



How Can We Secure

the U.S. Pharmaceutical Supply Channel?

By Kit-Bacon Gressitt

The often-postponed federal drug pedigree requirement, enacted in the Prescription Drug Marketing Act (PDMA),¹ was to have finally been implemented December 2006. It would require a pharmaceuticals distributor to document every entity that has had possession of a vial or bottle of medication the distributor handles. The common belief is that pedigrees will help secure the supply channel, preventing drug counterfeiting and diversion and the multiple transactions that often increase a drug's price and put it at risk of being mishandled.

Instead of being at long last implemented, the federal pedigree requirement has languished since December, awaiting resolution of a court challenge to its constitutionality. In the ongoing void of a nationwide requirement, individual states have tried to pass their own pedigree laws, resulting in mass confusion. Within the varying efforts to secure the U.S. pharmaceutical supply channel, "who's passed what and what's effective when" is more circular than the classic Abbott and Costello routine "Who's on First."

Worse, this has been the status quo for many moons. Despite the Food and Drug Administration's comprehensive 2004 report

"Combating Counterfeit Drugs" and its updates,² Despite the 2005 publication of the frightening exposé by Katherine Eban, "Dangerous Doses: A True Story of Cops, Counterfeiters and the Contamination of America's Drug Supply."³ Despite Florida's once passionate but ultimately tepid legislative effort to lead the nation in securing the pharmaceutical supply channel. Despite countless U.S. media reports of drug diversion, mishandling and counterfeiting. Despite the mournful and outraged pleas of families harmed by a channel lacking integrity. Despite all this, the U.S. pharmaceutical supply channel remains unsecured. This failure begs the question "How can we fix it?" and the answers vary, depending on who is asked.

FFF Enterprises, a specialty pharmaceuticals distributor and sponsor of *IG Living*, believes the solution is simple. "Don't do it—secondary distribution that is—just don't do it!" said Patrick M. Schmidt, FFF's president and CEO. Secondary distributors are those who buy pharmaceuticals from other distributors or from healthcare providers, rather than directly from manufacturers. "Ours is not a popular position," Schmidt said, "and some people in the industry think if you eliminate secondary distributors in an effort to secure the supply channel, there are U.S. sites of care we won't be able to reach. I don't believe that. Just ask FedEx or UPS or DHL."

¹ U.S. Prescription Drug Marketing Act of 1987: www.fda.gov/cder/regulatory/PDMA.

² "Combating Counterfeit Drugs" 2004, "FDA Counterfeit Drug Task Force Report" 2006, www.fda.gov/counterfeit.

³ "Dangerous Doses" by Katherine Eban, Pub. 2005; Reprint edition 2006, www.dangerousdoses.com.

FFF is a manufacturer-authorized distributor of record (ADR) for all U.S.-licensed plasma products, including intravenous immune globulin (IVIG or IGIV), a recognized target of diversion, unethical pricing and counterfeiting. Although ADRs are not required to provide pedigrees for medications purchased directly from manufacturers, FFF has been voluntarily providing electronic pedigrees for its customers since 2004. Yet Schmidt is not convinced pedigrees are the solution.

"I'm not sure the supply channel can ever be completely fixed, although there has been a lot of progress," Schmidt said. "But the pedigree requirement stops short as long as there are exemptions. ADRs and manufacturers should not be exempt. And now people know enough about pedigrees to be dangerous. Many providers know to ask for them but don't have the wherewithal to verify the pedigree information, and pedigrees can be counterfeited. We've seen pedigrees with transactions hand-written in."

In fact, FFF was recently provided copies of pedigrees obtained by the state of Georgia Drugs and Narcotics Agency in the course of an audit of a secondary distributor. The pedigrees, filled in by hand, documented several instances of IVIG transactions that began with FFF's purchase of the product from the manufacturer and sale to an infusion clinic. The infusion clinic sold the product to a physician who has a wholesale license. The physician didn't administer the IVIG to patients, but, instead, sold it under his wholesale license to a secondary distributor, which sold the product to another secondary distributor.

All told, the various secondary channel transactions reflected in the documents from Georgia resulted in price increases ranging from about 50 percent to 100 percent.

"We cut off the infusion clinic immediately, as did the manufacturer," explained Chris Ground, FFF's senior vice president of national accounts. "The clinic's sales of product obtained from FFF violated its agreement with FFF, its agreement with its group purchasing organization (GPO) and the GPO's agreement with the manufacturer. But the pedigree didn't stop the bad behavior; it just documented it. What the pedigree did *not* document was whether the IVIG was handled, stored and shipped properly; whether the temperature was maintained; whether the product's integrity was maintained. That IVIG was ultimately infused into critically ill patients, at an exorbitant price. Is that the IVIG you would want for yourself or for a loved one? To an informed reader, that pedigree tells a dangerous story; it doesn't do anything to instill confidence in the product."

If pedigrees aren't the fix, despite significant hope and dollars invested in them, the quest for channel integrity could become a windmill tilt. But Schmidt sees better defined business practices and a more astute buyer as the answer.

"Ultimately, the question is, do secondary distributors add value to the channel? We don't believe so," Schmidt said. "The secondary

channel exists to exist, to make money and to prey for shortages—and I mean that to be spelled p-r-e-y.

"FFF's distribution practices are a sharp contrast," Schmidt continued. "We purchase only from the manufacturer and ship only to the healthcare provider. That's the only true solution. That means no transactions between distributors, no manufacturer sales to unauthorized distributors, no secondary channel for healthcare providers to sell into. If all manufacturers, all ADRs and all healthcare providers accept this practice as the industry standard, the channel will be as secure as it possibly can be, and we won't need regulation. Short of that, it's the government's responsibility to protect its people."

Jayne E. Juvan, a healthcare law attorney with Benesch, Friedlander, Coplan & Aronoff, posts a health law blog⁴ where she has tracked the legal challenge to the federal pedigree requirement. The case was filed against the U.S. Department of Health and Human Services (HHS) by a group of secondary distributors (those who are not ADRs), led by RxUSA Wholesalers Inc. The plaintiffs are opposed to the federal pedigree requirement that exempts ADRs.

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Patrick M. Schmidt, FFF Enterprises

"RxUSA has argued that the law is unconstitutional because it treats different classes of individuals differently without having a rational basis for doing that," Juvan said, but she went on to explain that "[t]he Constitution allows us to do that. ... If it doesn't involve race or a fundamental right such as voting, the courts generally follow Congress."

Juvan expressed no expectation that RxUSA will prevail, but indicated the case could take years, holding up the federal pedigree requirement. Yet she echoed FFF's doubt that pedigrees can actually secure the supply channel.

"Supposedly, the average consumer stands to benefit from a more tightly regulated supply chain," Juvan said. "Whether that's actually [the case] is another question. Do the regulations make it less likely for counterfeits to make their way into the supply chain? There are arguments both ways."

And the argument has shifted to the states, a trend Juvan suggests could actually hinder channel integrity. "The federal government should say that states cannot legislate [pedigree requirements]," Juvan said. "Multiple standards could actually increase the ➤

⁴ www.JuvansHealthLawUpdate.com

likelihood that counterfeits will be introduced and could impede distributors' ability to conduct business."

While pedigrees remain the talk of the town, some industry watchers assume the U.S. supply will always have a percentage of counterfeit drugs. "The key," Juvan said, "is to make sure our percentages don't rise."

In 2005, **Congressman Steve Israel**, N.Y. 2nd District, introduced HR 2345 (commonly known as Tim Fagan's Law⁵) after hearing about then-16-year-old Fagan, an organ transplant patient, being infused with counterfeit Epogen. The boy's medicine went through 11 transactions between the manufacturer and the Fagans' refrigerator, including a deal at a strip club in Florida. Among other channel safeguards, HR 2345 would require drug pedigrees—paper or electronic—of all distributors, mandate manufacturer reporting of counterfeiting within two days, give the FDA drug recall authority and increase criminal penalties for counterfeiting.

The bill didn't progress in the Republican-controlled Congress, but with the transition to a Democratic majority, Israel's office is now preparing to reintroduce the bill in a form "very similar" to its original.

"If every member of Congress had a Tim Fagan in every district, this bill would have passed two years ago," Israel explained. "I would argue that every member *does* have a Tim Fagan, but the nature of counterfeit medicine makes it almost impossible to recognize that.

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Congressman Steve Israel, N.Y. 2nd District

There's no question that the economics of this issue have helped stall any progress on this bill, but even the industry has come to a fairly recent recognition that the threat of counterfeit medicines and a growing gray market are far greater challenges to their profits than paper pedigrees and increased FDA enforcement. Counterfeit medicine is now one of the fastest growing criminal enterprises in the U.S. It's easy to do, it's hard to get caught and it's highly profitable."

Although Israel's bill would eliminate the ADR pedigree exemption, essentially resolving the RxUSA case, it would not put an end to the types of transactions that inspired the bill. "I don't want to wipe out the secondary market," Israel concluded. "I just want the secondary market to thrive with a distribution system that has integrity. Sending Tim Fagan's Epogen to the strip club tells me there's a lack of integrity in secondary channels."

The **HHS Office of the Assistant Secretary for Planning and Evaluation (ASPE)** recently released a report on intravenous immune globulin.⁶ The report highlights some key characteristics of the secondary distribution channel:

"The IGIV marketplace has struggled with channel integrity and includes a significant secondary market outside of the authorized distribution channels. The secondary market is characterized by fluctuating prices and product availability.

"Prevailing IGIV prices in the secondary market are substantially higher than those in the authorized channel.

"In the last few years, in order to increase the integrity of the supply chain, each IGIV manufacturer has significantly reduced the number of its authorized distributors in the United States. Previously, manufacturers used large numbers of distributors, some of which were involved in reselling IGIV at a profit to other distributors (also known as the secondary market).

"Most manufacturers interviewed reported having a policy to eliminate any business relationships with an entity that supplies the secondary market. ... While IGIV manufacturers contend that they only sell to authorized distributors and providers, input from other sources contradicts this assertion. One GPO interviewed for the study reported that some manufacturers do indeed sell to secondary distributors at prices higher than that for allocated IGIV. Further, a secondary distributor interviewed for the study also indicated buying IGIV they sell directly from an IGIV manufacturer."

Flemming Nielsen, general manager of Octapharma USA, a global manufacturer of IVIG, confirmed some of the report's findings. Octapharma has reduced the number of its ADRs to five since entering the U.S. market in 2004, in an effort to secure its piece of the channel.

"Our direct distribution agreements indicate that our products are not for resale," Nielsen explained. "What usually happens is someone has acquired Octagam, and they call and want verification of the pedigree. Then we look into it and we get documentation that the product had been resold two, three, four times. We see that we sold it to the distributor, the distributor has sold it to the provider and then it has been sold out the back door. We will then tell the distributor not to sell to that provider anymore. ... We want to see that [it goes]

⁵ What does Tim Fagan's Law do? www.house.gov/israel/issues/counterfeitdrugs.htm.

⁶ U.S. Department of Health and Human Services, Office of the Assistant Secretary of Planning and Evaluation (ASPE), Analysis of Supply, Distribution, Demand and Access Issues Associated With Immune Globulin Intravenous (IGIV), February 2007: <http://aspe.hhs.gov/sp/reports/2007/IGIV/index.htm>.

from Octapharma to the distributor to the healthcare provider to the patient.”

Octapharma’s approach is labor intensive, which may not be feasible for big pharmaceutical companies. Nonetheless, Nielsen does see a channel integrity solution, one that isn’t regulated. “We sincerely believe that if you want to secure the channel there has to be a cooperative approach. ... As soon as [product] enters the channel, there has to be cooperation between the manufacturer, the distributor and the provider. We should be the ones to work this out together because we all want safe product and a secure channel for the patient.”

Martha Harbin was an organizer with Safe Drugs Now, a now-defunct consumer group formed to maintain the original requirements in Florida’s pedigree law. She believes she saw the government bow to the influences of business when the big three pharmaceutical wholesalers successfully lobbied the Florida Legislature to insert an exemption from pedigree requirements for ADRs in Florida’s law.

“We found some solace from watching the manufacturers’ press releases. They started announcing that they were voluntarily implementing some of the things that would have been required [by Florida’s law]. Like Pfizer announcing they wouldn’t sell to secondary distributors anymore.”

Harbin has come to believe the solution cannot be found at the state level. “If we continue to rely on the states to be the gatekeepers, there will be bad things happening. It’s going to take more for the public to become more involved and demand political change. It will take more media. The occasional instance of counterfeit drugs is not enough. I hope it’s not going to take something like the Tylenol situation in the ‘80s, but that was dramatic enough that it really caused a widespread awareness of the problem.”

Realistically, the public is slow to rally around a cause so difficult to understand. Today’s pharmaceutical supply channel is a tangled web, regardless of deceptive or honest practice: It is complex!

But, in a report to **U.S. District Court Judge Joanna Seybert**, presiding over the RxUSA v. HHS case, there is a seemingly quiet little statement that is actually screamingly simple: “[The Plaintiffs] purchase pharmaceutical products for resale almost exclusively from authorized distributors and not directly from manufacturers—primarily because manufacturers typically refuse to sell product directly to the Plaintiffs.”

That, coupled with the PDMA companion report by the Committee on Energy and Commerce that found “most of the drugs that were counterfeits, stolen, expired, or obtained through fraud were handled by secondary wholesalers” begs another question: If many manufacturers will not sell to secondary distributors and if secondary distribution is the primary entry point to the channel for dangerous drugs, can the

industry—can healthcare consumers—continue to tolerate the risks inherent in the secondary channel?

Harbin advocates for safety first: “[The manufacturers and distributors] need to put the safety of the consumer above everything else. They are in a unique position of public trust and that should motivate everything they do. In the end, that’s good business.”

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Martha Harbin, Safe Drugs Now

Good or bad, how the business of distributing pharmaceuticals will be regulated is unclear. National pedigree requirements remain stalled in the miasma of a court challenge. Pending state pedigree requirements have not resulted in an enthusiastic rush to comply with their intent—in fact, some industry meetings addressing state laws have been, at times, focused on forestalling the requirements if not outright avoiding them. Other states continue to dip a legislative toe or two in the muddied waters of pharmaceutical supply regulation. And the channel remains unsecured.

Meanwhile, healthcare consumers remain in ignorant risk—and may continue so, unless Harbin’s worst fears come true and consumers are painfully enlightened by a cataclysm of counterfeits. Woe to industry and government alike if losing consumer trust is what it takes to secure the U.S. pharmaceutical supply channel. Better would be an industry initiative that openly acknowledges all the risks and adjusts standard practices to mitigate the risks openly, effectively—and voluntarily. FFF’s model could be the most effective and least painful solution: from the manufacturer to the ADR to the healthcare provider.

As Israel commented, “It’s in the best interest of industry that American consumers have confidence in their products.” ■

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