FDA Conducts Preliminary Review of Agency's Diversion and Counterfeit Criminal Case Information

September 2011

"Drug counterfeiting, diversion, cargo theft and economically motivated adulteration are crimes of opportunity, and the opportunity is flourishing because of the dramatic way our world has changed in a relatively short period of time."[1]

Executive Summary

The United States has one of the safest drug distribution systems in the world due to the strict regulatory framework governing drug production and distribution. Nevertheless, the U.S. Food and Drug Administration (FDA) is concerned that the U.S. drug supply is increasingly vulnerable to a variety of illegal activities that could have serious public health implications, ranging from diversion and theft of legitimate drugs to drug counterfeiting. Diversion of legitimate drugs can present significant risks to public health because quality cannot be assured for products that leave – and are later reintroduced to – the legitimate supply chain. Counterfeit drugs present risks to consumers because they may contain inactive ingredients (providing no treatment benefit), or they may contain harmful ingredients or dosages.

Because FDA continues to see diverted, counterfeit, and other substandard products in the legitimate drug supply chain, the agency has been working to develop more proactive regulatory approaches to help combat these problems. As part of that effort, FDA collected information from judicial diversion and counterfeiting cases investigated by the agency's Office of Criminal Investigations (OCI) from 2003-2008. FDA then conducted a preliminary review of a subset of the case information to prepare this summary report.[2]

FDA's summary report highlights three examples of criminal drug schemes investigated by OCI. The report describes one drug counterfeiting case and two diversion schemes, which involve a wholesale distributor and a pharmacy/pharmacist, respectively. FDA also evaluated the types of drug products identified in the OCI cases and found that solid oral dosage forms (tablet or capsule) were the most common products. Finally, this review examined the types of trades affiliated with suspects identified in the OCI cases and found that wholesalers represented the greatest percentage of suspects (27%), followed by pharmacists (13%).

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[1] Keynote Address by Dr. Margaret Hamburg at Counterfeit Drug Interchange Conference in Washington, DC, hosted by the Partnership for Safe Medicines – October 8, 2010

[2] FDA conducted the review using a subset of the agency's diversion and counterfeit judicial case information, limited to cases OCI investigated from 2003-2008. Because the review provides a snap-shot of criminal activity and may not represent current drug supply trends, it does not contain statistical inferences, future trend predictions, or opinions.

FDA performed this review by examining OCI's diversion and counterfeit cases to: (1) describe potential threats to drug quality and integrity; (2) help identify where the U.S. drug supply may be vulnerable to diversion and counterfeiting; and (3) help identify the

types of drugs that have been involved in these diversion and counterfeiting cases. Having a better understanding of the types of schemes, products, and parties involved in drug diversion and counterfeiting cases advances FDA's public health mission. The review will help FDA prioritize risk management activities to protect the legitimate drug supply and help ensure drug quality and integrity.

1.0 Background

Today, maintaining the safety of America's medical products is a serious challenge. Complex global supply chains, international trade, the foreign sourcing and manufacture of regulated products, and the increase in the volume and complexity of imported products have forced FDA to reevaluate its approach to global supply-chain safety.[3]

For FDA to carry out its public health mission, it is important that the Agency find ways to improve the security of the drug supply chain for U.S. consumers. Our current approach involves examining ways to characterize potential threats and risks to the quality and security of the drug supply chain and to identify vulnerabilities of the drug supply chain to criminal activity. Current and emerging threats to the U.S. drug supply include intentional acts that can adversely impact the quality and integrity of prescription and over-the-counter (OTC) drugs, such as intentional adulteration of drug products, drug diversion, and counterfeiting. Intentional acts that might affect the quality and integrity of drugs can occur anywhere in the drug life cycle from initial manufacture through final distribution to the consumer. Finished drug products and components, from active pharmaceutical ingredients to inactive "excipients," are subject to adulteration, diversion and/or counterfeiting.

FDA believes that drug counterfeiting is relatively rare within the U.S. drug distribution system due in large measure to the extensive scheme of federal and state regulatory oversight and the steps taken by drug manufacturers, wholesaler distributors, and pharmacies to prevent counterfeit drugs from entering the U.S. drug supply. Nevertheless, counterfeiting and diversion do occur, and there has been an increase in these activities over the last decade. Therefore, FDA is concerned that the U.S. drug supply is increasingly vulnerable to a variety of illegal activities that could have serious public health implications. For example, FDA has identified and referred for legal action a range of criminal activities that can have direct public health consequences for U.S. consumers. These criminal activities range from counterfeiting a product, which may be inactive or contain harmful ingredients, to theft, to replacing a drug with a lower-dose and less expensive drug, and have become increasingly more sophisticated in nature. Recent examples, such as contamination of heparin with an active but allergenic compound and the deliberate substitution of diethylene glycol for glycerin in elixirs, demonstrate the risks to public health.

Diversion of legitimate drugs can also present significant risks to public health because the quality of the products that leave the legitimate supply chain cannot be assured. The grey market through which diverted drugs are distributed can serve as an entry point for

[3] FDA Strategic Priorities 2011 -2015 – April 20, 2011

counterfeit drugs into legitimate distribution channels. Diverted drugs are also difficult to detect, investigate, and quantify; therefore, it is hard to know or estimate the current extent of the problem.

2.0 Purpose

The purpose of this preliminary review is to describe potential threats to drug quality and integrity in addition to identifying risks and vulnerabilities of the U.S. drug supply to counterfeiting, diversion and possible adulteration. FDA hopes the results of this review will help the agency and industry prioritize risk management activities that can reduce the risks of counterfeiting, diversion, and other intentional acts that impact drug product quality and integrity.

3.0 Methodology

This study provides a preliminary review of case information related to criminal activity involving the movement of violative human drug products within the United States. The case investigations were conducted by FDA's Office of Criminal Investigations (OCI), and the review was conducted by FDA's Center for Drug Evaluation and Research (CDER). This review focuses on understanding the diversion and counterfeit information collected from cases investigated by FDA OCI spanning a five-year period from 2003-2008[4]. These results described in this summary report are based on a subset of OCI diversion and counterfeit cases that resulted in a judicial action[5] and includes information about the violative drug product(s) and the suspect(s) involved. At the time of this report, approximately 50% of the cases were examined, involving 188 different suspects and over 1200 different drug products. ***Since the information was limited to OCI judicial, diversion and counterfeit cases investigated from 2003-2008, the review and results presented should not be interpreted as a scientific representation of current drug supply chain trends or a comprehensive review of problems associated with the drug supply chain. Instead, these results should be viewed as an illustrative representation of certain problems and vulnerabilities that we have observed in the drug supply chain.***

4.0 Results

4.1 Criminal drug schemes

This review revealed various schemes and examples of the types of players in the supply chain, how different products enter the supply chain, and how fraudulent or diverted products were discovered. Having a better understanding of these characteristics will help us to identify potential vulnerabilities. Examples of three criminal drug schemes are described below.

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[4] This is only a representative sample of OCI judicial case information and is not intended to present a comprehensive study of all illegal supply chain activities.

[5] For the purposes of this preliminary report, a case that resulted in a judicial action means that an OCI investigation led to a case being filed in a court of law for which a final disposition was entered and the defendant(s) was sentence.

4.1.1 Counterfeit Scheme

Figure 1 depicts the association of details of a unique case used to determine the counterfeit scheme described in detail below. The case elements included: case identification (ID), the products found, where the products were made, the state where the products were found, and how the products were discovered. For this particular case, the products that were later confirmed as counterfeits were discovered and stopped at the border from entering the U.S. supply chain.

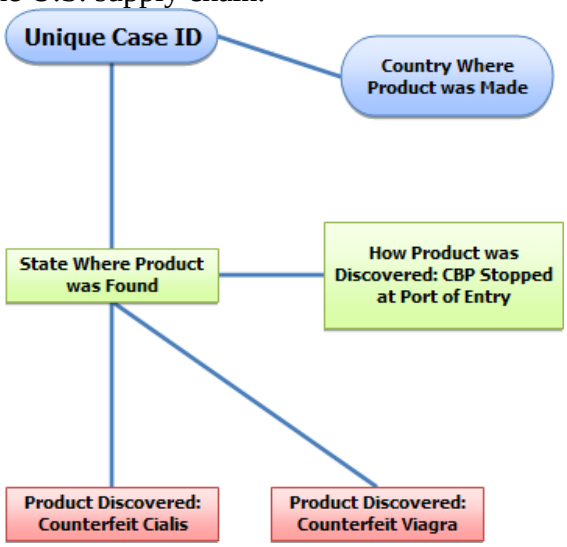

Figure 1: Diagram of details of a case and how associations were made to determine the counterfeit drug scheme.

Here is how the scenario unfolded:
The shipping documents identified the contents of the large package from China as health food, but when inspectors opened it, they discovered large quantities of tablets, which resembled the prescription drugs Viagra and Cialis. The inspectors called Pfizer, which manufactures Viagra and Eli Lilly, maker of Cialis. The pharmaceutical companies verified that the intercepted tablets were counterfeits.

The investigation conducted by special agents from Immigration and Customs Enforcement (ICE) and the FDA OCI led to a licensed pharmacist who owned a pharmacy in San Jacinto, Texas and had ordered the counterfeit drugs from China. When FDA OCI agents, posing as deliverymen, delivered the counterfeit drugs (1000 tablets of counterfeit Cialis and over 4500 tablets of counterfeit Viagra) to the pharmacist, he was arrested and ultimately convicted of conspiracy to introduce counterfeit and misbranded drugs into U.S. commerce. The investigation showed that the pharmacist paid 30 cents per tablet for the Chinese counterfeit drugs instead of the wholesale prices for the legitimate products, which was $9.55 per tablet for Cialis and $13.55 per tablet for Viagra. For the sake of making an illegal profit from the distribution of fake drugs, the pharmacist was willing to expose his customers to the risk of taking a potentially dangerous or contaminated counterfeit product. He was sentenced to two years in federal prison, without parole. (The Department of Justice press release can be found at: http://www.justice.gov/criminal/cybercrime/georgeSent.htm)

4.1.2 Diversion Scheme Involving a Wholesale Distributor

Drug diversion occurs when legitimate drugs are illegally bought, sold or otherwise circulated outside the legal distribution system that has been established to ensure their safety and quality. Diverted drugs may have been stolen from a warehouse or cargo truck, or illegally sold to a distributor or pharmacy. (Schematic in Figure 2)

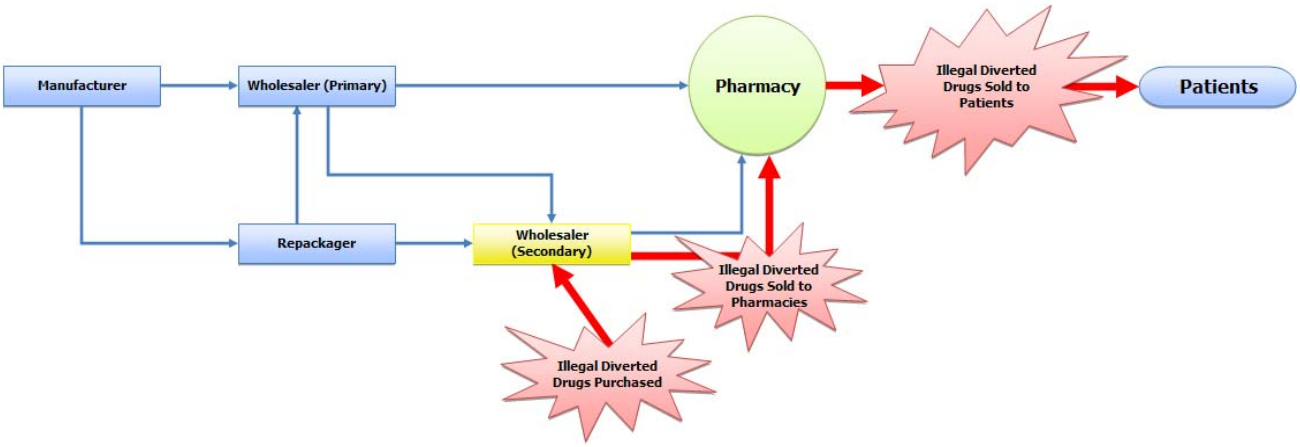

Figure 2: Illegal Distribution of Diverted Products
This schematic representation of the players of the supply chain shows how diverted product may enter back into the drug supply. The diverted drugs (depicted in red) are often purchased by unscrupulous wholesalers (depicted in yellow). The wholesalers sell the illegal diverted drugs to legitimate pharmacies (depicted in green) that may be unaware of that the drugs are illegal. The pharmacies subsequently sell the diverted drugs to patients.

When drugs are stolen or "diverted" outside of the legitimate supply chain and then re-introduced into commercial distribution, patients may be put at risk. There is no way of knowing how the drug was handled or maintained during the period of time when it was outside of the legitimate distribution chain. Some drugs require certain temperatures to ensure potency; all prescription drugs have a particular expiration date, beyond which they may not be safe or effective. Diverted drugs may sit in storage facilities with unregulated temperatures for a long time while the criminals wait for their opportunity to make big profits by selling its supply of diverted drugs.

Sometimes these diversion schemes constitute a large-scale criminal enterprise that spans several states and includes many links in the supply chain and multiple bad actors. Beginning in 2005, Federal and State authorities indicted multiple individuals and businesses with charges including conspiracy, money laundering, mail fraud, and drug diversion in a case that generated illegal revenue in the tens of millions of dollars from trafficking in black-market prescription medications. The last individual case was resolved in 2010, when an individual based out of New York pled guilty to funneling millions of dollars worth of illegally obtained prescription drugs to individuals and other secondary wholesalers operating in Utah, New York, New Jersey, and California, who were part of the criminal conspiracy. Most of the drugs involved in the scheme and purchased by the secondary wholesalers had been purchased or stolen from patients and/or stolen from manufacturers and then sold to drug wholesalers, who in turn, sold the drugs to pharmacies in various states. The drugs were then sold and dispensed to end-user patients. The diverted drugs in these cases were primarily expensive products used

to treat HIV/AIDS. (The press releases related to this case can be found at: http://www.ag.ny.gov/media_center/2006/aug/aug22b_06.html http://www.justice.gov/usao/ut/press/releases/Shafeek%20sentencing.pdf)

4.1.3 Diversion Scheme Involving a Pharmacy and Pharmacist

Product samples are supposed to be free; when the product is a prescription drug, selling a drug sample instead of distributing it for free to licensed physicians constitutes a crime. The FDA OCI has investigated several cases in which a drug company sales representative sold drug samples to a pharmacy, which then broke open the individual sample packages and sold them to patients at the retail price. In the majority of these cases, the pharmacy billed a health insurance company and sometimes Medicare and Medicaid, for the dispensed drug samples; these instances involve the additional crime of health care reimbursement fraud. (Schematic in Figure 3)

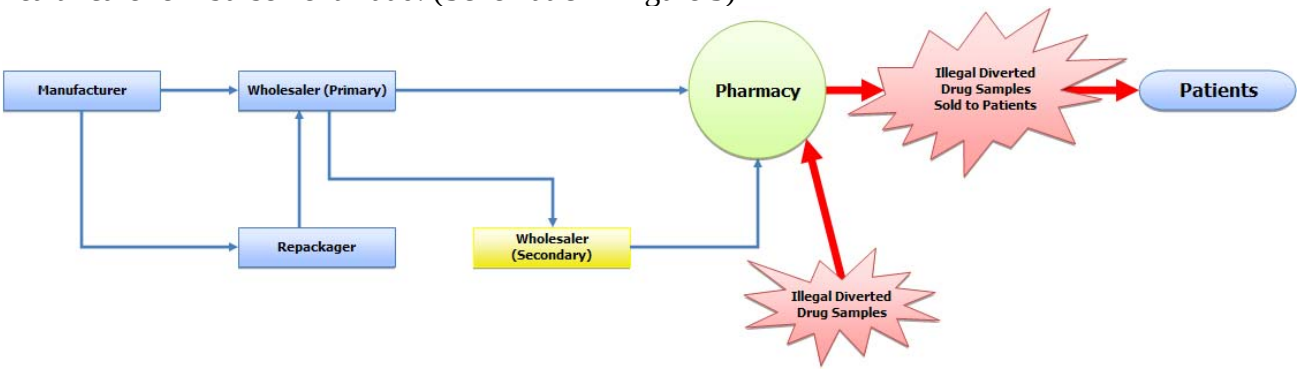

Figure 3: Illegal Distribution of Drug Samples
This schematic representation of the players of the supply chain shows how the diverted drug samples typically enter back into the drug supply. The diverted drug samples (depicted in red) are often times purchased by an unscrupulous pharmacy (depicted in green). The pharmacy sells the illegal diverted drug samples to patients.

One case involved a licensed pharmacist who owned his own pharmacy. The pharmacist was convicted of illegally selling prescription drug samples. The drug samples were obtained from numerous physicians' offices and other avenues. These drug samples were repackaged and sold to the public through his pharmacies and through pharmacies owned by others. The pharmacist was convicted and sentenced to 48 months probation, with 6 months home confinement. In addition, the sentence also included relinquishment of license, exclusion from participation in Medicare, Medicaid, and all other Federal health care programs, and payment of approximately $10.5 million to the United States.

4.2 Summary of Preliminary Results

This review of FDA OCI counterfeit and diversion judicial case data contains no statistical inferences, future trend predictions or opinions. The intent is to illustrate examples of the types of schemes that can threaten the integrity of the supply chain and the drugs that flow through it on a daily basis. Our initial review focused on identifying the type of drug products identified in each case, the U.S. supply chain location where the product was found, and the types of suspect(s) involved in these counterfeit and diversion schemes. ***Relative frequencies (e.g., percentages) are used for convenience of presentation of the results; the percentages cannot estimate either probabilities of occurrence or risk.***

4.2.1 Drug Products

The drug products that were involved in each case were reviewed. Of the OCI cases that had the highest number of different drug products involved, the top 10 of these cases were reviewed. The top five brand products identified in the counterfeit and diversion cases reviewed were: 1) Zyprexa, 2) Viagra, 3) Lipitor, 4) Zoloft, and 5) Risperdal. Focusing exclusively on drug product types, the most common form of counterfeit or diverted products were solid oral dosage forms (tablet and capsule). Injectables, inhalers, topical products and solutions were also observed in this review.

4.2.2 Suspect Type

In this review, we wanted to learn what types of suspects were involved in these criminal schemes. We looked at the two types of suspects; individual or company. (Fig.5). This analysis shows that approximately 14% of the suspects were classified as a company, while the remaining 86% were classified as individuals.

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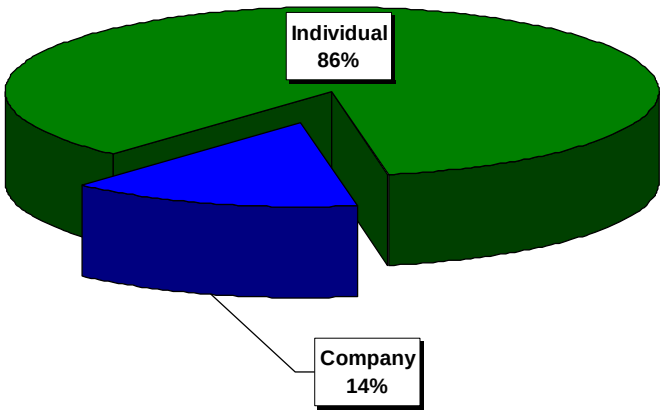

Figure 5: Percentage of identified occurrences by suspect type

4.2.3 Suspect Trade

We also wanted to identify the type of trade in which the suspects were affiliated. The trade of the suspects included a Broker, Doctor, Importer, Manufacturer, Pharmacist, Pharmacy, Repackager, Sales Representative, Wholesaler, Other Practitioner, or Other ("Other" was designated if the suspect did not fall into one of the previously listed trades. Some examples of what was included in the "Other" category include: individual, consumer/patient, truck driver, shipper.). Wholesaler was the trade associated with the greatest percentage of suspects (individual and company). Figure 6 depicts the trades identified for each type of suspect within cases information, as a percentage of the total counts. The results of all the suspect types showed a dominance of Wholesalers, Pharmacists, and Other trade groupings, accounting for approximately 70% of all suspect trades.

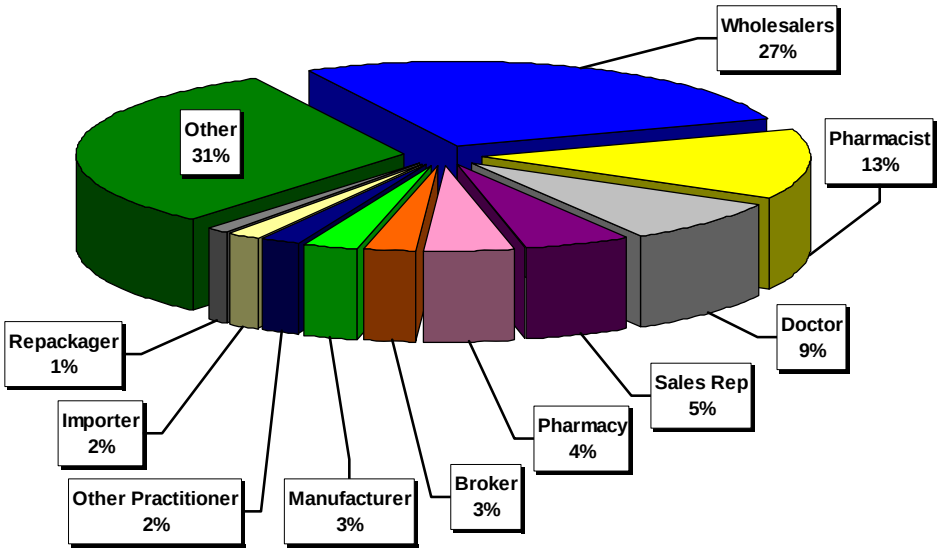

Figure 6: Percentage of all suspects grouped by type of trade

5.0 Summary

This preliminary review is a novel approach to help the agency identify and illustrate vulnerabilities in the U.S. drug supply chain. It is important to mention that the current review was conducted using a limited subset of the Agency's counterfeit and diversion judicial cases. Therefore, the results may not be representative of current drug supply chain trends. This review is intended to provide some insight into the schemes, types of products, and supply chain participants involved. We recognize that to conduct a more in-depth analysis and to achieve a full understanding of the supply chain complexities and the possible sources of sampling bias, additional data sources, such as those from industry, would be necessary. This report provides results from an initial review of the OCI case information and does not contain statistical inferences, future trend predictions or opinions. FDA expects to conduct further analysis and report as appropriate.