

Statement of

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INTRODUCTION

Mr. Chairman and Members of the Committee, I am William K. Hubbard, Senior Associate Commissioner for Policy, Planning and Legislation at the U.S. Food and Drug Administration (FDA or the Agency). I appreciate the opportunity to discuss our mutual concerns related to the importation of drugs into the United States. This topic encompasses a range of issues, including the importation by individuals of prescription drugs through the mail or in person; the purchase of drugs from foreign sources over the Internet; and the potential introduction of counterfeit drugs into the U.S. drug supply.

FDA is also concerned about legislative initiatives that, while intended to provide drug price relief to consumers, would severely damage the system of drug regulation that has come to be known as the "gold standard" for drug safety throughout the world. Last month, speaking at a biotechnology summit in Canada, Secretary Thompson said "Opening our borders to reimported drugs potentially could increase the flow of counterfeit drugs, cheap foreign copies of FDA-approved drugs, expired and contaminated drugs, and drugs stored under inappropriate and unsafe conditions. In light of the anthrax attacks of last fall, that's a risk we simply cannot take."

PERSONAL IMPORTATION OF DRUGS THROUGH THE MAIL

Under the Federal Food, Drug, and Cosmetic (FD&C) Act, unapproved, misbranded, and adulterated drugs are prohibited from importation into the United States. In general, all drugs imported by individuals fall into one of these prohibited categories. This includes drugs that are foreign versions of FDA-approved medications, and drugs that are dispensed without a prescription. In addition, under the Act, FDA-approved drugs that are manufactured in the U.S. and exported may not be reimported by anyone other than the manufacturer.

The volume of prescription drugs for personal use imported through the mail has increased dramatically in recent years. According to testimony by the U.S. Customs Service (Customs) before the House Government Reform Committee in May 2000, seizures of parcels containing scheduled or controlled substances at international mail facilities increased by 450 percent in FY 1999, primarily due to drug sales over the Internet. FDA estimates that approximately two million parcels containing FDA-regulated products for personal use enter the U.S. each year through international mail facilities. This estimate is based on an extrapolation of data obtained during a pilot project conducted at the international mail facility in Carson, California, which is discussed in more detail below.

At mail facilities, Customs officials identify parcels that may violate the FD&C Act for FDA examination. FDA inspectors then determine if these products should or should not be permitted to enter the country. If detained, FDA must issue a notice to the addressee describing the potential Federal violation and provide the individual with an opportunity to respond and provide reasons why the drug parcel should be allowed entry. If the addressee does not respond or provides an inadequate response, FDA will give the parcel back to Customs to have it returned to the exporter. Due to the requirements for notice and an opportunity to respond, the detention and further processing of mail parcels consumes

large amounts of FDA resources. In addition, considerable storage space is needed to hold the large number of detained parcels until replies are received from the addressees.

Recent advertisements in U.S. newspapers and magazines claim that Congress has made the personal importation of drugs a legal practice. Other advertisements and certain Internet sites state that personal importation of up to a 90-day supply of prescription medications is legal. Neither of these claims is true. As we will discuss in more detail below, we are seeing an increasing number of Canadian pharmacies and U.S. intermediaries marketing prescription drug products directly to U.S. citizens, in violation of state pharmacy laws and the FD&C Act.

From a public health standpoint, importing prescription drugs for personal use is a potentially dangerous practice. FDA and the public have no assurance that unapproved products are effective or safe, or have been produced under U.S. good manufacturing practices. FDA cannot assure the public that re-imported drugs made in the U.S. have been stored under proper conditions or that they are even the real product, because the Agency does not regulate foreign distributors or pharmacies. Therefore, unapproved drugs and re-imported approved medications may be contaminated, subpotent, superpotent, or counterfeit. In addition, some websites based outside the U.S. offer to dispense prescription drugs without a prescription by a licensed practitioner or a physical examination, bypassing the traditional doctor-patient relationship. As a result, patients may receive inappropriate medications due to misdiagnoses, they may fail to receive appropriate medications or other medical care, or they may take a product that could be harmful, or fatal, if taken in combination with other medicines they might be taking.

Personal Importation Policy

Under FDA's personal importation policy, as described in guidance to the Agency's field personnel, FDA inspectors may exercise enforcement discretion in limited circumstances to permit the importation of certain unapproved prescription medication for personal use.

First adopted in 1954, the policy was last modified in 1988 in response to concerns that certain potentially effective treatments for AIDS patients were not available in the U.S. but were available in other countries. The Agency expanded the guidance for humanitarian purposes to allow individuals suffering from serious medical conditions to acquire medical treatments legally available in foreign countries but not approved in the U.S.

The policy is articulated in guidance to FDA field personnel and is not a license for individuals to import unapproved, and therefore illegal, drugs for personal use into the United States. Because the policy does not apply to medications that are already available in the U.S., even if sold under the same name, only a very few drug products available from foreign sources, especially Canada and Mexico, meet the personal importation criteria.

The current personal importation policy permits the exercise of enforcement discretion to allow entry of an unapproved prescription drug only if the intended use is for a serious condition for which effective treatment may not be available domestically; the product is considered not to represent an unreasonable risk; the product is for personal use; there is no known commercialization or promotion to U.S. residents by those involved in the distribution of the product; and the individual seeking to import the product affirms in writing that it is for the patient's own use and provides the name and address of the U.S. licensed doctor responsible for his or her treatment with the product or provides evidence that the product is for the continuation of a treatment begun in a foreign country.

FDA's personal importation policy, as written, is difficult to implement with respect to mail shipments

of drugs. This is due, at least in part, to the difficulty faced by Customs or FDA inspectors, or even health care practitioners, in identifying a medicine simply by its appearance or its labeling, which may falsely identify a product. From a practical standpoint, FDA inspectors cannot visually examine drug products contained in a mailed parcel and accurately determine their identity or the degree of risk posed to the individual who will receive these drugs. Also, largely due to the advent of Internet sites selling prescription drugs from all points around the globe, the volume of parcels containing prescription drugs has increased dramatically, beyond the ability of Customs and FDA staff to efficiently process.

Due to the huge volume of drug parcels entering the U.S. through the international mail and courier services, the requirements for notice and hearing, and our limited resources, it is difficult for FDA to detain and refuse mail imports for personal use. As a consequence, tens of thousands of parcels that FDA does not review are eventually released by Customs and sent on to their addressees, even though the products contained in these parcels may violate the FD&C Act and pose a health risk to consumers. We do not believe this is an acceptable public health outcome.

CARSON MAIL FACILITY PILOT

In early 2001, FDA and Customs conducted a survey of imported drug products entering the U.S. through the Carson City, California, mail facility (the Carson pilot). The purpose of the Carson pilot was to provide a means for examining incoming mail shipments of pharmaceutical products over a specified time frame to identify both the volume and the types of drug products entering the U.S. We also wanted to better assess the level of effort and human resources required to handle drug importations at a mail facility, and to better understand the public health implications these importations may have for U.S. consumers.

The Carson pilot ran for a five-week period, with FDA inspectors present for 40 hours per week, a much higher staffing level than is normally possible. Although Customs took a baseline sample which indicated they could have set aside for FDA review an estimated total of 16,500 international packages (650 packages per day), FDA was able to examine only 1,908 packages during the five-week pilot, or an average of 381 packages per week. Unexamined packages were sent on to the addressees. Of the 1,908 packages examined by FDA, 721 parcels originating in 19 countries were detained and the addressees notified that the products appeared to be unapproved for use in the U.S., misbranded and/or a drug requiring a doctor's prescription.

Analysis of the Carson Pilot Drug Parcels

FDA's Center for Drug Evaluation and Research (CDER) reviewed listings of the products detained during the Carson pilot to define better the nature of the risk to public health from the types of products coming into the U.S. through personal importation. CDER's review demonstrates that there are serious public health risks associated with many of the 721 drug shipments (composed of 197 different drugs) detained at Carson. There are primarily two types of risks that consumers of these drugs would face. The first risk arises when consumers take drugs of unknown origin or quality. Second is the very significant risk associated with taking many of these drugs without first obtaining a physician's prescription and without the continued oversight of the physician.

In general, FDA has no information to establish where these drugs were actually manufactured and whether current Good Manufacturing Practice requirements were followed. There is also no assurance that the drugs were packaged and stored under appropriate conditions to avoid degradation or contamination. Approximately eight percent of the shipments contained drugs that could not be identified because they contained no labeling; some of these contain only foreign language labeling.

Most of these drug shipments were contained in plastic bags; one shipment contained drugs taped between magazine pages.

Several drugs do not appear to correspond with any FDA-approved drugs and the risks are therefore difficult to assess. One drug had been reviewed for FDA approval but was denied approval due to cardiac abnormalities and because its efficacy could not be demonstrated. Several shipments contained three drugs that were once approved by FDA but have been withdrawn from the market based on serious safety concerns.

The vast majority of the shipments were identified as containing prescription drugs, which by definition have a degree of toxicity and/or risk associated with them such that they are not safe for use except under the supervision of a licensed health care practitioner (Title 21, U.S.C. section 353(b)). We believe that very few foreign Internet sellers require a prescription from a practitioner licensed in the U.S. before dispensing drugs to U.S. residents. Moreover, after detention notices were issued to the intended recipients of the 721 drug shipments, fewer than four percent responded with evidence of prescriptions or that a physician would provide oversight of the use of the drugs purchased from abroad.

A number of controlled substances were identified, including lorazepam, codeine sulfate, loperamide, chlordiazepoxide, chloral hydrate, and diphenoxylate. These drugs have the potential for abuse, addiction or life-threatening overdose. A physician's prescription and oversight are essential for managing these risks. Additionally, drugs having potentially serious adverse side effects including diabetes, hypertension and serious infection were included in the Carson shipments, as were many drugs with serious contraindications and/or possible drug or food interactions for which physician oversight is essential.

Many of the drugs identified in the Carson pilot are intended to treat conditions that only physicians can properly diagnose. Consumers who bypass physician diagnosis and prescribing may be exposing themselves to risks and toxicities that cannot be justified by offsetting benefits. For example, almost ten percent of the shipments were for antibiotics, despite the fact that consumers are generally not able to diagnose whether their symptoms are caused by bacterial or viral infections. Several drugs listed are potent steroids, which are generally prescribed for conditions that are not self-diagnosable.

Based on these observations, FDA believes that the type of drugs that are coming into the country for personal use, as demonstrated by the Carson pilot, pose substantial risks to the public health.

INTERNET DRUG SALES

Based on a survey conducted in early 2000 by FDA's Office of Criminal Investigations (OCI) and a subsequent study by the General Accounting Office, there appears to be roughly 300 to

400 Internet sites selling prescription drugs to consumers, with approximately half located domestically and half located outside the U.S. FDA has long taken the position that consumers are exposed to a number of risks when they purchase drugs from Internet sites that are not operated by pharmacies licensed and operating within state pharmacy law or sites that dispense foreign drugs. These outlets 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. FDA cannot provide consumers with any assurance that these products were manufactured under current good manufacturing practice standards. Taking an unsafe or inappropriate medication puts consumers at risk for dangerous drug interactions and other serious health consequences.

Internet sites that provide prescription drugs by having consumers fill out a questionnaire rather than seeing a doctor can pose serious health risks. A questionnaire generally does not provide sufficient information for a healthcare professional to determine if that drug is appropriate or safe to use, if another treatment is more appropriate, or if the consumer has an underlying medical condition where using that drug may be harmful. Finally, it must be noted that in the case of foreign based web sites, if consumers have an adverse drug reaction or any other problem they have little or no recourse because the physical location or operator of the "pharmacy" often is not known or the seller is beyond the consumers' reach. FDA has no ability to take effective action against these foreign operators on behalf of U.S. citizens.

Over the last twelve to eighteen months, FDA has noticed a proliferation of websites that offer drugs purportedly from Canada directly to U.S. consumers. As noted earlier, a number of these websites claim that drug sales from Canadian pharmacies directly to U.S. consumers are legal. This is false. Some websites purport to offer "U.S. approved" drugs, however, it is highly unlikely that the drugs are in fact approved by FDA. Some web sites are actually ordering services that take orders from consumers that are then fulfilled by supposed Canadian pharmacies. However, under state law, these ordering services are likely participating in the practice pharmacy without a license to do so.

A number of Canadian drug websites and U.S. ordering services indicate that the Canadian drugs are dispensed pursuant to existing prescriptions that are rewritten by a Canadian doctor in order to comply with Canadian law. However, the dispensing of medication on a prescription written by a physician who has not seen the patient or conducted a physical exam is generally contrary to state medical practice standards. Additionally, Dr. Henry Haddad of the Canadian Medical Association has said that under the Canadian Code of Ethics, physicians have a responsibility to do a history, physical exam and discuss the risks and benefits of the medication with the patient. He went on to say that the approval of prescriptions for patients they have not seen "Is something Canadian physicians should not be doing" (Associated Press, 6/26/02).

Some of these sellers have become so emboldened that they have solicited state Medicaid programs to import drugs from Canada. One Canadian pharmacy recently sent packages of prescription drugs to more than 500 U.S. consumers in a single shipment. Another boasted that since it added Internet sales to its local pharmacy a year ago, the store has gained about 100,000 U.S. customers. An ordering service based in Florida has announced plans to open 500 storefront shops nationwide within three years (Orlando Sentinel, 6/3/02).

Some recent criminal cases indicate the seriousness of the risks to public health that confront regulators with regard to Internet drug sales, but also illustrate the progress that is beginning to be made in combating this problem.

Norfolk Men's Clinic

On February 16, 2002, a federal jury in Alabama convicted Anton Puztai and Anita Yates of charges arising out of the operation of the online pharmacy that illegally sold prescription drugs over the Internet to consumers. On June 18, Puztai and Yates were sentenced respectively to over 15 years and 6.5 years of incarceration. Puztai, an Australian citizen, and Yates, a resident of Clanton, Alabama, were convicted of conspiracy to commit violations of the FD&C Act, conspiracy to commit money laundering, mail fraud, dispensing misbranded drugs, and operating a drug repackaging facility not registered with FDA. From fall 1998 to the summer of 2000, the defendants operated a website called Viagra.au.com, also known as Norfolk Men's Clinic, and related sites, that sold Viagra, Xenical, Celebrex, Propecia, and Claritin-D to consumers.

In September 1999, OCI received information regarding the Norfolk Men's Clinic and the website. Based on this information, several covert purchases were made via the Internet. Search warrants were executed in October 1999 that resulted in the seizure of prescription drugs along with numerous business records. Additional covert purchases were made from part of the Internet operation in West Virginia. Based on these purchases and numerous interviews, several individuals were indicted. In addition to defendants Puzstai and Yates, the president of a prescription drug wholesaler located in Miami, Florida, and the company itself, pled guilty to distributing midbranded drugs and to obstruction of justice. In conjunction with the indictment, a second search warrant was executed in Clanton, Alabama along with two search warrants in West Virginia. While most of the drugs sold in this operation were domestic product, some appeared to have originated in New Zealand.

Medications Express

On June 7, 2001, Gerald Bevins was convicted in U.S. District Court for the Southern District of California of conspiracy to defraud the U.S. and commit offenses against the U.S. by introducing misbranded drugs into interstate commerce and smuggling. On September 4, 2001, Bevins was sentenced to serve twenty-four months in prison. The case was initiated on information received from Customs concerning an Internet web site called Medications Express. Bevins sold Mexican prescription pharmaceuticals from this website and claimed that no doctor's prescription was necessary. He continued to sell Mexican prescription pharmaceuticals through the mail from Sun City, California, even after discontinuing the Medications Express web site. Bevins, his wife and daughter, would receive orders via mail, travel to Tijuana, Mexico to purchase the pharmaceuticals, and smuggle them back into the U.S. The three packaged the pharmaceuticals into commercial courier boxes and shipped them to customers around the U.S. The drugs supplied by Bevins were labeled in Spanish and included Ritalin, Valium, Rivotril, and steroids.

Canadian Drug Store, Inc.

On May 14 of this year, the Ontario College of Pharmacists, a Canadian government agency, filed charges under Ontario law against The Canadian Drug Store Inc. for unlawfully operating an unlicensed pharmacy and using an un-registered pharmacist in filling prescriptions for U.S. residents. The College also filed charges against a licensed pharmacist, pharmacy, and physician in Ontario for helping to facilitate the delivery of prescription and non-prescription drugs to U.S. residents. A drug wholesaler was charged with supplying medications to a non-licensed pharmacy.

According to a statement released by the College, "There are many websites selling prescription and non-prescription medicines that have not been accredited as legitimate pharmacies by pharmacy regulators in either Canada or the U.S. The public needs to know that some websites presenting themselves as online "pharmacies" or "drugstores" may be operating without a pharmacy license and dispensing prescriptions without the oversight of a licensed pharmacist."

Total Remedy / Prescription Center II

According to news accounts, a Los Angeles pharmacy and two pharmacists were assessed penalties of almost \$90 million in a state Board of Pharmacy proceeding this past May for filling more than 3,500 illegal prescriptions over the Internet. The case was under a new law enacted in 2001 that creates a requirement in California to fill prescription pursuant to a "good-faith medical examination." The Internet site concentrated on filling prescriptions for "lifestyle" drugs such as Viagra and Propecia (Associated Press, 5/29/02).

Pillbox Pharmacy

In March of this year, a Texas pharmacist, three doctors, two corporations and an individual were charged in a federal indictment alleging that they conspired to illegally dispense drugs in connection with an Internet pharmacy operation. The indictment charged one pharmacist, three physicians and two corporations, the S&H Script Shop and the Pillbox Medical Center, with conspiring to illegally dispense controlled substances and commit money laundering. According to the indictment, between January 1, 2000, and June 12, 2001, the defendants grossed more than \$7.7 million from the Internet sales of just two drugs alone. The indictment alleges the doctors would issue prescriptions without establishing a patient history, performing a mental or physical exam, using appropriate diagnostic or laboratory testing, or providing any means to monitor medication response. The charges were the result of an 18-month investigation by FDA, the DEA and the Internal Revenue Service, working with the U.S. attorney's office. In April, the pharmacist and two corporations pled guilty to illegally dispensing controlled substances, and agreed to forfeit \$1 million.

Other Enforcement Activity

To date, OCI has initiated 296 Internet drug investigations with each case involving a variable number of websites from one to 25 or more. These cases originated from multiple sources including interception at mail facilities, web based research, consumer complaints, and a variety of others. OCI has effected 112 Internet-related drug arrests and obtained 72 convictions. OCI currently has 101 open Internet drug investigations.

Currently, FDA has 90 sites under active review for possible regulatory or civil action.

Warning letters have been sent to 55 domestic online sellers. Additionally, FDA has sent 137 "cyber letters" to operators of Internet sites in many countries, including Canada, that offer to sell online prescription drugs or unapproved drugs. These sites may be engaged in illegal activity such as offering to sell prescription drugs to U.S. citizens without valid (or in some cases without any) prescriptions. Cyber letters are sent over the Internet to the suspect websites to warn the operators that they may be engaged in illegal activities, and inform them of the laws that govern prescription drug sales in the U.S. Cyber letters have a deterrent effect and FDA has seen positive results from using them. FDA also sends copies of its cyber letters to the home governments of targeted websites when the locations can be identified. Follow-up depends on the ability and willingness of the foreign regulatory bodies to investigate and take actions against website operators who are illegally shipping drugs to other countries.

In cooperation with the Department of Justice (DOJ), FDA has obtained five preliminary injunctions against the sale of illegal products, including one product marketed as a weight-loss aid containing a potent thyroid hormone which could cause heart attacks or strokes, and an unapproved cancer therapy. Additionally, 15 product seizures, 11 product recalls, and the voluntary destruction of 18 violative products have been achieved, generally pertaining to unapproved new drug products including gamma hydroxybutyric acid, gamma butyrolactone, Triax, 1,4 butanediol, and laetrite. Forty-five foreign shippers have been placed on Detention Without Physical Examination and added to Import Alert 66-57 for targeting sales of unapproved new drug products to the U.S.

IMPORTATION AT LAND BORDERS

FDA is aware that a number of U.S. citizens travel to other countries to purchase medications at a lower cost. However, many prescription drugs available from foreign sources are either unapproved foreign

versions of FDA-approved drugs or products for which there is no U.S. approved counterpart. In either case, these products are unapproved drugs prohibited from importation by section 505 of the FD&C Act. In FDA's experience, many drugs obtained from foreign sources that purport to be the same as U.S. approved prescription drugs are of unknown quality. FDA cannot provide adequate assurance to the American public that the drug products they purchase in other countries are the same products approved by FDA.

FDA is developing a program to better warn U.S. citizens about these dangers and the potential risks to their health when purchasing such drugs. We have begun to provide brochures to consumers crossing U.S. borders to make such purchases and are installing posters at borders stations warning of the dangers inherent in purchasing drugs outside the U.S.

Within the last two years, FDA has conducted three surveys at U.S. borders to gather data on drug products carried by individuals entering the U.S. While these border surveys involve land traffic rather than mail importation, the results show some similarities to the findings from the Carson mail pilot, but also some significant differences.

Southwest Border Survey (August 2000)

A survey of prescription drugs being brought by pedestrians into the U.S. at eight ports of entry along the 2,000 mile border with Mexico was conducted by FDA's Southwest Import District (SWID) with the assistance of other agencies. The survey looked at activity during four hours on a Saturday (August 12, 2000) at eight border ports in California, Arizona, and Texas. The purpose of the survey was to determine what specific types of products are being imported, and who is importing these products. The data collected from over 600 interviews indicated that the most common importers of prescription drugs were older male Caucasians with prescriptions from the U.S., bringing back primarily antibiotics or pain relievers for their own use. Prescriptions were held by 63 percent of the persons interviewed (59 percent U.S. prescriptions and 41 percent Mexican). The most common drugs and their indications that were purchased in Mexico during the survey were as follows: Amoxicillin (antibiotic), Glucophage (diabetes), Premarin (estrogen), Dolo Neurobion (vitamin supplement), Vioxx (inflammation), Retin-A (acne), Tafil (anxiety), Celebrex (arthritis), Penicillin (antibiotic), Viagra (impotence), and Carisoprodol (analgesic). While many of these products are already available as FDA-approved drugs in the U.S., some are unapproved for sale in this country.

Canadian Border Survey

On January 6, 2001, in cooperation with Customs, FDA conducted a survey to obtain a snapshot of prescription drug products being brought into the U.S. from Canada via passenger vehicles. During the eight-hour survey at three ports of entry in New York, Michigan and Washington, a total of 10,374 passenger vehicles and 58 buses crossed into the U.S. Of these, 33 passenger vehicles (35 individuals) were referred by Customs to be interviewed. These individuals brought in a total of 47 containers of drug products from Canada. The types of products included pain medicines -- primarily A-222 (a combination of acetaminophen, caffeine, and codeine) or similar products. The indicated reason for import was that the products were available over-the-counter (OTC) in Canada and cost less than in the U.S. The next largest group of products was herbal products, with the reason for importation being that the products were not available in the U.S. Other products included Tobradex (antibiotic/ steroid ophthalmic for individuals having laser eye surgery); Claritin and Allegra (allergies) purchased OTC in Canada; Sibelium capsules (calcium channel blocker); and a variety of OTC products sold in Canada and not available in the U.S.

Some of these drugs are unapproved foreign versions of FDA-approved drugs, although some approved for sale as prescription drugs in the U.S. are sold as over-the-counter medications in Canada.

Southwest Border Survey (April 2001)

On April 11, 2001, FDA, Customs, and other agencies conducted a survey of prescription drugs being brought into the U.S. at seven ports of entry along the U.S./Mexican border. This survey coincided with both Easter vacations, college spring break and the end of the snowbird season, when tourists from Northern states visiting along the Southern border return home. During the four hour survey, a total of 586 persons brought in a total of 1,120 drugs. Approximately 56 percent had a prescription for the medicines (61 percent were U.S. prescriptions, 39 percent were Mexican). The most common drugs purchased in Mexico were: Amoxicillin (antibiotic), Premarin (estrogen), Claritine (allergy), Terramicinia (antibiotic), Ampicillin (antibiotic), Ibuprofen (analgesic), Penicillin (antibiotic), Vioxx (inflammation), Tafil (anxiety), Dolo Neuorobian (vitamin supplement), Glucophage (diabetes), Celebrex (arthritis), Naproxen (analgesic), Retin-A (acne), Ventolin (pulmonary disease), and Valium (controlled substance/ nervous system depressant). As in the earlier survey, many of these products are already available as FDA-approved drugs in the U.S., while some are unapproved for sale in this country.

Controlled Substances

Although we do not know, nor is it possible to clearly determine, the amount of controlled substances brought into the U.S. purportedly for personal use, it is likely that such medicines are frequently imported for resale and pose a public health risk. The Agency has been working with both Customs and DEA to streamline and clarify Federal import policies specifically related to the importation of controlled substances.

COUNTERFEIT DRUGS

FDA continues to believe that the quality of drugs in this country is high, and that the public can continue to have confidence that the drugs sold in the U.S. market are authentic. The Agency, however, takes very seriously any allegations or information regarding the counterfeiting or adulteration of drug products. As the drug manufacturing and distribution system has become more global in nature, the challenge of protecting against counterfeit, adulterated or substandard drugs has become more difficult. We are concerned about a spate of drug counterfeiting and tampering cases that have occurred in recent months, and we believe these incidents caution against any weakening of the current regulatory system.

The manner in which FDA handles these types of counterfeit and tampering incidents are driven by two primary goals that are often, but not always, complementary. First and foremost, FDA works with consumers, manufacturers, wholesalers, distributors, state agencies and others in order to determine the composition of the unsuitable product and the extent to which it has been introduced into the distribution chain, and we use this information do whatever is necessary to protect the public health. Second, OCI, with the support and cooperation of other FDA components and other law enforcement agencies, attempts to bring the perpetrators of criminal acts to justice. It must be noted, however, that the need to publicize the existence of a counterfeit or adulterated product in order to alert professionals and the public to potential dangers may compromise the successful conduct of criminal investigations.

Regular FDA district field investigators often work closely with OCI special agents in these cases. They follow up at specific wholesalers, distributors, hospitals or pharmacies identified as having received counterfeit product to conduct tracebacks on particular lots and to determine sources, quantities involved

and the distribution of product to retail outlets. The FDA's Forensic Chemistry Center (FCC) and/or the drug and biologic review divisions provide field personnel with the labeling and packaging of authentic product for comparison with counterfeit product. FDA also posts information to its MedWatch site to inform consumers and health care professionals about safety concerns related to counterfeited or tampered products.

OCI opened 55 counterfeit drug cases from October 1998 through June 2002. During that time we have made 26 arrests with 20 convictions. We have seen a gradual increase in the incidence of finished dosage form counterfeit activity over the last few years. So far this year we have 16 cases opened, 12 arrests, and seven convictions. Eight of these arrests and five convictions are attributable to the latest eight counterfeit drug appearances.

The current focus on drug counterfeiting and the public perception of a more dramatic increase in counterfeit drug activity is due to the fact that the latest several counterfeits have appeared in the wholesale market and received wider distribution than has been the case historically. This is due to the existence of an illicit wholesale drug diversion network that has grown up around tiered pricing and economic fraud.

This system consists of criminal middlemen who knowingly solicit closed door pharmacies, such as a hospital or nursing home supplier, to over-order certain drugs based on fraudulent demand. The drugs are then sold into the wholesale drug diversion network. The diverter typically offers a 25 percent kickback to the closed door pharmacy and diverts the excess drugs into the illicit wholesale diversion system. This system depends on the diverter maintaining confidentiality for the closed door pharmacy since the pharmacy would lose its preferred pricing should the manufacturer discover the fraudulent arrangement. False pedigrees are the hallmark of the system as each wholesaler passing the drugs on to the next faces being "cut out" if the subsequent buyer knows the identity of his supplier's source. It is easy to see how this system of "willful blindness" facilitates the entry of counterfeit and otherwise unsafe drugs into the marketplace. Unfortunately these illegal schemes net huge profits. From October 1998 to June 2002, OCI opened 255 Prescription Drug Marketing Act diversion cases, executing 464 arrests and resulting in 337 convictions, with fines and forfeitures totaling approximately \$32 million.

The following examples of counterfeit drug products and tampering incidents may help to illustrate the types of activity we have recently encountered.

Serostim (somatropin (rDNA origin) for injection), Serono Laboratories

In late 2000 and early 2001, FDA became aware of consumer complaints about adverse effects and a recall at the distributor level of Serostim. FDA enforcement personnel and criminal investigators became involved and engaged FDA field offices nationwide, which included investigative follow-up at other distributors and the manufacturer. In January 2001, Serono issued a press release regarding the apparent counterfeiting of one particular lot. An additional press release and Dear Health Care Professional letter were issued by the company in May 2001, regarding a second lot.

In May 2002, Serono became aware that counterfeit Serostim displaying a fake lot number had been distributed. Preliminary information indicates that the counterfeit product may have been distributed via the Internet. Laboratory analysis by FDA shows that the product contains no active ingredient, and it has been determined that the product did not originate from Serono.

On May 16, Serono issued a letter advising Serostim handlers to be aware of the counterfeit lot even though it has not shown up in normal distribution channels.

Neupogen (filgrastim), Amgen, Inc.

In the spring of 2001, based on observations by a distributor about product appearance, Amgen analyzed a suspect lot and determined that the vials contained only saline solution. Investigation by the company and FDA revealed that the lot did not display a legitimate Neupogen lot number, but one that had been assigned to a lot of Epogen, another Amgen product. The FCC performed additional analysis. In May 2001, Amgen issued 17,000 Dear Health Care Professional letters nationwide informing patients, physicians, pharmacies and wholesalers about the counterfeiting of Neupogen. Later that month, Amgen reported to FDA on product with four lot additional numbers having wrong expiration dates, indicating either counterfeit lot numbers or that expiration dates were changed to make them more saleable by extending dates. In June, Amgen updated its Dear Health Care Professional letter with information on additional confirmed and suspected counterfeit lots.

Epogen (epoetin alfa), Amgen, Inc.

In May 2002, FDA, state regulators and Amgen became aware that potential counterfeit Epogen may be in commerce. Amgen analysis indicated that a counterfeit product labeled as Epogen 40,000 U/ml vials with a particular lot number contained a clear liquid having active ingredient approximately 20 times lower than expected. Samples of the authentic product as well as the counterfeit product were sent to FCC for analysis. On May 8, Amgen issued a letter advising health care professionals about the counterfeit Epogen and describing the differences between authentic and counterfeit packaging so that physicians can identify the authentic product. Further investigation revealed that a major wholesale distributor was holding approximately 1,600 cartons of counterfeit product. The majority of this counterfeit product was tracked back to a wholesaler located in the western U.S. On May 24, Amgen issued a second advisory letter to warn health care professionals that two additional counterfeit lots of Epogen were discovered.

Combivir (lamivudine plus zidovudine), GlaxoSmithKline

In the spring of 2002, GlaxoSmithKline (GSK) received four complaints that bottles containing 60 tablets of Combivir were being replaced with Ziagen tablets. In addition, the firm determined that counterfeit Combivir labels were placed on authentic bottles of Ziagen tablets. Both medicines are used as part of a combination regimen to treat HIV infection. A GSK health hazard evaluation of this situation determined that if an individual takes the wrong tablet and is sensitive to abacavir sulfate (Ziagen), a potentially life threatening hypersensitivity reaction could occur. GSK has stated that the incidents appear to be isolated and limited in scope, and no injuries or adverse reactions have been reported. However, in May, distributors were advised to initiate recall to their customers. GSK also issued a press release to alert patients, pharmacists and physicians to watch for third party tampering that incorrectly labels Ziagen as Combivir.

Zyprexa (olanzapine), Eli Lilly & Co.

In the winter and spring of 2002, Eli Lilly received complaints from four pharmacies in four states that the product Zyprexa had been removed and replaced with white tablets labeled as aspirin. Zyprexa is indicated for the treatment of schizophrenia and acute bipolar mania. The tampering situations occurred in two strengths and in three different lots. The company determined that the tablets from two of the complainants were non-Lilly tablets and looked the same in both complaints. FDA has determined the manufacturing source of the white tablet marked as aspirin and is continuing to investigate. On May 4, Lilly issued a press release and Dear Health Care Professional letter concerning the tampering situation. The company stated in their press release that these incidents appeared to be isolated and limited in

scope.

Procrit (epoetin alfa), Amgen/Ortho Biotech

In May 2002, based on requests from state health authorities, Amgen obtained and analyzed samples of 40K vials of Procrit from a certain wholesale distributor. The analysis indicated that a counterfeit drug product labeled as Procrit 40,000 U/ml vials with a certain lot number contains a clear liquid having active ingredients approximately 20 times lower than expected. Samples of the authentic product as well as the counterfeit product were sent to FCC for further analysis. Investigators are continuing following up at wholesalers and distributors identified as receiving the counterfeit product. One major wholesale distributor was found to be holding approximately 339 cartons of counterfeit product. In June, Ortho Biotech issued a Dear Health Care Professional letter and press release which details the differences between authentic and counterfeit packaging so that physicians can be certain they have the authentic product.

In addition to the above cases, OCI has made a number of recent arrests relating to counterfeit AIDS and cancer drugs, as described below.

Serostim, (somatropin (rDNA origin) for injection), Serono Laboratories

In November 2000, Nicholas Hanson was arrested by a task force of OCI, U.S. Postal Inspection Service, and Iowa State Police on charges of conducting an ongoing criminal enterprise. Hanson was the leader of a small group that counterfeited Serostim. He imported the human growth hormone through the Internet from China, via Express Mail. At the same time, Jeremy Gansen was arrested by the same task force and charged conducting an ongoing criminal enterprise related to the misbranding and distribution of human growth hormone and steroids. Gansen assisted Nicholas Hanson in the counterfeiting of Serostim.

Nutropin AQ (somatropin (rDNA origin) for injection), Genentech

In July 2001, an individual was arrested in Texas by OCI and subsequently indicted in August 2001 by a Federal Grand Jury. He was charged with counterfeiting Nutropin, trafficking in counterfeit goods and controlled substances violations. He subsequently plead guilty to counterfeiting Nutropin and distributing controlled substances. In December 2001, a second individual was indicted by a Federal Grand Jury in Texas for counterfeiting the above Nutropin, conspiracy to defraud the FDA, aiding and abetting and controlled substances violations. He is a fugitive and a provisional international arrest warrant is being sought for his arrest. He will be extradited to the U.S. In April 2002, two additional individuals involved in the distribution of counterfeit Nutropin were arrested by OCI and DEA for selling heroin to an undercover agent.

Finally, in May 2002, a fifth individual was arrested by OCI for selling counterfeit Nutropin, and he subsequently plead guilty to the charge.

FDA remains strongly concerned about any possibility that counterfeit or otherwise unsafe drugs may find their way into the American drug supply. We will remain vigilant as we refine and improve the programs and procedures that we use to ensure the availability of safe medications for consumers. We also believe that proposals that have been put forth in Congress to allow either the reimportation of drugs by persons other than the original manufacturer, or to allow consumers to import drugs for their own personal use, will provide additional avenues for unscrupulous individuals to place counterfeit, substandard or otherwise dangerous drug products into U.S. commerce and into citizens' medicine

cabinets, as discussed below.

DRUG IMPORTATION LEGISLATION

Currently, new drugs marketed in the United States must be approved by FDA based on demonstrated safety and efficacy; they must be produced in manufacturing plants inspected and operated in conformance with FDA's current Good Manufacturing Practice (GMP) requirements; and their shipment and storage must be properly documented and subject to inspection. This "closed" regulatory system has been very successful in preventing unapproved, adulterated or misbranded drug products from entering the U.S. stream of commerce. Legislation that would establish other distribution routes for drug products, particularly where those routes routinely transverse a U.S. border, creates a wide inlet for counterfeit drugs and other dangerous products that can be injurious to the public health and a threat to the security of our nation's drug supply.

In particular, S. 2244, recently introduced by Senator Dorgan and others, would create two new pathways for drugs to enter the U.S. outside of the current drug regulation system that, while not perfect, has a remarkable record of protecting the public from contaminated, ineffective, or counterfeit drugs. Of particular concern are the provisions for allowing individuals to import drugs directly from Canadian pharmacies. This would greatly exacerbate the growing problem of the hundreds of websites purporting to sell legitimate medications that are in fact selling unapproved or otherwise dangerous drugs to Americans. These personal importation provisions are so broad that they will over-ride existing statutes that allow FDA to refuse entry to prescription drugs from Canada if they are believed to be unsafe, ineffective, adulterated, contaminated or counterfeit.

Throwing the door open to drugs purchased by individuals directly from Canadian sellers will encourage unscrupulous individuals to devise schemes using Canada as a transshipment point for dangerous products from all points around the globe. Web sites touting the availability of supposedly legal drugs from Canada will spring up in large numbers, duping consumers that will have no way of knowing that the drugs may be illegal, counterfeit or contaminated.

S. 2244 would create a second route for transporting drugs into the U.S. outside of the existing regulatory system. The bill would allow pharmacists and wholesalers to purchase drugs from Canadian sellers over which U.S. authorities (FDA or others) have no jurisdiction or control.

Because the bill requires that the drugs comply with sections 501, 502 and 505 of the Act, it may be found, in practice, that for the bill to have its intended effect, U.S. manufacturers would have to sell drug products manufactured, labeled and intended solely for the U.S. market to Canadian distributors, specifically for re-sale to the U.S. As a practical matter, meeting these requirements would be very difficult, and it is unlikely that Canadian sellers and U.S. importers would be willing to endure them. Additionally, it is not clear as to how FDA could ensure that drugs reimported under this proposal would in fact comply with those sections of the Act, because the Agency has no practical ability to regulate or inspect Canadian facilities.

The bill attempts to ensure the safety of the drugs under 804(b) by requiring testing for authenticity. Unfortunately, authenticity can rarely be established solely through chemical analysis. That can only be assured by the multiple layers of safeguards that are built into the FDA's oversight system in which drug approval, regulation, inspections and surveillance tracks drugs over their entire life cycle. The testing required by S. 2244 would not protect against the threat of counterfeit drugs because no random sampling plan can protect against such criminal conduct. The threat of counterfeits does not depend on the integrity of the product itself, but on the integrity of those handling it. 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.

In addition, the bill would require drug manufacturers to disseminate their drug formulations and chemical fingerprints to potentially thousands of pharmacies and wholesalers. This information, currently protected as trade secret, could be worth millions of dollars, per drug, on the black market. Counterfeiters could obtain drug formulations and learn how to make their fake drugs look real and survive chemical analysis. Notwithstanding these very real safety concerns, it is questionable as to whether the bill would achieve the goal of bringing cheaper pharmaceutical products to U.S. consumers. Any cost savings that might be generated may well be absorbed by the fees charged by exporters, wholesalers, pharmacists and testing labs.

We would also like to recognize that the Administration is continuing to review this legislation and may have further comments. Finally, FDA notes that we will continue to offer our expertise and advice to the Congress, as we have in the past, in exploring any additional proposals which may be offered to address the drug pricing issue, including those involving reimportation.

CONCLUSION

Mr. Chairman, FDA remains concerned about any possibility that unsafe drugs may find their way into the American drug supply. We will remain vigilant as we refine and improve the programs and procedures that we use to ensure the availability of safe medications for consumers. We appreciate the Committee's interest in assuring that the American public has access to safe and affordable medicines and we look forward to working with you in furtherance of this goal. Thank you again for the opportunity to participate in today's hearing. I will be happy to answer any questions.