Denise Myshko

Cracking DOWN on Fake Drugs

The fight to protect the pharmaceutical supply chain is a global one, requiring law enforcement, regulatory agencies, and companies to come together for the health of patients.

Counterfeit goods are big business. But when it comes to counterfeit medicines, it's a public health issue as well. Counterfeit prescription medicines have become widespread and pervasive, and they have been found in every disease category, in both generic and branded medicines, and in every region of the world. Counterfeit drug incidents around the world have caused an estimated 700,000 deaths from malaria and tuberculosis alone, reports the International Policy Network. Counterfeiting groups thrive in countries where the laws are weak.

And the problem is growing. Counterfeiters have become so sophisticated, they often are able to duplicate new security features on packaging in months.

"Over the years, we've seen the scope of counterfeiting increase," says Richard Widup Jr., senior director, corporate security, at Purdue Pharma. "Wherever there is an opportunity for people to make some money, they will take full advantage of that. Sometimes the counterfeiting of pharmaceutical products is based upon the type of product, the volume, or the cost. In other instances, counterfeiting is market-driven, where in a particular market the product is in high demand. As a result, the counterfeiters see an opportunity to make a fair amount of money."

Counterfeiting is the second-largest industry in the world from a total revenue standpoint, says Kent Mansfield, president of TruTag Technologies.

"People might think about counterfeiters being in a back room with one machine," he says. "But some of these counterfeiting operations are sizeable. They have their own graphic artist and are good at emulating holograms that are already on the package so they can slip material into the market easily."

With globalization, pharmaceutical companies are looking overseas and into emerging markets and that gives the opportunity for individuals who want to take advantage of the system, says Drew Olson, senior manager, BDO Consulting.

"It's a difficult thing to police because of the Internet," he says. "Fraudsters have the ability to take advantage of the system."

The World Health Organization calls these SFFC (spurious/falsely-labeled/falsified/counterfeit) medicines, and the WHO has found these are everywhere in the world. They range from mixtures of harmful substances to products with inactive ingredients.

Counterfeiting of prescription drugs has increased over the last 10 years. In 2011, there were 1,986 incidents of worldwide counterfeiting, illegal diversion, and theft incidents involving medicines, according to the Pharmaceutical Security Institute (PSI). This is down slightly from 2,054 incidents in 2010, but the incidence has gone up steadily since 2002 when the institute identified just 196 incidents of counterfeiting, illegal diversion, and theft.

Industry experts agree drug counterfeiting is a complex problem with no easy solutions. Developing nations are still struggling with weak laws and enforcement, although that is beginning to change. Last year, for example, Chinese government authorities arrested almost 2,000 people as part of a crackdown on the sale of fake or counterfeit drugs.

Additionally, four global pharmaceutical industry groups agreed in July 2012 to work together to address counterfeit medications. The four associations — International Federation of Pharmaceutical Manufacturers & Associations, Pharmaceutical Research and Manufacturers of America, European Federation of Pharmaceutical Industries and Associations, and Japanese Pharmaceutical Manufacturers Association — aim to raise awareness about counterfeiting and develop ways to combat unsafe medicines. One such effort is the Center for Safe Internet Pharmacies, which was formed to address fake medicines sold through online pharmacies.

Fred Felman, chief marketing officer at MarkMonitor, echoes a report issued in February by the Institute of Medicine, and says there needs to be international cooperation to stop the trade of illicit pharmaceuticals.

"There needs to be recognition of the risks that are posed to consumers by not regulating counterfeit drugs internationally," he says.

In fact, the IOM report made several suggestions for how counterfeit drugs could be addressed, but many of them focused on the need for international cooperation between global law enforcement and regulatory agencies. One recommendation was for governments to establish or strengthen systems to detect substandard, falsified, and unregistered medicines. The report also suggests the World Health Assembly create an inclusive, transparent process for developing a code of practice on the global problem of falsified and substandard medicines.

Pedigree Law and Traceability

In the United States, the IOM recommends Congress authorize and fund the FDA to establish a mandatory track-and-trace system. The report indicates that tracking pharmaceuticals through the global distribution chain with unique serial numbers is a good defense against criminal infiltration.

At the federal level, there have been several attempts to implement a national pedigree requirement, but none has been successful. The Prescription Drug Marketing Act (PDMA) in 1987 originally contained a national pedigree requirement, but it was controversial at the time and was challenged. Regulators also tried to include a pedigree requirement in the Food

and Drug Administration Safety and Innovation Act, which was implemented last year, but that provision was not in the final law. The Food and Drug Administration Amendments Act of 2007, however, requires the Secretary of Health and Human Services to develop standards and identify effective technologies for securing the drug supply chain.

Several states, however, have moved in the direction to implement the pedigree law. Florida was the first state to implement such a law in July 2006. The pedigree required by Florida can be either paper or electronic, but must contain information that records from sale by a manufacturer to wholesaler or repackager until final sale to a pharmacy.

California's new e-pedigree law goes into effect Jan. 1, 2015, and applies to almost all prescription drugs intended for sale in the state. It requires an electronic track-and-trace system for prescription drugs that uses a unique identification number and should be established at the point of manufacture.

"A significant difference between the laws in California and Florida is that the pedigrees are only required at a lot level in Florida while the California law requires pedigree down to a sellable unit," says Scott Pugh, VP, solution and service innovation, at Verify Brand.

Verify Brand provides supply chain solutions specifically around serialization and traceability and digital authentication.

Mr. Pugh says currently the laws allow for an electronic document that follows the medication as it moves through the supply chain, but another model for traceability is emerging.

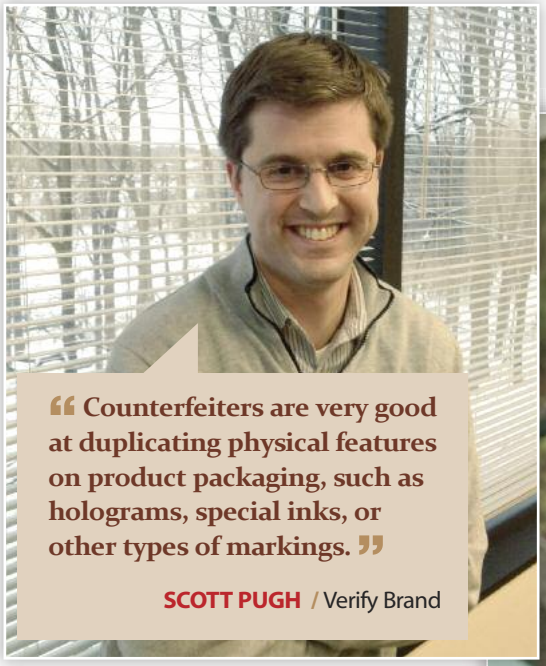
"A centralized model is coming into play, which means that instead of having a document that's traded from one partner to the next as that product flows, there is an IT solution that sits over top of the industry and all of the relevant parties — whether manufacturers, wholesalers, pharmacy, hospitals — submit their traceability information to a single database," he says. "This database would then be able to store and report on the full chain of custody or traceability of any single item from that centralized location."

He says the California Board of Pharmacy may accept a centralized model because they have stated they are not tied to any particular technology or standard to meet compliance as long as the solution meets all of the requirements of the law.

Internationally, a number of countries already have requirements for drug packages to be printed with 2D codes when they leave a manufacturer's plant.

Mr. Pugh suggests pharmaceutical companies consider a combination of methods to deter counterfeiters.

Counterfeiters are very good at duplicating physical features on a product, such as holograms or special inks or other types of markings," he says. "The strongest weapon against counterfeiting is to employ a combination of both physical security features and traceability. The more data we can capture about where products have been and where they are going, the harder it is for a counterfeiter to duplicate a product at different points in the supply chain."



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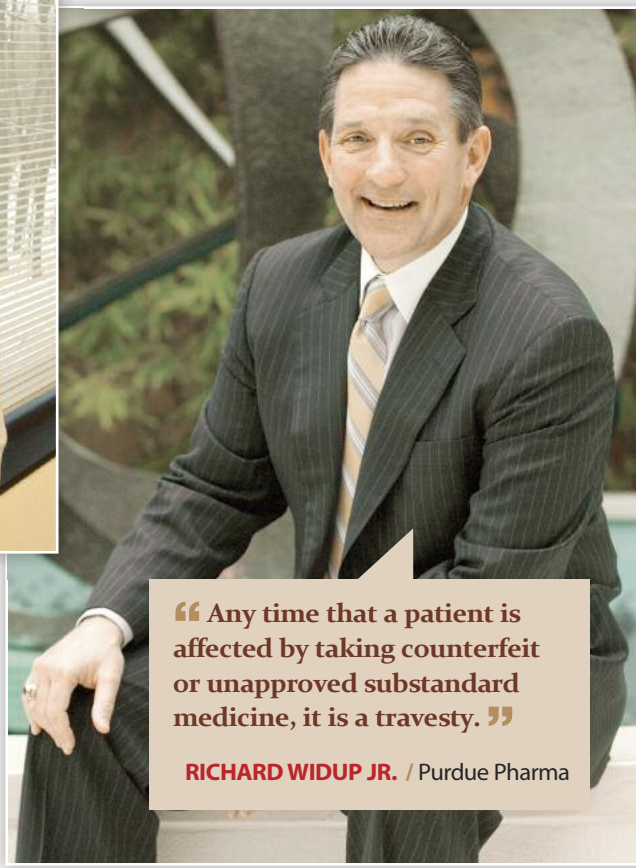

> "Any time that a patient is affected by taking counterfeit or unapproved substandard medicine, it is a travesty."
>
> **RICHARD WIDUP JR.** / Purdue Pharma

Counterfeiters, experts say, are very sophisticated and well-capitalized.

"This is a business to the counterfeiters," Mr. Pugh says. "They have a significant amount of resources that can be put toward whatever type of schemes, packaging, or whatever else might be required to pass counterfeit products off as authentic. "

Mr. Mansfield says companies need a multilayered approach to security that includes

Recent Examples of Counterfeit Medicines and Patient Impact

	Medicine	Country/Year	Report
1.	Avastin (for cancer treatment)	United States, 2012	Affected 19 medical practices in the US. The drug lacked active ingredient
2.	Viagra and Cialis (for erectile dysfunction)	United Kingdom, 2012	Smuggled into the UK. Contained undeclared active ingredients with possible serious health risks to the consumer
3.	Truvada and Viread (for HIV/AIDS)	United Kingdom, 2011	Seized before reaching patients. Diverted authentic product in falsified packaging
4.	Zidolam-N (for HIV/AIDS)	Kenya, 2011	Nearly 3,000 patients affected by falsified batch of antiretroviral therapy
5.	Alli (weight-loss medicine)	United States, 2010	Smuggled into the US. Contained undeclared active ingredients with possible serious health risks to the consumer
6.	Anti-diabetic traditional medicine (used to lower blood sugar)	China, 2009	Contained six times the normal dose of glibenclamide. Two people died, nine people were hospitalized
7.	Metakelfin (antimalarial)	United Republic of Tanzania, 2009	Discovered in 40 pharmacies. The drug lacked sufficient active ingredient

Source: World Health Organization

packaging security and other features to make counterfeiting more difficult. TruTag has developed a solution that uses micro-sized tags that are edible and can be incorporated in the tablet during manufacturing. These tags can be encoded with bar codes or serial numbers, which can help to identify products.

Counterfeiting and the Internet

The Internet has added even more complexity to an already complex issue. In more than 50% of cases, medicines purchased over the Internet from illegal sites that conceal their physical address have been found to be counterfeit, according to the WHO.

Online pharmacies often don't require a prescription and are not accredited by the National Association of Board of Pharmacy's VIPPS (Verified Internet Pharmacy Practice Site) program nor regulated by the FDA. NABP has reviewed more than 10,000 online pharmacy sites and only 3% of those online sites appear to be in compliance with pharmacy laws and practice standards.

"The evolution of online commerce and online supply chains has provided ways for people to source different materials from all over the world," Mr. Felman says. "One of the things that has enabled drug counterfeiting is the anonymity of the Web, which has created a place where intermediaries play a role in facilitating, communicating, shipping, and paying for goods of all sorts online."

Mr. Felman says this presents a challenge for law enforcement and governments. He says even just five years ago, there would be arrests that involved large bulk shipments of goods.

"These shipments could be stopped at the border," he says. "But now we are seeing a preponderance of counterfeit goods being sold and shipped in single parcels. This is almost impossible for border patrols to deal with." PV

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>
> **FRED FELMAN** / MarkMonitor

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> **DREW OLSON** / BDO Consulting

IOM Recommendations

In February, the Institute of Medicine issued a report to try to counter the problem of falsified and substandard drugs. The report found that counterfeit drugs are an international problem that requires international cooperation. Their recommendations include:

- Governments should establish or strengthen systems to detect substandard, falsified, and unregistered medicines. This surveillance should be integrated with established public health surveillance systems. Analysis and reporting should precisely describe the product's quality, packaging, and registration.
- The International Finance Corporation and the Overseas Private Investment Corporation should create separate investment vehicles for pharmaceutical manufacturers that want to upgrade to international standards. Governments can complement this effort by encouraging partnerships between local and foreign manufacturers.
- Procurement agencies should develop a plan, within the next three to five years, to comply with the World Health Organization Model Quality Assurance System for procurement agencies and work to remove any barriers to compliance.
- Regulatory authorities in low- and middle-income countries should use the International Conference on Harmonization Common Technical Document format for product registration to better harmonize their procedures and reduce application costs for manufacturers. To the same end, they should also conduct joint inspections and use a common inspection report.
- Governments and donor agencies should fund development of effective communication and training programs for consumers and health workers on understanding the quality and safety of medicine.
- State licensing boards should only license wholesalers and distributors that meet the National Association of Boards of Pharmacy accreditation standards. The FDA, in collaboration with state licensing boards, should establish a public database to share information on suspended and revoked wholesale licenses.
- Congress should authorize and fund the FDA to establish a mandatory track-and-trace system. In the interim, the FDA should convene a working group of stakeholders including the International Federation of Pharmaceutical Manufacturers and Associations and the Generic Pharmaceutical Association to promote voluntary track and trace for all supply chain actors in accordance with existing guidance.
- Governments in low- and middle-income countries should provide an environment conducive to the private sector establishing quality medicines retail in underserved areas. Government incentives could encourage this. To the same end, governments, the WHO, and the International Pharmaceutical Federation should support national pharmacy councils and education departments to train tiers of pharmaceutical personnel.
- The National Institute of Standards and Technology should fund the development of a central repository for existing and innovative detection, sampling, and analytical technologies, ranging from field and rapid screening tools to sophisticated laboratory-based assessments, to identify substandard and falsified medicines.
- The World Health Assembly, in partnership with the United Nations Office on Drugs and Crime and the World Customs Organization, and in consultation with major stakeholders, should institute an inclusive, transparent process for developing a code of practice on the global problem of falsified and substandard medicines. The code should include guidelines on surveillance, regulation, and law enforcement, empowering states and the international community to prevent and respond to drug quality problems.

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