Supply Chain Safety:
Where Are We Now?

New legislation, increased education, and high-tech tracking aim to curb the proliferation of compromised and counterfeit products in the pipeline.

By Trudie Mitschang

Supply chain safety made headlines in 2013, and not for positive reasons. In a well-publicized story, GlaxoSmithKline announced a recall of its asthma drug Ventolin after its contract manufacturer said that the syrup bottles might have been contaminated with glass particles. Also last year, *The New York Times* reported that the U.S. suffered shortages of injectable drugs due to quality failures at large manufacturers such as Hospira. And, in what "60 Minutes" described as "the worst pharmaceutical disaster in decades," 48 people died in a meningitis outbreak that was traced back to contaminated production in a Massachusetts compounding pharmacy.

While strides have been made in terms of improving the safety, efficacy and security of the pharmaceutical supply chain, there is still much work to be done. Millions of prescriptions are processed every year in the U.S., and simply keeping track of these legal medications is a daunting task. When you factor in the increasing numbers of illegally imported medicines and counterfeit drugs, it's easy to see how successfully policing the supply chain is easier said than done, especially when sales of counterfeit drugs continue to skyrocket.

According to the World Health Organization (WHO), global sales of counterfeit medicines in the marketplace and from online pharmacies represented an estimated $431 billion in 2012, and nearly 84 percent ($359 billion) had a direct impact on public health. Counterfeit formulations can range from random mixtures of inactive, ineffective preparations to harmful or even deadly concoctions, and all pose a very real threat to public health.[1]

"We've made progress in terms of awareness, but there is still a lot that needs to be done, including federal legislation and more education for both healthcare professionals and consumers," says Katherine Eban, investigative journalist and author of *Dangerous Doses*, an in-depth exposé on counterfeiting operations within the pharmaceutical supply chain. "Since my book was published, the FDA [U.S. Food and Drug Administration] has encouraged the industry to implement electronic pedigrees, but so far we're only seeing a response at the state level. Drug counterfeiting is a problem that is only going to get bigger as time goes on."

The Counterfeit Conspiracy

Federal officials document that, in recent years, many American consumers have purchased counterfeit versions of major brand-name drugs, including Adderall, Vicodin, Viagra and Xanax. Spurred by the success of these crimes, counterfeiters have begun feeding the pipeline with everything from counterfeit flu medications to cancer drugs. Counterfeit prescription drugs have become an exploding industry, with an estimated market worth $75 billion a year worldwide, fueled by online sales, global demand and skyrocketing profitability. Long the scourge of developing countries, fake drugs are now available at alarming rates within the United States.[2]

WHO defines counterfeit drugs as "those which are deliberately and fraudulently produced and/or mislabeled with respect to identity and/or source." Counterfeits are actually just one part of the broader problem of substandard pharmaceuticals, meaning products whose composition do not meet correct scientific specifications are consequently ineffective and often dangerous to the patient. The WHO fact sheet goes on to say that substandard medicines can result from many factors, including negligence, human error, insufficient resources or counterfeiting. Both branded and generic medicines can be considered counterfeit or substandard.

A drug may be considered counterfeit for many reasons, including:

- too much or not enough active ingredient
- no active ingredient
- the wrong active ingredient
- dangerous excipients and dyes
- the wrong ingredients but authentic packaging
- the correct ingredients but fake packaging
- the wrong ingredients, as well as fake packaging

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In today's global marketplace, no one is truly safe from the effects of counterfeit drugs. It's a growing problem worldwide, with drug counterfeiters actively defrauding consumers and interfering with patient therapies that are necessary to alleviate suffering and save lives. Even if the ingredients are correct, counterfeit packaging may include mislabeling, false expiration dates and inaccurate information about dosage and origin.

While both industrialized and developing countries are impacted by drug counterfeiting, developing countries typically suffer the highest number of fatalities, in part because of the high number of pirated drugs that are being used to treat serious diseases like malaria, tuberculosis and HIV/AIDS. WHO estimates that nearly 200,000 people die each year because of fake malaria drugs. It is also estimated that between 1 percent and 10 percent of drugs sold around the world are counterfeits, up to as many as 50 percent in some countries.[3]

An Evolving Problem in North America

For decades, North America has seen the lion's share of counterfeits show up in the lifestyle rather than life-saving drug category. Among the most popular counterfeits is Pfizer's Viagra, now considered one of the most counterfeited drugs in the world. According to John Clark, vice president of global security for the company, about 60 different Pfizer medicines and products are currently being counterfeited around the world — everything from Lipitor to Centrum vitamins. Other popular counterfeits include diet pills, hair restoration pills and other "vanity" medications that become the entryway for criminals looking for easy money.[1]

In 2012, a counterfeit version of the cancer drug Avastin was widely distributed in the U.S., and a fake version of the attention deficit hyperactivity disorder drug Adderall, in high demand because of a shortage, arrived in the U.S. through unethical Internet pharmacies. Avastin is an injectable drug, used often in combination with chemotherapy, to treat patients with colon, lung and other cancers. In the U.S., a 400-milligram vial of the authentic drug — the size that was counterfeited — costs $2,400, according to Genentech. The counterfeit Avastin was made of salt, starch and other chemicals, and packaged in counterfeit boxes that included French writing and Roche's name. In the U.S., the genuine product's boxes are labeled in English and bear the Genentech imprint.[4]

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In early 2013, FDA warned doctors that a fake version of the cancer drug Altuzan was being distributed in the U.S. This particular counterfeit contained no active ingredients, making it potentially deadly for patients seeking life-saving therapies.[4]

In response to these and other crimes, the FDA stated in a letter to the healthcare community: "FDA is requesting that the medical practices stop administering drugs purchased from any foreign or unlicensed source. FDA urges the healthcare community to examine their purchasing practices to ensure that they buy directly from the manufacturer or from licensed wholesale drug distributors in the United States." The letter went on to admonish healthcare professionals, pharmacies and wholesalers/distributors of the role they play in protecting consumers from the threat of unsafe or ineffective products that may be stolen, counterfeit, contaminated or improperly stored and transported.[5]

New Legislation Promises to Track and Trace

In response to the alarming number of new counterfeits in the U.S. supply chain, the U.S. House of Representatives passed a new "track and trace" bill late last year. According to a news release from the U.S. Senate HELP committee, the Drug Quality and Security Act (H.R. 3204) is intended to help ensure the safety of compounded drugs and will track all prescription drugs from the manufacturer to the pharmacy.[6]

When it comes to compounded drugs, the proposed legislation distinguishes compounders engaged in traditional pharmacy practice from those making large volumes of compounded drugs without individual prescriptions; defines FDA's role in oversight of outsourcing facilities; offers providers and patients information about compounded drugs; and clarifies current federal law regarding pharmacy compounding.

More specifically, traditional pharmacies will continue to be primarily regulated by state boards of pharmacy. But, compounders who wish to practice outside the scope of traditional pharmacy practice can register as outsourcing facilities subject to FDA oversight in much the same way as traditional manufacturers. Providers and patients have the option of purchasing products from outsourcing facilities that comply with FDA quality standards.

As far as the track and trace proposal, the legislation develops a pathway to unit-level tracing in the next decade; strengthens licensure requirements for wholesale distributors and third-party logistics providers; and establishes nationwide drug serial numbers, currently a huge roadblock when it comes to tracking and tracing products in the supply chain.[6]

Creating a Global Initiative

In March 2013, INTERPOL, the world's largest police organization, announced that it will partner with 29 of the world's largest pharmaceutical companies to create an enhanced pharmaceutical crime program to combat counterfeit medicines.[7] "With no country, no drug, no medical product immune from counterfeiting, a global effort is needed to combat this threat, which puts the lives of millions of people at risk every single day," said INTERPOL Secretary General Ronald K. Noble. "This support from a group of 29 companies from the pharmaceutical industry forms a bridge between the public and private sectors and will assist INTERPOL and each of its 190 member countries to more effectively tackle the problem of medical product counterfeiting."

The three-year deal will see the creation of INTERPOL's Pharmaceutical Crime Program to further build on the work of its Medical Product Counterfeiting and Pharmaceutical Crime (MPCPC) unit. According to INTERPOL, an essential part of the program is to raise public awareness of the dangers of fake drugs, particularly for people buying medicines online. WHO estimates that in more than 50 percent of cases, medi-

cines purchased over the Internet from illegal sites that conceal their physical address have been found to be counterfeit, yet most consumers remain ignorant of this fact.

"In the case of drug counterfeiting, it can mean the difference between life and death for a patient," said Christopher Viehbacher, chief executive officer, Sanofi. "It is estimated that 10 percent of medicines are fake, and these figures can go up to 50 percent, particularly in some poorer countries. This is why it is so important that industry members partner with INTERPOL to coordinate law enforcement operations around the world so that we can help curtail the threat of counterfeit medicines online and at the retail level."

"Drug counterfeiters put at risk the health of patients around the world by producing substandard and sometimes lethal medicines," said John C. Lechleiter, PhD, chairman, president and chief executive officer of Eli Lilly and Company. "Putting an end to counterfeiting requires broad, coordinated action on a global scale. This new initiative between the pharmaceutical industry and INTERPOL is aimed at helping ensure that patients can trust in the safety and efficacy of the medicines they rely on."

The Consumer Component

Human behavior will always be a wild card when it comes to regulating pharmaceutical supply chain safety. While new initiatives, laws and systems are steps in the right direction, the problem of supply chain safety is not simply about supply; it's also about demand. As consumers continue to be enticed by the availability of hard-to-find drugs and gray market pricing available through fake online pharmacies, many will continue to make purchases outside of the secure supply chain, despite the inherent risks. From travelers restocking their medicine cabinets while on vacation to Internet shoppers hoping to score deep discounts on pricey lifestyle medications, purchasing products well below retail has a high level of consumer appeal. For many Americans, the decision to seek alternative methods of obtaining prescription medication is a simple one: It's the only way they can afford the drugs they need. According to the Centers for Disease Control and Prevention, 25 million Americans did not take prescribed medication in 2009 due to the high U.S. drug costs, and the Commonwealth Fund found that 48 million American adults didn't fill their prescription because of high drug costs in 2010. By contrast, drugs purchased online from other countries can cost anywhere between 80 percent and 90 percent less than those sold in reputable U.S. pharmacies.[8]

According to many industry experts, education about the risks associated with online transactions needs to significantly increase. For example, many U.S. consumers would avoid making a pharmaceutical purchase from a third world country for obvious reasons. But, those same consumers might feel very comfortable purchasing from neighboring Canada. Unfortunately, that confidence is falsely placed: A 2005 FDA drug bust examined nearly 4,000 packages at airports in New York, Miami and Los Angeles, and found that 85 percent of the drugs ordered from what customers believed were Canadian pharmacies actually came from 27 other countries. Not surprisingly, a number of the products were also found to be counterfeit.[9]

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The battle to secure the pharmaceutical supply chain is far from over, and despite some victories, there are no simple solutions to this widespread and multipronged problem. Organized efforts by pharmaceutical companies, government agencies and consumer groups will need to pursue increased education and more stringent legislation if we ever hope to curb the distribution and sale of compromised and counterfeited drugs. ❖

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