BY DENISE MYSHKO

COUNTERFEIT DRUGS

Fighting an UPHILL BATTLE

THE COUNTERFEIT MEDICINES MARKET IS A REAL, CLEAR, AND PRESENT DANGER TO PUBLIC HEALTH. And while there have been efforts to minimize the threat of counterfeit and substandard medicines, there is a need to coordinate the efforts of all the various public and private stakeholders who are affected to address the different aspects of this global and growing problem.

Ellen Reilly *BearingPoint*

Counterfeiting impacts the brand and people's perception of the brand. Companies have to understand their entire supply chain — from raw materials to the consumer as well as the distribution process.

They're so hard to spot that even brand managers may have a hard time distinguishing a fake pharmaceutical product from a genuine one.

Manufacturers of counterfeit medicines have become so sophisticated they are able to accurately duplicate the look and feel of many products despite efforts by the industry to thwart counterfeiting.

Even when manufacturers put a new technology in place to distinguish their products from the fakes, it takes just one to three months before the counterfeiters have duplicated the technology, says Chris Clauss, director of sensor network solutions at IBM.

"We will never be able to stop counterfeiting 100% of the time," he says. "The trick is to raise the bar so high that counterfeiting is no longer profitable. There are many techniques and security measures that we can use to make it very difficult to create a counterfeit drug. The process to duplicate a product needs to be so difficult that it becomes economically untenable."

The World Health Organization (WHO) defines a counterfeit medicine as: "A medicine that is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients, or with fake packaging."

Counterfeit medicines are on the rise worldwide, as counterfeiters capitalize on the growing use of the Internet by consumers searching for inexpensive drugs. There is strong evidence of this pervasive problem; for example the Pharmaceutical Security Institute, a group funded by 26 drug makers, reports that seizures of fake drugs rose 24% to 1,513 incidents in 2007, and illicit versions of 403 different prescription drugs were confiscated in 99 countries.

Because the problem can go undetected and is so widespread, it is difficult to obtain precise figures on counterfeit products. Counterfeit medicines estimates range from less than 1% of sales in developed countries to more than 10% in developing countries, depending on the geographical area, according to the International Medical Products Anti-Counterfeiting Taskforce.

The FDA has estimated that worldwide sales of fake drugs exceed $3.5 billion per year, though others project much higher figures. The

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Chris Clauss *IBM*

Serialization is probably the single most important way to find counterfeit products in the supply chain. RFID has some additional benefits over bar code serialization but it is a more expensive technology.

Center for Medicines in the Public Interest, for example, predicts that counterfeit drug global sales could reach $75 billion by 2010.

In the United States, the Department of Homeland Security (DHS) seized counterfeit or pirated merchandise valued at about $200 million in 2007, an increase of about 27% compared with the previous year's total.

According to Customs and Border Protection officials, seizures of counterfeit imports coming into the United States rose by 22% — and by 141% in value — during the first half of fiscal year 2007.

DEFINING COUNTERFEITS

What makes counterfeits difficult to pinpoint is how varied the compositions can be.

"Counterfeit products can take many guises," says MaryAnn Hegedus, business development manager, brand enhancement, Colorcon. "A counterfeit drug can be an adulterated product mixed with an unaltered one. In other cases, the counterfeit product can contain a lesser amount of the active ingredient. It can be a different active ingredient or it could contain no active at all. Counterfeiters are very good at understanding manufacturing techniques, and in some cases the counterfeit product is coming from a legitimate manufacturing facility overseas. Counterfeiters have the knowledge and the ability to procure the goods."

Counterfeiters take inert ingredients, such as chalk and even dangerous chemicals, package them convincingly, and sell them to consumers.

Obviously, the problem is that such drugs may have no therapeutic effect and, worse, can be toxic.

According to the WHO, commonly counterfeited drugs include antibiotics, antimalarials, hormones, and steroids. Increasingly, the organization says anticancer and antiviral drugs are also being faked.

Peter Spellman, VP of products and Software as a Service (SaaS) at SupplyScape, says counterfeit drugs can enter the supply chain from many different avenues.

"The most common route is through a diversion of some type; the product gets into the supply chain in a nonsanctioned way or through an unprotected entry point," he says.

ACCORDING TO THE WHO

- **50% of medicines purchased over the Internet from sites that conceal their physical address are counterfeit.**
- **10% of medicines sold in developing countries are fakes.**
- **1% of medicines sold in developed markets, such as the European Union, are counterfeit.**

(Note: While it is generally suspected that the 1% figure in the EU is now much higher, it is still highly significant. Even the 1% figure would mean that, last year alone, more than 7 million U.K. and 16 million German prescriptions may have been filled with counterfeit medicines.)

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MaryAnn Hegedus *Colorcon*

The current estimate is that by 2010, counterfeiting will cost pharmaceutical manufacturers $75 billion. Counterfeited products can jeopardize patient safety and lead to a loss of credibility and damage to goodwill and public relations.

"Sometimes the counterfeit product is commingled with returns since these are not under the same amount of scrutiny as products in the forward supply chain."

Counterfeiting methods fall into varying degrees of complexity.

"There are uplabeling operations that are relatively low tech," Mr. Spellman says. "Conversely, in certain foreign countries counterfeiters have full production lines that resemble legitimate operations. The price, what counterfeiters can get for their products, is so high that operations are lucrative in all cases."

According to Ellen Reilly, managing director in the life-sciences practice at BearingPoint, one of the biggest challenges is stopping illegal drug manufacturers from infiltrating the supply chain.

"Branded manufacturers need to ensure they have agreements in place with their wholesalers and distributors up and down the entire supply chain and that all parties understand how they are helping to protect the manufacturing line," she says.

ATTACKING THE COUNTERFEITING EPIDEMIC

Experts say a multifaceted approach is needed to address the global counterfeiting problem.

Les Jordan *Microsoft*

The technology for RFID isn't there yet in terms of miniaturization of active tags, nor is the infrastructure widely deployed throughout the pharma industry. But, absolutely, companies should be conducting pilot programs and getting the infrastructure in place.

"There needs to be more awareness around Internet pharmacies; the delivery of a real medicine purchased online is rare," says Jim Thomson, chair of European Alliance for Access to Safe Medicines (EAASM). "The Internet is absolutely open to anybody who wants to buy their medicines without a prescription. People can self-medicate; they can remove themselves from the healthcare system and buy medicines online. But in 62.8% of cases, we found that the medicine was counterfeit or substandard."

Mr. Thomson says better enforcement is also needed.

"We need cooperation between enforcement agencies and regulators," he says. "The Internet trade only works because the money can be moved. If we remove the capacity for the money to move, then the counterfeiters don't have a business anymore. If the postal service and the couriers stop deliveries, then counterfeiters don't have a business. These are the choke points that can actually strangle this problem."

Global counterfeit drug sales could reach $75 billion by 2010.

In February 2006 the WHO launched the International Medical Products Anti-Counterfeiting Taskforce (IMPACT), which aims to build coordinated networks across and between countries to halt the production, trading, and selling of counterfeit drugs. IMPACT is a partnership comprised of all the major anti-counterfeiting players, including: international organizations, nongovernmental organizations, enforcement agencies, pharmaceutical manufacturers associations, and drug and regulatory authorities.

Additionally, Mr. Thomson says the European parliament is looking at the issue of parallel trade — that is the re-export of a product, on sale in one country at a lower price, to another country — and counterfeit pharmaceuticals and has promised to bring forward legislation.

"There will probably be a ban on repackaging, which is part of parallel trade," he says. "Often, products have to be repackaged to meet the regulations of the destination country. There will also probably be tighter pedi-

COUNTERFEITING AND ONLINE PHARMACIES

- Counterfeiters are attracted to two types of medicines: those that are used in high numbers and those that have a high monetary value.
- In developed markets, the products most commonly faked are those that are often referred to as lifestyle medicines, such as those for erectile dysfunction, hair loss, and weight management.
- Recently, fake versions of life-saving prescription medicines for cancer and serious cardiovascular diseases also are being sold to consumers online.
- 62% of medicines purchased online are fake or substandard, including medicines indicated to treat serious conditions, such as cardiovascular and respiratory disease, neurological disorders, and mental health conditions.
- 95.6% of online pharmacies researched are operating illegally.
- 94% of Websites do not have a named, verifiable pharmacist.
- More than 90% of Websites supply prescription-only medicines without a prescription.

Source: European Alliance for Access to Safe Medicines, Cardiff, United Kingdom. For more information, visit eaasm.eu.

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COUNTERFEITING: A PRIMER

Counterfeit medicines can be made and distributed by just a few people running a small-scale operation from a garage or commercial building. At the other end of the scale, multinational criminal networks collaborate in the high-volume production of counterfeit medicines (usually in Central and Eastern countries such as China and India) and they are distributed around the globe.

There is evidence to show that counterfeiters have used Oceania and the Islands of the Bahamas as an intermediate destination for fake medicines sent from China and the Middle East. From there, the products are distributed around Europe and other regions, having been sold via online traders masquerading as legitimate pharmacies based in Europe, the United States, and Canada.

Many counterfeit medicines are made in filthy backstreet "laboratories" in developing countries. These contaminated rooms are a far cry from the spotless, hygienic laboratory facilities and regulated manufacturing processes used by pharmaceutical companies.

Some medicines sold fraudulently in Europe may have been rejected originally by pharmaceutical companies due to quality control or related issues. These medicines are rightly disposed of, though it is not impossible for criminals to find them and try to sell them online. Other medicines may be thrown away because they fall out of date, but these too can sometimes reappear, perhaps in new (fake) boxes, via Internet-order deliveries.

Another key issue is that some medicines require refrigeration or other specific environmental conditions during transport and storage. If stored incorrectly their effectiveness can be reduced, rendering them useless or even dangerous. It is highly unlikely that medical products are handled correctly by criminal distributors. Counterfeit medicines have been discovered hidden during transportation within soft toys, large carrier bags, and cardboard boxes — a world away from the strictly regulated and sterile conditions required for licensed medicines.

How significant a problem is medicine fraud and counterfeiting? It is fundamentally impossible to declare the true magnitude of medicine counterfeiting on a global scale because of its clandestine nature. Counterfeit medicines are shipped covertly across a range of international jurisdictions and frequently traded via unofficial and uncontrolled Websites.

The European Alliance for Access to Safe Medicines (EAASM) knows, however, that the industry is growing rapidly each year because reports of suspicious packages and seizures of illicit goods are increasing continually.

The latest intelligence available on the incursion of counterfeit medicines reveals a worrying trend: the volume of counterfeit medicines seized in Europe has increased exponentially in recent years, with more than 500,000 products discovered in 2005 — twice the level found in 2004. In 2006, this figure was reported to have increased by more than five times, to 2.7 million. This explosion continued throughout 2007, according to the EAASM, and is rising all the time.

The Center for Medicine in the Public Interest, based in the United States, predicts that counterfeit medicine sales will reach about $71.2 billion globally by 2010 — an increase of more than 90% over just five years from 2005.

Source: European Alliance for Access to Safe Medicines, Cardiff, United Kingdom. For more information, visit eaasm.eu.

gree legislation. Europe is a little ahead of the United States in this respect, as we have routine unit dose packaging. There are very few examples of big tubs of tablets traveling around."

In the United States, Florida lawmakers in May 2008 passed the Anti-Counterfeiting Act, which increases penalties for counterfeiting activities. The act, introduced by Rep. Andy Gardiner (R-Orlando) in the House and Senator Alex Diaz de la Portilla (R-Miami) in the Senate, awaits Governor Charlie Crist's signature.

In addition to creating a tiered penalty system based on the quantity or retail value of counterfeited goods, the Anti-Counterfeiting Act increases the penalties for repeat offenders and those who disregard human life or safety when they counterfeit prescription drugs, automotive parts, and household goods.

In June 2008, the U.S. House Judiciary Subcommittee on Crime, Terrorism, and Homeland Security held hearings on "Online Pharmacies and the Problem of Internet Drug Abuse" and proposed the "Ryan Haight Online Pharmacy Consumer Protection Act of 2008" (H.R. 6353 and S. 980).

Additionally, the Food and Drug Administration Amendments Act (FDAAA), which was signed into law in September 2007, requires the FDA to develop standards and identify and validate effective technologies for securing the drug supply chain against counterfeit, substandard, adulterated, or expired drugs.

The law requires the FDA to develop standards for identifying, validating, and tracking prescription drugs and even suggests the use of promising technologies, including radio frequency identification technology (RFID); nanotechnology; encryption technologies; and other track-and-trace or authentication technologies.

Regulators at the FDA issued a request for comments that concluded in May. Regulatory officials say the agency received more than 60 comments to each docket, and they are in the process of evaluating what standards are currently available, what's being worked on, where the gaps are, and what's needed. The FDA is proceeding based on this collected information.

Since 2006, the federal Prescription Drug Marketing Act (PDMA) has required documentation of transactions. Some states, however, require more stringent pedigrees. In fact, 21 states have pedigree laws or rules today, and an additional 14 states have proposed pedigree legislation or rules.

"Pedigree laws are important, because they require the supply-chain participant to verify that the product has a certifiable chain of cus-

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Peter Spellman *SupplyScape*

Legislation, such as pedigree laws, is important; these laws require the supply-chain participant to verify that the product had a certifiable chain of custody back to the manufacturer.

tody back to the manufacturer," Mr. Spellman says. "This helps define the path of the product and provides some assurance of its authenticity. The problem thus far is that these are state laws, and for the industry this means there could be 50 different pedigree laws, which would make the supply chain very hard to manage."

SERIALIZATION AND RFID APPROACHES

Some states, such as California, have passed laws that will require the pedigree to be in an electronic format. But the law won't go into effect until 2011, despite earlier plans for a Jan. 1, 2009, starting date. This law requires unit-level tracking in an interoperable electronic system. Pharmaceutical manufacturers will be required to include a unique identifier (serialization number) placed on the smallest container saleable to a pharmacy.

While RFID is not necessary to meet the pedigree law, the technology is useful for tracking entire product lots, says Les Jordan, industry technology strategist, life sciences, at Microsoft.

"The industry is addressing the pedigree requirements through bar coding," he says. "RFID, however, provides a higher level of assurance. As this technology continues to evolve it will be particularly useful for tracking really high-profile drugs."

Mr. Clauss says RFID has some additional benefits over other technologies.

"There are some anticounterfeiting tricks that can be adopted using RFID that can't be done with bar codes, which makes it more secure but it is also a more expensive technology," he says.

Mr. Clauss says one anticounterfeiting technique is to write digitally generated content onto an RFID tag, which can then be verified later.

"Because RFID is an electronic delivery platform, we can do more than with a simple bar code," he says.

Mr. Spellman says the benefit of RFID is that it doesn't require line-of-sight readers.

"There are operational efficiencies with RFID, but it is expensive and companies have to retool their packaging lines," he says. "There is also some confusion in the industry as to what the right format is for serial number identification. There is no consensus yet in the industry on what this should be."

Mr. Clauss believes a mix of technologies — invisible inks, micro printing, color shifting ink, and holograms — should be used to address counterfeiting. ✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

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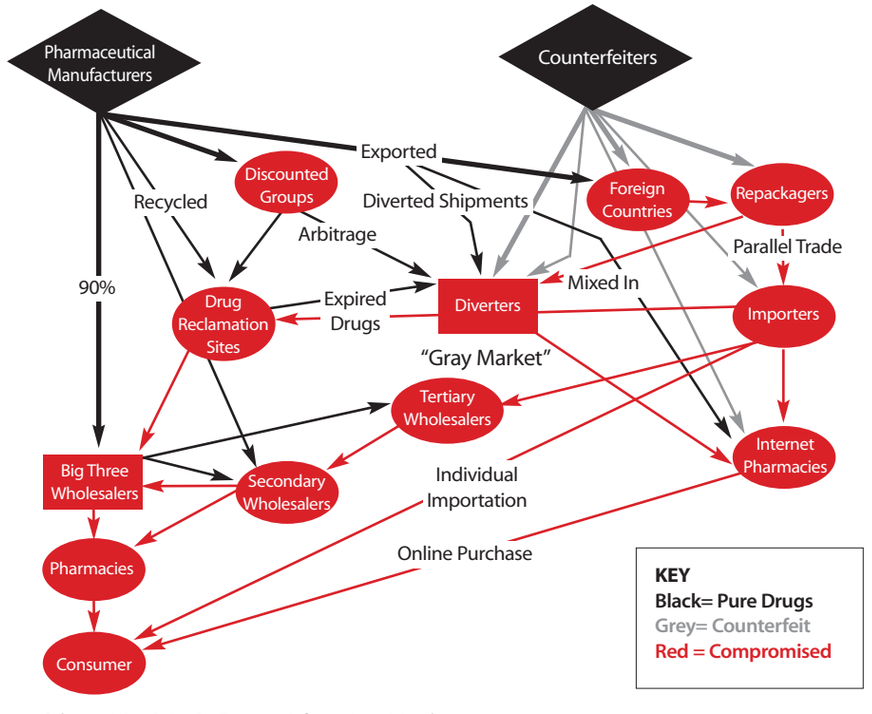

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