation.

2. Limiting Importation to Canada Would Not Minimize Safety Risks

Efforts to expand the current closed drug distribution system in the United States to include other geographic areas would increase the risk that adulterated, misbranded, and dangerous products would enter the drug supply in the United States. If our distribution system were expanded to include entities operating outside the United States, the ability to monitor, enforce, and account for drugs distributed throughout the world would be severely compromised. As more entities throughout the world, in varied geographic regions, transport and ship drug products, the likelihood of intentional interference with our drug supply would increase exponentially, and our ability to monitor and enforce against those interfering with our drug supply would decrease exponentially.

Suggestions that the benefits and protections of our closed drug distribution system can be maintained if expansion of the system is limited to Canada are also unfounded. On the contrary, even a limited expansion of the closed system to allow imports from Canada would pose serious risks to public health and safety. Canadian government officials have clearly indicated that they are unable to assure the safety of drug products shipped to the United States from Canada. Canada is simply unable to regulate its country's export market to ensure that exported drugs are safe and effective, and not counterfeit or contaminated.

U.S. and Canadian government officials have repeatedly documented a broad range of serious safety issues associated with drugs imported from, or transshipped through, Canada outside of the current closed U.S. drug distribution system. Canada is increasingly inundated with counterfeit drugs, drugs diverted from countries throughout the world, and drugs never approved by the FDA. Such drugs are currently transshipped through Canada into the United States, and implementing the importation provisions under the MMA or any other scheme would only increase the number of counterfeit and diverted drugs that reach the United States through Canada. Moreover, allowing importation from Canada outside of the current drug distribution system may encourage counterfeiters, terrorists, and

individuals interested in tampering with our drug supply to use Canada as a transshipment point for such drug products. The increasing prevalence of Internet pharmacies located in Canada (and throughout the world) that ship drugs into the United States would also make it exceedingly difficult to assure the safety of drug products at the border.

3. **There is No Basis for the HHS and FDA to Assume that Imported Drugs Are Safe**

Some have argued that the so-called small number of deaths associated with imported drugs under the current legal framework somehow supports the safety of imported drugs under the expanded MMA importation scheme. This argument is without merit.

As an initial matter, the MMA importation scheme would substantially alter the current legal framework and would provide for an influx of unapproved, adulterated drugs into the United States. Comparing outcomes expected under the MMA scheme to problems experienced under the current closed system is therefore entirely illogical.

Moreover, data obtained under the current system vastly underestimates the extent of the danger posed by imported drugs. Consumers are known to underreport drug-related injuries, particularly with regard to imported drugs that may have been obtained unlawfully. In addition, injuries caused by unapproved drugs may take time to develop. Not all counterfeit or adulterated products contain materials or dosages that would cause an immediate, severe reaction. Rather, products are often subpotent, and may therefore be ineffective. Negative effects based on the absence of efficacy may take time to develop, and may result in a patient's injury from an underlying condition that is not adequately treated, rather than from the drug itself. Accordingly, in many cases the injury may never be properly attributed to an adulterated drug.

Finally, our regulatory system is premised upon the belief that drugs must be presumed unsafe unless proven otherwise. This presumption underlies FDA's entire New Drug Application ("NDA") process, which requires manufacturers to demonstrate safety and efficacy before a drug product may be lawfully marketed in the United States. There is no rational reason for this presumption to be altered for imported prescription drugs. The "no bodies in the street" argument put forth by some advocates of importation turns this concept -- and the fundamental premise of the FDCA -- on its head, by presuming that a drug product is safe unless there is concrete evidence to the contrary. Although we must remain vigilant, as Americans we are privileged to have the most successful system for ensuring drug safety and efficacy in the world. HHS and FDA should be profoundly troubled by any proposed system that would allow drugs to enter the U.S. market without a demonstration of safety and efficacy, regardless of whether injuries or deaths have already been identified. Employing less stringent safety and efficacy standards for imported drug products would be illogical, misguided, and dangerous.

4. **There are no Safe Alternatives to Offset the Risks Posed by Imported Drugs**

Regardless of additional safety measures that might be implemented, an importation scheme such as that established under the MMA would always pose additional risks to public health and safety. The regulatory regimes employed by foreign countries are simply not capable of ensuring the safety of drugs exported to the United States. An analysis of Canadian laws and regulations, as well as the

laws of 24 other countries identified as potential significant sources of pharmaceuticals for importation into the United States, makes abundantly clear that foreign regulatory regimes are insufficient to protect American consumers. The primary purpose of drug regulatory regimes in these countries is to protect the domestic drug supply, not to ensure the safety, efficacy, or quality of drugs that are exported to the United States or elsewhere.

Canada's laws, for example, are designed only to ensure the safety of drugs intended for use by Canadian citizens, and do not generally have extra-territorial effect. Canada's primary food and drug law (the Federal Food and Drugs Act) specifically exempts certain exports from the Act and its accompanying regulations. Moreover, Health Canada - Canada's drug control agency - has stated on several occasions that its priority is ensuring the safety of drugs approved for sale in Canada, and that it cannot assure the safety of drugs exported from (or through) Canada into the United States.

In addition, the FDA cannot ensure the safety of drug imports by testing drugs upon importation. Ensuring that drug shipments are handled in compliance with FDA GMPs and safe distribution practices throughout the entire manufacturing, distribution, and storage process is critical to assuring drug safety. Test methods available at the border (*e.g.*, end-product testing) are incapable of ensuring that a drug product is FDA-approved, has been handled and stored in an appropriate and safe manner, and has not been commingled with unapproved or contaminated products. There is simply no test or test protocol that is available - or that could be established - to ensure that drugs coming into the country are FDA-approved and have been handled in a manner that guarantees product safety and efficacy.

Finally, existing anti-counterfeiting technologies are insufficient to prevent the importation of counterfeit or unapproved drug products. While a number of anti-counterfeiting technologies are available to help improve the safety of drug products distributed under the current legal framework, such technologies are not foolproof. Anti-counterfeiting technologies, while offering an incremental safety benefit under the current closed drug distribution system, cannot prevent the risks associated with importation of drug products once that system has been expanded. Further, while advanced authentication technologies, like watermarks and holograms, offer increased protection against counterfeits, repackaging and expert duplication techniques have allowed counterfeit operations to catch up to these technologies in the past. Advanced track-and-trace technologies (including electronic product codes and radio-frequency identification tags) offer the long-term potential for increased control and security. However, these technologies are years away from implementation. More importantly, track and trace technologies will only offer greater control of products within the closed system. They will not allow manufacturers and suppliers to track products coming from outside the system.

5. **FDA and HHS Are Well Aware of the Safety Risks Associated with Imported Drugs**

FDA and HHS are "on notice" that imported drugs pose significant health and safety risks based upon the number of unapproved drugs identified during FDA import blitzes and the documented dangers posed by imported drugs. There is simply no basis for a decision by HHS, in conjunction with FDA, that importation of drugs under the MMA or any other importation scheme could be done safely. Such a decision would undoubtedly be arbitrary and capricious, in light of the overwhelming and unambiguous factual record documenting widespread safety concerns and dangers associated with imported drugs.

C. The Costs, and Financial Impact, Associated with Importation Under the MMA Would be Exorbitant

Not only would it be impossible for the Secretary of HHS to certify that drugs brought into the United States under an importation scheme like that of the MMA would be safe, but it would also be impossible for the Secretary to certify that there would be any noticeable reduction in costs as a result of such a scheme. On the contrary, there are huge costs associated with importation that would far exceed any alleged benefits of such a scheme. While many of these costs are direct and obvious, many other costs are indirect and hidden – but would still be borne by consumers. The costs inherent in dismantling our current, closed drug distribution system by allowing importation outside of this framework would far outweigh any illusory benefits.

1. Price Reductions Would Have a Major Negative Impact on Pharmaceutical Profitability

Assuming drug importation will cause a significant volume of current sales in the U.S. to be sourced elsewhere, either at the wholesale or retail level, then at least from a pharmaceutical firm's point of view every dollar in sales that is transferred away from the U.S. and to another country is likely to be replaced by less than a dollar in revenue from the imported sale. This, by definition, will reduce profits (assuming costs remain constant).

A major reduction in profits would strike a painful – though perhaps not immediately fatal – blow to the current pharmaceutical industry. With the financial prospects for future discoveries in doubt, investors would surely demand that firms return their capital rather than invest it in new discoveries. Furthermore, any firm that did not comply would quickly lose its investors. The largest impact may be felt by early-stage pharmaceutical and biotechnology firms that rely on investor confidence in future returns for their financing.

2. Reduced Profitability Would Significantly Curtail Pharmaceutical Research and Development

U.S. investment in R&D for new medicines last year totaled more than \$27 billion, continuing a pattern of robust growth. In recent years, the industry has typically introduced 25-30 new medicines annually, suggesting on its face that it takes approximately \$1 billion per year to fund a research program that yields one new product per year. This estimate is consistent with outside analyses that have estimated the cost of developing a new drug at \$800 million - \$1.7 billion.

A reduction in profitability, and the attendant impact on capital markets, will necessarily lead to a reduction in pharmaceutical R&D. As larger firms consider cutting R&D projects, they will almost certainly look to cut earlier stage projects first. Projects that are far enough along in the development pipeline will be funded to completion, but early stage projects will not be supported. The combination of: (a) the disappearance of smaller firms reliant on capital markets to fund R&D projects; and (b) the shift away from early-stage research projects, coupled with the 10-15 year development timeline typical in this industry, means that it will likely be at least a decade before consumers notice the impact on the pharmaceutical research industry. The reduced investment in R&D will lead to a lack of new products, and those missing products have been estimated to be worth much more than the potential short-run savings from price controls.

Unfortunately, a decade from now it will be impossible for policymakers to reverse course, as the pharmaceutical pipeline would presumably be dry. Just as it would take at least 10 years for consumers to notice the lack of products being invented, it would take at least that long to re-energize the research-based pharmaceutical industry. Further, it would clearly be a challenge for the government to make credible commitments to a free-market pricing system at that time.

3. Importation Ultimately Leads to Delayed Access to New Therapies

The sole rationale for enacting importation legislation is to exploit the price differences that exist between the United States and certain other markets. None of those price differences is the result of free market forces, such as efficiencies or economies of scale. Rather, all of the price differences result from the fact that the other countries engage in government price controls. The rationale supporting importation is premised upon such foreign governmental price fixing. Thus, importation is nothing less than a clear step in the direction of price controls. Indeed, the debate over importation presents a critical choice to healthcare policymakers in America. We can continue to support a successful market-driven healthcare system where innovation and access to safe and efficacious medicines advance the standard of care year after year. Or we can slowly import a centralized and highly regulated healthcare system where prices are set by government bureaucrats rather than by the market forces that drive innovation. It is therefore appropriate and important to look at the impact that government regulated price controls have had on the access to innovative medicines in other markets. In Europe, for example, where centralized health systems are common, it takes an average of two years from the time a drug first becomes available on the market until it is accessible by most European consumers. Such delays are largely a result of the process used by foreign nations to establish reimbursement rates and establish price controls for new drugs. Rather than import the policies of foreign healthcare regimes, policymakers in the U.S. should endeavor with greater vigor to encourage other industrialized nations to support the innovation that brings them such tremendous advances in care.

4. Price Differentials Would Not be Passed on To Consumers

The proponents of importation assume that the relatively large difference in wholesale prices between the U.S. and Canada or other nations can be passed along to U.S. consumers by allowing importation from such countries. Whatever one believes about how the associated reduction in profits will impact the pharmaceutical and biotechnology industries, it is important to note that it is not at all clear that consumers will actually experience economic benefits that reflect the true difference in prices between countries.

While pharmaceutical manufacturers will feel the full brunt of the shift in sourcing from foreign countries, the dollars taken out of manufacturers' hands will be reallocated among multiple entities. Our experience in Europe demonstrates that the gains from importation will ultimately accrue to a new industry of middlemen, not to consumers. In addition, in light of the significant costs required to attempt to monitor the safety of imported drugs (which would come at significant taxpayer cost) there is significant reason to question whether consumers would actually experience any economic benefits under open importation.

Allowing imports is therefore the worst possible form of price control regime. For every dollar of desired price reduction, investment in research must be reduced by a multiple in order to make up for the money diverted to middlemen.

5. Allowing Expanded Importation Would Create Significant Liability Costs

A host of new and troubling liability issues would arise if importation of prescription drugs were permitted under the MMA or any other importation scheme; exposure to product liability claims would impose significant additional indirect costs on manufacturers, distributors, retailers, and individual states.

If products labeled with American brand names were imported without any assurance that they were indeed the products they claimed to be, and without any guarantee of safety or efficacy, American manufacturers could face a substantial number of new lawsuits based on the introduction of counterfeit or otherwise contaminated products into the United States. In many situations, it would be impossible to trace the origin and distribution chain of a product involved in a lawsuit, and the consumer might not even know that such a product was counterfeit. American manufacturers would therefore be sued in numerous cases that did not actually involve their products. This liability could extend throughout the distribution chain to wholesalers, distributors, retailers and even doctors who – like manufacturers – may have had nothing to do with the product at issue.

Even if a foreign entity were known to be truly responsible for harm caused by a particular drug product, strict liability principles could be asserted by plaintiffs to force American manufacturers, distributors, or retailers to pay for resulting damages. Many foreign exporters would lack adequate insurance or other resources to cover the costs of their wrongdoing. Thus, joint and several liability principles could potentially expose American manufacturers to large jury awards even if a foreign company was deemed by a jury to be almost entirely at fault.

States, too, would potentially face significant liability if foreign drugs imported into the U.S. under state plans injure American consumers. When imported drugs cause serious adverse reactions, are subpotent, or otherwise differ from the FDA-approved drugs, states that facilitate the provision of such drugs to consumers face serious liability risks. States could be sued, by individuals or via class action, under various tort and other theories – including theories of negligence, strict liability, breach of implied warranty of merchantability, failure to warn, and fraud or misrepresentation. Whether or not states are treated as merchants with a direct responsibility for ensuring drugs are safe, courts may nonetheless hold that states are, in fact, responsible for ensuring that unsafe drugs do not fall into the hands of consumers – particularly given that the potential injury to patients from imported drugs is both foreseeable and likely.

The State of Minnesota recently announced that it would permit its 120,000 state employees and their dependents to purchase prescription drugs from a pharmacy in Alberta, Canada. No doubt cognizant of its potential legal liability for damages to its employees resulting from the purchase of imported counterfeit or otherwise unsafe or dangerous products, the State posted a “disclaimer of liability” for the program on its Website. “The State of Minnesota makes no warranty, express or implied, of merchantability and fitness for a particular purpose, and accepts no legal liability, with respect to any product offered, or pharmaceutical care provided, by the pharmacies listed on this

Website.”³ The State of Minnesota, acknowledging the safety risks associated with imported drugs, nonetheless encouraged its employees to import such drugs and then declined to accept legal responsibility for any problems arising from the use of such drugs.

Ultimately, the substantial burdens and costs American pharmaceutical companies and U.S. states already bear under our tort system would increase dramatically if importation were permitted outside of the current system. It would be misguided for HHS and the FDA to condone an importation scheme that would allow American companies and the states to be held hostage as deep pocket defendants based upon plaintiffs’ injuries that were foreseeable and caused entirely by foreign companies or individuals.

The flip side of this is that enforcement of FFDCA requirements against foreign entities participating in the importation of drugs would be impossible. In order to discourage conduct that can lead to safety risks for the public, the FFDCA imposes criminal penalties on both corporate and individual violators. Even if corporate entities could somehow be prosecuted, most of the individuals participating in importation-related activities would be outside the jurisdiction of U.S. agencies. This lack of deterrent effect would certainly lead to more unlawful behavior and increased safety risks.

In sum, importation increases liability risks for U.S.-based companies while reducing the ability of regulatory agencies in the U.S. to prosecute unlawful conduct affecting American consumers. This is hardly a prescription for increasing American competitiveness.

6. **The Costs Required to Ensure Compliance at the Border Would be Exorbitant, And Safety Still Could Not Be Guaranteed**

As noted above, the FDA maintains tight oversight of the U.S. drug manufacturing and distribution process in order to maintain the integrity of the U.S. drug supply. The Agency and Congress have, through the FFDCA and its associated regulations, imposed a wide range of requirements on manufacturers, distributors and retailers, including manufacturing standards, licensing requirements, labeling requirements, and the NDA process.

The only way to assure the safety of any drug - including an imported drug – is to apply these requirements. It is essential that drugs comply with GMPs, labeling requirements, and the extensive safety and efficacy requirements of the NDA process. If imported drugs do not comply with these requirements, the FDA must refuse them admission into the United States under section 801 of the FFDCA.

Enforcing the above requirements and attempting to assure compliance at the border would require incalculable resources - time, money and personnel. We reasonably assume that counterfeiters and others interested in infusing the system with unsafe drugs would not comply with these requirements; thus, it would be insufficient for foreign countries and companies merely to adopt the FDA’s requirements. Rather, it will be imperative that U.S. officials inspect every package at the border. Although the costs associated with monitoring the border are not currently quantifiable with any precision, it is safe to assume that such costs would easily run into the billions if the

³ <http://www.advantage-meds.com/>

volume of cross-border trade is assumed to be large. These costs would, of course, in all likelihood be passed on to American taxpayers.

7. **HHS and FDA Must Not Discount the Loss of Consumer Confidence That Would Result from a New Importation Scheme**

There is another incalculable cost that should be incorporated into the analysis: costs associated with the widespread erosion -- if not complete loss -- of public confidence in drug safety and the officials charged with its protection. Historically, the occurrence of a drug crisis, based upon weaknesses in current laws and regulations, has led Congress to strengthen the Agency's regulatory powers. Subsequent to the Elixir Sulfanilamide tragedy in 1937, Congress strengthened the law and passed the FFDCA in 1938. Similarly, after thalidomide birth defect cases were identified throughout the world, Congress passed the Drug Amendments of 1962. In both cases, widespread consumer panic, and concerns over the safety provided by the current regulatory scheme, led Congress to act in an effort to restore confidence in the FDA.

More recently, Congress and the FDA reacted to events like the Tylenol® tampering scare in the 1980's by strengthening our laws to restore the public's faith that our drug supply is safe. We must not now underestimate the volatility of public perception in the face of potential dangers posed by imported drugs. HHS and FDA have witnessed public panic in the face of the anthrax scare of 2001, and should not now minimize the impact on the public of widespread adverse events associated with imported drugs. It would be the greatest irony if we now reverse the history of strengthening our drug distribution system and instead allow those charged with the responsibility for the safety of our drug supply to create the very conditions that would undermine it. Pfizer urges HHS and FDA to avoid such a terrible mistake, and to ensure that consumer confidence in our drug supply is maintained.

D. Conclusion

Safety risks inherent with expanded drug importation are significant, real, and greater than they were in 2001, when Secretary Thompson last refused to certify the safety of an importation scheme. In addition, the costs required to implement such a scheme, as well as to take the steps necessary to safeguard the U.S. drug supply, would be exorbitant and would not provide the desired results.

Based on the clear risks and costs that would result from an expansion of drug importation outside of our current closed system, HHS has absolutely no justification for certifying that the importation scheme presented under the MMA (or any other importation scheme) would pose no additional risks to public health and safety and would result in cost reductions. Based upon the factual record, a decision to certify would be arbitrary and capricious, and would expose American consumers to a wide range of significant dangers based upon the presence of counterfeit, adulterated and misbranded drugs in the U.S. drug supply.

More detailed responses to the specific questions posed by the FDA are provided below.

II. Scope and Volume of Unapproved Drugs Entering the United States Through Mail Shipments and at Border Crossings

A. Lack of FDA Resources and Tracking Mechanisms, FDA's Personal Importation Policy, and Internet Pharmacies Render It Exceedingly Difficult to Quantify the Number of Unapproved Imported Drugs

It is exceedingly difficult to quantify the number of unapproved drugs entering the United States through mail shipments and border crossings. FDA currently has no formal mechanism to track the numbers of imported pharmaceuticals and is unable, even informally, to inspect most of the packages that enter the United States. Moreover, the existence of unauthorized wholesalers, Internet pharmacies, and FDA's "personal importation policy" virtually assure the undercounting of unapproved drugs entering the United States.

As described below, FDA spot reviews of several international mail facilities and border crossings have confirmed that the rate of packages currently entering the U.S. exceeds FDA's management capabilities. FDA simply is not in a position to inspect the vast majority of packages entering the country, and thus cannot know precisely how many of those packages contain unapproved – and potentially dangerous – drugs.

In addition, even if FDA had sufficient resources and a tracking system were implemented, FDA's personal importation policy, the prevalence of unauthorized wholesalers, and the rising use of Internet pharmacies would continue to have a significant impact on the influx of imported drugs into the United States. Such factors would still render it exceedingly difficult to estimate the number of unapproved drugs entering the country.

B. Officials Currently Estimate that More than 20 Million Packages Containing Pharmaceutical Products are Imported into the U.S. Every Year and that a Significant Percentage are Unapproved and Dangerous

Officials from the FDA, U.S. Customs and Border Protection ("Customs"), and Congress all agree that prescription drug products are being imported into the United States in vast – and ever increasing – numbers. The past three years alone have witnessed significant growth in the number of prescription drugs crossing our borders. In 2001, FDA and Customs conducted a survey of the volume and types of imported drug products entering the U.S. through the Carson City, California mail facility.⁴ A baseline review of suspect international packages and packages that would customarily be set aside for FDA review indicated that an estimated 16,500 such packages could have been set aside by Customs for FDA inspection over the course of the five-week survey.⁵ Based in part on the Carson pilot study, FDA estimated that approximately 2 million packages containing

⁴ See, e.g., *Comparative Pricing of Prescription Drugs: Hearing Before the Subcomm. on Consumer Affairs, Foreign Commerce and Tourism of the Senate Comm. on Commerce, Sci. and Transp.*, 107th Cong. (2001) (statement of William K. Hubbard, then-Senior Assoc. Comm'r For Policy, Planning and Legislation, Food and Drug Administration); See also Nat'l Assoc. of Bds. of Pharmacy ("NABP"), *Position Paper on the Importation of Foreign Prescription Drugs*, 2 (March 2003).

⁵ *Comparative Pricing* hearing, *supra* note 3 (statement of William K. Hubbard).

FDA-regulated products for personal use were being imported into the United States annually from countries around the world.⁶

Since then, the number of prescription drugs being imported into the United States from other countries has been rising steadily.⁷ In 2003, the Miami International Mail Branch Facility alone received approximately 150,000 packages containing pharmaceutical products weekly, 600,000 monthly, and approximately 7 million annually.⁸ Extrapolating the Miami data nationally, more than 20 million packages containing pharmaceutical products are imported into the U.S. every year – a 1,000 percent increase over the 2001 estimate.⁹

Customs officials have confirmed this increase. In March of this year, Customs officials estimated that 40,000 packages of prescription drugs move through the John F. Kennedy mail facility in New York each day.¹⁰ In fact, FDA stated that, according to recent data from IMS Health, “approximately \$1.1 billion in pharmaceuticals were imported into the U.S. in 2003 (based on U.S. prices), despite federal laws prohibiting such actions.”¹¹

While imported drugs originate in a wide variety of countries, importation from Canada, in particular, is considerable. According to the National Association of Boards of Pharmacy (“NABP”), “nearly 70 pharmacies in Canada . . . shipped almost \$500 million dollars worth of prescriptions into the U.S. in 2002.”¹² This phenomenon has prompted at least one Congressman to conclude that the “the importation of [prescription drugs] from Canada alone – over the Internet, through cross-border traffic and, increasingly, through bulk shipments to U.S. ‘pharmacy storefronts’ – has become a multibillion-dollar business affecting the health and safety of hundreds, if not millions, of Americans.”¹³

⁶ *Continuing Concerns Over Imported Pharmaceuticals: Hearings Before the Subcomm. on Oversight and Investigations of the House Comm. on Energy and Commerce*, 107th Cong. 47-48 (2001) (statement of William K. Hubbard); See also Rep. James Greenwood (R-PA), *The Tide of Imported Medicines Must be Turned*, THE HILL, July 16, 2003, at 34.

⁷ As one Congressman stated, “Not much has changed since [the 2001 hearing] other than the volume of drugs.” *A System Overwhelmed - The Avalanche of Imported, Counterfeit, and Unapproved Drugs Into the U.S.: Hearing Before the Subcomm. on Oversight and Investigations of the House Comm. on Energy and Commerce*, 108th Cong. 2 (2003) (statement of Rep. James Greenwood, (R-PA)).

⁸ *See id.*

⁹ *Id.*

¹⁰ FDA Week, *Customs Says 40,000 Drug Parcels Go Through JFK Facility Daily* (March 19, 2004). Senator Norm Coleman (R-MN), after visiting the facility, indicated that many of these prescription drugs were counterfeit or controlled substances obtained without a prescription.

¹¹ See FDA Press Release, *FDA Partners with States to Warn Consumers that “Looks Can Be Deceiving”: Virginia Joins Growing List of State Partners in Effort to Educate Consumers About Unapproved Foreign Drugs; More Expected to Sign On in Coming Weeks* (April 13, 2004).

¹² See NABP Position Paper, *supra* note 3, at 1.

¹³ Greenwood, *supra* note 5.

While it is clear that vast numbers of drugs move across our borders each year, it is virtually impossible to determine the number of drugs that are, in fact, unapproved. This is due, in great part, to FDA's admitted inability to inspect all of the packages that come across our borders.¹⁴ Nevertheless, the FDA, industry trade associations, members of Congress, and Customs officials have all estimated that the number of unapproved, adulterated, contaminated, counterfeit, or otherwise prohibited imported drugs is substantial. These types of drugs enter the United States in great quantities through both mail facilities and land borders.

1. Significant Numbers of Unapproved Drugs Enter the United States through Mail Facilities

International mail facilities are a key entry point for vast numbers of imported drugs, yet the FDA has not been able to determine how many of these imports are unapproved. All evidence suggests, however, that the number is significant. During the 2001 survey of the Carson City, California mail facility, approximately 16,500 packages passed through customs for FDA review over a five-week period. The FDA, however, was only able to examine 1,908 packages - a mere 11.5% of the total number of packages- during this period.¹⁵ Of these, more than one-third were detained because they were unapproved for use in the U.S., were misbranded, or required a doctor's prescription.¹⁶

Similarly, in 2001, Congressman Peter Deutch (D-FL), Congressman James Greenwood (R-PA) and Congressman Bart Stupak (D-MI) visited the international mail facility near Dulles Airport in Virginia.¹⁷ The findings, according to Rep. Deutch, were "sobering." Prior to their arrival, Customs inspectors detained 167 parcels containing drugs in a mere 4 hours.¹⁸ During their visit, the Congressmen observed "a haphazard collection of unmarked and misbranded drugs."¹⁹ Many were unlabeled, some packages had false declarations, and most contained "no prescription nor any indication that a drug was being taken under supervision of a doctor or a pharmacist."²⁰ Moreover,

¹⁴ See, e.g., *Continuing Concerns* hearing, *supra* note 5, at 47-49 (Statement of William K. Hubbard). Hubbard cautioned that the FDA did not have sufficient personnel to inspect all packages containing prescription drug products for personal use that enter the United States (then estimated at 2 million per year), and thus could not determine the country of origin, describe the conditions under which the drugs were manufactured, or estimate what percentage might be counterfeit. *Id.* at 47.

¹⁵ *Id.* at 49. According to Mr. Hubbard, "the Carson pilot demonstrated that the rate of packages coming into the U.S. exceeds FDA's capacity to manage, thus, Customs is left with little choice but to forward the majority of packages to addressees." *Id.*

¹⁶ *Id.* FDA indicated it had "no information to establish where these drugs were actually manufactured and whether necessary current Good Manufacturing Practice requirements were followed." FDA also had "no assurance that the drugs were packaged and stored under appropriate conditions to avoid degradation or contamination."

¹⁷ See *Continuing Concerns* hearing, *supra* note 5, at 5-6, 12 (statements of Rep. James Greenwood (R-PA) and Rep. Peter Deutch (D-FL)).

¹⁸ *Id.* at 12 (statement of Rep. Peter Deutch).

¹⁹ *Id.*

²⁰ *Id.*

many of the packages contained dangerous drug combinations, drugs outside of their original containers, or drugs masked as another drug product.²¹

All evidence indicates that massive numbers of unapproved drugs continue to flow into United States mail facilities. In the past year, the FDA has conducted a number of “import blitzes” at mail facilities around the country. During these blitzes, the Agency has reviewed a mere fraction of the prescription drug products actually entering the country; nevertheless, the number of unapproved drugs identified in even these small-scale reviews has been astounding.

For example, in July and August 2003, the FDA, in conjunction with Customs, conducted a series of import blitzes in Miami, New York, and California.²² At each location, the agencies examined packages shipped via international mail through U.S. Postal Service facilities over a 3-day period. In total, 1,153 imported drug products were examined. Of these, approximately 88% were found to contain unapproved drugs.²³

Subsequently, on January 27, 2004, the FDA and Customs announced the results of their second import blitz, performed in November 2003, in Buffalo, Dallas, Chicago, and Seattle mail facilities and the Memphis and Cincinnati courier hubs. This blitz identified 1,728 unapproved drugs, including so-called “foreign versions” of FDA-approved drugs, recalled drugs, drugs requiring special storage conditions, drugs requiring close physician monitoring, investigational drugs, and drugs containing addictive controlled substances.²⁴

2. **Significant Numbers of Unapproved Drugs Enter the United States through Land Borders with Canada and Mexico**

Mail facilities are not the only points of entry for unapproved drugs. Rather, a recent series of land border patrols along the U.S.-Canadian and U.S.-Mexican borders reveals that substantial importation is also occurring at vehicular border crossings and that, as is the case at mail facilities, a significant percentage of these imported drugs are unapproved.

The Canadian border is fertile territory for the influx of unapproved drugs into the U.S. On January 6, 2001, for example, FDA and Customs conducted an eight-hour survey of passenger vehicles at three ports of entry along the U.S.-Canadian border. FDA detained 33 passenger vehicles (out of 10,374 passenger vehicles and 58 buses that crossed the border) and found 35 individuals carrying

²¹ *Continuing Concerns* hearing, *supra* note 5, at 6 (statement of Rep. James Greenwood).

²² FDA Press Release, *FDA/U.S. Customs Import Blitz Exams Reveal Hundreds of Potentially Dangerous Imported Drug Shipments* (Sept. 29, 2003).

²³ *Id.* See also *Prescription Drug Importation: Hearing before the Senate Comm. on Commerce, Sci. and Transp.*, 108th Cong. (2003) (testimony of John M. Taylor, III, Assoc. Comm’r for Regulatory Affairs, Food and Drug Administration).

²⁴ FDA News, *Recent FDA/U.S. Customs Import Blitz Exams Continue to Reveal Potentially Dangerous Illegally Imported Drug Shipments* (Jan. 27, 2004); see also NABP Press Release, *NABP/FDA: Public Safety is at Risk with Foreign Drug Importation* (Jan. 27, 2004); FDA Talk Paper, *FDA Takes Actions Against Illegal Drug Import Operations of Expedite-Rx, SPC Global Technologies, and Employer Health Options* (Jan. 22, 2004).

47 containers of drug products. Among the imported drug products were drugs prohibited in the U.S. and drugs only available with a prescription in the U.S.²⁵

The Mexican border is also a key entryway for unapproved drugs. For example, in August 2000, FDA's Southwest Import District, in conjunction with Customs, the Drug Enforcement Agency ("DEA"), the U.S. Department of Agriculture ("USDA") and others, conducted a survey of prescription drugs being brought by pedestrians into the U.S. at eight ports of entry along the U.S.-Mexican border.²⁶ During the four-hour survey, more than 600 people were interviewed. Of these, 63% were carrying prescriptions for medications they were bringing into the country (59% were U.S. prescriptions, and 41% were Mexican prescriptions).²⁷ Among the imported drug products were drugs restricted to a prescription in the U.S. but available OTC in Mexico, and a variety of products not available in the U.S.²⁸

A subsequent four-hour survey conducted on April 11, 2001 at seven points along the Mexican border found similar results.²⁹ Approximately 586 people brought 1,120 prescription drugs into the United States. Of these, 56% had a prescription for the drugs in question (61% were U.S. prescriptions, while 39% were Mexican prescriptions).

Drugs crossing the border from Mexico, officials say, "are difficult to trace and may be manufactured improperly, sorted incorrectly, mislabeled or contain an inaccurate amount of the active ingredient."³⁰ According to at least one estimate by American law enforcement officials, the level of counterfeits and substandard medications could be as high as 25%.³¹

While the numbers of unapproved drugs entering the United States cannot be determined with precision, it is indisputable that these numbers are significant, and rising. Considerable shipments of unapproved prescription drugs are finding their way into the United States through our land borders to the North and South, and by air, from sources around the world.

²⁵ See, e.g., *Continuing Concerns* hearing, *supra* note 5, at 51 (statement of William K. Hubbard); see also NABP Position Paper, *supra* note 3, at 3-4.

²⁶ See *Continuing Concerns* hearing, *supra* note 5, at 50-51 (statement of William K. Hubbard); see also *Comparative Pricing* hearing, *supra* note 3 (statement of William K. Hubbard); NABP Position Paper, *supra* note 3, at 3.

²⁷ See, e.g., *Continuing Concerns* hearing, *supra* note 5, at 51 (statement of William K. Hubbard).

²⁸ *Id.*

²⁹ *Id.* See also NABP Position Paper, *supra* note 3, at 3.

³⁰ Sarah Lunday, *When Purchasing Medicine in Mexico, Buyer Beware*, N.Y. TIMES, April 17, 2001, at F5.

³¹ *Id.*

III. Safety Concerns Posed by Unapproved Drugs

A. The Current United States Drug Regulatory System Must be Strengthened

The United States has a “closed” drug regulatory system specifically designed to ensure the safety and integrity of the American drug supply and keep potentially dangerous drugs out of the U.S. stream of commerce. Under this system, FDA exercises authority and oversight over drug products from “cradle to grave.”

Seventeen years ago, Congress investigated and recognized the need to strengthen the U.S. drug distribution system. At that time, Congress concluded that the safety of imported drugs could not be assured once such products were distributed outside the control of the drug manufacturer. Under those circumstances, distribution channels could no longer be effectively controlled and diversion and counterfeiting could not be prevented. These conclusions led Congress to pass the PDMA.³² Passage of this Act, which focused on prescription drug reimportation, confirmed the general importance of “closing” and securing the U.S. drug distribution system.

Currently, under this closed system, drugs intended for the U.S. market must meet the rigorous safety and efficacy requirements of the FDCA and its implementing regulations. Under the current system:

[m]ost retail stores, hospitals, and other outlets obtain drugs either directly from the drug manufacturer or from a small number of large wholesalers. FDA and the states exercise oversight of every step within the chain of commercial distribution, generating a high degree of product potency, purity, and quality. In order to ensure safety and compliance with current law, only the original drug manufacturer is allowed to reimport FDA-approved drugs.³³

The current closed regulatory system thus allows FDA and state authorities to protect the integrity of the drug supply and reduce safety risks by exercising strict control over all aspects of drug approval, manufacture, distribution and sale. The current closed system has ensured a high degree of drug safety and efficacy for the American public.

Nevertheless, the current closed drug distribution system is not without problems. Even with significant safeguards in place, this system has been breached, over time, by imported drug products. Whenever this has happened, serious safety problems have been identified. Widespread, growing safety concerns, due in particular to the expansion of worldwide counterfeiting and the diversion of unapproved drugs into the United States, make it imperative that the system be strengthened and secured. As explained below, weakening the system with the importation scheme established under the MMA – or any other scheme encouraging importation – would clearly be arbitrary and capricious, as it would create the very safety risks that the current system was designed to minimize.

³² 21 U.S.C. §§ 331, 333, 353, 381 (1999 & Supp. 2003). The President signed the PDMA into law in 1988 (Pub. Law No. 100-293) and it was subsequently amended in 1992 (Pub. Law No. 102-353).

³³ Letter from Tommy G. Thompson, Secretary, HHS, to Sen. James Jeffords (I-VT) (July 9, 2001).

In a report entitled “Combating Counterfeit Drugs – A Report of the Food and Drug Administration,” issued a mere three months ago, the FDA recommended that the Agency and other entities take action in multiple areas “to create a comprehensive system of modern protections against counterfeit drugs.”³⁴ Such steps include, but are by no means limited to: implementation of new technologies to better protect the drug supply; adoption of track-and-trace technology; state adoption and enforcement of anti-counterfeiting laws and regulations; increased focus on state licensure of wholesale pharmacies; increased criminal penalties; and adoption of secure business practices by all participants in the drug distribution chain.³⁵

Given the extensive work necessary, by FDA’s own admission, to keep counterfeit medications out of the U.S. market even under our current system, “opening” this system to allow importation of drugs from other countries would be misguided and contrary to FDA’s mandate to protect the public health. Opening the system, even on a small-scale basis, would undo the protections our closed system offers and would allow a steady stream of dangerous medicines to enter our drug supply.

B. Drugs Imported As a Result of Breaches in the Current Closed System Already Pose Significant Safety Risks

Multiple, serious threats to safety have been associated with imported drug products. FDA has repeatedly, and consistently, stated that significant public health and safety issues are raised by the importation of prescription drugs. As noted by a high-ranking FDA official:

[P]rescription drugs purchased from foreign countries generally are not FDA-approved, do not meet FDA standards, and are not the same as drugs purchased in the United States. Because the medications are not subject to FDA’s safety oversight, they could be outdated, contaminated, counterfeit, or contain too much or too little of the active ingredient. In addition, foreign dispensers of drugs to American citizens may provide patients with incorrect medications, incorrect strengths, medicines that should not be used in people with certain conditions or with other medications, or medications without proper directions for use.³⁶

In fact, a Federal District Court recently reached the same conclusion, noting that: “unapproved prescription drugs and drugs imported from foreign countries by someone other than the U.S. manufacturer do not have the same assurance of safety and efficacy as drugs regulated by the Food and Drug Administration Because the drugs are not subject to FDA oversight and are not

³⁴ *Combating Counterfeit Drugs: A Report of the Food and Drug Administration*, at i. (Feb. 2004).

³⁵ *Id.* at i-v.

³⁶ Letter from William K. Hubbard to David Work, Executive Director, North Carolina Board of Pharmacy (July 1, 2003); *see also* Warning Letter from David J. Horowitz, Esq., Director, Office of Compliance, Center for Drug Evaluation and Research, FDA to C. Bradley Stevens, President/CEO, CanadianDiscountDrugs, *et al.* (June 30, 2003).

continuously under the custody of a U.S. manufacturer or authorized distributor, their quality is less predictable than drugs obtained in the United States.”³⁷

Safety concerns associated with imported drugs are not merely hypothetical. In the past few years alone, government officials have identified the following categories of dangerous drugs that have been imported into the United States:

- Counterfeit innovator and generic drugs;
- Drugs that appear to be from Canada, but in fact have been transshipped through Canada from other countries;
- Sub-potent drugs;
- Super-potent drugs;
- Drugs containing no active ingredients;
- Drugs containing unlisted ingredients, which may pose a danger of allergic reactions, adverse reactions with other medicines, and in fact be contraindicated with certain medical conditions;
- Drugs not manufactured, shipped, or transported under drug GMPs;
- Drugs banned in the United States;
- Drugs recalled in the United States;
- Drugs never approved in the United States;
- Drugs with no labeling, incorrect labeling, or foreign language labeling only;
- Drugs available OTC in Canada but restricted to a prescription in the United States;
- Drugs inappropriately packaged;³⁸
- Animal drugs not approved for human use;
- Controlled substances;

³⁷ *United States v. Rx Depot, Inc.*, 290 F. Supp. 2d 1238, 1241 (N.D. Okla. 2003). In November 2003, The *Rx Depot* court granted the government a preliminary injunction to immediately prevent two companies, Rx Depot, Inc. and Rx of Canada LLC, from facilitating the importation of prescription drugs from Canada. Noting that the purpose of the FDA is to protect the public health, and stressing that the unapproved drugs were a clear violation of the FFDCA, the court found that an injunction was warranted. The judge held that the companies could not assure the safety of the drugs they had been importing, and thus, in violating the law, had put Americans at serious risk.

³⁸ Medicines purchased from sources outside the U.S. may be sold in packaging that does not meet U.S. regulatory standards for safety. They often violate both FDA and Consumer Product Safety Commission (CPSC) regulations for safe drug packaging by failing to utilize tamper-resistant and/or child resistant packaging. For example, FDA surveys have indicated that very few drugs mailed to the U.S. from Canada are in true “unit-of-use” containers, in which pills are packaged as individual units in tamper-resistant packaging. Such containers reduce medication errors and the likelihood of counterfeit drugs. Instead, FDA has found that drugs coming to the U.S. from Canada tend to be packaged in manufacturers’ “stock bottles.” These bottles are not intended for use by patients whose prescriptions are for more or less than 100 units, and generally do not include appropriate labeling and warnings. Thus, use of these bottles may lead to medication errors and allow patients to obtain greater quantities of medication than their doctors prescribe. The CPSC has also stated that “stock bottles” violate safe drug packaging statutes, and therefore place children at increased risk. See Letter from William K. Hubbard to Dr. Ron Kamath and Scott McKibbin, Illinois Special Advocates for Prescription Drugs (November 6, 2003).

- Drugs subject to risk management or restricted distribution programs in the United States, such as drugs that may produce birth defects;
- Drugs requiring supervised use - such as initial screening, careful monitoring, and careful dosing by a health care professional - imported in the absence of a prescription and physician monitoring;
- Unlicensed vaccines and biologics;
- Investigational products not authorized for use in the United States and not found to be safe;
- Foreign versions of FDA-approved drugs; and
- Drugs containing dangerous untested substances.³⁹

The FDA has documented hundreds of potentially dangerous imported drug shipments in its small-scale import blitzes. The FDA's July and August 2003 blitzes, for example, lasted a mere three days and were limited to mail facilities in Miami, New York City (JFK airport), San Francisco and Carson City, California. Yet in that short time, the blitzes found that 88% of 1,153 imported packages contained unapproved drugs. This small series of inspections identified hundreds of potentially dangerous imported drug shipments, including, but not limited to, the following:⁴⁰

- **Drugs different from those approved by FDA** – Drugs that require careful monitoring by health professionals, including Roaccutane (an unapproved version of Accutane®), from Thailand, and Taro-warfarin (an apparently unapproved version of Warfarin®), from Canada.
- **Drugs requiring careful dosing** – Unapproved versions of drugs such as Dilantin®, Synthroid®, and Glucophage®, which require individual titration and very careful dosing to avoid serious life-threatening side effects.
- **Drugs inappropriately packaged** – Drugs packaged in plastic bags, tissue paper, or letter envelopes, and arriving crushed and broken.
- **Drugs withdrawn from the market** – Drugs the FDA has withdrawn from the market for safety reasons, such as Dipyrone®, removed from the market in 1977 because of its reported link to severe blood disorders, some of which resulted in fatalities.
- **Animal drugs not approved for human use** – Drugs such as Clenbuterol®, from Costa Rica and China, approved for the treatment of airway disease in horses but not for human use, and

³⁹ Additional risks could also include the risk that a drug product would contain an unlisted ingredient that could cause an adverse reaction, create an adverse reaction in combination with other medicines, or be contraindicated with other medicines or medical conditions. In addition, if equipment used to manufacture or ship drug products is not cleaned, cross contamination may occur and result in unexpected drug residue.

⁴⁰ FDA Press Release, *supra* note 21.

banned by the International Olympic Committee as a performance-enhancing drug.

- **Drugs that carry risks requiring initial screening and/or periodic patient monitoring** – Unapproved versions of drugs such as Lipitor® and Pravachol®, for which initial screening and periodic patient monitoring by a medical professional is recommended.

Similarly, the FDA's November 2003 import blitz, which covered only four mail facilities (in Buffalo, Dallas, Chicago and Seattle) and two courier hubs (in Memphis and Cincinnati), identified a wide range of dangerous imported drugs, including but not limited to:⁴¹

- **Drugs with risk management and/or restricted distribution programs** – These drugs include Canadian manufactured Accutane®, a drug that, in the United States, requires patient screening and monitoring to avoid serious risks such as birth defects.
- **Drugs requiring initial screening or periodic monitoring to ensure safe use** - These drugs include Coumadin® and warfarin, Plavix® and tamoxifen.
- **Narrow Therapeutic Index Drugs** – These drugs require individual titration of the dose and very careful dosing in order to avoid serious and potentially life-threatening side effects.
- **Biologic drugs that should be administered by a healthcare provider and are not licensed by FDA** – These drugs include Influenza Virus Vaccine approved in Canada but not licensed by the FDA.
- **Investigational Products** – Unapproved drugs that may only be shipped pursuant to FDA's Investigational New Drug ("IND") regulations.
- **So-called "foreign versions" of FDA approved drugs** – These drugs vary from U.S. standards in potency and purity and may raise additional concerns regarding both safety and efficacy. Examples include:
 - **APO-Tamox** - an unapproved, foreign version of the anti-cancer drug tamoxifen;
 - **APO-Warfarin** - an unapproved, foreign version of the blood thinner warfarin. The potency of warfarin may vary depending on how it is manufactured, and the drug must be

⁴¹ See FDA News, NABP Press Release, and FDA Talk Paper, *supra* note 23.

carefully administered and monitored by a health professional in order to prevent potential bleeding problems;

- **APO-Carbamazapine** - an unapproved, foreign version of the anti-convulsant drug carbamazapine, which requires initial screening and monthly monitoring of blood and platelet counts to ensure safe use.

Given that the FDA found such a vast number of unapproved and dangerous drugs in such small-scale spot reviews, one can only imagine the number of such drugs that would be identified if the FDA conducted large-scale import blitzes over an extensive period of time and widespread geographic area. As explained below, based upon these documented safety concerns, the current drug distribution system in the United States needs to be strengthened, not weakened through importation.

C. Weakening the Closed Distribution System through Importation Would Only Increase Health and Safety Risks

FDA import blitzes and border surveys have confirmed that the safety concerns associated with imported drugs are significant and not merely hypothetical. Weakening or expanding the closed system would increase the number of dangerous drugs in the United States, and would place the health of American consumers at significant risk.

1. Importation Would Increase the Risk that Counterfeit Drugs Would Enter the United States

One of the most likely – and significant – dangers inherent in allowing the importation of drugs is the risk that counterfeit versions of FDA-approved drugs would enter the market directly from Canada or transshipped through Canada.

A recent FDA report reveals that our closed system of drug distribution, along with the joint efforts of regulators, law enforcement officials, manufacturers, distributors, and pharmacies, has worked to ensure that “counterfeiting is not widespread within the system of manufacturing and distributing pharmaceuticals legally in the United States. . . .”⁴² Nevertheless, the Agency has, in recent years, “seen growing evidence of efforts by increasingly well-organized counterfeiters backed by increasingly sophisticated technologies and criminal operations to profit from drug counterfeiting at the expense of American patients.”⁴³ While acknowledging that exact prevalence rates within the United States are unknown, the FDA stressed that counterfeiting outside the U.S. is widespread; counterfeiting operations have been identified in virtually all countries. The Agency speculates that in some countries, more than half of the drug supply may be counterfeit.⁴⁴

Due to the Agency’s significant concerns regarding counterfeit drugs, the Agency created a Counterfeit Drug Task Force in 2003. The Task Force found that:

⁴² *Combating Counterfeit Drugs*, *supra* note 33, at 1.

⁴³ *Id.* at i.

⁴⁴ *Id.* at 2. For example, the report notes that more than 50% of anti-malarial medications in Africa may be counterfeit.

[W]hen consumers order medications from outside the U.S. (e.g., internet purchases, cross-border purchases), whether safe or unsafe, a portal of entry is created for counterfeit drugs into the U.S. distribution system. Counterfeiters can take advantage of this entryway by combining many small purchases from foreign countries into one and selling them to U.S. wholesalers or other unsuspecting entities. Due to the extensive resources involved in preventing small quantities of drugs from entering the U.S., as the volume of unapproved drug imports increases, it is more difficult for FDA to use its existing resources to identify and stop unsafe importations.⁴⁵

As the Task Force noted, the potential for counterfeit drugs to arrive in the United States via Canada or other countries is decidedly real. According to the World Health Organization (“WHO”) and the FDA, counterfeits exist in both industrialized and developed countries and constitute more than 10% of the world drug supply.⁴⁶ WHO estimates that up to 25% of the medicines consumed in poor countries are counterfeit or substandard.⁴⁷ In 2002, one WHO official indicated that approximately 70% of the reports it had received since 1982 on counterfeit drug cases were reported by developing countries, and less than 30% came from developed countries.⁴⁸ He indicated that counterfeiting occurs in both branded and unbranded products across a wide variety of therapeutic categories.⁴⁹ The same official reported the WHO’s findings that 43% of counterfeit drugs reported to the organization (and for which ingredient information was available) contained no active ingredient, 24% were poor quality, 21% contained low ingredient content, 7% contained the wrong ingredient, and 5% were packaged incorrectly.⁵⁰

Examples of counterfeit and substandard medications are numerous. For example, in 2002, 60% of all pharmaceuticals in Nigeria were counterfeit, substandard, or expired.⁵¹ A 2001 study revealed that 38% of 104 anti-malarial drugs on sale in Southeast Asian pharmacies did not contain any active ingredients.⁵² That same year, more than 100,000 deaths occurred in China as a result of counterfeit

⁴⁵ *FDA Counterfeit Drug Task Force Interim Report*, 11-12 (Oct. 2003).

⁴⁶ See World Health Organization, *Substandard and Counterfeit Medicines*, November 2003, at <http://www.who.int/mediacentre/factsheets/fs275/en>.

⁴⁷ *Id.*

⁴⁸ Lembit Rágo, M.D., Ph.D., Coordinator, Quality Assurance and Safety: Medicines, Essential Drugs and Medicines Policy, Health Technology and Pharmaceuticals Cluster, World Health Organization, *Counterfeit drugs: Threat to Public Health*, Presentation before The Global Forum on Pharmaceutical Anticounterfeiting, Geneva, Switzerland (Sept. 22-25, 2002), at 5.

⁴⁹ *Id.* at 7, 9.

⁵⁰ *Id.* at 8.

⁵¹ World Health Organization, *supra* note 45.

⁵² *Id.*

pharmaceuticals.⁵³ In 2000, 30 Cambodian deaths were traced to fake malaria medication, and more than 2,500 people died in Niger in 1995 after receiving fake malaria vaccinations.

The widespread existence of counterfeit drugs in other countries is significant because these drugs are making their way into the United States. For example, in 2000, investigations by the U.S. House Commerce Subcommittee on Oversight and Investigations revealed that the FDA had linked adverse drug reactions in 155 U.S. citizens to drug ingredients originating from China. At that time, the FDA indicated that 4,600 foreign, bulk drug suppliers to the U.S. had not been inspected.⁵⁴

Pfizer has experienced the consequences of counterfeiting first-hand. In April 2003, a substantial amount of counterfeit Lipitor® – the best-selling cholesterol-lowering medication in the world - was discovered in the U.S. distribution system. Pfizer became aware of the counterfeiting problem through consumer complaints. However, the counterfeit product was so visually similar to the legitimate product that many consumers did not know they had a counterfeit version, and very few complaints were received. Investigation by Pfizer and the FDA identified a large-scale, sophisticated international operation involving many companies. Manufactured in Costa Rica, with active pharmaceutical ingredients sourced from Sweden and excipients and tooling sourced from the U.S., the counterfeit drugs were introduced into the U.S. market by repackagers who commingled the product with authentic product and utilized the secondary wholesale network to distribute it to pharmacies throughout the United States. Ultimately, 18 million tablets were recalled.

Similarly, an August 5, 2003 raid in several locations throughout Taiwan found extensive evidence of counterfeit, fake, and otherwise prohibited drugs, including raw materials, tools and equipment, semi-finished drugs, and finished drugs ready for sale. Particularly large quantities of counterfeit Pfizer products were identified. In total, approximately 66,638 tablets of counterfeit Viagra®, 19,650 counterfeit Norvasc® drugs, and 9 large cartons of packaging and inserts for both drugs were seized.

The Pharmaceutical Research and Manufacturers of America (“PhRMA”) has also confirmed the significant level of counterfeit drugs in the U. S. and has indicated that, since 1998, the FDA has opened 78 investigations into counterfeit or tampered drugs.⁵⁵ These investigations have led to 25 convictions for conspiracy to introduce counterfeit drugs.⁵⁶ Moreover, PhRMA notes that a study by Global Options Inc. found that a third of online prescription drugstores holding themselves out as Canadian do not actually ship their products from Canada.⁵⁷ Rather, drugs may come from

⁵³ German Pharma Health Fund e.V., *Counterfeit Medicines – an Unscrupulous Business*, at http://www.gphf.org/web_en/projekte/minilab/hintergrund_arzneimittelfaelschungen.htm.

⁵⁴ See, e.g., *Continuing Concerns* hearing, *supra* note 5, at 6 (statement of Rep. James Greenwood); see also Jayanthi Iyengar, *A Bitter Pill for Indian Drug Industry*, ASIAN TIMES, Dec. 21, 2002.

⁵⁵ See Pharmaceutical Research and Manufacturers of America, *What You Should Know...Gutknecht-Emerson Bill: Counterfeit Drugs on the Rise*, Vol. 1, Issue 7 (July 23, 2003).

⁵⁶ *Id.*

⁵⁷ *Id.*

countries such as Mexico, which, the U.S. State Department has warned, may have counterfeit or substandard products in as much as 25% of total drug product circulation.⁵⁸

Importantly, the Agency has indicated that it is unaware of any feasible testing requirements that would be capable of ensuring that drug shipments do not contain counterfeit products. Increasingly, counterfeit products have been commingled with authentic products within the same shipment or bottle, making detection virtually impossible.⁵⁹ While the Agency, in its recent anti-counterfeiting report, emphasized the role of “track-and-trace” technology in efforts to prevent counterfeiting, it also indicated that the use of such technology would not be feasible until at least 2007. Unfortunately, such technology, while beneficial, will not solve the counterfeiting problem. As counterfeiting techniques become more sophisticated, counterfeit drugs become more difficult to detect and the risks to public health and safety become even more pronounced. This issue is addressed in greater detail in Section VI.

Given all of the available evidence that counterfeit drugs are already in the U.S. market, and that counterfeiting is increasing steadily in other countries, any policy – state or federal – that permits drugs to be imported legally constitutes a direct invitation to counterfeiters to flood our market with their products.

2. **Importation Would Increase the Risk that Adulterated Drugs and Drugs that Fail to Comply with FDA GMPs Will Enter the United States**

There is no way to ensure or guarantee that drugs imported outside of the current legal framework have been manufactured, distributed and stored in accordance with the FDA’s strict GMP standards and general safety requirements. Thus, consumers purchasing imported drugs risk a myriad of dangers from adulterated products. Such products may be subpotent or superpotent, or may not contain any active ingredient at all. Because compliance with GMPs cannot be ensured with foreign imports, consumers also risk ingesting contaminated or expired drug products. As the FDA has noted:

The reason that Canadian or other foreign versions of U.S.-approved drugs are generally considered unapproved in the U.S. is that FDA approvals are manufacturer-specific, product-specific, and include many requirements relating to the product, such as manufacturing location, formulation, source and specifications of active ingredients, processing methods, manufacturing controls, container/closure system, and appearance. . . . Frequently, drugs sold outside of the U.S. are not manufactured by a firm that has FDA approval for that drug. Moreover, even if the manufacturer has FDA approval for a

⁵⁸ *Id.*

⁵⁹ *See, e.g.*, Letter from Lester M. Crawford, Deputy Comm’r, Food and Drug Administration, to Sen. Thad Cochran (R-MS) (July 17, 2002) (“Moreover, some of the testing requirements cannot even be met, as there is no testing that can ensure that a shipment of drugs does not contain counterfeits. Since counterfeits can easily be commingled with authentic product, either by the case, by the bottle, or by the pill, there is no sampling or testing protocol sufficient to protect the public against the grave public harm they pose.”).

drug, the version produced for foreign markets usually does not meet all of the requirements of the U.S. approval, and thus it is considered to be unapproved.⁶⁰

It has also been noted that foreign sources:

may dispense expired, subpotent, contaminated or counterfeit product, the wrong or a contraindicated product, an incorrect dose, or medication unaccompanied by adequate directions for use. . . . The drugs may not have been packaged and stored under appropriate conditions to prevent against degradation, and there is no assurance that these products were manufactured under current good manufacturing practice [“GMP”] standards.⁶¹

Testing a product when it reaches the U.S. border is incapable of guaranteeing that the product is not adulterated. There is no test or test protocol available that can test for every possible contaminant that may have been introduced into a drug product, nor can testing methods ensure that drug handling has been proper throughout manufacturing, storage, and distribution; there is simply no testing protocol that can identify whether drugs have been exposed to improper amounts of light, humidity, heat, cold, etc. throughout the drug distribution process.

As it is impossible to guarantee that imported drugs are not adulterated and have been handled in compliance with GMPs and safe distribution practices from manufacture through distribution and storage, it is simply not possible for the Secretary to certify that such drugs are safe and effective.

3. Importation Would Increase the Risk of Product Tampering

Opening our borders, even on a limited basis, would increase the vulnerability of the nation’s drug supply to product tampering. Tampering with both OTC and prescription drugs is a serious concern even under our closed drug distribution system.

In May 2002, for example, GlaxoSmithKline issued a press release alerting patients, pharmacists and physicians that third-party tampering appeared to have occurred with its Combivir® and Ziagen® prescription drug products.⁶² Both medicines are used as part of combination regimens to treat HIV infection. After receiving four reports of suspect bottles that were labeled to contain 60 tablets of Combivir® but, in fact, contained Ziagen® Tablets, the company determined that counterfeit labels for Combivir® Tablets had been placed on two bottles of Ziagen®. Labels on another two bottles were also suspect. The tampering incident had the potential for serious adverse reactions in a small number of patients.⁶³ In addition, the replacement of Combivir®, which contains two antiviral

⁶⁰ Letter from William K. Hubbard to Robert P. Lombardi, Esq. (Feb. 12, 2003).

⁶¹ *A System Overwhelmed* hearing, *supra* note 6, at 23 (statement of William K. Hubbard).

⁶² FDA Press Release, *GlaxoSmithKline Alerts Patients, Pharmacists and Physicians to Watch for Third-Party Tampering that Incorrectly Labels Ziagen® as Combivir®* (May 10, 2002).

⁶³ Approximately 5% of individuals who receive an ingredient in Ziagen® develop a potentially life-threatening hypersensitivity reaction. While the condition subsides upon discontinuation of use, such patients are advised never to take the medication again, in order to avoid more severe symptoms, within hours, that may include life-threatening

drugs, with Ziagen®, a single antiviral, had the potential to decrease the effectiveness of a patient's treatment regimen.

Drug tampering is not a new problem; for decades, it has been associated with numerous deaths and serious injuries. FDA has been rightfully concerned about drug product tampering for more than 20 years. The Agency first implemented regulations to protect consumers from tampering with OTC drug products in 1982, in response to a widely publicized tampering incident in which seven people in the Chicago area died after ingesting Extra-Strength Tylenol® capsules that had been laced with cyanide.⁶⁴ The regulations, which were intended to alert consumers to potential tampering by making a breach of the packaging visible, required that any OTC drug product intended for retail sale (with several exceptions) be packaged in "tamper-resistant" packaging.⁶⁵

While the new regulations did reduce the risk of tampering, it soon became evident that OTC drugs were still vulnerable. In 1986, three deaths resulted from tampering with two-piece, hard gelatin capsules.⁶⁶ Subsequently, FDA amended its regulations to require that OTC drugs in two-piece, hard gelatin capsule form be packaged using at least two tamper-resistant packaging features, or with at least one such feature if the product featured a tamper-resistant capsule seal.⁶⁷

Unfortunately, even these precautions were insufficient to protect the public from product tampering. In 1991, two deaths were associated with Sudafed® capsules contaminated with cyanide - despite the fact that the capsules met FDA's tamper-resistant standards and bore many obvious signs of tampering.⁶⁸ This tragedy, the investigations that followed, and FDA's continuing review of tampering risks led the Agency in 1998 to mandate the sealing of these capsules using tamper-evident technology and to change its regulations to require that OTC drug packaging read "tamper-evident," rather than "tamper-resistant."⁶⁹ The change reflected FDA's acknowledgment of and concern about its inability to prevent tampering altogether; the new words "appropriately underscore the importance of heightening consumer awareness to any evidence of tampering, rather than implying that a particular package is difficult to breach or is tamper-proof."⁷⁰

The regulatory history associated with tamper-resistant packaging regulations provides clear indication that, despite the government's best efforts to reduce the risk under our closed drug

hypotension and death. Patients taking Combivir® who had previously experienced a hypersensitivity reaction to the ingredient in Ziagen® and received the altered drugs were at risk of having this life-threatening reaction.

⁶⁴ See 47 Fed. Reg. 50442 (Nov. 5, 1982).

⁶⁵ See 47 Fed. Reg. at 50443-44.

⁶⁶ See 63 Fed. Reg. 59463, 59463 (Nov. 4, 1998) (discussing the history of OTC tamper-resistant packaging requirements).

⁶⁷ See 54 Fed. Reg. 5227 (Feb. 2, 1989).

⁶⁸ See 63 Fed. Reg. at 59463.

⁶⁹ *Id.* at 59463-64.

⁷⁰ *Id.* at 59464.

distribution system, the risk of product tampering cannot be eliminated. Allowing drug importation would only increase the risk that products that have been altered in possibly life-threatening manners will find their way into the U.S. market. HHS and the FDA should take particular note of tampering concerns identified by third parties while Congress was considering allowing reimportation in 2002:

. . . Congress should consider the possibility that a deranged individual, like the Unabomber or the criminal who poisoned Tylenol in the 80's might take advantage of the reimport law to randomly poison prescription drugs which will be offered for sale in the United States if [reimportation is authorized]. Not only would reimportation make it easier for these individuals to put tainted products into the American drug supply, drug importation legislation cannot impose a foolproof chain of custody requirement, and this would severely hamper the ability of manufactures [sic] and public health officials to recall tainted medicines. The sort of panic that such an incident would create cannot be over-emphasized and the danger to health posed by millions of Americans refusing to take medications which they fear are contaminated would be unprecedented.”⁷¹

Given that Congress and FDA have expressed concern for years about the already significant risks of tampering under our current closed drug distribution, the FDA should advocate against any proposal to expand our distribution system. Such an expansion would only make the system more vulnerable to drug tampering and increase the very real risk that tampered drugs will find their way into the hands of American consumers.

4. Importation Would Increase the Risk of Terrorism

Since September 11, 2001, the nation has been painfully aware of its vulnerability to risks that were previously unthinkable. As recent events around the world have shown, terrorists are willing to strike civilian targets by virtually any means. The FDA should not discount the possibility that terrorists might seek to launch an attack on our public health system. To the extent that our borders are opened to medicines even from a select list of countries, we run the risk of exposing ourselves to domestic attack.⁷²

Canada, in particular, may be the country of choice for terrorists seeking easy access to the United States. A research arm of Congress has found that Canada - a technologically advanced, modern liberal democracy with relatively lax immigration laws, flexible asylum policies, technological advancement, and long borders and coastlines - has become “a favored destination for terrorists and international criminals.”⁷³ According to the Canadian Security Intelligence Service, “more than

⁷¹ Anthony E. Daniels and Philip R. Manuel, *Dangerous Medicine: American Consumers at Risk from Prescription Drug Reimportation*, Manuel, Daniels, Burke International, LLC, Sept. 16, 2002, at 5.

⁷² *Id.* at 5.

⁷³ LaVerle Berry et al., Fed. Research Div., Library of Congress, *Nations Hospitable to Organized Crime and Terrorism*, at 146. (Oct. 2003).

50 terrorist groups are believed to be operating in Canada.”⁷⁴ Canada’s Special Senate Committee on Security and Intelligence has also indicated that “a few terrorists can ultimately gain entry to the United States by circumventing Canadian and United States border controls.”⁷⁵

The FDA has specifically acknowledged the increased risk of terrorism that would be posed were Canadian borders legally opened to drug importation. Lester Crawford, then-FDA Deputy Commissioner, when asked in a 2002 Congressional hearing whether importation from Canada posed greater challenges in light of current terrorism concerns than it did previously, responded:

The problem would be if it becomes apparent to the rest of the world, including the world of terrorists that we are not interdicting shipments of drugs that come from Canada or Mexico, the contiguous States, either one or both, then I think this is a signal to a would-be terrorist that this might be a way to enter the United States.⁷⁶

A more recent analysis conducted by a leading international risk management organization concluded that, “[c]urrent legislative proposals to allow the importation of drugs from Canada would create new, lucrative opportunities for terrorists in Canada seeking to generate funds from drug counterfeiting. Legalizing the importation of drugs would also facilitate a terrorist attack on the medicine supply. Instead of smuggling drugs across the border, a strike could be launched by sending tainted drugs through the mail system or adulterating drugs bound for the U.S.”⁷⁷ In light of analyses such as these, HHS and FDA should put renewed energy into strengthening our drug distribution system, rather than weakening it. Certainly, any scheme that would weaken the system in a manner that would expose American citizens to the very real possibility of a terrorist attack – as would importation outside the current legal framework - should be rejected.

5. Importation Would Negatively Impact Risk Management and Pharmacovigilance Programs

The legalization of drug importation would also have a significant, negative impact on the ability of the FDA and the pharmaceutical industry to conduct effective drug risk management and pharmacovigilance programs. One of the key functions of both FDA and pharmaceutical companies is to monitor and assess safety-related events that are reported for approved drugs. By tracking reported adverse event data, the Agency and the drug manufacturers are able to determine whether labeling changes or other corrective action for a marketed product are warranted.

⁷⁴ *Id.* at 147 (citing Canadian Security Intelligence Service Director Ward Elcock, in Jonathan Dube, *Safe Haven for Terror?* ABCNEWS.com Jan. 14, 2000).

⁷⁵ *Id.* (citing Canada, Senate, Special Committees on Terrorism and Public Safety, *Response to Recommendations of Senate Special Committees on Terrorism and Public Safety*, Jan. 1999).

⁷⁶ *Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriation For 2003: Hearings before the Subcomm. on Agriculture, Rural Development, Food and Drug Admin. and Related Agencies of the House Comm. on Appropriations*, 107th Cong. (2002) (statement of Lester M. Crawford, Deputy Comm’r, Food and Drug Administration).

⁷⁷ Global Options, Inc., *An Analysis of Terrorist Threats to America’s Medicine Supply* (May 2003).

The presence of adulterated, misbranded and counterfeit drugs on the market would interfere with this function by compromising adverse event data and Medwatch reports. If, for example, a consumer ingests counterfeit Lipitor® and experiences an adverse event which they or their doctor report to FDA and/or Pfizer, that event will be entered into the Lipitor® post-marketing safety database, even though the offending product was not, in fact, Pfizer's Lipitor®. It is unlikely that Pfizer or FDA would be able to differentiate between reports involving "true" brand products or reports involving adulterated, misbranded or counterfeit products. "False positive" data will be entered into the database along with data for legitimate products, with no way to distinguish between the two. This could increase both the number and type of adverse events reported for a particular product. FDA and the regulated industry would have a difficult time implementing and maintaining effective risk management and pharmacovigilance programs on the basis of faulty adverse event data. These significant "data skewing" hazards would thus compromise risk management programs and pharmacovigilance systems, ultimately compromising the health of the American consumer.

D. Limiting Expansion of the Closed System to Imports from Canada Would Not Ensure Product Safety

Any effort to expand the closed system to include other geographic regions would increase the risk that dangerous products will enter the U.S. drug supply. As more entities throughout the world distribute drug products, the likelihood of interference with our drug supply would increase exponentially. At the same time, our ability to monitor and account for drugs distributed throughout the world, as well as to enforce against those interfering with our drug supply, would decrease exponentially.

Significant safety repercussions would result, even if expansion of the closed system were limited to Canada. Canadian government officials have clearly indicated that they are unable to assure the safety of drug products shipped to the United States from Canada.⁷⁸ Canada is simply unable to regulate its export market to ensure that exported drugs are safe and effective, and not counterfeit or contaminated. As noted by FDA, "even if the Canadian system is every bit as good as ours . . . the Canadian system is open to vulnerabilities by people who will try to enter the [United States] market because . . . that's where the money is."⁷⁹

1. Drugs Imported to the United States from Canada Pose Real Risks to Public Health and Safety

Canada's drug supply is inundated with drugs that are counterfeit, adulterated, misbranded, dangerous, and unapproved by the FDA. In particular, as the FDA has acknowledged, Canada has experienced – and continues to experience – significant problems with counterfeiting and wholesale

⁷⁸ During a July 9, 2002 hearing before the Senate Special Committee on Aging, William K. Hubbard reported that Canadian officials expressly told him that if drug importation from Canada into the U.S. became legal, they could not take responsibility for the safety of the products. See *Buyer Beware: Public Health Concerns of Counterfeit Medicines: Hearing before the Senate Special Comm. on Aging*, 107th Cong. 82 (2002).

⁷⁹ *Comparative Pricing* hearing, *supra* note 3 (statement of William K. Hubbard).

diversion. The Royal Canadian Mounted Police has acknowledged that Canada has an “established counterfeit industry” and that counterfeiting in Canada has reached “an epidemic.”⁸⁰

While Canada regulates its own supply of drugs for sale to Canadian citizens, it does not regulate transshipped drugs that are not intended for use in Canada. Therefore, FDA has repeatedly expressed concern that a bill that allows importation from Canada would make Canada “a transshipment point for legitimate or non-legitimate manufacturing concerns throughout the world, and in many cases we would not be able to determine the true country of origin.”⁸¹ There is simply no way to prevent importation of these drugs into the United States. In the absence of any feasible testing mechanism to ensure that drug shipments do not contain commingled counterfeit products, FDA has repeatedly indicated that the opportunity for potentially dangerous counterfeit drugs to enter the U.S. would substantially increase if importation from Canada were permitted.

Internet pharmacies located in Canada – like others throughout the world - pose an additional threat to U.S. consumers. Such sites make it particularly easy for customers to order prescription drugs from locations outside the United States, but are exceedingly difficult for the FDA to monitor. Statements from the Internet export operators themselves demonstrate their intent to find new sources of inexpensive products. If drug importation from Canada is permitted, it would be much harder to control drugs coming into the United States and to prevent the commingling of counterfeit drugs with FDA-approved drugs.

The FDA is clearly aware of the serious risks posed by Canadian drug imports. The Agency has repeatedly stressed that it cannot assure the safety of drugs arriving from Canada, and that Canadian officials are not able to provide such a guarantee. In particular, former FDA Commissioner Mark B. McClellan has historically been a staunch opponent of drug importation and has expressed significant concerns about the safety of drugs from Canada.⁸²

Some have suggested that limiting such drug imports to those from
Canada would address these potential safety concerns. But FDA

⁸⁰ Dr. Merrill Matthews, Jr., *The Ethical Dilemmas of Prescription Drug Reimportation*, Institute for Policy Innovation Ideas, Issue No. 19 (April 2003).

⁸¹ Letter from Lester M. Crawford to Sen. Thad Cochran, *supra* note 58 (“Legislation that would establish other distribution routes for drug products, particularly where those routes routinely traverse a U.S. border, creates a wide inlet for counterfeit drugs and other dangerous products that are potentially injurious to the public health and a threat to the security of our nation’s drug supply.”); *see also* Letter from William K. Hubbard to Dr. Ram Kamath and Scott McKibbin, *supra* note 37 (“An importation plan such as [Illinois], with no reliable anti-counterfeiting measures included and with some fundamental misunderstandings of how drugs are distributed in Canada, could encourage counterfeiters to increasingly use Canada as an entry point for the U.S. market.”); *see also* Warning letter from FDA to Carole Becker, President, Discount Prescriptions from Canada, Inc. (Feb. 18, 2004) (“Moreover, there is a possibility that drugs, which come to U.S. consumers through Canada, or purport to be from Canada, may not actually be Canadian drugs. In short, drugs delivered to the American public from foreign countries may be very different from products approved by FDA and may not be safe and effective. For all of these reasons, FDA believes that operations such as yours expose the public to significant potential health risks.”).

⁸² *See, e.g.*, Letter from Mark B. McClellan, Commissioner, Food and Drug Administration, to Diane C. Gorman, Assistant Deputy Minister, Health Products and Food Branch, Health Canada (February 12, 2004) (“[W]e continue to find numerous safety problems involving prescription drugs being mailed into the United States from Canada outside of effective regulatory oversight.”)

cannot guarantee the safety of Canadian drugs. Additionally, Canadian health officials have made clear in public statements that they can provide no assurance as to the safety and authenticity of drug products shipped to Canada for resale in other countries. In fact, the Agency has concrete examples of drug products shipped to Canada that violate safety provisions established by FDA and by state pharmacy authorities, and we have seen instances of internet sites that offer to sell FDA-approved drugs, but upon further investigation we have determined that the drugs they sell are adulterated, sub-potent, or counterfeit.⁸³

Dr. McClellan has also noted:

We have seen many examples of drugs that appear to be from Canada but pose significant dangers to American consumers. Examples include expired drugs, substitution of the wrong drug, unrefrigerated shipments of drugs that must be kept cool, sale to American women of drugs that are potent causes of birth defects (and so are tightly controlled in the U.S.), failure to include proper instructions and warnings, and other problems that would rarely be seen in purchases from licensed U.S. pharmacies. We have seen Internet sites purporting to be Canadian that appear to be in other countries, and Canadian pharmacies that claim to sell only U.S.-made drugs that actually send the consumer drugs from developing countries. While FDA works to protect Americans from such potentially unsafe unapproved drugs, we do not have the ability or the resources to assure the safety of unapproved imported drugs that claim to be “just as good” as FDA-approved drugs. Consequently, FDA cannot condone any program that encourages Americans to use unapproved and potentially unsafe drugs.⁸⁴

Unless and until the FDA can guarantee that drugs being imported into the United States from Canada are safe – and it has repeatedly acknowledged that it cannot do so - it is a farce to suggest that importation from Canada poses fewer or less serious risks than importation from other countries.

2. **FDA and Other Government Officials Are Aware of, and Have Acted to Prevent, the Dangers Posed by Imports from Canada**

The specific risks associated with imports from Canada are widely known not only to the FDA, but also to officials from HHS, Congress, Customs, and the Office of Management and Budget, among others.⁸⁵ In addition to the statements made by former FDA Commissioner McClellan (see above),

⁸³ Letter from Mark B. McClellan to Sen. Thad Cochran (R-MS) (June 19, 2003).

⁸⁴ Letter from Mark B. McClellan to Gov. Rod R. Blagojevich, State of Illinois (September 23, 2003).

⁸⁵ See, e.g., Executive Office of the President, Office of Management and Budget, *Statement of Administration Policy: S.1427, Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill, FY 2004* (Nov. 5, 2003)

the FDA has also taken a wide range of actions to alert companies and consumers to the serious risks associated with imported drugs.⁸⁶

The FDA has issued numerous Warning Letters to companies importing drugs from Canada outside of the current legal framework. In these Warning Letters, the Agency has expressed its dire concerns over Canadian drug importation. For example, on September 16, 2003, the FDA issued a Warning Letter to CanaRx Services, Inc. of Detroit, Michigan, a company that ran an Internet website and mail operation. The FDA notified the firm that its operation illegally caused the shipment of prescription drugs from a Canadian pharmacy into the U.S., subjecting Americans to dangerous imported drug products. The FDA had evidence that the company shipped insulin in a manner that did not ensure proper refrigeration and storage conditions, and considered these operations to be illegal and a risk to public health. Then-Commissioner McClellan stated, “[f]irms like this should not continue to profit through illegal actions that put the health of the American public at risk. . . . Our investigation has shown that CanaRx operates a drug purchasing arrangement that channels drugs through companies other than licensed pharmacies and does not consistently use shipping practices that ensure its drugs are safe and effective.”⁸⁷

In February of this year, the FDA also issued a Warning Letter to Discount Prescriptions, Canada, after learning that the company ran an operation that sent U.S. prescriptions, credit card information, and paperwork to CanAmerican Drugs, Inc. (“CanAm”), in Manitoba, Canada. Under the companies’ arrangement, CanAm would then arrange for a corresponding prescription from a Canadian doctor, fill the prescription, and send the drugs directly to the U.S. consumer. The FDA warned:

(“. . . [T]he Administration believes that allowing importation of drugs outside the current safety system established by the Food and Drug Administration would threaten public health and result in unsafe, unapproved, and counterfeit drugs being imported into the United States.”); *Administration’s FY 2003 Budget Proposals for Prescription Drugs*, Hearing Before the Senate Committee on Finance, 107th (2002) (Testimony of Mr. Tom Scully, Administrator of the Centers for Medicare and Medicaid Services) (“Well, we have opposed [importation] for FDA reasons, which is that it’s impossible for us to regulate and monitor. . . . FDA obviously decides what is safe and efficacious. There’s no way for FDA to monitor and regulate drugs coming in from Canada or Mexico or other countries. . . . [T]he Clinton Administration took exactly the same position, that it wasn’t related to health policies, it was related to health safety, and the fact that there’s no way for us to guarantee the safety of patients for drugs coming back in over the borders.”); *Continuing Concerns* hearing, *supra* note 5, at 9 (statement of Rep. John D. Dingell (D-MI)) (“Our systems for protecting U.S. consumers from drugs of poor or dangerous quality are eroding, as recent evidence bears out. . . . This is not a new problem, and FDA has been put on notice about it for years. . . . Customs now freely admits that while the present system envisions that its staff hold all pharmaceuticals for FDA review when they enter the country, in reality, *most* are delivered to consumers without knowing whether these drugs are safe.”).

⁸⁶ FDA has engaged in a wide range of activities, including but not limited to the issuance of Warning Letters and press releases, publication of articles, and dissemination of advertising warning health professionals and consumers of the risks posed by imported drugs.

⁸⁷ FDA Press Release, *FDA Warns CanaRx Services About its Illegal Internet Website and Mail Operation Obtaining Unapproved and Potentially Risky Drugs from Canada*. (Sept. 16, 2003); Warning Letter from FDA to Joseph K. Todd, Jr., Regional Manager, CanaRx Services, Inc. (Sept. 16, 2003); Warning Letter from FDA to Robert Howard, Shipping Manager, CanaRx Services, Inc. (Sept. 16, 2003); Warning Letter from FDA to G. Anthony Howard, Shipping Manager, CanaRx Services, Inc. (Sept. 16, 2003); *see also* Letter from William K. Hubbard to Gregory Gonot, Deputy Attorney General, State of California (Aug. 25, 2003) (noting shipment of insulin to U.S. from Canada without proper refrigeration).

Prescription drugs purchased from foreign countries generally are not FDA-approved, do not meet FDA standards, and are not the same as the drugs purchased in the United States. Drugs from foreign countries do not have the same assurance of safety as drugs actually regulated by the FDA. Because drugs from foreign countries have been manufactured, shipped, held and/or repackaged outside of FDA's safety oversight, they could be outdated, contaminated, counterfeit or contain too much or too little of the active ingredient. In addition, foreign dispensers of drugs to Americans may provide patients with incorrect medications, incorrect strengths, medicines that should not be used in people with certain conditions or with other medications, or medications without proper directions for use. These risks are exacerbated by the fact that many of the products that you are soliciting U.S. consumers to buy are indicated for serious medical conditions.⁸⁸

Given that HHS and FDA are well aware of the serious dangers that are already posed by imported drugs from Canada, they should not permit even a limited expansion of the drug distribution system to include drugs imported from Canada. Such a decision would undoubtedly be arbitrary and capricious, in light of the overwhelming and unambiguous factual record documenting widespread safety concerns and dangers associated with imported drugs.

E. Safety Risks Cannot be Quantified

Based on the FDA's import blitzes and the overwhelming evidence of extensive counterfeiting practices worldwide, it is clear that unapproved, adulterated, misbranded, counterfeit and otherwise dangerous drugs are currently entering the United States in significant numbers. The FDA must assume that the number of such drugs that would enter the United States under any importation scheme would increase exponentially. Given the FDA's inability to process the vast number of imports coming into the country, however, as well as the difficulties in tracking which unapproved drugs end up in the hands of consumers, it is impossible to quantify, with any precision, the actual number of Americans who have been injured to date, or who may be injured in the future.

It should be emphasized that adverse reactions and ineffective products are routinely underreported. Such underreporting is likely to be accentuated with regard to imported drugs as many of these drugs are imported outside of the legal and regulatory system. Consumers who have ordered drugs online from pharmacies in Canada, or who have crossed into Mexico or Canada to bring back medication, may be reluctant to report to the FDA and/or their doctors if they suffer an injury as a result. This may be particularly true where there has not been any physician involvement in prescribing the drug in the first place.

Moreover, injuries caused by unapproved drugs may take time to develop. Not all counterfeit or adulterated products contain poisonous materials or excessive dosages that would be likely to cause an immediate, severe reaction. Rather, products are often subpotent, and may therefore be ineffective. Injuries based on the absence of efficacy may take time to develop; a drug may simply

⁸⁸ Warning Letter from FDA to Carole Becker, *supra* note 80.

fail to be fully effective at treating the underlying condition, and the condition may become worse and injure the patient over time. In such circumstances, the consumer or his/her doctor may never attribute the adverse health consequences to the adulterated drug itself.

On several occasions, the FDA has been asked to explain why the Agency has not documented numerous deaths and injuries from imported drugs, given the extensive risks these drugs pose. FDA official William K. Hubbard has consistently explained in Congressional testimony that it is simply not possible to know how many people have been injured based upon the absence of reporting and tracking. In addition, he has noted that efficacy problems may not be identified immediately, and may not be attributed to the actual drug:

Well, one answer is that we believe that people that purchase these products in such surreptitious ways tend not to want to report them if they do have a problem. And to be quite honest, there could be lots of people out there whose blood pressure is not being controlled or whose infections are not being adequately treated or otherwise are not getting adequate treatment, and they are slowly – their health is slowly deteriorating. But we won't know that, because they were unhealthy to begin with.⁸⁹

Mr. Hubbard confirmed the same position in 2003, when he was asked to opine as to the number of American citizens who have died as a result of taking imported drugs.

We believe that is an unknowable thing . . . because there is no system that tracks such injuries. And people that buy these drugs will tend to be not the sort of people that would report. They recognize that they bought them outside of the normal practice to buy them. But . . . the more likely injury from these drugs is that someone would not have their disease treated. You do not take a fake drug and have an adverse effect because it just does nothing. What happens is your illness is not treated, and that effect can occur over many months or even years. . . .

Generally many of these drugs themselves are not going to immediately hurt you. They are just not going to help you. And the purpose of taking a drug, of course, is to treat an illness, not to just take a placebo or a sugar pill. And many of these drugs in fact are just that, they are subpotent or they are lacking in any active ingredient. You would not expect an injury from that, but you also would not get the medicinal treatment that the drug was intended for.⁹⁰

⁸⁹ *Examining Prescription Drug Importation: A Review of a Proposal to Allow Third Parties to Reimport Prescription Drugs: Hearing Before the Subcomm. on Health of the House Comm. on Energy and Commerce, 107th Cong. 52-53 (2002) (statement of William K. Hubbard).*

⁹⁰ *A System Overwhelmed* hearing, *supra* note 6, at 63-64 (statement of William K. Hubbard).

While it is simply not possible to predict or assess the number of deaths and/or serious injuries that would result if importation were permitted outside the current legal framework, there is no doubt that the potential for such serious adverse events would be significant. The Secretary, therefore, should not permit any expansion of our current closed drug distribution system.

IV. FDA's Inability to Ensure the Safety of Drug Imports by Testing Drugs Upon Importation

A. Overview

In its Federal Register notice, FDA questioned what the Agency should do to assure the safety of imported drug products. Specifically, FDA questioned whether it should “examine all imports,” or use “a sampling method, along with testing” to assure safety.⁹¹ Pfizer believes that any notion that testing all imports, or a percentage of imports, would somehow assure the safety of all imported drugs is misguided. No testing conducted at the border, or upon importation, would ever be sufficient to ensure the safety of imported drug products.

Drug safety can only be assured if drug shipments are handled by appropriately licensed and inspected entities and if drug products are in compliance with FDA GMPs throughout the entire manufacturing, distribution, and storage process. If drug importation were permitted outside of the current legal framework, a wide range of unapproved drug products would appear at our borders – including drugs never approved by the FDA, counterfeit drugs, contaminated drugs, banned drugs, drugs mishandled in the distribution process, and drugs diverted from around the world into the United States (through Canada, for example).

There is no test or test protocol that could be established to ensure that imported drugs are FDA-approved and have been handled in a manner that guarantees product safety and efficacy. There is no test or test protocol capable of testing for every possible contaminant that could have been added (intentionally or unintentionally) to a drug product. Moreover, even though test methods exist to authenticate that a drug product contains the stated active ingredient(s) and is not counterfeit, testing can not guarantee that the product was handled in an appropriate manner (*e.g.*, stored and distributed such that it was not exposed to sunlight, heat, cold, freezing, or other ambient influences that might compromise safety or efficacy).

The potential commingling of authentic, FDA-approved products with contaminated or counterfeit drugs within the same package also precludes the ability to test at the border for product safety and efficacy. Indeed, the FDA has stated:

[T]here is no testing that can ensure that the shipment of drugs does not contain counterfeits. Since counterfeits can easily be commingled with authentic product, either by the case, by the bottle, or by the pill, there is no sampling or testing protocol sufficient to protect against the grave public harm they pose. No random sampling plan will be able to detect and protect such criminal conduct since the threat does not depend upon the nature of the reimported product, but upon the integrity of those handling it.⁹²

⁹¹ 69 Fed. Reg. 12810, 12811 (Mar. 18, 2004).

⁹² Letter from Lester Crawford to Sen. Thad Cochran, *supra* note 58 (emphasis added).

Testing a product after it has been manufactured and processed is known as “end-product testing.” FDA has always taken the position that end-product testing is insufficient to ensure drug safety, efficacy, and quality. Moreover, such testing would be infeasible due to massive associated costs and the numerous procedural impediments that would exist at the border. The complexity and resources associated with such efforts would also inevitably compromise other important border control efforts, both with respect to other FDA-regulated products and other Homeland Security objectives.

B. Testing Drug Products at the Border Would Not Ensure the Safety of Drug Imports

End-product testing cannot guarantee the safety and efficacy of imported drug products. FDA has long taken the position that end-product testing is not a viable means of assuring that a drug was manufactured, processed, and handled in accordance with FDA standards.

FDA’s drug GMP regulations ensure that drug products are consistently produced and controlled according to quality standards by covering all aspects of manufacture and distribution, including: (1) personnel (*e.g.*, disease control, cleanliness, education and training, and supervision); (2) buildings and facilities (*e.g.*, sanitation, plant construction and design, sewage, and plumbing); (3) equipment (*e.g.*, design, construction, and maintenance); (4) control of components and drug product containers and closures (*e.g.*, storage, testing, and retesting of components, containers, and closures); (5) production and process controls (*e.g.*, written standard operating and testing procedures and control of microbiological contamination); (6) packaging and labeling controls; (7) holding and distribution; (8) laboratory controls; (9) records and reports; and (10) returned and salvaged products.⁹³

The detailed procedures required by the GMP regulations are essential given that each regulated process could affect the quality of the finished product. GMPs ensure that manufacturers have proof that the correct procedures have been implemented in each step of the manufacturing process – every time a product is made.

FDA has repeatedly stated that end-product testing is an unacceptable, ineffective and insufficient way to ensure product safety. In 1987, for example, FDA published a guidance document, entitled “Guidelines on General Principles of Process Validation,”⁹⁴ which stated in no uncertain terms that process validation, not end-product testing, is the “key element” in assuring product quality. According to those guidelines, “[q]uality cannot be inspected or tested into a finished product.”⁹⁵ The FDA’s guidelines explained that:

Due to the complexity of today’s medical products, routine end-product testing alone often is not sufficient to assure product quality for several reasons. Some end-product tests have limited sensitivity In some cases, destructive testing would be required to show that the manufacturing process was adequate, and in other situations,

⁹³ 21 C.F.R. Parts 210 and 211 (2003).

⁹⁴ FDA’s Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, and Center for Devices and Radiological Health, *Guidelines on General Principles of Process Validation* (May 1987, reprinted Feb. 1993).

⁹⁵ *Id.*

end-product testing does not reveal all variations that may occur in the product that may impact on safety and effectiveness. . . .⁹⁶

Similarly, the WHO has emphasized the need to build quality into the manufacturing process, rather than to attempt to test the quality of a finished product.⁹⁷ Recognizing that GMPs provide the gold standard for product safety, the WHO has observed that:

GMP[s] prevent errors that cannot be eliminated through quality control of the finished product. . . . Without GMP[s] it is impossible to be sure that every unit of a medicine is of the same quality as the units of medicine tested in the laboratory.⁹⁸

If HHS were to allow importation outside the current closed system, the FDA would be unable to confirm that the imported product was handled in accordance with GMPs throughout its chain of custody, and could not assure that the product was unadulterated. End-product testing is simply not an effective method for ensuring compliance with GMPs, or ensuring that drugs were handled, distributed, and stored in an appropriate manner to prevent adulteration.

Accordingly, if HHS permitted commercial and personal importation of prescription drugs, checked only by end-product testing, the Department would essentially be establishing a safety standard for imported drug products that is far inferior to the safety standard required for domestic drug products. The influx of inferior imported drug products would significantly compromise the overall U.S. drug supply, which is currently the safest in the world.

C. The Costs and Procedural Impediments Associated with Border Testing Are Excessive

As noted previously, it is currently estimated that over 20 million packages of drug products are imported into the United States each year.⁹⁹ It is entirely unrealistic to assume that each of the more than 20 million packages would be opened and subjected to a battery of end-product tests. We believe it is virtually impossible for one to estimate the number of people required for such a massive undertaking. Moreover, the time required to conduct the testing would significantly impact drug distribution and, potentially, the health of individuals waiting to obtain the release of their drug shipments.

⁹⁶ *Id.*

⁹⁷ See World Health Organization, *Good Manufacturing Practice (GMP) in Pharmaceutical Production*, at <http://www.who.int/medicines/organization/qsm/activities/qualityassurance/gmp/orggmp.shtml> (last visited Apr. 19, 2004).

⁹⁸ *Id.*

⁹⁹ It is important to note that this 20 million package estimate reflects what is currently – and in all probability unlawfully – imported. If importation were made legal, the actual number of packages entering the United States from abroad would increase substantially.

The specter of end-product testing also raises the question of what tests should be utilized, and who should conduct the tests. Product identity authentication tests are complex, multi-faceted, and proprietary.¹⁰⁰ It is unclear who would conduct the tests (the MMA provides only that testing would be conducted by the importer or manufacturer at “qualified labs” that would be “qualified” by the FDA) and who would bear the associated financial burden. The FDA certainly lacks the resources to engage in such testing, as does Customs.

Moreover, even if testing each package of imported drugs were feasible, doing so would not protect public health. FDA officials have already documented their concerns regarding the commingling of authentic products with counterfeit or contaminated products within the same bottle and shipment. In light of this very real concern, true safety testing would require analyzing each tablet or capsule – and not simply one sample within a large lot or package.

In practice, we believe the costs associated with such testing would well exceed initial estimates provided by the FDA. Authentication testing alone, for solid oral dosage form drug products, entails four tests to assess: (1) identity; (2) potency; (3) purity; and (4) dissolution. Performing these extensive tests on a single batch ordinarily requires two to four days. Based upon the number of required tests and the applicable time-line, typical authentication testing would clearly be cost-prohibitive for every drug batch. Moreover, authentication testing for certain types of drug substances may be even more complex and time-intensive.

In a letter to Senator Thad Cochran (R-MS), the FDA conceded that end-product testing generally “would be an enormous undertaking” and “would be costly and time consuming, both for the government and importers.”¹⁰¹ More recently, former FDA Commissioner Mark B. McClellan stated in a letter to House Energy and Commerce Committee Chairman Billy Tauzin that the government resources associated with product testing would likely be substantial, with initial estimates projecting the cost of partial testing at over \$50 million.¹⁰² Importantly, this estimate would represent only a portion of all related costs; in testimony before the Senate Commerce,

¹⁰⁰ Proprietary test methods clearly constitute “trade secrets” under both Federal and state law. Moreover, compelling disclosure of authentication trade secrets to multiple parties, with multiple employees, located throughout the United States, would inevitably lead to the unauthorized disclosure of proprietary trade secrets, whether that disclosure be intentional or unintentional. It is axiomatic that the Fifth Amendment’s Takings Clause prohibits the government from taking “trade secrets” without just compensation. See *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1001-04 (1984); *Philip Morris, Inc. v. Reilly*, 312 F.3d 24, 32-46 (1st Cir. 2002) (*en banc*). To determine whether a particular regulation effects an unconstitutional taking, courts balance three factors: (1) the economic impact of the regulation; (2) whether the governmental action interferes with reasonable investment-backed expectations; and (3) the character of the governmental action. *Reilly*, 312 F.3d at 33. Here, the economic impact would be substantial and would clearly interfere with the reasonable expectation that drug company “trade secrets” would be protected against disclosure to non-governmental entities. In addition, the character of the government action would be highly suspect because the testing program established by the MMA would be entirely ineffective and would not ensure public health safety. Accordingly, requiring drug companies to disclose test methods to non-governmental entities such as wholesalers and importers would constitute a “regulatory taking” and would require the government to provide “just compensation” to drug manufacturers.

¹⁰¹ Letter from Lester Crawford to Sen. Thad Cochran, *supra* note 58.

¹⁰² Letter from Mark B. McClellan to Rep. W.J. “Billy” Tauzin, Chairman, House Comm. on Energy and Commerce (July 18, 2003).

Science and Transportation Committee on March 11, 2004, McClellan estimated these costs to be as high as hundreds of millions of dollars.¹⁰³

Pfizer believes that given the serious safety concerns related to bioterrorism, counterfeit drugs, mislabeled or adulterated drugs, pharmacy quality and safety practices, and physician supervision, it is safe to assume that costs incurred based upon implementation of a drug importation scheme could easily run into the billions of dollars. These costs, which would in all likelihood be passed on to American taxpayers, would dwarf any potential costs savings allegedly associated with the MMA or any other scheme encouraging importation.

¹⁰³ *Options for Safe and Effective Prescription Drug Importation: Hearing Before the Senate Comm. on Commerce, Science and Technology, 108th Cong. (2004) (Testimony of Mark B. McClellan); see also FDA Week, \$58 Million for Canadian Rx Reimportation Program Based on Outdated Estimate, (March 19, 2004).*

V. **Existing Legal Authorities Prevent the Secretary From Certifying that Prescription Drugs Imported into the U.S. from Canadian Wholesalers and Pharmacies Are Safe**

Numerous provisions of the FFDCA prevent the Secretary from certifying that prescription drugs imported into the U.S. from Canadian wholesalers and pharmacies are safe and in compliance with FDA legal and regulatory requirements. Specifically, Sections 501, 502, 505, and 801 of the FFDCA establish adulteration standards,¹⁰⁴ mandatory labeling requirements,¹⁰⁵ the NDA requirements,¹⁰⁶ and import requirements,¹⁰⁷ respectively. Compliance with these provisions is essential to establishing safety. Accordingly, FDA cannot distinguish between safety issues and issues associated with compliance with the provisions of the FFDCA. Both concepts are inextricably linked, and until it can be determined that the drugs imported from, or through, Canada meet these provisions, the Secretary cannot certify to the safety of the MMA importation scheme.

A. **Adulterated Products Are Not Safe - Compliance with GMPs Is Essential to Establishing Product Safety**

Although other provisions of the FFDCA inhibit the Secretary's ability to certify that drugs imported outside of the current legal framework are safe, section 501(a)(2)(B) of the FFDCA is particularly instructive because of the absolute necessity for a drug product marketed in the U.S. to comply with current GMPs.¹⁰⁸

Under the FFDCA, a drug is adulterated if "the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with good manufacturing practice to assure that such drug meets the requirements of [the FFDCA] as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess."¹⁰⁹ The purpose of § 501(a)(2)(B) is to "provide assurance that drug product quality would not fall below that which is feasible and available under contemporary technology."¹¹⁰

In accordance with its authority under this section, FDA promulgated GMP regulations, which can be found at 21 C.F.R. parts 210 and 211. These quality control regulations are designed to prevent "super and sub-potency, product mix-ups, contamination, and mislabeling."¹¹¹ They provide that the "failure to comply with any [GMP] regulation set forth in parts 211 through 226 . . . shall render

¹⁰⁴ 21 U.S.C. § 351 (1999 & Supp. 2003).

¹⁰⁵ 21 U.S.C. § 352 (1999 & Supp. 2003).

¹⁰⁶ 21 U.S.C. § 355 (1999 & Supp. 2003).

¹⁰⁷ 21 U.S.C. § 381 (1999 & Supp. 2003).

¹⁰⁸ 21 U.S.C. § 351 (1999 & Supp. 2003).

¹⁰⁹ 21 U.S.C. § 351(a)(2)(B) (1999 & Supp. 2003); *see also U.S. v. Barr Labs., Inc.*, 812 F. Supp. 458, 465 (D.N.J. 1993).

¹¹⁰ 43 Fed. Reg. 45014, 45020 (Sept. 29, 1978).

¹¹¹ *Barr Labs.*, 812 F. Supp. at 465.

such drug to be adulterated under Section 501(a)(2)(B) of the [A]ct and such drug, as well as the person who is responsible for the failure to comply, shall be subject to regulatory action.”¹¹² Indeed, it is well recognized that “the employment of [GMPs] will assure that a particular drug is safe and reliable.”¹¹³ “The ultimate test of GMP, therefore, is whether it results in a product which possesses the characteristics which the manufacturer represents it to have and whether the methods used to produce it are designed to assure that result.”¹¹⁴

Clearly, section 501(a)(2)(B) and its implementing regulations provide a substantial obstacle for the Secretary to certify that drugs imported from Canada are safe. The GMP regulations set minimum standards for drug manufacturers and are critical to ensuring quality control and protecting public health. As noted in the previous section, upon importation there is no way to test drugs to ensure that they have been manufactured, shipped, stored, and distributed in accordance with GMPs and under appropriate and safe distribution conditions. Accordingly, the Secretary would have no way of knowing whether imported drug products comply with the requisite GMP requirements. In the absence of an assurance that imported drug products were handled, shipped, stored, and distributed in accordance with GMPs, such products must be assumed to pose a significant safety hazard and are adulterated as a matter of U.S. law.¹¹⁵

B. Misbranded Products Are Not Safe – Compliance with Labeling Requirements Is Essential to Assure Product Safety

Not only is the issue of adulteration a major concern with respect to drugs imported from or through Canada, but adequate labeling is also a crucial safety component. Under the authority of Section 502 of the FFDCA, FDA has established specific labeling requirements for prescription drugs. Ordinarily, these requirements are met via the package insert, which must include: a description of the product, clinical pharmacology, indications and usage, contraindications, warnings, precautions, adverse reactions, drug abuse and dependence, overdose, and dosage and administration information.¹¹⁶ The labeling information serves as “the primary mechanism through which FDA and drug manufacturers communicate essential, science-based prescribing information to healthcare professionals.”¹¹⁷ In addition, many prescription drug products are also accompanied by patient package inserts and “medication guides” intended for use directly by consumers, as well as associated risk management programs that rely upon various labeling elements, from registries to informed consent forms to educational materials, to ensure patient safety.¹¹⁸

¹¹² 21 C.F.R. § 210.1(b) (2003).

¹¹³ *U.S. v. Bel-Mar Labs., Inc.*, 284 F. Supp. 875, 882 (E.D.N.Y. 1968).

¹¹⁴ *U.S. v. Morton Norwich Prods, Inc.*, No. 75-CR-114 (N.D.N.Y. May 11, 1976) (emphasis added).

¹¹⁵ *U.S. v. 789 Cases*, 799 F. Supp. 1275, 1286-87 (D.P.R. 1992).

¹¹⁶ 21 C.F.R. § 201.57 (2003).

¹¹⁷ 65 Fed. Reg. 81082, 81082 (Dec. 22, 2000).

¹¹⁸ *See, e.g.*, Lotronex® and Accutane® risk management programs.

As discussed in Section III, drugs imported from or through Canada, however, may not include the critical information required in FDA-approved drug labeling.¹¹⁹ Without this information, it would be impossible for consumers to determine even the simplest of facts about the imported drug such as whether the product they obtained is the correct prescription (*i.e.*, active ingredient, strength, dosage form, etc.) to treat their condition. The drug labeling also may lack vital information such as possible contraindications, adverse reactions, and other precautions associated with the drug product. In the absence of an assurance that drug products imported outside of the current legal framework will contain appropriate, mandated product labeling, such products must be assumed to pose a significant safety hazard and are misbranded as a matter of U.S. law.¹²⁰

C. Unapproved Products Are Not Safe - Compliance with Section 505 of the FFDCA Is Essential to Guarantee Product Safety

Congress has mandated, and the FDA has implemented, extensive and strict controls on the process of approving new drugs for marketing. Federal laws and regulations governing the NDA process, under section 505 of the FFDCA, illustrate the breadth and depth of information the FDA requires.¹²¹ Extensive information is required in an NDA to ensure product safety and efficacy, including but not limited to:

- **Chemistry, Manufacturing, and Controls (“CMC”) Information** – nomenclature, structural characterization, validation of process and controls, justification of specifications, and stability tests.
- **Nonclinical Pharmacology and Toxicology Information** – the drug’s pharmacological actions, toxicological effects, significance to reproduction, and results from animal testing.
- **Human Pharmacokinetics and Bioavailability Information** – a description of all studies of the drug in humans and an analysis of the pharmacokinetics and metabolism of the drug’s active ingredients.
- **Clinical Data and Safety Information** – all clinical investigations of the drug, including pharmacology studies, controlled-studies, uncontrolled-studies, studies for other uses of the drug, commercial marketing experience, evidence supporting dosage, and safety information.

¹¹⁹ Even if drug manufacturers were required to provide copies of drug labeling to importers and distributors, based upon the number of drug products distributed in the United States (in varying strengths and dosages), the number of individuals in the distribution scheme to whom the requirement would apply, and the practical impossibility of proof-reading lengthy drug labeling, it would be virtually impossible for the FDA or other government officials to adequately review the labeling of all imported drug products. Such a requirement would therefore not be sufficient to eliminate, or even minimize, the issues associated with drug misbranding.

¹²⁰ *U.S. v. 789 Cases*, 799 F. Supp. at 1286-87.

¹²¹ 21 C.F.R. Part 314 (2003).

- **Pediatric Use Information** – studies showing the safety and effectiveness of the drug, and its benefits and risks to the pediatric population.
- **Samples and Labeling Information** – samples of the drug for FDA testing, copies of the drug product label and all product packaging.

NDA submissions also require supporting data, statistical analyses, methodological diagrams, literature reviews, and updates of changes occurring during the application process.

All of this information is necessary for FDA to determine that drug products meet the safety and efficacy requirements established under Section 505 of the FFDCA. Yet the FDA would have no way of confirming whether a drug product at the border was actually approved by the FDA and therefore in compliance with the numerous requirements imposed by Section 505. Based upon the presence in Canada of drugs never approved by the FDA, counterfeit drugs, contaminated drugs, and drugs diverted into Canada from throughout the world and the inability to adequately test imported products for such safety issues, the Secretary would have no way of knowing whether imported drug products are safe.

Since the MMA requires the use of safeguards to ensure absolute compliance with Section 505 of the FFDCA, and such safeguards are nonexistent, the Secretary should be compelled to again refuse to certify to the safety of imported drugs.

D. Section 801 of the FFDCA, Along With Its Underlying Purpose, Prohibits the Importation of Drugs Outside of the Current Legal Framework

The importation provisions of the FFDCA create another obstacle for the Secretary to certify that the imported drugs meet the requirements of the Act and are safe. Under Section 801 of the FFDCA,¹²² FDA must refuse imported food, drugs, devices, and cosmetics admission into the U.S. “if it *appears* from the examination of such samples or otherwise” that:

- (1) the article “has been manufactured, processed, or packed under unsanitary conditions,”
- (2) the article is “forbidden or restricted in sale in the country in which it was produced or from which it was exported,” or
- (3) the article is “adulterated, misbranded, or in violation of section 505 [*e.g.*, unapproved “new drugs”].”¹²³

FDA has historically interpreted this provision as a mandate to refuse to admit not only adulterated FDA products that have been tested and proven to be unsafe, but also products, *with or without any*

¹²² 21 U.S.C. § 381 (1999 & Supp. 2003).

¹²³ *Id.* at § 381(a) (emphasis added).

physical examination that are: (1) misbranded, (2) unapproved “new drugs,” or (3) not manufactured in accordance with GMPs.¹²⁴

The courts have concluded that Section 801 gives FDA extremely broad authority to bar the entry of FDA-regulated products into the U.S. Courts have found that the term “appears” is “a striking and clear indication of Congress’ intent to forego formal procedural requirements,” and that it permits FDA to bar FDA-regulated products “without the introduction of testimony or evidence.”¹²⁵

With regard to drugs imported outside of the current legal framework, FDA has stated that:

[U]napproved prescription drugs and drugs imported from foreign countries by someone other than the U.S. manufacturer do not have the same assurance of safety and efficacy as drugs regulated by the [FDA]. Because the drugs are not subject to FDA oversight and are not continuously under the custody of a U.S. manufacturer or authorized distributor, their quality is less predictable than drugs obtained in the [U.S.]. For instance, the drugs may be contaminated, counterfeit, or contain erratic amounts of the active ingredient or different excipients. Also, the drug may have been held under uncertain storage conditions, and therefore be outdated or subpotent.¹²⁶

FDA is clearly on notice that drugs imported from Canada outside of the current legal framework pose significant safety risks. Such imported drugs would therefore, by definition, “appear” to be in violation of FDA requirements, and - as noted in the previous section - no product testing would be able to ensure product safety. Accordingly, under the statutory mandate of Section 801 of the FFDCa, FDA would be compelled to prohibit the importation of these drug products.

E. No Level of Additional Risk is Acceptable for Imported Drugs

The overriding purpose of the FFDCa is to protect the public health.¹²⁷ Congress has incorporated this paramount objective into FDA’s current mission statement by mandating that FDA “promote the public health” by ensuring that “drugs are safe and effective.”¹²⁸ In addition, FDA has indicated that the Agency’s mission is “to promote and protect the public health by helping safe and effective

¹²⁴ FDA Office of Regulatory Affairs (“ORA”), *FDA Import Program System Information*, at http://www.fda.gov/ora/import/ora_import_system.html. (last visited Apr. 19, 2004).

¹²⁵ See, e.g., *Seabrook Int’l Foods, Inc. et al. v. Harris*, 501 F. Supp. 1086, 1090 (D.D.C. 1980), *aff’d* 674 F.2d 38 (D.C. Cir. 1982); see also *Sugarman v. Forbragd*, 405 F.2d 1189, 1190 (9th Cir. 1969); *Balmaceda v. United States*, 815 F. Supp. 823, 826 (E.D. Pa. 1992) (“[T]he language of the statute clearly affords the FDA with discretion to act without requesting or relying on the results of the testing of samples).

¹²⁶ *United States v. Rx Depot, Inc.*, 290 F. Supp. 2d. at 1241-42 (citing declaration from T. McGinnis, FDA Director of Pharmacy Affairs).

¹²⁷ See, e.g., *U.S. v. Bacto-Unidisk*, 394 U.S. 784, 798 (1969).

¹²⁸ 21 U.S.C. § 393(b) (1999 & Supp. 2003).

products reach the market in a timely way, and monitoring products for continued safety after they are in use.”¹²⁹ As a public health agency, it is inconceivable that FDA would ever advocate for a program that would create a significant additional level of public health risk, particularly if the Agency cannot assure the same level of safety for imported drugs as consumers expect from drugs purchased through state-licensed pharmacies.

The public relies on FDA to safeguard the nation’s drug supply. Consumers expect that the prescription drugs marketed in the U.S. have been evaluated by FDA and determined to be safe and effective. Because of the FDA’s efforts, the U.S. has been a leader in providing safe and effective drugs and has implemented one of the most developed drug approval processes in the world. The public has confidence in the drugs they purchase, and this confidence would be seriously jeopardized if HHS determines that it is permissible to import drugs into the U.S. that may be less than safe and effective. The result would be similar to that seen in other countries, where the government cannot guarantee the safety or effectiveness of drugs and it is common to encounter counterfeit, subpotent or superpotent drug products on the market.

In light of the grave concerns that have been raised about the safety and efficacy of drug products imported from Canada, exposing American consumers to increased health and safety risks by permitting importation of these drugs would create a significant public health hazard and strike a tragic blow to the integrity of FDA’s regulatory framework.

¹²⁹ See FDA, *Protecting Consumers, Protecting Public Health: Overview*, at <http://www.fda.gov/oc/opacom/fda101/sld001.html> (last visited Apr. 19, 2004).

VI. Anti-Counterfeiting Technologies

A. Anti-Counterfeiting Technologies Are Not Sufficient to Prevent the Import of Counterfeit or Unapproved Drug Products

The safety risks associated with imported drug products are not limited to the introduction of counterfeit drugs into the U.S. market. Imported drugs may be unapproved, adulterated, contaminated, and diverted from countries throughout the world. Accordingly, even if anti-counterfeiting technologies were capable of preventing counterfeit drugs from entering the U.S., they would be incapable of eliminating other risks not necessarily associated with counterfeits.

The most effective way to protect the American public from counterfeits is to strengthen the closed U.S. drug distribution system. Only by requiring heightened diligence and increased accountability from those who operate within the closed U.S. drug supply chain can the introduction of counterfeits into the drug distribution system be effectively avoided. While anti-counterfeiting technologies may add an incremental safety benefit when utilized under this closed system, there is no way they can assure the safety of the drug supply if that system is expanded to allow the importation of drugs from foreign sources.

FDA recently recognized that “[b]ecause the capabilities of counterfeiters continue to evolve rapidly, there is no single ‘magic bullet’ technology that provides any long-term assurance of drug security.”¹³⁰ Pfizer agrees that there is no “magic bullet” technology that provides long-term assurance of drug security. However, while we continue to believe that no technology would adequately protect the American public from the safety concerns associated with drugs imported outside of the current legal framework, we nevertheless recognize that a combination of rapidly improving track-and-trace and product authentication technologies has the potential to provide a greater level of security for a closed U.S. drug supply system.

Several different types of anti-counterfeiting technologies - authentication technologies, track-and-trace technologies and unit-of-use technologies - have existed for many years. These technologies, while different, are complimentary. They should be understood as a series of barriers that: (1) start with overt and recognizable features identifiable to the public as an intimate part of the packaging; (2) incorporate covert security features used by inspectors, often requiring simple verification instruments and readers; and (3) utilize unequivocal forensic level features to prove authenticity. Generally, authentication technologies allow end users or professionals to make certain that a drug is, in fact, the product it appears to be. Track-and-trace technologies allow end users or professionals to determine where the product has been and how it moved from place to place. Finally, unit of use technologies include all container closure systems and tamper-proof labeling.

¹³⁰ *Combating Counterfeit Drugs*, *supra* note 33, at i.

Authentication technologies fall into three categories:¹³¹

- **Overt authentication technologies** - Protective measures that are easily visible to the naked eye, such as holograms, color shifting inks, and watermarks;
- **Covert authentication technologies** - Protective measures that are not visible without the use of special equipment, such as invisible bar codes and certain inks and dyes that absorb UV light; and
- **Forensic authentication technologies** - Protective measures that can only be identified using sophisticated analytical equipment, usually found in a forensic chemistry lab, such as chemical markers, taggants, and other unique chemical properties of a substance.

Track-and-trace technologies include:¹³²

- **Radio-frequency identification (“RFID”)** - A technology that involves the placement of electromagnetic chips/tags containing product-specific information onto cartons, pallets, and individual products; and
- **Barcodes** - Symbols on labels that are read by a scanner to identify a product. Bar codes can also function as authentication technologies when combined with certain covert elements.

Despite their potential, however, all counterfeit-resistant technologies have significant limitations. First, even with such technologies, drug products are merely resistant to counterfeiting – they are not counterfeit-proof. The experience of the U.S. Treasury is instructive. The U.S. Government employs a number of different counterfeit-resistant technologies on its bank notes, including special color-shifting inks, embedded threads and micro-printing. In order to stay ahead of counterfeiters, the government redesigns its notes every seven to ten years. The government recently introduced a redesigned \$20 bill incorporating a host of new counterfeit resistant technologies; yet only three weeks after the debut of the new \$20 bill, the press reported that a number of “computer-generated phonies have turned up.”¹³³ As this example illustrates, all counterfeit technologies are capable of being defeated by determined counterfeiters.

When it comes to anti-counterfeit technology, the least costly, most easily monitored technologies are also the most easily defeated. For example, overt authentication technologies offer potential benefits in that they can theoretically be used for real time product verification. These technologies, however, are easier to counterfeit than covert features, and thus provide the least assurance of

¹³¹ *FDA Counterfeit Drug Task Force Interim Report*, *supra* note 44, at 16-17.

¹³² *Id.* at 17.

¹³³ *New \$20 Not So Counterfeit Proof* (MSNBC Report, October 30, 2003).

authenticity. From a practical standpoint, many of these anti-counterfeiting features, whether overt or otherwise, may be either too unsophisticated or too complex to be cost effective and/or provide real time verification of drug products. Pfizer recognizes that new printing technologies, based on sophisticated image generation techniques, are being marketed as solutions for product authentication. However, we believe such technologies are not entirely effective because as the resolution of scanners increases, the ability of such techniques to provide a barrier to the counterfeiter diminishes.

The limitations associated with authentication, track-and-trace, and unit-of-use technologies are generally well known. For example, authentication technologies only supply limited information about individual items. Additionally, authentication technologies are more easily compromised because individual counterfeits can only be reconciled with a batch that may constitute a large number of units. Moreover, these products must be distributed collectively in batches. Repackaging and expert duplication techniques have allowed counterfeit operations to catch up with authentication technologies in the past. Track-and-trace technologies, on the other hand, offer long-term potential for increased control and security, but are costly and time-consuming to develop. These technologies are years away from implementation. In addition, unit-of-use packaging may be undesirable in situations where, for example, physicians choose a dosing regimen that differs from what is available from the manufacturer.

It is clear that anti-counterfeit technologies must be combined to be truly effective. Unfortunately, the costs of implementing multiple counterfeit-resistant technologies are significant. Authenticating covert features and taggants typically requires specialized equipment or testing; these features can and should be authenticated only by the manufacturer. These tests often cannot be performed on site or require a manufacturer's representative to travel to the site. In addition, tests for taggants may take up to several days to perform in order to accurately determine whether or not a drug is counterfeit. Where a large drug shipment is of questionable authenticity, the entire shipment would have to be withheld from commerce until the testing was completed, and the resulting delay in shipping could be considerable.

Pfizer is actively reviewing and testing new distribution technologies that offer the potential for increased security within the current closed U.S. drug distribution system. New track-and-trace systems, utilizing Electronic Product Codes ("EPC") that are scanned by bar code or radio frequency technologies, are potentially promising. Systems of this kind may ultimately form the cornerstone for long-term product integrity efforts. Unfortunately, there are tremendous technological and economic hurdles involved in the development and implementation of these new technologies. Issues surrounding RFID technology, for example, include data ownership and accessibility, global standards for tags, the high costs of tags and readers and the ability of supply chain partners to fund and support the investment required to adopt this technology.

It should also be noted that Pfizer has also been reviewing track-and-trace technologies through the Healthcare Distribution Management Association ("HDMA"). Pfizer is a member of HDMA, and Pfizer representatives sit on several boards and committees. In 2003, the HDMA developed a broad position statement utilizing EPC in healthcare and an educational white paper on RFID and EPC. The HDMA has also developed the HDMA Healthcare Foundation EPC/RFID Research Study. Through this study, the HDMA hopes to identify the factors impeding implementation and to make recommendations about how the HDMA and its member companies can accelerate the value

delivered of RFID to the pharmaceutical industry. Pfizer has agreed to co-sponsor and fund the study with Johnson & Johnson.

Pfizer has also participated in other industry groups looking at new technologies. For example, Pfizer played a role in the National Association of Chain Drugstores (“NACDS”) Task Force, which culminated with NACDS’s submission to the FDA Counterfeit Drug Task Force. Task forces such as these are important to moving industry-wide concepts forward.

Once these new technologies are developed and implemented, Pfizer believes they will be helpful in reducing the number of counterfeit drugs in the United States under our current legal framework. Pfizer does not believe, however, that any anti-counterfeiting technologies will be sufficient to prevent counterfeit products from entering the U.S. market if HHS permits importation.

B. Costs Associated with Developing and Employing Anti-Counterfeiting Technologies Would Be Exorbitant

There are numerous anti-counterfeiting technologies, ranging from covert to overt, that can be applied to pharmaceutical products. Many of these types of features are already used on products and packages by the U.S. pharmaceutical industry. These technologies, however, are only capable of reducing the number of counterfeit products that enter the market – they are not capable of eliminating and preventing counterfeiting altogether.

The ultimate cost and success of using such technologies cannot be appreciated until the requirements for a particular product are clearly defined and the supply chain for that product is fully understood. The process for developing and deploying anti-counterfeit technology is product-specific and therefore time and resource intensive. In order to determine the anti-counterfeiting technology requirements for a particular product, a number of factors must be evaluated, including, but not limited to:

- Is the product high risk?
- Is there “intelligence” that helps identify what level of authentication is warranted?
- Is there a need for a high degree of authentication (taggant vs. overt features)?
- Who is being targeted as the likely “authenticator” (the patient, dispensing pharmacist, wholesaler, field investigator, Customs inspector, internal lab analyst, etc.)?

Once the above factors are evaluated, an appropriate strategy can be developed for specific pharmaceutical products. It is common to pursue a multi-layered approach utilizing a variety of covert, semi-covert, and overt technologies. The solution’s robustness must be considered in selecting the appropriate technology. Specifically, consideration must be given to how difficult the feature will be to detect and to replicate.

Once selected, the supply chain for the technology must also be secured. The security of the feature itself (for example, the taggants or inks) must be guaranteed throughout its particular supply chain. For example, in considering a printed component with a covert ink, one must evaluate all points in the chain, from the ink's point of origination to its delivery at the printer and the subsequent delivery of the printed components to their respective manufacturing/packaging sites.

Actions must be taken by those deploying the technology to ensure each tablet, vial or component intended to be marked with a covert or semi-covert feature is marked in a manner that does not compromise the integrity of the effort. When considering a particular technology, it is also important to determine an appropriate validation approach, as the chosen approach will vary in difficulty across technologies and components.

Costs can only be estimated once all of the above-listed issues have been adequately defined. Pfizer's experience to date in following the above approach to develop a labeling system utilizing a mixture of overt, semi-covert and covert features in a container label demonstrates a five-fold increase in the cost of that label. Presently this approach is utilized on a limited number of specific Pfizer products. If this approach were extended to all products Pfizer markets in the US - as would be required if drug importation is legalized -Pfizer estimates that the total incremental labeling cost would be well over \$32 million per year.

Importantly, this estimate represents the cost of applying counterfeit technologies merely to the product labels. Thus, this represents a mere fraction of the overall costs that would be involved in achieving the overall security of these products. Although Pfizer does not currently have an estimate for the cost of deploying the full range of anti-counterfeiting technologies across its product line, we believe costs would likely be at least in the hundreds of millions per year.

VII. Financial Implications and Impact on Research and Development

A. The Price Cuts Required to Satisfy Policymakers Would Significantly Impact Industry Profits and R&D Capabilities

1. R&D Today Requires Extensive Investment and Significant Risk

U.S. investment in R&D for new medicines last year totaled more than \$27 billion, continuing a pattern of robust growth. In recent years, the industry has typically introduced 25-30 new medicines annually, suggesting on its face that in equilibrium it takes approximately \$1 billion per year to fund a research program that yields one new product per year. This estimate is consistent with outside analyses that have estimated the cost of developing a new drug at \$800 million - \$1.7 billion. A recent article on one Phase III trial that we are conducting on a promising medicine estimated the cost at \$800 million simply for the Phase III trial – that cost comes after ten years of investment to develop the molecule to that point. Overall, Pfizer invests nearly \$8 billion annually in R&D.

Investing in new medicines is a risky but potentially rewarding proposition. When a new molecule is identified as a potential medicine, on average it takes between 12 and 15 years to earn FDA approval. Of course, most molecules turn out to fail in scientific trials; only one out of every 5,000-10,000 compounds makes it from the test tube to the medicine cabinet. Even among those molecules that make it to clinical testing, only one out of five earns approval. Furthermore, market approval is no guarantee of a financial windfall; research conducted in 2002 showed that only 3 out of every 10 prescription drugs that reach the market succeed in producing revenue that matches or exceeds the typical R&D cost for a new product.¹³⁴

Investors must have a high tolerance for risk and a great deal of patience if they are to allocate capital to finding new medicines, and the rewards for success must match that risk tolerance and patience. Indeed, researchers have demonstrated that “incentives” are a crucial driver in pharmaceutical R&D. For example, research done at Columbia and Wharton in 2003 showed that the rate of introduction of orphan drugs started to rise dramatically in 1983 when Congress passed the Orphan Drug Act, providing increased exclusivity for orphan drugs. The new incentives increased orphan drug introductions by a factor of 5.¹³⁵

The U.S. system is currently the only system in the world that recognizes the importance of maintaining a value-based marketplace for new medicines that is robust enough to attract investor capital to such a risky enterprise. The U.S. supports an R&D infrastructure that evolved over decades through a careful collaboration of government, industry and academic efforts. However, nothing can force investors to fund continuously risky healthcare R&D projects. Such investments must be justified by their potential payoffs in order to maintain capital flows into the industry. If the market for pharmaceuticals suddenly becomes heavily regulated, investors must seriously consider moving their capital into other areas. This would be true no matter what the mechanism – importation is one possibility, but the same analysis would apply to any other type of government-

¹³⁴ H. Grabowski et al., *Returns on Research and Development for 1990's New Drug Introductions*, 20 PHARMACOECONOMICS 11-29 (Supp. 3 Dec. 2002).

¹³⁵ F. LICHTENBERG & J. WALDFOGEL, DOES MISERY LOVE COMPANY? (Nat'l Bureau of Econ. Research (“NBER”), Working Paper No. 9750, June 2003).

imposed price or profit control. A significant shift of capital out of the early-stage industry would reinforce the message to the research-based companies and their executives that investors no longer prefer to fund new projects.

2. Price Reductions Would Have a Major Impact on Profitability

The current enthusiasm for allowing consumers and other payers to import drugs from Canada and elsewhere depends on the notion that such importation will save payers money. If this assumption is incorrect – as many, including the Congressional Budget Office, assume – then the debate over importation is not worth having. Our comments proceed taking the proposals at face value, i.e., on the assumption that importation will indeed cause a significant volume of current sales in the U.S. to be sourced elsewhere, either at the wholesale or retail level. If that is the case, then at least from a pharmaceutical firm’s point of view, every dollar in sales that is transferred away from the U.S. and to another country is likely to be replaced by less than a dollar in revenue from the imported sale, and will therefore reduce profits. How large a reduction in profits depends upon two factors: (1) the difference in the prices we charge between the U.S. and the country we will import from (e.g., Canada) and (2) the total volume of sales in the U.S. that are replaced by sales from foreign countries.

Importation supporters believe that Canadian prices are substantially lower than U.S. prices. Such claims are difficult to prove because of the extreme variability in retail price in the U.S. (cash prices within a given neighborhood – prices set by retailers who all face similar wholesale costs, rather than by drug manufacturers - can vary by 30% or more, according to various state Attorneys General reports). Whatever the price difference, it is large enough to have attracted the attention of policymakers and the public, and can be assumed to be large enough that legal importation would spur a large shift away from U.S. wholesalers and toward wholesalers in other countries.

When sales are shifted to foreign sources, U.S. revenues decline by the amount of the shift while costs remain largely unchanged. As a result, the full revenue reduction will be subtracted from profits. It is well known that a majority of industry sales and profits currently come from the U.S., hence reductions in revenues can be presumed to have a major impact on overall profits. Some importation proponents have argued that lower prices will spur increased demand, potentially offsetting the price reductions. However, if such gains were possible, surely firms would have already lowered their own prices directly.

As we will discuss later, a major reduction in profits would strike a painful – though perhaps not immediately fatal – blow to the current pharmaceutical industry. But, as discussed above, with the financial prospects for future discoveries in doubt investors would surely demand that firms return their capital rather than invest it in new discoveries. Furthermore, any firm that did not comply would quickly lose all of its investors. The largest impact may be felt by early-stage pharmaceutical and biotechnology firms that rely on investor confidence in future returns for their financing.

3. Reduced Expected Future Profits Would Cause Fewer Projects to Meet or Exceed the Threshold Level of Expected Return

Pfizer’s investment in R&D amounts to about \$22 million *per day* in shareholder funds spread across many promising projects. As with any business investment, each project must be forecast to exceed a minimum level of expected profits in order to warrant funding. Expected profits are a function of

two major factors: the expected therapeutic impact (number of people with the condition to be treated, improvement on existing therapies, etc.) and the expected revenues from the product. It is our fiduciary responsibility to shareholders to ensure that their money is invested wisely, i.e., that if our R&D projects do not meet the minimum threshold level of return, we do not put investor money into such projects. Projects cannot continue if they are not promising therapeutically, and they also cannot continue if the expected revenues are insufficient to warrant the investment.

Government-imposed price reductions reduce current revenues and expected future revenues, as discussed above. A necessary result is that a certain proportion of R&D projects that previously would have exceeded the minimum threshold level of return will no longer exceed that threshold, even assuming the threshold level that investors require does not change when the price controls are introduced. When fewer R&D projects warrant funding, our fiduciary responsibility will be to reduce our investment in R&D. In a later section of these comments we will address the types of projects most likely to be impacted by such a reduction.

4. **Effective Price Cuts (via Importation or Other Means) Would Increase the Perceived Risk of Future Market Interference**

In addition to reducing the number of potential R&D projects that would have met the previous investment threshold, importing government price controls through importation will have a second, equally serious impact on the perceived risk of R&D investments. In short, a willingness to impose price cuts today will likely be viewed by investors as increasing the chance of future price cuts. As investors evaluate potential alternative investments, they must evaluate potential revenues as well as the potential variance from those expected revenues. Just as interest rates on corporate bonds increase as risk increases, investors demand a higher return for riskier investments. The net result from the industry's standpoint is that the minimum level of return required would increase if price controls were imposed. This would cause an additional number of projects to miss the cut, causing a further, potentially large reduction in R&D.

5. **Stock Price Declines Would Reflect the Belief That Profits Will Be Forever Lower Under Price Controls**

Lower stock prices for existing firms will be a natural result of reduced investment in R&D and reduced investor confidence in the pharmaceutical industry. A lower stock price does not impact a given firm's ability to invest in projects – rather, the lower price simply reflects the downturn in expected future profits. However, lower stock prices industry-wide will have an impact on potential entrants' ability to raise capital for new ventures, as investors evaluate the long term prospects for early stage companies in large part based on the market values assigned to successful companies in the industry where the new venture will compete.

B. **Reduced Profits and R&D Investment Would Have a Significant Negative Effect on Current and Future Consumers**

1. **Reductions in Expected Profits Would Damage Established Firms, and Cause Newer, Smaller Firms to Fail Altogether**

As discussed above, government-imposed or government-enabled price reductions in the U.S. would cause major – though perhaps not immediately fatal – reductions in profits for currently

profitable pharmaceutical firms. However, as discussed in a recent working paper that simulates firm survival rates in the industry,¹³⁶ the larger, more immediate impact of price controls will be on smaller, newer firms. Such firms attract investment dollars based solely on the prospects for future returns, and cannot finance investment in new products out of existing revenue streams. As a result, while larger firms might be able to weather a price control storm using existing resources as a cushion, venture-based firms – largely small biotech and pharmaceutical firms that are often viewed as a critical growth industry by policymakers – will have great difficulty securing funding and will therefore disappear.

2. Early Stage Research Would Disappear Sooner Than Late-Stage Research; Consumers Might Not Notice a Difference in Product Flow for About 10 Years

As larger firms consider cutting R&D projects, they will almost certainly look to cut earlier stage projects first. Projects that are far enough along in the development pipeline will be funded to completion, but early stage projects will not be supported. The combination of a) the disappearance of smaller firms and b) the shift away from early-stage research projects, coupled with the 10-15 year development timeline typical in this industry, means that it will likely be at least a decade before consumers notice that anything has changed in the pharmaceutical research industry. However, at that time it will be impossible for policymakers to reverse course, as the pipeline would presumably be dry at that point. Just as it would take at least 10 years for consumers to notice the lack of products being invented, it would take at least that long to re-energize the research-based pharmaceutical industry. Further, it would clearly be a challenge for the government to make credible commitments to a free-market pricing system at that time.

3. Importation Ultimately Leads to Delayed Access to New Therapies

The sole rationale for enacting importation legislation is to exploit the price differences that exist between the United States and certain other markets. None of those price differences is the result of free market forces, such as efficiencies or economies of scale. Rather, all of the price differences result from the fact that the other countries engage in government price controls. The rationale supporting importation is premised upon such foreign governmental price fixing. Thus, importation is nothing less than a clear step in the direction of price controls, and it is important to look at the impact that government regulated price controls have had on the access to innovative medicines in other markets.

In addition to stemming the flow of private investment funds into R&D for new medications, price controls have created issues of patient access to certain medications in other countries. Fewer products are launched in Europe, which affects how quickly doctors and patients access advanced treatments.¹³⁷ According to a 2002 report by HHS, it takes an average of two years from when a drug first becomes available on the market to when it is accessible by most European consumers.

¹³⁶ D. FILSON & N. MASIA, THE EFFECT OF R&D SCALE ON THE PROBABILITY OF LONG TERM FINANCIAL SUCCESS IN THE RESEARCH-BASED PHARMACEUTICAL INDUSTRY (Claremont Graduate University, Working Paper, 2004).

¹³⁷ Jim Gilbert, *Addressing the Innovation Divide*, at 3.

The delays in access are attributed largely to the process foreign nations have created for establishing reimbursement rates and price controls for the new drug.¹³⁸

In research conducted in 2003, Patricia Danzon and colleagues showed that pharmaceutical price regulation negatively impacted patients' access to new medicines in Canada and Europe.¹³⁹ The researchers looked at 85 new chemical entities (NCEs) launched globally between 1994 and 1998. Analyzing access in terms of both the number of products reaching market and the average time to market, the U.S. led the pack with 86% of the products reaching patients, at an average delay of just 4.2 months. In Canada, by contrast, only 66% of the products reached patients, at an average delay of 12.2 months. In France, only 53% of the products reached patients, at an average delay of 14.9 months. Finally, in Portugal, only 31% of the products reached market, at an average delay of 22.1 months.

These delays in access to new medicines are not surprising in centralized health systems that employ draconian measures to ration care. Annual studies of health care waiting times by The Fraser Institute show that patients in Canada are now waiting an average of 18 weeks for treatment, almost twice as long as they waited in 1993.¹⁴⁰ The average waiting time between referral by a general practitioner and consultation with a specialist rose from 3.7 weeks in 1993 to 8.3 weeks in 2003. The average waiting time between specialist consultation and treatment increased from 5.6 weeks in 1993 to 9.5 weeks in 2003. The total waiting time for patients from referral to treatment, across 12 specialties and 10 provinces, is now 17.7 weeks. The researchers describe how the unrecognized costs of long wait times may include lost work time, decreased productivity associated with physical impairment and anxiety, and physical and psychological pain and suffering:

A working person incapacitated by an illness bears the costs of the loss of work. These costs are not included among those associated with running the health care system. Cancer patients who must drive long distances to regional health centers or to the United States for radiation therapy bear costs in terms of lost time that are neither included in health costs nor in any way compensated for by the health care system. A woman with a lump in her breast, who is told she must wait four weeks for a biopsy to determine whether the lump is cancerous, finds little comfort in the advice from her physician that epidemiological research shows that it does not matter to the outcome if the biopsy is delayed that long. The woman's anxiety and tangible psychological pain are not included in the costs of operating the health care system.

¹³⁸ Assistant Secretary for Planning and Evaluation, U.S. Dept. of Health and Human Services, *Securing the Benefits of Medical Innovation for Seniors*, at 10 (July 2002).

¹³⁹ P. DANZON ET AL., THE IMPACT OF PRICE REGULATION ON THE LAUNCH DELAY OF NEW DRUGS, (NBER Working Paper No. 9874, July 2003).

¹⁴⁰ The Fraser Institute, *Hospital Waiting Lists in Canada* (13th ed. 2003).

All of these are characteristics of the Canadian health care experience. Unfortunately, researchers offer little prospect for improvement: “This grim portrait is the legacy of a medical system offering low expectations cloaked in lofty rhetoric. Indeed, under the current regime—first-dollar coverage with use limited by waiting, and crucial medical resources priced and allocated by governments—prospects for improvement are dim. Only substantial reform of that regime is likely to alleviate the medical system’s most curable disease—longer and longer waiting times for medical treatment.”

In the U.S., studies show that 63% of patients receive treatment within one month, with only 5% of patients waiting over 4 months – the Canadian average.¹⁴¹ Thus, the choice for policymakers in the U.S. could not be more stark: continue to support a successful market-driven healthcare system where innovation and access advance the standard of care year after year or slowly import a centralized, cumbersome and highly-regulated healthcare system where treatment is rationed by ever-increasing wait lists and delayed access to important new therapies.

4. **Research Suggests that Reduced R&D Investment Resulting from a \$1 Reduction in Profits Costs Consumers \$3 Worth of Products That Otherwise Would Have Been Invented**

Ultimately, the argument over whether to impose price cuts on the pharmaceutical industry boils down to estimating the value of the products that *would have been* invented without such controls. Economists at the University of Chicago investigated that question, and found that each dollar in savings achieved via price controls today causes a certain number of future products to disappear, and that those “missing” products are worth \$3 to today’s consumers in present value terms.¹⁴²

C. **Practical Economics of Importation Show That the Benefits are Smaller Than Believed by Most**

1. **Much of the Potential Price Difference Would Not Be Passed Along to Consumers**

There is another important dimension to the importation debate that affects consumers. As mentioned above, importation’s proponents assume that the relatively large difference in wholesale prices between the U.S. and Canada or other nations can be passed along to U.S. consumers by allowing importation from such countries. Whatever one believes about how the associated reduction in profits will impact the pharmaceutical and biotechnology industries, it is important to note that it is not at all clear that consumers will actually see price reductions that reflect the true difference in prices between countries. While pharmaceutical manufacturers will feel the full brunt of the shift in sourcing the lower-priced countries, the dollars taken out of manufacturers’ hands will be split among consumers, other payers, wholesalers, retailers, and a new industry of middlemen who would facilitate the trade.

¹⁴¹ R. Blendon et al., *Inequities in Health Care: A Five-Country Survey*, 21(3) HEALTH AFFAIRS 182-191 (May/June 2002).

¹⁴² J. HUGHES ET AL., “NAPSTERIZING” PHARMACEUTICALS: ACCESS, INNOVATION, AND CONSUMER WELFARE (NBER Working Paper No. 9229, Oct. 2002).

Since importation is akin to the parallel trade that Europe has been struggling with for some 30 years, it is important to take a serious look at the lessons learned. Our experience in Europe demonstrates: (i) that the gains from parallel trade ultimately accrue to the middlemen rather than to the consumers; (ii) that the substantial losses to manufacturers in innovation markets like the United Kingdom (“U.K.”) negatively impact future research funding; and (iii) that the increased movement of goods across markets threatens product integrity.¹⁴³

A recent London School of Economics study found that anywhere from half to up to 89% of the potential gain to consumers or payers from parallel trade is, in fact, realized by the parallel traders.¹⁴⁴ The study’s author found that “[t]here is no evidence of sustainable dynamic price competition in destination countries, with no corresponding indirect cost savings. The supposed benefits of this system need to be reviewed.”

The LSE study’s findings were echoed by a March, 2004 study by Dr. Stefan Szymanski of the Imperial College London.¹⁴⁵ Dr. Szymanski investigated the impact of parallel trade on the welfare of consumers, purchasers and producers in the U.K. Dr. Szymanski estimated that parallel traded pharmaceuticals account for 20 per cent of the U.K. market and that parallel traded products sell at around 15 per cent cheaper than products originating in the domestic market. Based on these figures, Dr. Szymanski calculated a gain of up to £480million for the U.K. economy from parallel trade (assuming all parallel trade profits remain in the U.K.) against a £770 million loss to U.K. manufacturers. Given the significant net loss, Dr. Szymanski concluded that “overall parallel trade has a negative impact on the U.K. economy, notwithstanding the short-term benefits.”

So, the net impact of legalized importation would seem to be a transfer of wealth from R&D-based pharmaceutical firms to middlemen who will make the market in traded pharmaceuticals. Under such a scenario, a 50% price difference between the U.S. and Canada – assuming that Canadian prices remain low – may translate into a 15% or 20% discount to actual U.S. consumers. Meanwhile, the analysis of profitability from the previous section would remain unchanged – while consumers would only experience a small discount, pharmaceutical firms would be impacted dramatically.

2. Potential Price Reductions Would Come at Significant Taxpayer Cost

The FDA and Health Canada have made it clear that neither the U.S. nor the Canadian regulatory systems can ensure the safety of products shipped from or through Canada to the United States. While providing additional resources to the FDA, Customs, or a new regulatory body may help mitigate the safety concerns, the potentially large resources required, however, must be factored in when considering the potential cost savings under a legalized importation regime. Given the serious safety concerns related to bioterrorism, counterfeit drugs, mislabeled or adulterated drugs, pharmacy quality and safety practices, and physician supervision, it is safe to assume that such costs will not be

¹⁴³ Patricia M. Danzon, *The Economics of Parallel Trade*, PHARMACOECONOMICS (1998).

¹⁴⁴ P. Kanavos et al., London School of Economics, *The Economic Impact of Pharmaceutical Parallel Trade: A Stakeholder Analysis* (2004)

¹⁴⁵ S. Szymanski & S. Hall, Economic and Social Research Council (“ESRC”), *Intellectual Property Rights: Trading in Pharmaceuticals* (2004).

trivial, and could easily run into the billions if the volume of cross-border trade is assumed to be large.

3. Price Differences Between Countries Would Likely Diminish Over Time

Two significant drivers of the price differences between the U.S. and other countries have been: (1) government price controls on pharmaceuticals in foreign countries; and (2) the strength of the U.S. dollar over the past decade. Some have suggested that legalizing importation will allow firms to negotiate better deals with foreign governments, which will allow prices to rise in those countries. If true, that would further diminish the capacity for U.S. consumers to achieve savings on medicines by accessing foreign sources. However, there is reason to question whether foreign prices would really rise very much. A willingness to consider compulsory licenses, combined with an increase in pricing systems that set prices indirectly (through generic reference pricing or other mechanisms) rather than directly (by negotiating prices for specific drugs) may mean that foreign prices will not rise much at all. As to exchange rates, it is worth considering what would happen if the dollar were to weaken significantly (as predicted by some economists). Suddenly prices in the U.S. would look low relative to prices paid in other countries, again limiting the potential benefits for consumers looking to take advantage of foreign price controls.

4. Importation is Not Free Trade

There are some who would argue that parallel trade (or importation) is simply free trade. However, this is a smoke screen that allows proponents of importation to avoid the need to address the economic downside of price controls. Whatever you call it – importation, parallel trade or product diversion – it is not free trade. Leading economists have demonstrated that parallel trade in pharmaceuticals does not yield the normal efficiency gains that we expect from trade because countries achieve low pharmaceutical prices by aggressive regulation, not through superior efficiency.¹⁴⁶ In fact, parallel trade reduces economic welfare by undermining price differentials between markets. Pharmaceutical R&D is a global joint cost of serving all consumers worldwide; it accounts for roughly 30% of total costs. Optimal pricing to cover joint costs (Ramsey pricing) requires setting different prices in different markets, based on inverse demand elasticities. By contrast, parallel trade and regulation based on international price comparisons tend to force price convergence across markets. Everyone loses from this kind of price convergence. Consumers in low income countries will face higher prices or loss of access to new drugs, and the research-based companies in the higher income countries will be constrained in the ability to fund future research.

D. The Decline of Pharmaceutical Industries in Other Countries Exemplifies the Long-term Impact that Price Controls Would Have on the U.S. Pharmaceutical Industry

Other countries that implemented price controls years ago have seen a decline in their pharmaceutical industries, experienced losses in their national economies and forced citizens to wait longer for breakthrough medications (assuming their patients can get the new medications at all).

¹⁴⁶ Danzon, *supra* note 142.

Many factors have contributed to the decline of the pharmaceutical industry in Europe, and price controls in Europe also affect firms outside of Europe. However, price controls may be the strongest signal that a government can send that it does not recognize the importance of rewarding innovation. The experiences of these countries highlight the need to maintain the delicate balance that exists between the high risk of research and the rewards for innovation in the United States for the U.S. pharmaceutical industry.

Over the past ten years, investment in R&D endeavors within the United States has increased dramatically, especially as compared to investment in Europe, as pharmaceutical companies channel an increasing amount of their overall R&D funding into the United States.¹⁴⁷ This trend was spotted as early as 1991 by the U.S. International Trade Commission, which wrote: “The enactment of cost-containment programs, price controls, or both, on a national level often results in decreased levels of R&D spending in that these programs reduce revenues that can be reinvested in R&D programs.”¹⁴⁸ Ten years later, the European Federation of Pharmaceutical Industries and Associations (“EFPIA”) confirmed that the situation had worsened dramatically as European price controls squeezed the ability of European companies to finance R&D. EFPIA’s Annual Report for 2002 concluded that: “the U.S., over the last decade, has overtaken Europe both in terms of innovative efforts (R&D investment) and in terms of the output of its innovative activity (new molecular entities launched on the world market).”¹⁴⁹

Key benchmarking indicators show that between 1990 and 2002, R&D investment in United States rose more than fivefold, while in Europe it only grew 2.5 times. In 1990, major European research-based companies spent 73% of their worldwide R&D expenditure on the EU territory. However, by 1999, they were spending only 59% in the EU territory. The U.S. is now the leading inventor of new medicines. Indeed, of the top 10 worldwide products in 2002, 8 originated from the U.S. against 2 from Europe. Furthermore, 70% of the sales of new medicines launched on the world markets during the period 1998-2002 were made in the U.S., compared to only 18 % in Europe. Whereas the European pharmaceutical market was still the world’s largest market in 1990 (representing 37.8% of the world market), it now only represents half the share of the North American market (25.4 % compared to 50.9 % of the world pharmaceutical market).¹⁵⁰

European companies are increasingly deploying their R&D resources in the U.S. where the incentives for innovation support a robust research infrastructure. In May 2002, the Swiss-based Novartis company announced that it would move the center of its worldwide research operations from Switzerland to Cambridge, Massachusetts. With an initial investment of \$250 million, the new research facility in Cambridge opened with room for 400 scientists and technology experts. Novartis has plans to expand the research site to house upwards of 1,000 scientists.

¹⁴⁷ PhRMA, *Pharmaceutical Industry Profile 2003* at 16.

¹⁴⁸ U.S. Int’l Trade Comm’n, *Global Competitiveness of U.S. Advanced-Technology Manufacturing Industries: Pharmaceuticals: Report to the Senate Finance Committee* (September 1991).

¹⁴⁹ European Fed’n of Pharmaceutical Indus. and Ass’ns, *2001-2002: A Year in Review*, at 15 (Brussels, Nov. 2002).

¹⁵⁰ European Fed’n of Pharmaceutical Indus. and Ass’ns website, at <http://www.efpia.org/>.

The loss of substantial research resources and the delayed access to new medicines are just some of the “hidden” costs that Europeans are paying for their excessive control of pricing according to a new study from Bain and Company.¹⁵¹ In fact, Bain’s research suggests that the social and economic costs to Europe in the form of delayed access to drugs, poorer health outcomes, lowered investments in R&D and the drain on high-value pharmaceutical jobs are a high price to pay in return for lower prices at the pharmacy counter. Bain’s study contends that European bargains at the pharmacy counter result in:

- Less drug innovation – as evidenced by just 44 NMEs launched between 1998 and 2002 in Europe down from 81 introduced between 1993 and 1997, while in the U.S., 85 NMEs were launched between 1998 and 2002, a 77% increase over the previous period;
- Fewer high-value jobs – the U.S. created 42% more high value pharmaceutical jobs than Europe from 1990 to 2001;
- Loss of corporate research centers – after nearly even spending on R&D expenditures in 1992, U.S. pharmaceutical expenditures grew by 11% (compounded annually) in the period from 1992 to 2002, while European expenditures grew by only 8%; and
- Delayed access to the most advanced drug treatments – the average delay from initial drug launch to market is 33% longer in Europe than in the U.S. – one reason is the lengthy reimbursement negotiations that follow government approval in Europe.

These warning signs are merely a glimpse of what might lie ahead for the industry and patients across the globe. “Europe has to realize the free ride is not free,” said Paul Rosenberg, Bain Vice President and co-author of the study. “We’re not talking about altruism here – this is about enlightened, self-interest by governments and business leaders alike.”

The impact of price controls is having an intense impact on the sustainability of innovation in Germany. Pharmaceutical research in Germany is in jeopardy after the country’s most recent wave of price controls, including reference prices and a mandatory 16% rebate. Indeed, a report from January 2004 states that: “The future for the development of new drugs looks so bleak that the industry might not be able to survive in the country.”¹⁵²

¹⁵¹ J. GILBERT & P. ROSENBERG, ADDRESSING THE INNOVATION DIVIDE: IMBALANCED INNOVATION (Bain & Co, Inc.) (2004).

¹⁵² B. Rossiter, *More Reform Less Research*, MED AD NEWS, at 4 (January 2004).

E. Conclusion

Importation is proposed as a way for U.S. consumers to save money on medicines. There is significant reason to question whether consumers really would save money under open importation, but if savings are possible they will clearly come directly from the bottom line of pharmaceutical firms. Reductions in expected profit for new and existing R&D projects will imply that many such projects will no longer clear the required rate of return to justify investment. Further, a policy decision to control prices, explicitly or implicitly, will cause investors to perceive that similar moves are likely in the future and will cause investors to demand a higher minimum rate of return as compensation for taking on additional risk. Both of these factors will lead to a large-scale reduction in R&D investment as a natural consequence of investor preferences – managers that did not comply with such preferences would surely lose their jobs. Smaller firms will be hit first, as their financing requirements are higher relative to ongoing revenues, but larger firms would also scale back their investment or risk getting sued by their shareholders. The reduced investment in R&D will lead to a lack of new products beginning in a decade or so, and those missing products have been estimated to be worth much more than the potential short-run savings from price controls.

Finally, as price control schemes go, importation does not have much to recommend it. Importation is an extremely inefficient way to impose price controls in the U.S.; every dollar of price savings passed along to consumers will necessarily mean more than a dollar in losses for pharmaceutical firms and a commensurately large reduction in R&D. While pharmaceutical firms would feel the full brunt of the shift in sales out of higher-priced markets and toward lower-priced markets, consumers would only gain a fraction of the price difference as the middlemen have proven adept in this industry at extracting most of the available gains. In this way, importation provides the worst of both worlds – little in the way of price savings, but a large and negative impact on R&D into future cures. Furthermore, this would leave pharmaceutical firms open to additional price controls down the road, as consumers will probably not feel enough of a price reduction to stop seeking regulatory solutions. The costs of these policies – in terms of lost products for future generations – will not become clear until well after many of today's policymakers have retired and many pharmaceutical and biotechnology firms have exited the R&D business altogether.

The risk to the research base in the U.S. is enormous. As one Pfizer researcher noted in commemorating Pfizer's 150th anniversary: "It is much easier to lose a science-based, innovation-directed culture than to reinvent it. Innovation in medical research is really something that is very fragile; it is progress that should not be taken for granted at all."¹⁵³

¹⁵³ *The Importance of Innovation in Pharmaceutical Research*, THE PFIZER JOURNAL (1999) (quoting clinical researcher Scott Hopkins).

VIII. Liability Issues

The importation of prescription drugs would raise a host of new and troubling liability issues for entities throughout the U.S. distribution chain. American manufacturers, distributors, wholesalers, retailers, and doctors, as well as individual states, would face the possibility of a substantial number of new lawsuits based upon introduction of counterfeit or otherwise contaminated products into the United States. The tort system in this country already imposes substantial burdens and costs on these American entities, and these burdens would be dramatically increased by the importation of prescription drugs.

Importation would create situations where it would be impossible to trace the origin and distribution chain of a product involved in a lawsuit. Therefore, American entities would be sued throughout the United States but would not be in a position to demonstrate that the injuries alleged are attributable to the actions of foreign actors in the supply chain. Even if there is enough information for patients or American companies to identify and sue foreign exporters, those exporters can advance defenses in American courts that will make it more difficult – and expensive – for an American entity to demonstrate that the foreign actors were truly at fault for the injuries alleged. Finally, it would be virtually impossible for U.S. regulatory agencies to impose criminal liability on foreign entities, as these entities would fall outside U.S. jurisdiction. Importation would thus increase liability risks for U.S. entities while reducing the ability of U.S. regulators to prosecute unlawful foreign conduct.

A. The Unknown History of Imported Drugs Would Make U.S. Entities the Targets of Complex Litigation

Probably the most profound litigation difficulty that would be generated by importation of pharmaceuticals outside the current legal framework would be the difficulty in establishing who had contact with the product before it entered this country. In some cases, a patient would not know that the drug he or she ingested came from abroad. In others, no records would exist indicating where the product came from. Even in cases where the parties were known, unraveling what happened to a product would involve expensive fact gathering and discovery in a foreign country. Thus, American manufacturers would be sued in numerous cases that did not involve their products.

Litigation involving imported products would be extremely complex – and hence very expensive. Individuals bringing lawsuits have an incentive to sue all potential defendants simultaneously, and defendants have an incentive to bring all potentially responsible parties into the litigation. In a case involving an imported drug this could include: (1) a Canadian exporter; (2) a foreign manufacturer who exported into Canada; (3) a foreign pharmacy that filled an individual's prescription; (4) a foreign doctor writing that prescription; (5) an American wholesaler or pharmacy who imported the product; (6) the American pharmacy that filled the prescription; (7) the American company that manufactures the product; (8) the American company who marketed the product in this country; and (9) the American physician who prescribed the drug. Lawsuits involving this range of parties would lead to difficult problems in gathering facts, and would generally complicate legal issues based upon the involvement of foreign parties and the serious concerns regarding the solvency of the types of companies and individuals who would distribute drugs outside the current U.S. distribution system.

Individual states that assist consumers in obtaining imported drugs would also potentially face significant liability if drugs imported into the U.S. under state plans injure American consumers, cause serious adverse reactions, are subpotent, or otherwise differ from the FDA-approved drugs. Consumers would have various tort and other theories available - including theories of negligence, strict liability, breach of implied warranty of merchantability, failure to warn, and fraud or misrepresentation – under which to sue states, individually or by class action. Whether states are treated as merchants selling imported drugs directly to consumers or as secondary actors merely facilitating the movement of imported drugs through the distribution chain en route to consumers, courts may likely hold that states are, in fact, responsible for (1) making sure drugs in the state are safe drug and (2) ensuring that unsafe drugs do not fall into the hands of consumers. States’ risk of liability may be particularly great given that the potential injury to patients from imported drugs is both foreseeable and likely. The FDA has already put states on notice that their facilitation of drug importation puts citizens at risk:

When you recommend to your citizens that they go outside of our regulatory system and enter into a “buyer beware” gray zone, you assist those who put profits before patient health. Your actions also shine a bright light on a path that can (and, indeed, is) used not only by profiteers masquerading as pharmacists, but by outright criminals who do not pause before actively feeding counterfeit drugs into the marketplace.¹⁵⁴

The State of Minnesota recently announced that it would permit its 120, 000 state employees and their dependents to purchase prescription drugs from a pharmacy in Alberta, Canada. No doubt cognizant of its potential legal liability for damages to its employees resulting from the purchase of imported counterfeit or otherwise unsafe or dangerous products, the State posted a “disclaimer of liability” for the program on its Website. “The State of Minnesota makes no warranty, express or implied, of merchantability and fitness for a particular purpose, and accepts no legal liability, with respect to any product offered, or pharmaceutical care provided, by the pharmacies listed on this Website.”¹⁵⁵ The State of Minnesota, acknowledging the safety risks associated with imported drugs, nonetheless encouraged its employees to import such drugs and then declined to accept legal responsibility for any problems arising from the use of such drugs.

Clearly, then, in the event of an injury caused by a drug imported under a state plan, that state could be deemed to have known (or to have been in a position where it should have known) of the risks inherent in such drugs, and could therefore face a serious risk of liability.

B. Even Where Claims Against Them Are Without Merit, American Entities Would Have to Clear Enormous Hurdles to Avoid Liability in Such Lawsuits

In cases where the patient or American pharmaceutical companies or other entities could identify foreign companies in the chain of distribution, they would face a blizzard of legal tactics that would slow the progress of these lawsuits to a crawl and raise the cost of them significantly. Foreign

¹⁵⁴ Letter from William K. Hubbard to Gov. Tim Pawlenty, State of Minnesota (Feb. 23, 2004).

¹⁵⁵ <http://www.advantage-meds.com/>

companies could challenge whether American courts can exercise jurisdiction over them. Even if foreign companies can be parties in American lawsuits, they could argue that a case nevertheless should be heard in the foreign country based upon foreign laws – and that fact gathering should proceed under the complex procedures of the Hague Convention. Thus, even in cases where there is no valid claim against them, American companies would incur additional expense rebutting these claims, and they could be forced to litigate claims in a foreign nation and/or under potentially different legal standards.

In some cases involving adulteration of an imported drug product by a foreign entity, plaintiffs may sue an American manufacturer claiming that the manufacturer failed to take adequate steps to prevent tampering with the product. These cases could proceed to trial even if the American company complied fully with FDA's regulations (and can prove it). Courts in many states treat FDA regulations as mere "minimum standards" and allow plaintiffs' lawyers to seek huge damage awards by claiming that companies should be held to some un-codified higher authority. Thus, a jury could impose massive liability on an American pharmaceutical company for an adulterated product even if the company packaged its product exactly as FDA says it should.

Moreover, in some cases involving products imported into the United States, the exporter may include non-U.S. labeling or foreign patient information for the drug. If that labeling or foreign patient information is provided to American patients, it is possible that a patient would claim that American manufacturers failed to prevent the dissemination of the foreign labeling or failed to warn patients directly that they might receive unapproved labeling information. Again, American companies would be drawn into a morass of litigation even though they did nothing wrong.

C. Under Alternative Theories of Liability, American Entities May be Forced to Pay For Foreign Wrongdoing

The consequences of this new system would be swift and costly. Basic principles of liability and fault would be turned upside down and inside out, to the detriment of the American company attempting to demonstrate that it did nothing wrong. Rather than lower the costs of prescription drugs in the United States as drug importation purports to do, this system would cause drug prices to escalate as American manufacturers, distributors, wholesalers and retailers are forced to litigate an encyclopedia of new issues that importation will engender.

To make matters worse, most of the foreign exporters would lack adequate insurance and therefore would be unable to pay for their wrongdoing. Under the law applicable in many states, an American entity may be required to pay for this liability even though the foreign actor was truly responsible. Finally, American companies named in suits involving foreign drug imports would have no certainty that juries hearing these questions would even accept the evidence proving that a foreign company caused a product to be adulterated, counterfeit, or otherwise rendered harmful. Thus, American companies would be at risk of being held hostage, as the "deep pocket" defendant, by plaintiffs seeking damages for personal injuries caused by foreign companies or individuals.

Finally, in some cases involving counterfeiting, adulteration, degradation or importation of an unapproved product by a foreign entity, plaintiffs might sue American entities on alternative theories of liability, even if the primary responsibility for the alleged injury lay with the foreign exporter. In those cases, the American entity would face the prospect of a trial in which they could be found liable for a tiny fraction of the alleged damages but have to fund the entire judgment under

principles of joint and several liability. Based upon the manner in which this principle is applied in many states, a plaintiff who obtains a large award after the jury finds a foreign company 99% at fault and an American company 1% at fault can decide to collect the entire judgment from the American company. The American company would then be left to bring a lawsuit seeking contribution from the foreign exporter. These rules place enormous pressure on American entities to settle cases where their liability is limited or non-existent.¹⁵⁶ In effect, American companies would be forced to serve as a litigation insurer for companies that lawfully or unlawfully enter the pharmaceutical import-export market.

The problem of joint and several liability would be compounded by the nature of the companies who would likely enter the pharmaceutical export business. These entities may be little more than fly-by-night operators with no real expertise in the sale of pharmaceuticals let alone the assets to pay a judgment. Given the difference between the Canadian and American tort systems, it is quite likely that drug exporters in Canada will not have significant insurance. Further, even in cases where the exporters have insurance, it may not cover cases arising in the United States relating to imported drugs.¹⁵⁷ Moreover, even if the foreign exporter is brought into an American court, and a judgment is entered against the exporter and it has resources available, a plaintiff may not be able to enforce the judgment.¹⁵⁸ Further, Canadian provinces could enact legislation specifically intended to block enforcement of American judgments related to imported drugs. Both British Columbia and Quebec did exactly that with regard to judgments imposing liability for damages caused by asbestos produced in those provinces.¹⁵⁹ These risks would create strong incentives for plaintiffs' lawyers to bring American companies into their lawsuits to make certain there is a deep pocket to pay for a potential jury verdict.

In conclusion, the basic principle of the American legal system is that liability should not be imposed absent a showing of fault, a principle that potentially would be completely reversed in litigation over an imported drug. There is the real possibility that an American pharmaceutical manufacturer would be required to pay for damages caused by exporters who cannot be identified, are not subject to the American court system, or cannot pay for the damage that they have caused. Absent sweeping changes to the American tort system, it will be impossible to ameliorate all of the potential liability risks associated with drug importation.

¹⁵⁶ This is not a theoretical concern. Drug manufacturers recently confronted this type of problem in a case where a Missouri pharmacist had diluted cancer drugs. After jury selection, the drug companies settled with the plaintiff for fear that they would have to pay 100% of any damages awarded. *Missouri Pharmacist Hit with \$2.2 Billion in Damages for Diluting Cancer Drugs*, 18(8) ANDREWS PHARMACEUTICAL LITIG. REP. 3 (2002).

¹⁵⁷ See G. Gonzalez, *Canadian Drug Controversy Generating New Side Effects*, BUSINESS INSURANCE, Jan. 19, 2004 (Canadian insurance companies may not extend coverage to Canadian doctors writing prescriptions for American patients).

¹⁵⁸ See www.state.gov/www/global/legal_affairs/canadian_annex-3.html (note of Canadian government suggesting that Canadian courts will not enforce punitive damages awards of American courts).

¹⁵⁹ See The Court Order Enforcement Act, 2 REVISED STATUTES OF BRITISH COLUMBIA [R.S.B.C.] ch. 75, § 40 (British Columbia); and CODE CIVIL [C. CIV.] arts. 3129, 3151, 3165(2) (Quebec).

IX. Regulation by Foreign Health Agencies

A. Introduction

Because the MMA, if enacted, would specifically authorize imports from Canada, we have conducted an analysis of Canadian laws and regulation, both federal and provincial, to ascertain whether Canada specifically has protections in place sufficient to safeguard the health and safety of American consumers should importation be authorized under the MMA. Thereafter, the laws of 25 countries, identified as potential significant sources of pharmaceuticals for importation into the United States, were analyzed.¹⁶⁰ Canada is also included in the 25-country analysis.

The analysis of these laws and regulations makes clear that the United States cannot rely on the laws of other countries to protect American consumers. Although these countries have relatively sophisticated drug regulatory schemes, the primary purpose of those schemes is to ensure the safety, efficacy, and quality of products in their domestic markets. The regulatory schemes were neither intended nor designed to ensure the safety of products intended for export. Similarly, it is apparent that the foreign health regulatory authorities would lack the resources or political will to impose new or additional protections for exported or transhipped drug products.

Delegating responsibility for the safety of the U.S. drug supply to foreign authorities and bureaucrats would, in essence, gut our regulatory system and the FDA's ability to assure drug safety. In passing the FFDCA, Congress never authorized the delegation of any powers, including the power to ensure the safety and efficacy of drug products, to foreign sovereigns. Moreover, FDA regulations expressly limit the delegation of authority from the Secretary of HHS to U.S. government officials.¹⁶¹ Permitting the safety of imported drug products to be determined by foreign health authorities would violate Federal law and would cause the American public to be held hostage to the vagaries of other countries' regulatory limitations, resource decisions and whims.

In addition, importation, by delegating responsibility to these foreign authorities, would completely undermine the level of accountability our current closed system affords. It is not clear who – if anyone – could be held accountable for injuries resulting from a drug that was under the oversight of a foreign authority. Even if a company were able to identify a foreign entity responsible for such an injury, it is unlikely that the company would be able to pursue civil action against that entity. Moreover, any foreign actor would likely be immune from FDA's enforcement authority. Thus, there would be one standard of liability for U.S.-based actors, and an entirely different (and much looser) standard for actors operating outside the United States. This undermines the very reliability of the U.S. drug distribution system, and leaves consumers with little recourse but to sue American companies for injuries sustained as a result of foreign actors. (See Section VIII, above).

¹⁶⁰ The countries include Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Liechtenstein, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, South Africa, Spain, Sweden, Switzerland, and the U.K.

¹⁶¹ See e.g. 21 C.F.R. Part 5.

B. Canadian Drug Regulation

1. Background

Canadian law, both at the federal and provincial levels, does not have protections in place to ensure the safety of drugs that are exported from, or transhipped through Canada.

a. Federal Food & Drugs Act [“F&D Act”] and Health Canada

The F&D Act and its regulations are designed to protect the health of Canadians and do not contain provisions that ensure the safety of drugs that are exported from or transhipped through Canada. Similarly, the Act and its regulations do not generally have extra-territorial effect. Enforcement of the F&D Act is the responsibility of the Health Products and Food Branch (“HPFB”) of Health Canada, which is responsible for drug quality, safety and efficacy. It regulates drugs imported into and manufactured for sale in Canada.

b. F&D Act Exemption for Exported Drugs

The F&D Act contains an “Export Exemption” which explicitly states that the Act and its regulations do not apply to exports from Canada, if certain requirements are met. The Export Exemption is available, and the Act does not apply to a drug, where: (1) the drug is not manufactured for consumption in Canada; (2) the drug is not sold for consumption in Canada; (3) the package is marked in distinct over-printing with the word “Export” or “Exportation”; and (4) a certification has been issued confirming that the package and its contents do not contravene any known requirement of the law of the country to which it is to be exported. Thus, the provisions of the F&D Act that ensure drug safety are not applicable to such exported drugs.

The Export Exemption does not contain any reference to the place of manufacture, but only requires that the drug not be manufactured “for consumption in Canada”. For that reason, there are differences of opinion with respect to the exact scope of the Export Exemption, and specifically, whether it: (a) applies only to drugs manufactured in Canada for export; or (b) also applies to drugs manufactured outside of Canada and then imported to Canada, for the purpose only of export or transshipment. This issue remains untested and unsettled.

c. Provincial Regulation of Health Care Professionals

At the provincial level, governments and self-regulatory bodies regulate the practices of health care professionals, including physicians and pharmacists. To the extent that Canadian physicians or pharmacists are involved in the export of drugs from Canada, they may be subject to review and sanction by their respective regulators. For example, the Ontario College of Pharmacists (the “OCP”), which regulates the practice of pharmacy in Ontario, adopted a “Policy for Ontario Pharmacies Operating Internet Web Sites” in 2001. This Policy requires that Internet pharmacies in Ontario comply with all of the regulatory requirements that apply to accredited pharmacies. Under the Policy, OCP-regulated pharmacists may not co-sign or re-write prescriptions for out-of-country patients. The OCP and other provincial regulatory bodies were instrumental in charges being laid against a pharmacist, other individuals and The Canadian Drugstore Inc., with respect to the operation of an Internet pharmacy. This Internet pharmacy was not accredited in Ontario and did

not operate in compliance with the OCP Policy. The pharmacist and others pled guilty to offenses under provincial legislation.

d. Prescription Drugs Are Not Covered by Export Control Requirements

The Export and Import Permits Act (the “Export Act”) gives the federal cabinet the authority to establish an Export Control List (the “List”). The List includes products such as arms, munitions and products or raw materials for products that are required for Canada’s defense. The Export Act generally prohibits the export of products on the List to countries that are included on an Area Control List. Currently, the List does not include pharmaceuticals. Accordingly, the Export Act cannot be relied upon to prohibit or limit the export of drugs from Canada into the United States.

2. Canada is Unlikely to Modify its Law to Regulate Exported or Transshipped Drugs

As discussed below, it is unlikely that Canada will be willing or able to amend the F&D Act, or make other legislative or regulatory changes to ensure the safety of exported or transshipped drugs.

a. The Role of Health Canada

The role of the HPFB, which includes the Therapeutic Products Directorate (“TPD”),¹⁶² is to: “. . . take an integrated approach to the management of the risks and benefits to health related to health products and food by . . . minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and promoting conditions that enable Canadians to make healthy choices. . . .” The TPD evaluates and monitors the safety, effectiveness and quality of drugs and other therapeutic products for Canadians. Clearly, the focus of the HPFB is on the health of Canadians. There are no indications that Health Canada would be willing to implement new or additional regulations or procedures in order to ensure safety of exported or transshipped drugs.

b. Health Canada and Provincial Regulators

On October 27, 2003, Health Canada wrote to provincial regulatory authorities on the issue of Internet pharmacies. The letter was triggered by significant interest in Canadian-based Internet pharmacies, by the U.S. FDA and by U.S. and Canadian media. In this letter, Health Canada clarified that its regulatory authorities and responsibilities are contained in the F&D Act and its regulations and its primary role regarding Internet pharmacies is limited. “Health Canada’s primary role with respect to the safety, quality and effectiveness of prescription drugs is twofold: first, through the regulatory review prior to market authorization, and second, through post-market surveillance and compliance/enforcement activities once a product is marketed.”

As noted in this letter, safe products of good quality do not guarantee safe usage, and the federal role of Health Canada is not sufficient to protect Canadians from the potential harm of incorrectly prescribed drug products. The letter further noted that the F&D Act and its regulations trigger

¹⁶² Available at <http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt>.

provincial regulation. Specifically, the regulations require that prescription drugs may only be sold at the retail level if prescribed by a provincially licensed practitioner. The October 27, 2003 letter emphasized the critical role played by licensed practitioners within each province and territory, and of their regulatory bodies. The letter requested that medical and pharmacy regulators and associations emphasize, with their members, the importance of both federal and provincial requirements.

c. **Health Canada/FDA Meeting - November 2003**

Canada's reluctance to apply the F&D Act to drug exports is exemplified by its reaction to statements made by the FDA Commissioner in November, 2003. On November 18, 2003, senior officials from Health Canada met with FDA officials to sign a Memorandum of Understanding ("MOU") to enable the two regulatory authorities to share information. The MOU focused on information relating to post-market safety of therapeutic products; information related to the review and evaluations of new product submissions; and information on investigations and enforcement.

During that meeting, then-Commissioner of FDA Mark B. McClellan commented on the Internet pharmacy issue, indicating concern at the potential for unapproved and mislabeled medications to be imported into the United States from Canada. According to press reports, Dr. McClellan expressed the hope that Health Canada would take a leadership role in addressing the FDA's concerns. In response, Health Canada issued a press release clarifying its position on Internet pharmacies, emphasizing that drugs approved for use in Canada are safe, that its systems are among the most rigorous in the world and that these systems do assure the safety, quality and efficacy of prescription drugs. Certain statements within this press release highlight Health Canada's priorities and form the foundation for the view that Health Canada is unlikely to implement amendments to the F&D Act, or other regulatory changes, for the purpose of ensuring the safety of exported or transhipped drugs:

"Health Canada's priority and mandate is the safety of drugs approved for sale in Canada."

"If any Canadian laws have been violated, Health Canada will take necessary measures to protect the health and safety of Canadians. The U.S. FDA has an obligation to enforce its own laws."

With these statements, Health Canada confirmed that its role relates to drug safety in Canada only, and that it does not perceive an obligation to persons outside of Canada.

The November 18, 2003, Health Canada press release also emphasizes the importance of provincial regulation of health professionals, including pharmacists. Referring to its October 27, 2003, letter to provincial regulators, the press release notes that Health Canada continues to work with the provinces and territories and the regulatory colleges in order to prevent any negative impact from Internet pharmacies on Canadians. This statement is noteworthy with respect to its emphasis on the potential impact of Internet pharmacies on Canadians. Clearly, Health Canada is unwilling to extend its activities in order to ensure the safety of exported or transhipped drugs.

C. General Legal Framework for Drug Regulation in 25 Countries

Twenty-five countries, including Canada, have been identified as the most significant potential sources of pharmaceutical products for importation and use in the United States market. An examination of each country's laws shows that all of the identified countries have relatively sophisticated drug regulatory schemes. The primary purpose of these regulations is to ensure the safety, efficacy, and quality of products in their domestic markets. The regulatory regimes, however, were neither intended nor designed to ensure the safety of products intended for export.

Products intended for export are subject to meaningful oversight or regulation in some respects. However, because of gaps in some national regulatory regimes, countries cannot always ensure the safety, efficacy, and quality of the products that are imported, distributed, or manufactured within their borders for the purpose of export. In particular, the laws in many of the countries do not ensure that products imported for the sole purpose of export are safe, effective, and of the quality required for American consumers.

1. Overview

Similar to most developed countries, the 25 countries under review ensure the safety, efficacy, and quality of pharmaceutical products in two ways. First, products are subject to government pre-approval or authorization before marketing. This authorization provides a level of assurance of a product's safety and efficacy for its intended medical purpose, as well as its quality. Second, the countries require that manufacturers and distributors of medicinal products hold government authorizations or licenses that are usually conditional on compliance with certain standards of GMP or good distribution practice ("GDP").

All of the 25 countries exercise a degree of control over products that are intended for their domestic markets. However, this level of oversight does not always extend to products intended for export. The requirement for a marketing authorization is usually only triggered if a product is intended for the local market. With limited exceptions, the mere act of import and export of a product to or from these countries does not require a marketing authorization. While a number of jurisdictions require that manufacturers and distributors hold authorizations and comply with GMP or GDP, even if products are intended for export, others do not. Even where the requirements apply, the GMP or GDP standards may differ from their United States equivalents.

The gaps in national drug regulations are more numerous and pronounced where products are imported for the sole purpose of re-exportation. With few exceptions, the countries reviewed either explicitly or implicitly exclude transshipped products from various aspects of their medicines laws. Even where elements of national law do apply, evidence suggests that local drug regulators attach a low enforcement priority to transshipped products.

While controls in some countries are tighter than others, there is no guarantee that products that are exported from any of these jurisdictions to the United States will have been subject to sufficient control and oversight by the foreign country's regulatory agency to guarantee their safety. The following discussions provide illustrative examples of a number of the countries' regulatory weaknesses and deficiencies in this respect.

2. Manufacturing Licenses and Compliance with GMPs Often is Not Required for Imported and Exported Products

In regulating the manufacture of medicinal products, countries tend to define “manufacturing” broadly to include drug processing, assembly, division, packaging, and labeling, in addition to the initial manufacturing. Manufacturing also includes the associated sourcing of materials, quality control, release, storage, and distribution.¹⁶³ Any activities undertaken to prepare products for export to third countries such as the U.S. are likely to constitute manufacturing. Adequate regulation of these activities is essential to ensure the quality and correct handling and storage of such products.

Each of the 25 countries requires that manufacturers hold government licenses or authorizations. Governments usually grant licenses only after inspecting the applicant’s facilities. The licenses provide a degree of comfort as to the manufacturer’s suitability and the competence of associated staff. Yet no government requires manufacturing applicants to submit information about the safety and efficacy of the products being manufactured. Manufacturing license applicants are only required to submit information regarding their production processes and/or control of pharmaceutical manufacturing operations.

Many of the countries consider the importation of medicinal products to be a manufacturing operation requiring a manufacturing permit or equivalent distribution license, but licensing requirements do not always apply to these activities. For instance, Ireland¹⁶⁴ and the U.K.¹⁶⁵ do not require an importer to hold a license as long as the importer does not own the products, acts solely as a carrier or import agent for products imported from a country outside the European Economic Area (“EEA”), and delivers the products to a licensed manufacturer or wholesale distributor. Under U.K. law, the importer may hold the goods for an unlimited time. Ireland, though, requires the import agent to be licensed if it holds medicinal products for an appreciable length of time (*i.e.*, more than 48 hours). Where no license is required, there can be no guarantee that the importer will store and handle products appropriately.

Each country requires drugs for the domestic market to be manufactured in accordance with the country’s standards of GMP. Belgium, Canada, Denmark, Israel, and New Zealand exempt some licensed manufacturers, importers, and/or exporters from the GMP requirement entirely. Licensed importers in Denmark do not have to ensure compliance with GMP if control certificates for the products are available from other countries.¹⁶⁶ Products that are manufactured in Belgium or in Israel for export may meet the destination country’s specifications, rather than the local GMP requirements.¹⁶⁷ Similarly, New Zealand’s law does not expressly require export-only products to be

¹⁶³ Under European Community law, imports from outside the European Community or European Economic Area (“EEA”) are manufacturing operations. Imports from other EEA Member States do not require a license.

¹⁶⁴ Medicinal Products (Wholesale Licenses) Regulations (S.I. 39, 1993).

¹⁶⁵ Medicines (Exemption from Licenses) (Wholesale Dealing) Order 1990 (S.I. 566, 1990).

¹⁶⁶ Executive Order on Good Manufacturing (GMP) and Good Distribution (GDP) Practice for Medicinal Products (EO No. 264, April 4, 1997).

¹⁶⁷ Decree on the Manufacturing, Distribution and Supply of Medicines (*Koninklijk Besluit betreffende de fabricage en distributie in het groot en de terhandstelling van geneesmiddelen*) (June 6, 1960) (Belgium); Pharmacists Regulations [Medicinal

manufactured in accordance with New Zealand's standards of GMP.¹⁶⁸ It also does not require manufacturers of export-only products to hold a valid manufacturing permit.

Germany allows licensed manufacturers to meet a lower GMP standard when manufacturing products for foreign markets. Products meet this standard if they are neither unsafe nor significantly diminished in quality as a result of deviations from recognized pharmaceutical principles and practices.¹⁶⁹ Significant deviations from European GMP standards could violate this requirement. Yet manufacturers may deviate from this lesser standard if the destination country allows the lower-quality product to be imported.¹⁷⁰

Even where a country's GMP requirements apply in full to products intended for export, these standards may not be adequate to ensure the quality of products for the U.S. market. Each country's GMP standards may differ from American GMP standards. The current movement towards the international harmonization of GMP is limited in scope and effect. For example, the International Conference on Harmonization has developed standards for the manufacture of active pharmaceutical ingredients, but many jurisdictions, including the European Community ("EC"), have yet to adopt them formally. Standards for most elements of drug production, including the manufacture of inactive ingredients and finished medicinal products, have not been harmonized and may vary significantly between countries.

This variability in national requirements is evidenced by the fact that the U.S. has yet to enter into working mutual recognition agreements ("MRAs") with any of the 25 countries. Operative MRAs could allow the U.S. to rely on another country's GMP regime and inspections as assurance of adequate manufacturing controls. The U.S. has yet to implement the MRA that it executed with the EC in 1997. The U.S. has agreed to share certain GMP inspection and enforcement information with countries such as Australia, Canada, and Japan, but has not executed full MRAs.

3. Distribution Licenses Often Are Not Required for Imported and Exported Products

Distribution licenses and compliance with GDP can provide some assurance that pharmaceutical products are appropriately handled, stored, and transported, and that the products are not exposed to harm or degradation during distribution. However, compliance with GDP and/or the terms of distribution licenses does not require formal quality control testing. These licenses therefore provide only limited assurance that product quality has not been compromised during the distribution process.

Moreover, Austria, Canada, Germany,¹⁷¹ Greece, Israel, New Zealand,¹⁷² and the U.K. exempt some or all exported products from compliance with these requirements. For instance, Austrian law

Preparations] § 29(a)(6) (1986) (Israel).

¹⁶⁸ See Medicines Act § 42 (1981).

¹⁶⁹ Medicines Law (*Arzneimittelgesetz*) [hereinafter "AMG"] arts. 5 & 8.

¹⁷⁰ AMG § 73a.

¹⁷¹ Germany is in the process of amending its national laws to bring such products within the scope of its wholesale

requires licenses only to distribute products that are placed on the domestic market. Distribution of products solely for export purposes requires no license.¹⁷³ The U.K. requires a wholesale dealer's license only to export products to other EEA member states.¹⁷⁴ Companies exporting drugs from the U.K. to the U.S. do not have to be licensed and do not have to meet GDP requirements. As a result, there can be no guarantee that companies exporting to the U.S. have maintained product quality through correct handling, storage, and transport.

4. **Imported and Exported Products Often Are Not Subject to a Marketing Authorization Requirement**

Most countries require companies to obtain a marketing authorization before marketing a medicinal product domestically. The marketing authorization requirements and procedures in most of the 25 countries are similar to the FDA's approval process, and require the submission of data demonstrating the product's safety, efficacy, and quality.

While each of the 25 countries requires domestic products to be authorized, the marketing authorization requirement is triggered in most countries only if the product is "placed on the market," "supplied," "sold," or "distributed" within the relevant jurisdiction. Thus, in most countries, a product may be imported or exported without a marketing authorization. As long as the product is not placed on the domestic market, the product need not be approved by the national regulatory agency. Imported and exported products may therefore be of uncertain safety, quality, and efficacy.

a. **Imports - Most Countries Do Not Require Marketing Authorization and Cannot Guarantee Safety and Efficacy**

In most of the 25 countries, medicines may be imported even if the products are not authorized for marketing by the national regulatory agency. Only Canada, Germany, Ireland,¹⁷⁵ Israel,¹⁷⁶ Luxembourg,¹⁷⁷ and Switzerland require marketing authorizations prior to import. Certain products may be exempt from these requirements.¹⁷⁸

distribution regulations.

¹⁷² Medicines Act § 33 (1981). No license is required to export a product that could be lawfully sold in New Zealand.

¹⁷³ AMG § 63(1).

¹⁷⁴ Medicines Act § 481(b) (1968).

¹⁷⁵ Products may be imported into Ireland from another EC member state without an Irish marketing authorization. Medicinal Products (Licensing and Sale) Regulations, art. 3 (S.I. 142, 1998).

¹⁷⁶ Pharmacopoeia Ordinance [New Version] § 47A (1981).

¹⁷⁷ Law on Marketing and Advertising of Medicines, art. 4 (Apr. 11, 1983).

¹⁷⁸ Exemptions for transshipped products are discussed in detail below.

The other countries do not require adequate assurance that a product is safe and effective before import. Some of the countries impose more limited requirements, but these requirements are insufficient to guarantee that the products are safe and effective for their intended use. For instance, Australian law requires most imported and exported products to be listed on the Australian Register of Therapeutic Goods (“ARTG”). Listing requires only compliance with basic quality and safety criteria, and does not require stringent review of the product’s effectiveness. Australia’s Therapeutic Goods Administration can conditionally list medicines that do not meet the standards for the domestic market by specifying that they are for “export only.”¹⁷⁹

A number of countries require imports to be authorized by or notified to the regulatory agency. These notification requirements are generally administrative and are not intended to allow regulatory agencies to prohibit the importation of the product on safety or effectiveness grounds. Imports into Austria from outside the EEA must be authorized by the Ministry of Health and Women Products.¹⁸⁰ France requires prior authorization of all imports. Applications for authorization must include only such information as the product description, the import quantity, the purpose or intended use of the import, and the importer’s contact information.¹⁸¹ Similarly, Italian law requires prior authorization to import drugs, even if the products will not be marketed in Italy.¹⁸² The regulatory agency does not consider the product’s safety and efficacy when authorizing imports. Furthermore, no authorization is required to import products into Italy that meet particular requirements demonstrating their quality.¹⁸³ Neither Austria, France, nor Italy requires the requestor to submit the information necessary to determine whether an imported product is safe, effective, and compliant with GMP standards. As a result, products imported into Austria, France, or Italy may have undiscovered dangers.

The South African government allows some “gray market” goods to enter the country. These medicines are imported (and possibly manufactured) by an entity other than the manufacturer named in the official product registration, even though the medicines have the same name as product registered in South Africa. Product composition and quality is deemed to be identical to that of the registered medicine. The importer is not required to actually demonstrate the gray market product’s equivalence, safety, efficacy, or quality. Without such information, it is not possible to determine the risks that these products pose to consumers.

¹⁷⁹ Therapeutic Goods Act § 28 (1989); Therapeutic Goods Regulations (1990).

¹⁸⁰ Law on Importation of Medicinal Products (*Arzneiwareneinfuhrgesetz*). The import into Austria of any product that is subject to a marketing authorization in an EEA country need only be notified to the Ministry of Health and Women Products.

¹⁸¹ *Id.*; see also PUBLIC HEALTH CODE (*Code de la santé publique*) [hereinafter “CSP”] art. R. 5142-14.

¹⁸² Legislative Decree 178/1991.

¹⁸³ Authorization is not required for: (1) products manufactured in and imported from other EC member states; (2) products exported by an EC member state for which the exporting country has granted a certificate of quality control, regardless of their country of manufacture; and (3) imports from non-EC member states with which Italy has entered into an agreement ensuring the quality of medicinal products. *Id.*

b. **Exports - Most Countries Do Not Require Marketing Authorizations Prior to Export**

Almost all of the 25 countries exempt exported products from marketing authorization requirements.¹⁸⁴ Some countries require no safety or efficacy showing whatsoever for exported products, while others require exporters to demonstrate the product's quality. For instance, the Netherlands expressly excludes export-only medicines from its marketing authorization requirement,¹⁸⁵ while Belgium has created a simplified license procedure for export-only products that are not registered in Belgium.¹⁸⁶ This Belgian "declaration" need only include the complete qualitative and quantitative composition and chemical-pharmaceutical dossier. This showing is insufficient to guarantee that the products are safe and effective for the intended use.

Japan broadly exempts from marketing authorization requirements all drugs and "quasi-drugs" that are manufactured in Japan for export.¹⁸⁷ The manufacturer need only notify the regulatory authority of the products that will be manufactured for export.¹⁸⁸ The Japanese interpret "manufacturing" broadly to include "packaging." As a result, licensed manufacturers may import out-of-date medical products under the notification of re-exportation, re-package them as new products, and export them to foreign destinations. Such practices would be unlawful only when the products have "decomposed" or are otherwise harmful.

France and Denmark do not require exported products to be authorized by the relevant national regulatory agency, but do require exporters to explain why the product is not authorized.¹⁸⁹ This explanation need not include a safety or efficacy showing, and it does not appear that either country could prevent the exports on safety or efficacy grounds. The French regulatory agency (the "AFSSAPS") may prevent the export only for quality reasons, although it may inform the destination country that the product is not authorized in France. Denmark's voluntary export register lists exported products that meet product component, quality, storage, and manufacturing requirements.¹⁹⁰ Listed products are not subject to safety and efficacy requirements. Thus, products can be removed from the list only for non-compliance with quality requirements. Because the listing is not mandatory, this authority may be inadequate to assure product quality.

¹⁸⁴ Luxembourg and Norway have determined that their marketing authorization requirements apply to export-only products. Law on Wholesale Distribution of Medicines, arts. 1 & 2 (Jan. 6, 1995).

¹⁸⁵ Decree on the Registration of Medicines (*Besluit registratie geneesmiddelen*) art. 21.2 (Sept. 8, 1977). Similarly, Austria exempts products that are stored in such a way that no consumer (e.g., patient or physician) can access them, even if they ultimately are intended for the Austrian market. AMG § 2(11).

¹⁸⁶ Decree on the Manufacturing, Distribution and Supply of Medicines (*Koninklijk Besluit betreffende de fabricage en distributie in het groot en de terhandstelling van geneesmiddelen*), Article 3§1.7.a (June 6, 1960).

¹⁸⁷ Enforcement Order of the Pharmaceutical Affairs Law, art. 15. This manufacturing is not exempt from the licensing and GMP requirements.

¹⁸⁸ Similarly, the Spanish Medicines Agency ("SMA") must be notified of exports of authorized products. The SMA must grant prior approval for the import of any product that is not authorized for marketing in Spain. Law 25/1990 on Medicines; Circular 8/2002.

¹⁸⁹ Medicinal Products Act § 9(5).

¹⁹⁰ Ministry for the Interior and Health, Circular no. 14 (Jan. 29, 1998).

5. Regulation of Transshipped Products

Most countries exercise insufficient regulatory control, oversight, and supervision of transshipped products to assure the products' quality, safety, and efficacy. Indeed, these products are often completely unregulated. As a result, most jurisdictions cannot guarantee that products transshipped through their territory are subject to proper handling and storage, and are safe and effective for their intended use.

Transshipped products are often exempt from national marketing authorization requirements. Of the 25 countries, only Norway requires transshipped products to meet the requirements that apply to domestic products. The transshipment of products *via* Norway is subject to marketing authorization requirements, government supervision, and licensing. Switzerland also requires all transshipped products to hold a valid marketing authorization, unless they are otherwise exempt. Some countries also exempt transshipped products from licensing and GMP/GDP requirements. This exemption may be limited to products that are stored in customs warehouses or that are not manufactured or altered while they are in the country.

Some jurisdictions, including Austria, Finland, and Liechtenstein, exempt transshipped products from all national regulation without limitation. For instance, Austria's Law on the Importation of Medicinal Products specifically states that transshipping is not considered to be importation. Accordingly, the import does not have to be approved by the Ministry of Health and Women, and no marketing authorization is required.

Australia, Belgium,¹⁹¹ France, Greece, Iceland, the Netherlands, and the U.K. exempt transshipped products from marketing authorization requirements. Products also may be exempt from licensing and GMP/GDP requirements in these countries. In theory, products could undergo substantial change during trans-shipment without demonstrating their continued safety and efficacy.

Israel, Luxembourg, Australia, and Belgium exempt transshipped products from the marketing authorization requirement subject to particular conditions. Israel exempts transshipped products from marketing authorization and quality control requirements as long as the products are not "manufactured" in any way while within the country. Luxembourg requires a marketing authorization if the products are stored outside of customs warehouses. Australia requires transshipped products to be listed in the ARTG unless they never clear customs and are part of a continuous carriage within the control of a single person. Products must comply with basic quality

¹⁹¹ If products are imported into Belgium from outside the EC for re-exportation to a non-EC destination, Belgian law does not require that the products have an approved Belgian or European marketing authorization. The exporter need not even file the full declaration, described in section 4(b) above, if the product: (1) will be exported without any further processing or handling within Belgium; (2) clearly indicates the person responsible for the marketing of the products in the destination country and, if different, the manufacturer; and (3) does not refer to any person established in Belgium. The exporter is required only to declare the medicine to the inspection services and show that the products meet quality standards (compliance with GMP, testing of raw materials and the finished product, any other examinations necessary to ensure product quality, and licensure and compliance with WHO GMP standards). The importer does not have to provide a chemical-pharmaceutical dossier (normally part of the declaration) or a batch release. If the products remain under customs control, Belgium can exert little power, as the inspection services cannot access or inspect the products. All transshipments must be licensed.

and safety criteria in order to be listed in the ARTG, *e.g.*, sponsors must show that the foreign manufacture of products meets “GMP clearance of overseas manufacturers.” The products may not be required to meet the standards for domestically marketed products.¹⁹²

Portuguese law does not require transshipped products to be approved for marketing in Portugal, in the country of manufacture, or in the destination country.¹⁹³ Products imported into Portugal may be re-exported, even if they are not authorized in Portugal, if the source country authorized either the product’s marketing or manufacturing. The destination country need not have authorized the product. If a product is exported on the basis of the source country’s manufacturing authorization, therefore, it is possible that no country will ever examine the product’s safety and efficacy.

Some of the countries, including Ireland,¹⁹⁴ Italy,¹⁹⁵ Japan, Spain, and Sweden,¹⁹⁶ require businesses to hold manufacturing or distribution licenses in order to transship products.¹⁹⁷ France¹⁹⁸ and the Netherlands¹⁹⁹ require licenses only if the products are removed from customs warehouses or customs control. Greece,²⁰⁰ Iceland, and the U.K.²⁰¹ require licenses if the transshipped products will be “manufactured” in some way within the country. Licensees must comply with the general licensing requirements, which often include compliance with local GMP or GDP. These countries may regulate the business of transshipping, warehousing, storage, and related activities, and generally supervise the movement of products through their territories.

The licensing requirements do not ensure that drug products are safe and effective. They also may not ensure product quality. For instance, transshipped products that remain under customs control in Germany are subject to the lessened GMP requirements described above.²⁰² The German health

¹⁹² Therapeutic Goods Act § 28 (1989).

¹⁹³ Decree-Law 72/91 (Feb. 8, 1991); Directorate-General for Customs’s Guidelines (“Circular”) No. 46/2000 and 55/2000, on import/export of medicines.

¹⁹⁴ Medicinal Products (Licensing and Sale) Regulations art. 4(d) (S.I. 142, 1998).

¹⁹⁵ Legislative Decree 178/1991; Legislative Decree 538/1992.

¹⁹⁶ Pharmaceutical Act § 17 (1992:859).

¹⁹⁷ Ireland and Sweden require a manufacturer’s license only if the products are imported from outside of the EEA.

¹⁹⁸ An import authorization is required to import medicines from an EEA country for storage in a national import warehouse pursuant to article 277 A of the General Tax Code. CSP art. R. 5142-2 (inserted by Decree No. 2004-83, January 27, 2004, on import of medicines for human use). Products that will not be stored in a customs warehouse require a different type of authorization.

¹⁹⁹ These products only require an import license and compliance with Dutch GMP and GDP if they are imported from a non-EC country for re-export outside the EC. Decree on the Registration of Medicines (*Besluit registratie geneesmiddelen*), art. 21.2 (Sept. 8, 1977).

²⁰⁰ Ministerial decision A6a/9392/91/92, art. 10.

²⁰¹ Medicines Act § 14 (1968).

²⁰² AMG § 73 (2) No. 3.

authorities can inspect these products for compliance with the lessened GMP requirements, but cannot otherwise exercise oversight. Japan's regulatory gap is more substantial. Japan requires importers to notify the authority of the products that will be imported for re-export. Licensees could legally import or domestically procure outdated or expired medical products under such a notification, re-package them as new products and export them to foreign destinations. This practice is unlawful only if the products are "decomposed" or otherwise harmful.

D. Conclusion

As documented above, in the 25 identified countries, regulatory regimes are not capable of ensuring the safety of drugs exported to the United States. It would accordingly be misguided and dangerous to permit American consumers to be exposed to products for which safety has not been assured. Allowing drugs to enter the United States from foreign sources, under the MMA or any other importation scheme, would essentially hand over responsibility for the safety of our drug supply to foreign entities that have virtually no ability to ensure that drugs leaving their countries are not counterfeit, adulterated, or unapproved.