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Fake Avastin Shows Very Little Protects Drug Supply

As drug counterfeiters step up their sales of bogus medicines, global health regulators have few protections in place to prevent them from reaching patients, and new laws aimed at addressing the problem could be years away.

Scrutiny of the supply chain has grown since fake versions of Roche's cancer drug Avastin (bevacizumab) turned up at U.S. oncology practices late last year, sparking an international investigation that so far stretches from southern California back to Turkey with a stopover in a Cairo suburb.

Drug manufacturers, distributors, pharmaceutical security experts and regulators interviewed by Reuters identified vulnerabilities all along the supply chain and called for comprehensive measures to protect patients and punish perpetrators.

The World Health Organization (WHO) estimates that less than 1% of medicines available in the developed world are likely to be counterfeit. Globally, however, the figure is around 10%, while in some developing countries up to a third of medicines are estimated to be bogus.

Problems include the lack of a system to track medications as they change hands, loose regulation that allows potential counterfeits to enter the system and a willingness by legitimate distributors and medical practices to look the other way even when medicines appear to come from a questionable source.

"Right now you have a situation where one shady wholesaler can introduce something and that can then pass through multiple actors in the system," said Allen Coukell, director of medical programs at the Pew Health Group who co-authored a report on counterfeit medicines. "Once they've gone outside the legitimate supply chain they can't be sure they're protecting patients."

Europe beginning in 2016 will require a unique identifier on all medicine packages. The United States has no national system for tracking drugs, but a California law requiring serial numbers goes into effect in 2015, and the FDA and U.S. legislators have called for universal tracking systems to combat counterfeiting.

The fake Avastin contained a variety of chemicals but none of the life-extending medicine. It has so far been traced back to Turkey via an illiterate Syrian businessman who procured it for an Egyptian firm, parties involved in the transactions told Reuters.

"The business about counterfeit Avastin really demonstrates how easy it is to be fooled," said Sandra Kweder, deputy director of the FDA's Office of New Drugs. "Often these outfits, they're in business one day and out the next."

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WHO said newer technologies are helping counterfeiters produce and sell more convincing fakes.

"Nowadays, access to all sorts of copying technology and printing technology for labels is much, much easier than it used to be," said Lembit Rago, coordinator for quality and safety of medicines at WHO in Geneva. "Online pharmacies add another layer to the picture by concealing where the stuff comes from."

Although the Egyptian firm was not registered with the national health ministry, it was able to sell the fake medicine to Swiss distributor Hadicon AG. It then passed through licensed distributors in Denmark and Britain before shipping to U.S. dealers the FDA has accused of peddling unapproved medicines.

Hadicon Chief Executive Klaus-Rainer Toedter said the company was the "victim of a major international fraud."

"The perpetrators certainly acted in a highly professional manner and knew that drugs would not be allowed to be opened once smuggled into the delivery chain," he said in an emailed statement. "Hadicon has been badly damaged by the misuse of its position as an intermediary."

The drugs were sold in the United States by Montana Healthcare Solutions and Tennessee-based Volunteer Distribution, which are under FDA investigation. The agency named 19 oncology practices that might have purchased counterfeit Avastin.

"The counterfeiters are so good at what they do, and they're so good at making a product that looks real, it's easy for someone to say, 'well, I didn't know, it looked right,'" said Ilisa Bernstein, another FDA official. She added that in some cases they are helped by "willful blindness" on the part of customers.

A source at one of the 19 practices described Montana Healthcare's sales representative as "a good con man."

"He had a legitimate business license and he had a legitimate distributor's license, or it seemed he did," said the source, who asked not to be named because the source did not have permission to speak to the media.

The source at one of the practices said it purchased drugs from Montana Healthcare's list of U.S. products and not from its offering of "lower-priced European alternatives," which included Avastin under its Turkish brand name. But they acknowledged that the very fact that such drugs were being sold should have raised a red flag that Montana Healthcare was breaking U.S. laws.

"Counterfeiters will attack the weakest area in any supply chain," said Tod Urquhart, a sales director for Norway-based Kezzler AS, which sells technology such as encryption software to help identify tampering or counterfeiting.

"If anybody ever tells you there is a silver bullet for this they really aren't right. You have to take a multitude of measures," said Urquhart.

But even the most sophisticated safeguards, such as encryption software or radio frequency identification (RFID) tags, can be undermined, counterfeit medicine experts said.



"If you're a doctor running a (U.S.) clinic and you're willing to dispense medicines with French packaging, what good is an RFID tracker?" said Tom Kubic, president of the Pharmaceutical Security Institute, a non-profit, industry-supported organization. "You've got to have some integrity on both ends."

Chris Valine, a spokeswoman for the Medical Board of California, where 16 of the practices named by the FDA are located, said any doctor found to be purchasing unapproved medicines from overseas or otherwise putting patients in harm's way could face sanctions ranging from a public letter of reprimand to revoking the doctor's license to practice.

"It's dishonesty, it's gross negligence, it's unprofessional conduct," she said.

The counterfeit drug trade has become a lure for terrorist and criminal organizations in part because penalties are much smaller compared to traditional illegal drugs, such as heroin and cocaine, according to details from a 2009 workshop organized by the U.S. mission in Nigeria that was obtained by Wikileaks.

Roche is "aware of cases where counterfeiters have tried to forge basically our entire portfolio," said spokesman Daniel Grotzky, citing fake versions of Avastin and other cancer drugs found in China and Syria. At the same time, the company doesn't have a way to track its medications once they leave the plant.

"With counterfeiting we rely on outside parties to report if they notice anything," he said.

Kezzler, the Norwegian company that sells technology to help identify tampering or counterfeiting, worked with Roche in India a few years back to help eradicate counterfeiting of some of its drugs there using unique serial numbers hidden under labels designed to make any tampering obvious, as well as other technology. The problem then moved to Egypt, Urquhart said.

Plans for Kezzler to work with Roche in Egypt were scuttled due to political instability there, Kezzler officials said.

Roche's Genentech division, which manufactures Avastin and other cancer drugs and sells them in the United States, said it only contracts with licensed, fully vetted distributors, such as the large U.S. wholesalers McKesson Corp and Cardinal Health. Those companies said they get drugs only directly from their FDA-approved manufacturers.

Morris & Dickson, a Louisiana-based company that is one of Genentech's contracted distributors, said it stopped selling medicines to secondary suppliers in the 1990s.

"The secondary market in and of itself wasn't bad, but it became an entry point for counterfeit drugs. The nefarious side of the trade got into it," said Paul Dickson, the company's chief operations officer.

He speculated that reimportation of medicines sold much more cheaply in Africa and Asia may be supplying the so-called gray market and allowing for counterfeits to enter the system.

While the problem is smaller in the United States than elsewhere, the temptation for doctors to seek cheaper



versions of drugs is growing as newer medicines command very high prices while reimbursement rates are cut.

Larger hospitals are likely to have more quality controls in place than individual clinics, but there are still concerns. The Mayo Clinic, for example, gets the vast majority of its drugs and supplies from Cardinal Health.

But drug shortages pose a unique problem "where you have to begin to look for outside sources," said Robert Wolf, pharmacotherapy director for hematology and oncology at the Mayo Clinic's cancer center. Avastin was not in short supply however.

A U.S. Senate bill that calls for far harsher penalties for counterfeit drug trafficking and for a universal system to track drugs through supply and distribution chains passed this month but it was not clear if or when it might be adopted as law.

"If we had a system of serialization and authentication it would be a major check against counterfeit or stolen drugs from entering the system," Pew's Coukell said.

The lack of a U.S. tracking system and free trade throughout the European Union, where regulations vary widely from country to country, helps facilitate the entry of counterfeits into the system, security experts said.

The California law that goes into effect in 2015 "should create pressure for a national system because wholesalers and manufacturers operate nationally, so they don't want a patchwork of state laws," Coukell said.

There are also questions about whether legitimate drugs, some of which need to be kept refrigerated, are being properly protected when they pass through less developed markets.

"We've seen medicines sitting on the dock at the Suez Canal literally for months in the sun and who knows how it's been handled," the Pharmaceutical Security Institute's Kubic said. "You may get it cheaper, but how do you know what you really get?"

Source: Medscape Pharmacists

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