

The Quest for a Secure

The catalyst for a movement to rid counterfeit prescription drugs from the United States supply channel sits in a butter dish in the Fagan family's refrigerator at their home in New York. It is two vials of Epogen, an anemia-fighting drug taken by Tim Fagan, now 20, following a liver transplant in 2002. One vial has a legitimate label for Epogen's strongest dosage (40,000 U/ml), and the other was relabeled (or "uplabeled") by a counterfeiter, from 20,000 to 40,000 U/ml. While Fagan did not die from being injected with the fake drug, his red blood cell level did not rebound as it should have and he had agonizing side effects.

The only detectable difference between the two thumbnail-sized vials is that the counterfeit drug's label had no Celsius degree symbol next to the words "Store at 2 to 8 C." Unless one has a magnifying glass at the ready, the difference is not readily seen.

"I am a pharmacist, and most pharmacists I know can't easily make the distinction between real and counterfeits," says Carmen A. Catizone, executive director of the National Association of Boards of Pharmacy (NABP).

Neither can most healthcare consumers. Tim Fagan's parents purchased the Epogen at a local CVS pharmacy. They eventually discovered the counterfeit had made its way through a zigzag chain of distribution from the drug's maker, Amgen, through two of the three major national drug wholesalers to a series of secondary wholesalers in South Florida up to the Fagans' pharmacy in New York. The traditional buying and selling habits of large wholesalers includes buying back product from secondary distributors (discounted from the price at which it originally sold or at increased pricing during shortages). This practice makes the underregulated pharmaceutical supply channel vulnerable to counterfeiters embedded in the gray secondary wholesale market.

What types of drugs are most susceptible to counterfeiting? Not surprising, counterfeiters target widely used and popular drugs, such as Lipitor and Viagra, and

expensive, injectable therapeutics such as Procrit and Epogen, and, yes, immune globulin.

How prevalent is counterfeiting? According to a statement presented to a House of Representatives subcommittee last November, attorney Donald deKieffer noted that in 2003, the World Health Organization and the FDA estimated that counterfeits made up 10 percent of the global medicines market.

In the last four years, following criminal investigations stemming from the Fagans' case and others in states such as Florida and Nevada, strides have been made by both the public and private sector to stop the disturbing crime of pouring adulterated, mislabeled and possibly lethal drugs into the U.S. drug supply.

Unfortunately, like the Fagan evidence that helped spur public awareness of this issue, the toughest federal legislative proposal to secure the safety of the drug supply channel from manufacturer to pharmacy sits on the shelf—in this case, a subcommittee of the U.S. Congress' House Energy and Commerce Committee.

The bill, the Counterfeit Drug Enforcement Act of 2005 (also known as Tim Fagan's Law, HR 2345), was introduced in Congress in May 2005 by Representative Steve Israel, D-N.Y., Fagan's congressman. A companion Senate bill (S. 1978) was introduced by Senator Charles E. Schumer, D-N.Y., in November 2005 and is sitting in the Senate Committee on Health, Education, Labor and Pensions.

Of eight major proposals in Fagan's Law, four of them go even further than current regulation by the FDA under the Prescription Drug Marketing Act (PDMA) enacted in 1988, further than existing state laws, and further than drug wholesalers' self-policing commitments. These proposals are: increasing criminal penalties against counterfeiters (up to life imprisonment if convicted of counterfeiting); mandating that a manufacturer must alert the FDA of a counterfeited drug in two days; giving the FDA recall authority for prescription drugs (currently it can only request, and ultimately sue to require, that private companies recall



Pharmaceutical Supply Channel

By Angela Macropoulos

product); and requiring a drug pedigree, a record of the chain of custody of a specific unit of medication as it moves through the supply channel from manufacturer to pharmacy. The requirement for a full and contiguous drug pedigree is the bill's linchpin.

This June, the FDA lifted an 18-year stay on the PDMA's pedigree regulations, which will result in implementation of a federal pedigree requirement. However, the federal regulations contain a significant loophole, because they do not require a pedigree from an "authorized distributor of record" of a drug. The PDMA defines an authorized distributor of record as a wholesaler that has an "ongoing relationship" with the manufacturer to distribute the drug.

Katherine Eban, the author of the book "Dangerous Doses," which compellingly chronicles schemes of making and distributing counterfeit drugs in South Florida and ties the tale to Tim Fagan's own bad medicine, says that the authorized distributor loophole is bad because it allows distributors to continue to be able to launder the origin of the drug. "So long as a company is an authorized distributor, there is an assumption that it got it directly from the manufacturer. And the regulation's murky definition of who is an 'authorized distributor' is too permissive," Eban says.

Eban adds that drug manufacturers have been unwilling to disclose who their authorized distributors are, presumably to protect competitive pricing advantages. "The efforts to make the chain more transparent have been stymied," she adds.

Last November, a hearing on counterfeit drugs was held by the U.S. House of Representatives Committee on Government Reform. Among those who testified were Eban and Kevin Fagan, Tim's father, who has become an enthusiastic advocate for this issue. Although the hearing encouraged other congressional representatives to sign on to Tim Fagan's Law, it continues to languish in the House subcommittee.

"It makes no sense," says Eric Turkewitz, a lawyer who

represented the Fagan family in a civil action related to the counterfeit Epogen. "There is nothing partisan in this bill, and it's all for the public's benefit. Where a counterfeited drug could affect millions of lives, who could be against it?"

Eban says that there is some public and political confusion that tangles the effort to preserve the integrity of the supply chain into the argument against importation of cheaper drugs. "Some congressmen take the position that the talk about supply chain safety is a ruse by pharmaceutical companies to prevent drug importation or re-importation," she says.

Catizone of the NABP stresses that, while it is perceived that Canada has a secure supply chain, Canada could obtain drugs from other countries that do not.

Ultimately, while Representative Israel holds that "all politics is personal," when describing how the Fagan family's story has been compelling in articulating his legislative effort, another chestnut, "business is business," continues to hold sway in the battle to eliminate counterfeit drugs.

For example, the Florida Legislature passed a law in 2003 that initially required full pedigrees for 34 of the most commonly counterfeited drugs. The Florida law would have implemented an expansion of the pedigree requirement, effective July 1, for all drugs. Instead, HB 371 was introduced in 2005 to weaken the additional pedigree requirement. It was supported by the Healthcare Distribution Management Association (HDMA), and Governor Jeb Bush signed it into law right before Florida's legislature adjourned this summer.

Martha Harbin, communications director for Safe Drugs Now, a Florida coalition dedicated to the implementation of drug pedigree laws, says that by hiring well-respected lobbying firms within Tallahassee, the HDMA successfully argued against the more rigorous pedigree requirements and in favor of business interests.

Kevin Fagan, who went down to Florida in May to

lobby against passage of HB 371, is not surprised. ➤
“There are more drug lobbyists than there are members of Congress,” he says.

Harbin says that the Safe Drugs Now coalition is still reeling from its loss. “Government will put more effort in making sure that CDs, DVDs or purses are not counterfeited,” she says.

But there is also political action on the horizon nationwide. For example, in New York, state Assemblywoman Amy Paulin, D-Scarsdale, and state Senator Nick Spano, R-Yonkers, have co-sponsored a bill that requires a full pedigree in electronic format or other emerging technology (A.2957 and S.3278). Wholesalers nationwide have argued previously that they needed time to go from paper to e-pedigrees, but New York’s proposed law, if passed, would force electronic tracking by December 2007. It also increases registration fees for drug wholesalers and manufacturers, and requires that wholesalers post a surety bond of \$100,000 or more.

Paulin says that mandating a surety bond this high will weed out bad apple wholesalers. She is optimistic that the law will pass when legislative session resumes in January. Paulin believes that states should do their part in closing the breaches in the porous drug supply channel. “What the FDA regulations now do is merely to provide a minimum standard. There is no reason in the world why states should not try to take leadership roles on this issue,” she adds.

Not all efforts are political. In 2005, the NABP, a professional association representing the states’ boards of pharmacy, started the Verified-Accredited Wholesale Distributors Program (VAWD). VAWD accredits wholesalers through on-site inspection of their facilities and evaluation of their operating practices. This accreditation process is required in Indiana, and 10 states recognize VAWD in lieu of a state inspection by the individual state pharmacy’s board. The association’s inspectors consist of former employees of the FDA, the Drug Enforcement Agency and the state boards.

“It is intended to fill in the gaps of the federal and state regulatory side,” says Catizone.

In the meantime, the big three drug wholesalers pledged in 2005 not to buy brand-name pharmaceuticals from the secondary market, and CVS agreed that it would not purchase from middlemen who buy from the secondary market.

As for Tim Fagan’s Law, Congressman Israel is undaunted in his effort to establish a national standard for drug supply channel safety. He recognizes that the current Congress and presidential administration do not consider it a priority issue. “My attitude is to fix bayonets and charge. I tend to take on issues that have been relegated to the sidelines,” says Israel.

But it is the personal aspect of this issue that seems to inspire Israel to continue his efforts. “Tim Fagan proved that a single person can catalyze change for millions of Americans,” Israel says. “Any person who is a medical consumer can learn the lesson of Tim Fagan.” ■

What Can You Do About Counterfeit Drugs?

- Encourage your representative and senator to support the Counterfeit Drug Enforcement Act of 2005 (HR 2345).
- Talk with your healthcare providers about where they buy your drugs.
- Ask your pharmacist if the pharmacy has a policy of not dealing in the secondary wholesale market. Other than the general explanation of side effects given with the dispensed drug, ask if the pharmacist has heard of any other possible side effects.
- Be conscious of new or different side effects from those you’ve had previously or that are disclosed with the drug’s packaging.
- If the drug is ineffective from the start or stops being effective, be suspicious and take it back to the pharmacy.
- Be familiar with your medicine. Examine its shape, color and size.
- Look at the packaging. Is it clear, clean and sealed? Look particularly at the quality and preciseness of the labeling.
- Be sure to keep samples of your medicine for evidence and comparison. Remember, the reason the Fagan family was able to identify the bad Epogen is because they had a good vial to compare it to.
- Most of all, observe your symptoms.
- Check for warnings and announcements from the FDA website and from state pharmacy boards and boards of health. Also explore your pharmacy’s website.
- If you or your doctor suspect a medicine is bad, you or your doctor should submit a report to the FDA on its MedWatch site. Submission forms can be found at <http://www.fda.gov/medwatch/report/consumer/consumer.htm>.