D. W. Howell, Director of Global Product Protection, Eli Lilly and Company

Testimony before HHS' Task Force on Drug Importation, April 5, 2004

I. Executive Summary

My name is D.W. Howell II. I am the director of global product protection for Eli Lilly and Company. The global product protection office was formed in January 2003 to intensify our ongoing anti counterfeiting efforts for Lilly products. Prior to 2003 I was Lilly's director of global security for 20 years; before that I was an FBI agent for 11 years, in various field assignments.

There are four key themes I would like to focus on in my testimony:

1. The prescription drug counterfeiting business has become a highly sophisticated, globalized endeavor, encompassing highly specialized distribution syndicates that deliver high-quality replicas of packages containing counterfeited drug product.

2. Counterfeit product is largely produced in China and India and destined for the developed world – including numerous countries targeted as potential U.S. importation sources under several versions of importation bills.

3. We test the counterfeit materials we recover during investigations and find wide variance in quality and sterility of the end product – some have no active ingredient, some have unrecognizable content, some have too much or too little active ingredient, and most are made in unhygienic settings.

4. Drug quality and safety would be threatened by the legalization of drug importation, as sophisticated counterfeiting activities would likely increase exponentially.

My testimony before your task force is focused on the increasingly sophisticated activities of counterfeit pharmaceutical networks as they pertain to Eli Lilly and Company products. But let me be clear. By "sophistication," I am not referring to the quality of a knock-off's ingredients, but instead to the highly developed packaging and printing replication capabilities used to mimic the approved product, the increasing anonymity afforded to these syndicates by the Internet, and their intricate and quick-responding distribution systems.

In the last several years, we have noticed an increase in the counterfeiting of Lilly products. Counterfeits today are being sold through complex distribution networks with packaging that is often indistinguishable from our own, even by experts.

Previously, our experience with counterfeit products was mainly limited to relatively unsophisticated operations producing copies of our antidepressant Prozac®. The distribution systems were limited and disorganized, and the packaging did not resemble Lilly's.

With the advent of the Internet, a whole new era of counterfeiting has begun. It is now feasible to rapidly distribute counterfeit product with relative anonymity. We have identified several criminal syndicates who now manufacture, package, and distribute counterfeits on a global basis.

These syndicates deal in illicit drugs and receive funding from identified organized criminal elements. We have been advised by law enforcement entities that in some instances these syndicates are linked to terrorist organizations in the Middle East, Afghanistan, and Pakistan and to drug cartels in Mexico.

In many cases, counterfeits are produced in facilities in China and then distributed to Korea, Taiwan, or surrounding countries for packaging and distribution. These syndicates often manufacture knock-offs in filthy, unsanitary conditions. Importantly, these products don't stay in Asia; they travel to the major Western pharmaceutical markets – some of the same countries that have been identified as prospective sources for a potential U.S. supply of imported pharmaceuticals in recently proposed importation bills.

As part of our investigative process, we have tested these knock-offs, and we find a range of potential safety concerns. In some, cases the product is subpotent. In others, it is suprapotent or mixed with other active ingredients or with unknown substances. In other cases, these counterfeits contain no active ingredient at all. In some cases, the chemical composition is similar to our own. We believe all of these scenarios raise significant safety issues because the counterfeits are produced in unsanitary conditions with absolutely no regulatory oversight.

I'd like to walk you through some recent counterfeiting investigations involving Lilly or its products.

- In one case, with the cooperation of the Taiwanese authorities, we identified an illicit drug ring in Taiwan that was producing counterfeit Lilly product on the same machines that produced methamphetamines. From the photographs of this raid, which have been included in my testimony, you can see that the sterility of the product is highly dubious, and the product was clearly a counterfeit. Multiple arrests and prosecutions are currently underway in Taiwan based on this illegal activity. These counterfeits were destined for major Western markets and for Internet sales.

- In a different case, counterfeit Lilly product originated in China and was moved through Korea and into the Middle East. In this instance, Israeli authorities discovered the operation. Subsequent raids and arrests have occurred in Israeli locations that were producing counterfeit packaging to contain the Chinese-originated counterfeit tablets for distribution in Israel.

- In another recent case, we detected counterfeit Lilly product from China, destined for the U.K., being transported via Belgium, disguised as a shipment of computer parts.

- In 2003, we conducted a raid in Los Angeles with other companies and federal and local law enforcement. We learned that a Vietnam-based organization was importing pharmaceutical products from Canada into the U.S. – including Zyprexa®, a Lilly product for schizophrenia and bipolar disorder. In this case, the counterfeiting was twofold: this operation stripped our Zyprexa out of its legitimate packaging, filling the original bottles with iron tablets, and distributed these bottles for consumption outside of the U.S. As a second step, they placed the legitimate Zyprexa tablets into counterfeit bottles for consumption in the U.S. marketplace. The counterfeiters mixed multiple strengths of Zyprexa in the same bottle before sending them out to secondary U.S. distributors.

- In another instance in China, documents that emphasized the counterfeiter's capability to provide counterfeit versions of nearly 50 branded pharmaceuticals – including cholesterol-lowering drugs and AIDS drugs – were seized with counterfeited drugs. These products were destined for Korea and European markets.

In the case of chronic use medicines, such as drugs to treat schizophrenia, AIDS or high cholesterol, this is not a matter to be taken lightly – as treatment with a sugar pill masquerading as a legitimate drug or treatment with inappropriate dosage levels could result in significant adverse consequences for the patient.

As you can see from these examples and the type of activities I have described, we have significant concerns regarding counterfeit syndicates and the flow of product into the U.S. from Canada, the Internet, and other illegal and unsafe distribution channels.

Finally, I can also report that our company has received patient- or physician-initiated reports in the U.S. of instances where a drug alleged to be a Lilly product was purchased from Canada and resulted in patient harm. In one case, a diabetic patient experienced adverse events after taking insulin that was improperly stored and shipped or was past the expiration date. This patient ended up in a coma.

Keep in mind that my testimony is based on today's environment, which is relatively closed – the nation's drug supply is FDA-approved and the distribution channels are straightforward and transparent. Now imagine the impact these highly evolved counterfeiting rings could have in a world where drug importation was legalized

II. Lilly's anticounterfeiting activities

Lilly anticounterfeiting and antidiversion activities can be divided into five categories:

- Active monitoring and investigation of reports of counterfeiting
- Risk-based use of authentication and tamper-resistant technologies
- Active management of product distribution channels
- Development and evaluation of new countermeasure technologies
- Internal restructuring to maximize organizational alignment

Each of these categories plays a significant role in our multipronged approach to reducing the risk of counterfeit Lilly drugs. I am responsible for the active monitoring and investigation of reports of counterfeiting.

Lilly has an active security program that investigates reports of suspected counterfeiting from all regions of the world. Lilly has security professionals in domestic and international offices regularly monitoring United States and international markets to locate drug diverters and counterfeiting operations.

Our security team is made up of former law enforcement professionals with collectively more than 100 years of experience. Some come with extensive knowledge of information technology and the Internet, and they have added immeasurably to our ability to identify rogue Internet pharmacy operators who sell counterfeits of Lilly products. They work with private investigators and alongside law enforcement personnel, participating in international investigations that identify and gather evidence about counterfeiting operations, illegal drug diversion networks, and the people who operate them.

As team members develop evidence about illegal activity, they present the case to government officials, who often conduct law enforcement operations, such as raids and arrests, based upon that evidence. Our team also directly assists law enforcement investigators in distinguishing counterfeits from authentic Lilly products during investigations. (*For additional information on Lilly's anticounterfeiting activities please see Appendix A)*

III. The prescription drug counterfeiting business has become a highly sophisticated, global endeavor, encompassing highly specialized distribution syndicates that deliver high-quality replicas of tablets (containing counterfeit drug ingredient), packaging, and labels.

A. Counterfeit Drug Packaging Is Virtually Impossible to Differentiate From Packaging for Legitimate, FDA-Approved Drug Products

Lilly has invested billions of dollars in drug research and development, testing and clinical trials, manufacturing and facilities, and the drug approval process to ensure the highest quality, safety, and efficacy of our drug products. Our investment in product packaging is also substantial.

Counterfeiters, however, invest minimally in the production or acquisition of drug products and focus the majority of their efforts on producing external packaging to give the false impression that their counterfeit substitutes are authentic. Through our investigative efforts, we have discovered counterfeit Lilly products that reflect an increased level of sophistication – especially in terms of drug packaging.

Historically, counterfeiters struggled to match certain types of packaging characteristics (*e.g.*, printing on foil). Poor quality in packaging material assisted investigators and health care professionals in identifying suspect drug products in the market. Today, counterfeit packaging is often virtually indistinguishable from authentic packaging, and, to the naked eye, counterfeit packaging and print may appear flawless. *(See Appendices B & C for photographs)*

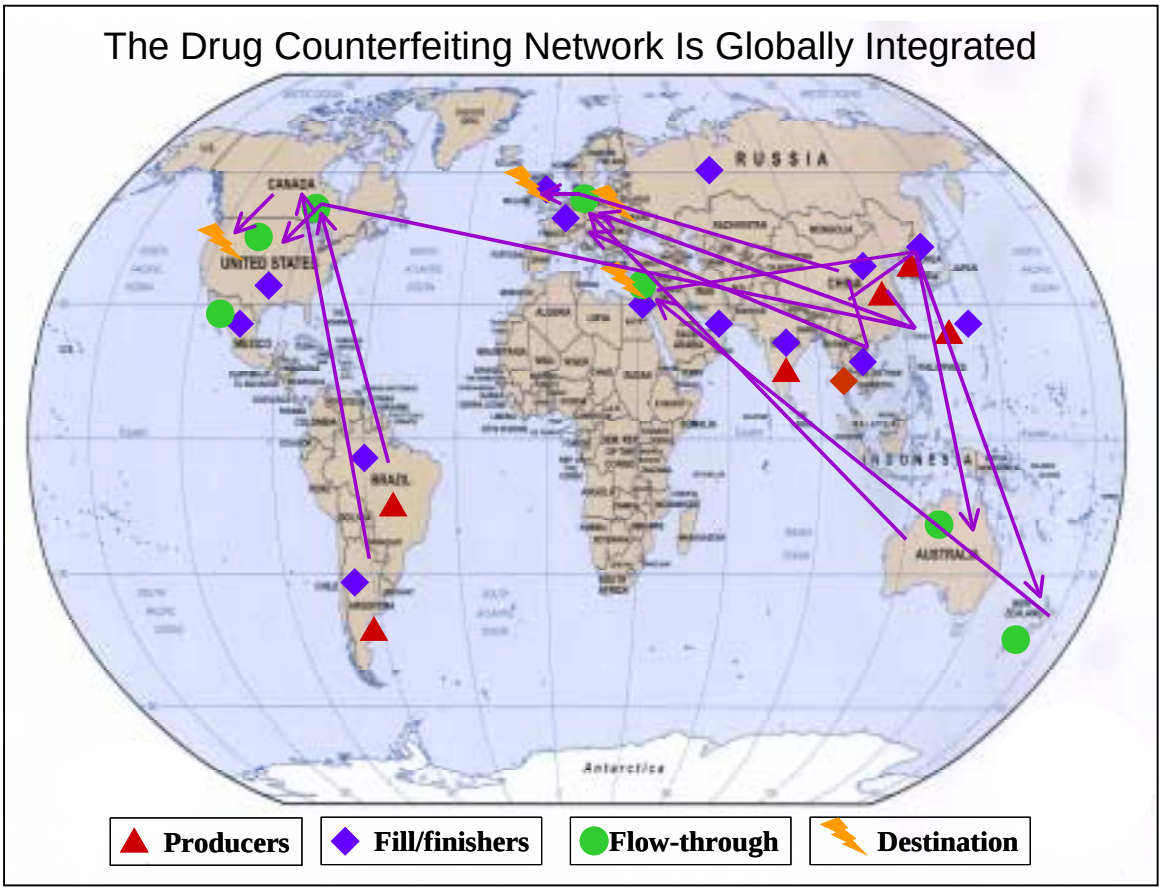
For example, in a recent investigation in Taiwan, our security team saw the use of sophisticated packaging equipment that was housed and operated in a "clean" building used for counterfeiting drug packaging and labeling. Conversely, the fake drug product destined for the aforementioned packaging itself was being "manufactured" next to methamphetamine, a substance strictly regulated under the Controlled Substances Act and routinely associated with illicit drug traffickers and organized crime. The drug production facility was filthy and used rusted machines that were caked with dirt, unknown chemicals, and contaminants. *(See Appendix D for photographs)*

B. Increasing Sophistication of Counterfeiting Distribution Syndicates

Lilly also is concerned that counterfeiting operations have become better coordinated. Our investigations have found links between counterfeiting and organized crime. This connection may spring from the fact that the penalties for counterfeiting are less severe than those for trafficking in controlled substances. We also have seen evidence that counterfeiting may be used as a "front" business by criminal enterprises to launder money. These factors have contributed to an increase in complexity among drug counterfeiters, who now have more assets available to them to disguise the source of

proceeds from illegal activities and have developed more complex organizational structures to shield their operations from investigators.

This very complex web of drug counterfeiting involves producer countries, distributor countries, and destination countries.



In many cases, the counterfeit product is produced in facilities in China and then shipped to Korea, Taiwan, or surrounding countries for packaging and distribution. As mentioned above, manufacturing of these knock-off is done in filthy, unsanitary conditions.

Syndicates represent primarily illicit drug distribution networks and have participants and funding from identified organized criminal elements. Our intelligence reports that these groups are located in Thailand, Cambodia, and other areas of Southeast Asia, trafficking in illicit drugs from South America. We have been advised by law enforcement that in some instances these syndicates are linked to terrorist organizations in the Middle East, Afghanistan, and Pakistan and to drug cartels in Mexico.

Importantly, these products don't stay in Asia; they are shipped to the major Western pharmaceutical markets – including many of the same countries that have been identified as prospective sources for U.S. drug importation in recently proposed importation bills.

Our investigations do not stop with raids. We test the counterfeit materials we recover during these investigations and find wide variance in quality of the end product and a broad range of potential safety concerns. In some cases, the product is subpotent, in others it is suprapotent or mixed with other active ingredients or unknown substances. In other cases, these counterfeits contain no active ingredient at all. In some cases, the chemical analysis is similar to our own. We believe all of these products represent significant safety issues, because they are produced in unsanitary conditions with absolutely no regulatory oversight.

Since I began collecting evidence of counterfeited Cialis ® in 2002, we found the following variations: versions with no active ingredient; versions containing caffeine; versions with a mixture of counterfeit Cialis and counterfeit Viagra® (Pfizer); versions with unknown ingredients; versions containing dietary supplements, and versions containing other counterfeited ED drugs.

C. A catalog of some of the counterfeiting investigations on which Lilly has participated:

1. In one case, product originated in China and was moved through Korea and into the Middle East. In this instance, Israeli authorities discovered the operation. Subsequent raids and arrests have occurred in Israeli locations that were producing counterfeit packaging to contain the Chinese-originated counterfeit tablets for Israeli distribution.

2. In another recent case, we detected counterfeit Lilly product from China, destined for the U.K., being transported via Belgium, disguised as a shipment of computer parts.

3. In another case from China, approximately 50,000 counterfeit erectile dysfunction pills from numerous manufacturers were intercepted. Additionally, materials were found that emphasized the counterfeiter's capability to provide counterfeit versions of nearly 50 branded pharmaceuticals, including cholesterol-lowering drugs and AIDS drugs. These products were destined for European markets and Korea.

4. Yet again in China, local authorities seized nearly 200 boxes of counterfeit Cialis® and additional quantities of other counterfeited erectile dysfunction medicines. Lilly/ICOS Corporation neither manufactures nor sells Cialis in China.

5. In the fall of 2002, Eli Lilly and Company and other pharmaceutical companies began to work with the Los Angeles County Sheriff's Department and the Food and Drug Administration (FDA) on suspicion that a global importation/counterfeit scheme was being conducted in the Los Angeles area. In February 2003, a search warrant was executed against NuCare Pharmaceuticals and NDT Pharmaceuticals. Enforcement organizations involved included the Los Angeles County Sheriff's Department HALTT team, U.S. Customs, the FDA, and the California state authorities. Following the execution of the search warrant, large quantities of pharmaceuticals and computer

equipment were seized. Upon review of information gathered, the following conclusions have been drawn:

- NuCare and NDT Pharmaceuticals had been conducting a global importation/counterfeit scheme.
- Operation sites included Canada, Asia, Sweden, Los Angeles, Houston, and New York.
- The importation source for much of the product was Canada, specifically an organization named, PharmaExp Montreal.
- The method of operation included importing product and relabeling and repackaging said product. Personnel completed the relabeling and repackaging in a nonsterile, noncontrolled environment. This product was then integrated into the U.S. distribution system. Vitamins (usually iron tablets) would then be placed into the original package and shipped to destinations outside the U.S.
- Sales of repackaged/substituted Zyprexa were estimated to be in excess of $20,000/week. Total receipts for the organization for all imported/counterfeit product totaled approximately $1,000,000/week
- The FDA is conducting ongoing enforcement activities regarding this situation.

6. On August 12, 2002, Lilly received a complaint from a pharmacist that a bottle of Zyprexa appeared to contain round, white tablets instead of Zyprexa tablets (See Appendix E for photos). Lilly received the bottle for further analysis and found that the package contained 71 round, white tablets that were imprinted with "ASPIRIN -L-"on one side of each tablet (the opposite side of each tablet was completely smooth). This particular imprint on the aspirin tablets is associated with a specific manufacturer (L. Perrigo) and has a product code of 411.

In addition, the following observations were made:

- The bottle, cap, and label all compared favorably to Lilly's "house" sample of the same lot; however, the package literature was not affixed to the bottle.
- There was no evidence that package literature was ever affixed to the bottle as there was no adhesive residue present on the area of the bottle where the package literature normally is attached.
- There was no desiccant present in the bottle.

- There appeared to be residue of some type of adhesive with attached cotton filaments around the mouth of the bottle. No glue is used in the process of applying the induction seal liners to Zyprexa bottles.

- Lilly received seven additional complaints of aspirin being discovered in Zyprexa bottles in spring and winter 2002.

(See Appendix E for photos)

7. On June 20, 2003, the FDA warned consumers that: SIGRA, STAMINA Rx, STAMINA Rx for Women, Y-Y, Spontane ES, and Uropin, all products manufactured by NVE, Inc., in Newton, New Jersey, and distributed by Hi-Tech in Norcross, Georgia, contained tadalafil, the active ingredient in Cialis. It is not clear where the tadalafil powder originated. However, it appears to be counterfeit material rather than diverted, authentic Cialis that was manufactured by Eli Lilly and Company.

D. *The advent of the Internet has introduced another layer of complexity to the battle against drug counterfeiting.*

Much of my testimony has been devoted to a discussion of the front end of the counterfeiting distribution chain. The advent of the Internet has introduced another layer of complexity to the importation story, with the potential to link a U.S. consumer directly to a counterfeiting operator or dealer, rather than to a legitimate retailer who genuinely believes his goods destined for U.S. import are legitimate. Couple this with the increasing public demands for drug importation from Canada and we see the potential danger of unwittingly turning a developed country with a safe drug supply into a potential gateway for counterfeit drugs.

While the Internet is a powerful information and economic tool that has improved our lives in numerous ways, it has also greatly complicated pharmaceutical manufacturers' abilities to protect their products. According to Carmen Catizone, executive director of the National Association of Boards of Pharmacy (NABP), the NABP believes there may be as many as 500 independent websites that offer prescription medications for sale direct to consumers (House Committee on Government Reform, March 27, 2003).

Further, there is no guarantee that a website is based in Canada. According to a report by GlobalOptions, Inc., a consulting firm specializing in security issues, approximately one-third of purported Canadian websites were actually hosted outside Canada. Not all Internet drug sellers with Canadian addresses are licensed. Consumers ordering drugs from Internet drug sellers have no guarantee that the medicine they are getting is either American-made or FDA-approved, regardless of what the Internet seller claims.

The evidence that suspect drug supplies are being diverted to Canada is mounting. According to Industry Canada, a department of the Canadian federal government,

between September 2002 and September 2003 there was a significant increase in Canadian imports of pharmaceuticals from Singapore, Ecuador, China, Iran, Argentina, Thailand, and South Africa. The majority of these countries have documented counterfeiting problems and none of these countries has a Mutual Recognition Agreement (MRA) with Canada on Good Manufacturing Processes (GMP) for prescription medicines.

COUNTRY	2002 TO 2003 CHANGE IN TRANSHIPMENTS	%INCREASE
Singapore	$13.8 TO $17.9 M	**+30%**
Ecuador	$.74 TO $2.2 M	**+198%**
China	$24.9 TO $35.5 M	**+43%**
Iran	$.049 TO $1.41 M	**+2,753%**
Argentina	$.22 TO .72 M	**+221%**
South Africa	$.28 TO $.51 M	**+84%**
Thailand	$.61 TO $.92 M	**+52%**

Source: Industry Canada, Trade Data Online
<www.strategis.ic.gc.ca> (20 November 2003)

Even if Canada did control these exports, its regulatory system would be quickly overwhelmed. Currently, the total Canadian legal prescription drug market is extremely small compared to that of U.S. Even creating a modest U.S. demand for drugs transshipped through Canada by lifting the current importation ban would pose an enormous challenge to that distribution and regulatory system.

E. While Anticounterfeiting Technology Is Feasible, No Single Technology Would Provide a Long-Term Solution to Counterfeiting

In February 2004, the FDA released its final report on "Combating Counterfeit Drugs." We strongly concur with the report's opinion that, "because the capabilities of counterfeiters continue to evolve rapidly, there is no single 'magic bullet' technology that provides any long-term assurance of drug security."

As we look at the most viable anticounterfeiting technologies, this assessment is important to consider. Importantly, the most reasonable timeline for the introduction of radio frequency identification (RFID) – the technology Lilly believes is most promising and is currently evaluating, is 2007.

We believe that RFID is years away from being a useful product protection technology. It will require development and installation of complex and costly computer networks and readers throughout the supply chain to track product as it proceeds through

distribution. Issues with cost, standardization of the electronic product code (EPC), technical limitations, consumer privacy, and data management remain unresolved.

I'd like to return to the point made earlier in my testimony – that these counterfeiters have access to the latest counterfeiting technology. In particular, they are quickly mastering the appearance of anti-counterfeiting technology on the packaging they produce. This is much like the phenomenon seen when the U.S. Treasury introduced a new $20 bill – viable counterfeits have already made their way into the marketplace.

The above analyses have all been done assuming an environment where drug importation remains illegal. Given the increasing sophistication of the drug counterfeiting currently penetrating our ostensibly closed U.S. pharmaceutical market, it may be useful to do scenario modeling around the potential for counterfeiters to quickly obsolete anti-counterfeiting technology in a world where importation is legal. The computer software and movie and music entertainment industries could serve as potential case studies for the task force to gain an understanding of the impact of counterfeiting on an industry.

In particular, the manner in which web music downloads now compete with CD and cassette sales might serve as a good proxy for the potential for legalized drug importation to change competitive dynamics and create a potential explosion in drug counterfeiting businesses.

E. Counterfeiting- and Importation-related Safety Concerns Do Touch Patients

While the focus of my work and my expertise is at the beginning of the counterfeiting distribution chain, I can report that our company *has* received patient- or physician-initiated reports in the U.S. of instances where a drug alleged to be a Lilly product was purchased from Canada and resulted in patient harm. In one case, a diabetic patient experienced adverse events after taking insulin that was improperly stored and shipped or was past the expiration date. This patient ended up in a coma.

This case is one example of the voluntary, unsolicited reports that come to Lilly from consumers and health care professionals, and the company is not in position to determine causality between the medicine and the adverse event, or even if the product was made by Lilly. The company is also not in a position to extrapolate to what extent the adverse event and safety reports it does receive are the result of patients taking counterfeited or otherwise imported drugs.

Other cases of patient safety being infringed also exist.

- According to research conducted by Beau Dietl and Associates, a young man in Georgia died after taking medicine he ordered from a South African website.

- According to a story in a *Washington Post* series on the dangers of buying drugs over the Internet, a teenager died after over-dosing on controlled substances and "some [of the medicines] came from overseas."

- An 82-year-old man with prostate enlargement bought a drug from an Arizona-based website that said the drug was produced in the U.S. and sold in Canada. He received a Tupperware container of drugs for prostate enlargement that contained knock-offs made in India. (The counterfeit medicine was labeled "Gabatin." The current FDA list of approved drug products contains no such medicine.) The container had no labeling or warnings.

- In a recent FDA investigation of Expedite-Rx and Rx Depot (storefront operations that send U.S. prescriptions, credit card information, and paperwork to a Canadian pharmacy), an FDA investigator brought a prescription for Serzone to Rx Depot that called for 60 pills, with one pill to be taken twice each day for 30 days. The investigator received 99 pills of APO-Nefazodone, an unapproved, foreign-manufactured version of the active ingredient in Serzone. In addition, the APO-Nefazodone package did not indicate that more than the prescribed number of pills was sent; instead, the labeling simply instructed the patient to take one pill two times a day. If the patient took the drug as instructed in the package sent from the Canadian pharmacy, he or she could have an increased risk of liver failure, which might be associated with taking the drug for an excessive period.

IV. Conclusion

Drug counterfeiting networks have reached such a high level of sophistication; one that will only continue to improve if the U.S. market is opened up to legalized drug importation. The counterfeiting business has become a fast-moving, deeply entrenched, globalized endeavor, encompassing highly specialized distribution syndicates delivering highly professional packaging replicas nonetheless containing counterfeited drug product. The counterfeiting chain is well-established: counterfeit product is largely produced in China and India and destined for the developed world – specifically, to numerous countries targeted as potential U.S. importation sources under several versions of importation bills.

Our testing of counterfeit materials reveals high variance in quality and sterility of the end product – some have no active ingredient, some have unrecognizable content, some have too much or too little active ingredient, and most are made in unhygienic settings. In the case of chronic use medicines, such as drugs to treat schizophrenia, or AIDS, or high cholesterol, this is not a matter to be taken lightly – as treatment could mean life or death.

The focus of the importation debate is well intentioned, but misguided. The American public has been led to believe the only issue is price. This assumes that the product they obtain in the U.S. is the same as that which would be imported—that is, that there is no difference in quality, only in price. In many cases, this assumption is false (e.g., counterfeit).

The real issue for the American consumer should be a weighting of price and quality. There is a good reason that counterfeit products are cheaper—their manufacturers do not have to invest in high quality research, development and manufacturing and distribution operations. They do not have to conduct clinical trials to demonstrate safety or efficacy. They do not have to even do the bioequivalence tests we require for generics to be approved for use in the U.S.

A fundamental founding principle of the food and drug laws in this country is that the producer has the burden of proof to demonstrate that the product is safe and, in the case of pharmaceuticals, effective. We have never asked the consumer to bear this burden. We have never required the government to bear this burden. Yet, now, it seems that the U.S. Congress is ready to shift this burden of proof to everyone but the marketers of the products that would be imported.

It was only a few decades ago that this burden of proof protected U.S. consumers from the terrible birth defects of thalidomide, a seductive and hypnotic drug that was found to be responsible for malformed offspring when used during pregnancy. Are we willing to undercut the FDA now and alter the very standards that have protected our own generation?

As mentioned before, my expertise lies in security issues and anticounterfeiting activities, and this has been the focus of my testimony. I would be remiss, however, in not, for the record, briefly reiterate the numerous other reasons that Lilly believes legalized drug importation is a bad idea. Drug importation subjects patients to numerous other safety risks; it provides questionable cost savings; it would ostensibly import price controls, damaging our capacity to innovate; and it would have significant negative impact on the U.S. economy.

While I am not qualified to speak to these important issues, Eli Lilly and Company would be pleased to provide other experts to testify on these matters in additional venues. I would be happy to direct you to the appropriate resources within the company.