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WHITE PAPER

Beyond Pedigree:

The Role of Infrastructure in the Pharmaceutical Supply Chain

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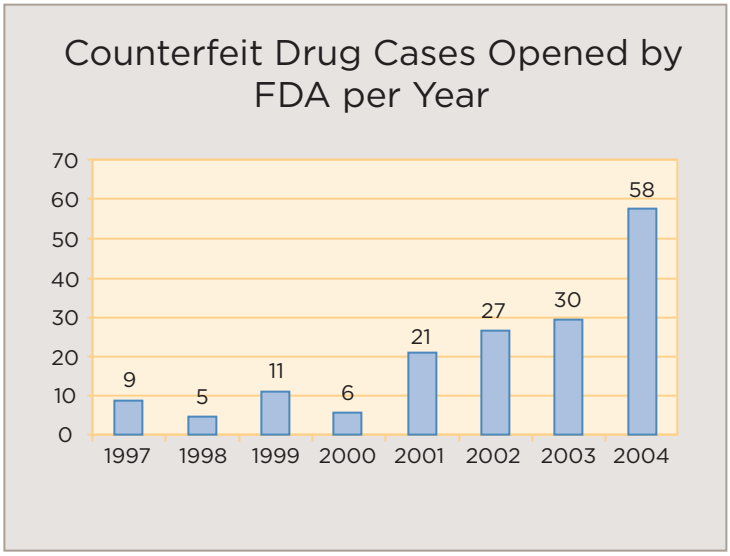
In an agency meeting October 15, 2004, John M. Taylor III, associate commissioner for regulatory affairs at the Food and Drug Administration (FDA), acknowledged that, "No single magic bullet will solve the counterfeit drug problem. Rather, we need a multi-pronged strategy. And many new technologies are available to counter the threat."

To address and combat the increasing occurrence of counterfeit drugs, Federal and State regulators are pursuing solutions that require the tracking, recording, and communication of a drug "pedigree." A drug's pedigree represents the complete history of a given product's chain of custody from the manufacturer to the point of dispensing. Much of the early work around implementing solutions has focused on support of the pedigree through electronic solutions, both in terms of applications for managing pedigrees and sensory technologies for capturing data, such as radio frequency identification (RFID) tags. An equally crucial element to the success of these measures is the network or infrastructure that will allow the captured data to be stored, shared, and authenticated. In this paper, VeriSign addresses the growing counterfeit problem, new requirements for electronic pedigree, and the challenges the industry faces in implementing solutions in the most efficient and effective way possible.

The Growing Counterfeit Drug Issue

According to the FDA, the number of investigations involving counterfeit drugs has increased over 90 percent from 2003 to 2004.



Source: *Combating Counterfeit Drugs: A Report of the Food and Drug Administration Annual Update* May 18, 2005

The actual number of cases may be small compared to the overall volume of drugs purchased, but the risk to patients from a single case of counterfeit drugs may cause serious harm or even be life-threatening. The following incidents are actual examples of the growing threat:

- In May 2002, thousands of vials of Procrit (epoetin) labeled as containing 40,000 units were found to contain only 2,000 units, and later that year, other vials of Procrit were found to contain nothing but Miami tap water.
- In the spring of 2003, there were reports that some Lipitor (atorvastatin) pills tasted bitter, caused a burning sensation on the tongue, and were too large.
- In February 2004, several Web sites sold unsuspecting consumers contraceptive patches, under the Ortho Evra brand name, that contained no active ingredient.

Source: Paul M. Rudolf, M.D., J.D., and Ilisa B.G. Bernstein, Pharm.D., J.D., "Counterfeit Drugs" *New England Journal of Medicine*, April 2004

The prescription drug supply chain in the United States is unlike any other industry's supply chain in the world. It handles highly sensitive materials and satisfies a far-reaching demand across large markets and small niches. The distribution process is complex, with prescription drugs passing through a number of entities along the supply chain. The consumer or patient may purchase a drug that has passed through as many as five or six entities along the way, including:

- Manufacturers
- Contract Packagers
- Primary Wholesalers
- Secondary Wholesalers
- Retail Pharmacies
- Hospitals
- Closed or Institutional Pharmacies
- Doctor's Offices and Clinics
- Mail Order
- Repackagers
- Internet Pharmacies

Fortunately, the vast majority of prescription drugs received by patients are safe. However, given the complexity of the supply chain and the variation in regulations covering different entities and different geographies; opportunities exist for counterfeit or adulterated drugs to enter the supply. Multiple transactions of the same product increase the risk of mishandling, faulty storage, mislabeling, tampering, compounding, and counterfeiting of drugs. Pricing differences among various markets and regions create a strong illegitimate profit motive. Dangerous counterfeit drugs, originally introduced into the drug supply by malicious individuals and organizations, can be unknowingly sold by legitimate companies to unsuspecting customers.

To ensure the safety of prescription medications, manufacturing and packaging processes are primarily regulated at the federal level by the FDA. The remaining processes in the supply chain are typically regulated at the state level. In a rationale for its ground-breaking

program, the State of Florida explains, "The U.S. Congress mandated state regulation of the drug distribution market because pharmaceuticals, including prescription drug samples, which have been mislabeled, misbranded, improperly stored or shipped, have exceeded their expiration dates, or are outright counterfeits have been injected into the national (and international) distribution system in astonishing numbers."

Source: *http://www.doh.state.fl.us/pharmacy/WebPage/News_CorrespondenceHTML/HowItAffectsYourPractice.htm.* Article title: "The Florida Drug and Cosmetic Act: How It Affects Your Practice"

The Need for Drug Pedigree

As far back as 1988, Congress passed the Prescription Drug Marketing Act (PDMA) with a drug pedigree requirement. However, the burdens of manual record keeping have caused the FDA to be hesitant in its implementation of these requirements. At the state level, Florida is leading the way with the adoption of legislation and rules that require detailed pedigrees for all drug sales to retail pharmacies and other dispensing parties. Florida requires that these pedigrees record the complete chain of custody—all the way back to the original purchase from the drug's manufacturer. The Florida regulations also include the following requirements:

- Every party engaged in the wholesale distribution of a prescription drug (except the manufacturer of that drug) must provide a pedigree
- Pedigrees must be provided prior to wholesale distribution
- A drug for which the required pedigree is nonexistent, fraudulent, or incomplete is considered "adulterated" and cannot be sold. The law stipulates that parties involved with adulterated pedigrees are at risk for felony prosecution if they:
    - Fail to authenticate the pedigree and attempt to further distribute a drug
    - Falsely swear or certify that pedigree papers have been authenticated
    - Falsely represent factual content of a pedigree or knowingly omit required information

The implementation of pedigree requirements in the pharmaceutical supply chain is seen as an inevitable improvement to the safety of the U.S. drug supply. The next two years will likely see many states adopting laws similar to those in Florida—in fact, many states are looking to Florida's legislation as well as the Model Rules for the Licensure of Wholesale Distributors developed by the National Association of Boards of Pharmacy® (NABP®). NABP represents the state boards of pharmacy in all 50 states, and has developed the Model Rules, which include recommended language for developing state laws or pharmacy board rules regarding drug pedigree requirements.

California recently passed a law requiring pedigrees to be transmitted from a seller to a buyer of all prescriptions drugs beginning in January 1, 2007. Indiana has also passed a law requiring pedigrees for some transactions starting on June 30, 2006.

The Emergence of the Electronic Pedigree

In its February 2004 report "Combating Counterfeit Drugs," the FDA stated that the adoption and common use of reliable "track and trace" technology is feasible by 2007. The ability to track a specific drug product through the supply chain and trace its exact journey will help secure the integrity of the drug supply by providing an accurate drug pedigree. Some of the functional requirements for an electronic pedigree solution may include:

- Authentication of each owner listed on the pedigree of a drug product, traced from current owner back to the original manufacturer and shipment
- Validation that the drug product referenced on the pedigree matches the physical product received
- Reconciliation of product on hand to ensure it has a pedigree, and confirmation that only products with pedigrees are shipped to customers
- Association of pedigree information to outbound shipments
- Confirmation that shipped products have complete and accurate pedigrees

While the functional requirements for each state regulation may differ, the need for authenticated data, secure communication, and comprehensive reporting are fundamental to a viable pedigree program. The challenges that arise from the need for an information and network infrastructure are different than those of any other electronic system in today's drug supply chain. By its very nature, a pedigree requires validated information to pass from one authenticated party to another without any compromise to its integrity. The parties involved in the manufacture, distribution, and dispensing of drug products will be forced to rely on each other—and on a common network or infrastructure—in order to securely authenticate, record, store, and share pedigree information.

At a high level, the following is a list of some of challenges the industry faces:

- **Transaction Volumes**—Pedigrees will require a significant increase in the amount of information shared between trading partners.
- **Information Storage**—Each player in the supply chain will need to maintain complete, accurate, and secure records of drug pedigrees for multiple years.
- **Reliability**—Pedigree information must be available before a product can be shipped—if it is not, shipping the product could result in a felony charge.
- **Certification**—Each player in the supply chain must authenticate the chain of custody back to the manufacturer, maintain a secure record of this authentication, and certify that the shipments have complete and accurate pedigrees.

No matter what specific regulations are enacted, pharmaceutical manufacturers, distributors, and retailers must address the information and network infrastructure needs in order to comply with pedigree laws in a large-scale environment.

Beyond Pedigree to Intelligent Infrastructure

MANAGED SERVICE MODEL

Like other VeriSign services that secure and handle sensitive financial and proprietary transactions, our capabilities are delivered as a managed service. This service model is available in a number of different deployment options and augments, rather than replaces, existing execution systems critical to a business in the pharmaceutical industry. A service-based model minimizes upfront investment and allows a company to pay for capacity requirements only when needed, while gaining the benefits of proven intelligent infrastructure services.

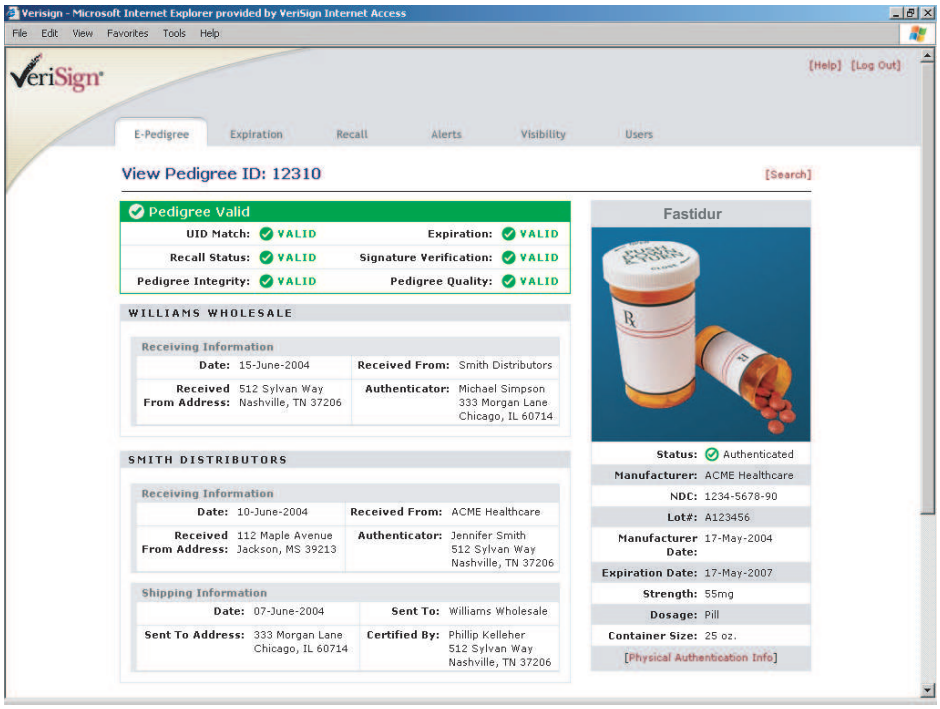
As a leading provider of Intelligent Infrastructure Services for today's complex, global networks, VeriSign is uniquely qualified to address the challenges arising from pedigree regulation. VeriSign operates large-scale intelligent infrastructures that enable over 14 billion daily Internet interactions, such as email delivery and Web site look-ups; facilitate three billion daily telecom interactions including caller ID, wireless content and SMS messaging; and secure over $100 million in e-commerce every day. In fact, VeriSign was founded as a provider of Internet security services, and today provides encryption and authentication services for nine out of 10 *Fortune* 500 companies and the top 10 U.S. banks.

VeriSign is bringing that expertise in authenticating entities and protecting information exchange online to bear on the challenge of recording and sharing the pedigree of products as they move through an increasingly complex supply chain.

In 2004, VeriSign was selected by EPCglobal to operate the authoritative root of the EPCglobal Network.™ Based on the expertise that earned that designation, as well as in-depth discussions with many players in the pharmaceuticals supply chain, VeriSign is leveraging its infrastructure to develop network services supporting the unique needs of this industry. To enable companies to immediately capitalize on this existing reliable and scalable infrastructure, VeriSign offers a pedigree solution that addresses the existing and proposed legislation faced by the industry. This solution goes beyond the mere capture of data to infrastructure services that enable the secure sharing, recording, and storage of data to guarantee authentic, comprehensive pedigrees.

As mentioned above, the information and network requirements of pedigrees place unique challenges on the members of the drug supply chain. VeriSign services have been designed to support real-world use cases expected by the industry, including the following:

- Inbound processing of notifications
- Serialized and non-serialized products
- Authentication and signing of pedigrees
- Certification of pedigrees
- Recalls/returns/damaged goods considerations
- Integration with existing receiving, put-away, picking, and shipping processes
- Repacking
- Hardcopy pedigree handling



Screen shot from the VeriSign solution showing the pedigree data with indications that the electronic data has been authenticated and that various attributes have been checked to ensure the product can be distributed

The VeriSign solution was developed to ensure a safe and secure supply chain through the application of our proven services and expertise. All VeriSign solutions are built on established intelligent infrastructure that reliably handles high transaction volumes, storage requirements, service reliability, and certification requirements on a daily basis. It is exactly this experience and these capabilities that will enable drug manufacturers, distributors and retailers to implement a successful pedigree system and ensure a safe and efficient pharmaceutical supply chain.

To learn more about how VeriSign can help you address pedigree, send an email requesting more information to epedigree@verisign.com.

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