Facing the Pedigree Challenge

This paper addresses what has led to the regulations regarding drug pedigrees, requirements for electronic pedigree, and the challenges the industry faces in implementing solutions efficiently and effectively.

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In an agency meeting in 2004, John M. Taylor III, associate commissioner for regulatory affairs at the Food and Drug Administration (FDA), acknowledged, "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."

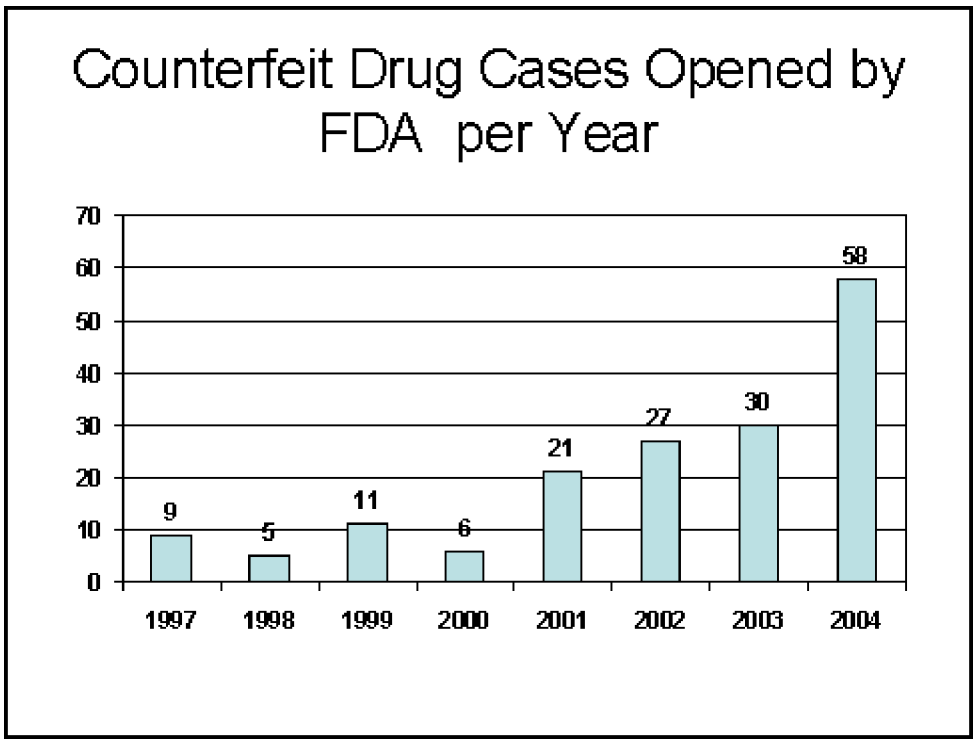
Federal and state regulators and the participants in the drug supply chain (i.e., manufacturers, wholesalers and pharmacies) are pursuing strategies to continue to provide a safe and secure drug supply. One regulatory strategy is to require the tracking, recording and communication of a drug "pedigree."

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 RFID tags. While there are many advantages in leveraging this technology to track drugs, widespread adoption has not yet occurred.

As various regulatory deadlines approach, attention has shifted to how pedigree data will be captured, stored, shared and authenticated in advance of industry adoption of RFID. In this paper, VeriSign addresses the what has led to the regulations regarding drug pedigrees, 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 increased over 90% from 2003 to 2004.



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 often cited when discussing the potential threat of the growing threat:

- In May 2002, thousands of vials of Procrit (epoetin) labeled as containing 40,000 units were found to contain only 2000 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.

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

It is important to note that while there have been a number of publicized counterfeit drugs, the true nature of the problem has not been documented. It would be very difficult to calculate the actual risk of receiving a counterfeit drug in the U.S.

The prescription drug supply chain in the United States 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	Retail Pharmacies
Contract Packagers	Closed or Institutional Pharmacies
Repackagers	Mail Order and Internet Pharmacies
Primary Wholesalers	Doctors' Offices and Clinics
Secondary Wholesalers	Hospitals

All of these legitimate entities provide valuable and necessary functions. The vast majority of prescription drugs received by patients have been properly acquired, handled and sold. However, given the number of potential players in the supply chain and the variation in regulations and laws covering each kind of player; opportunities may exist where unscrupulous individuals could get around the safeguards established by the industry.

The Rationale 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 recordkeeping have caused the FDA to be hesitant in its implementation of these requirements and has stayed the PDMA requirements for a pedigree while industry explored ways to adopt a workable pedigree model.

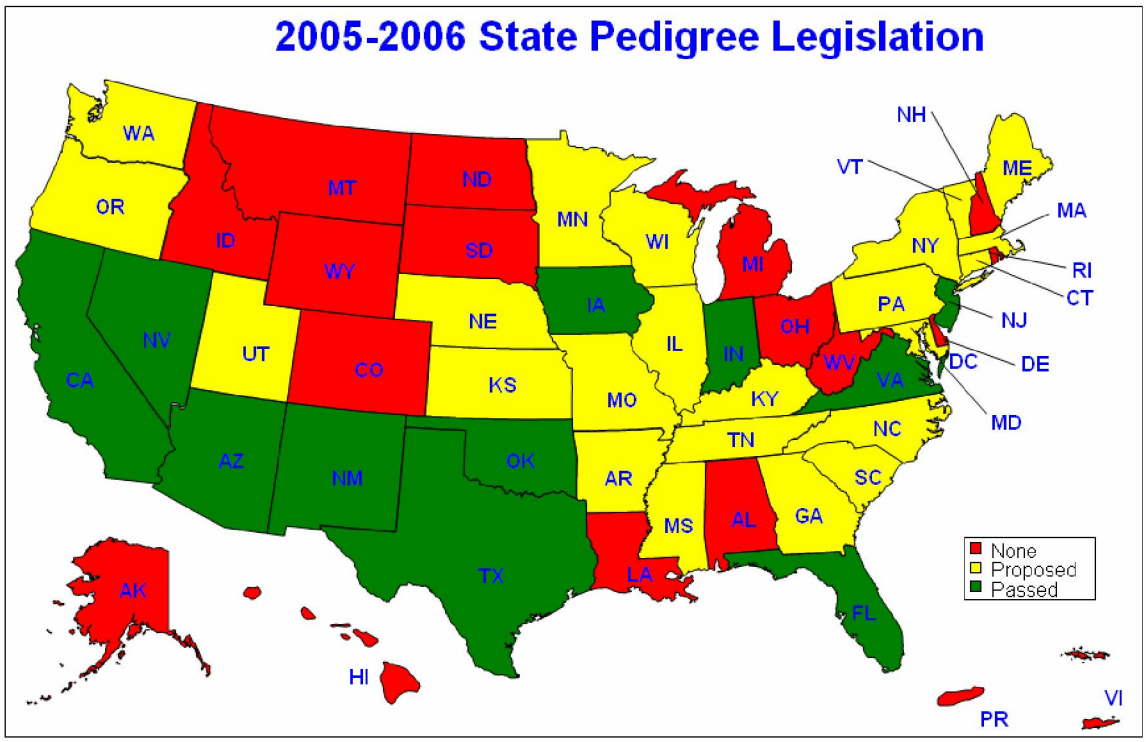
The FDA has recently publicly voiced concern about the pace of adoption. Acting FDA Commissioner Dr. von Eschenbach reconvened the Counterfeit Drug Task Force to assess the progress that has been made in adopting electronic track and trace technologies, and to look at the obstacles that have been encountered and what measures should be taken to quickly overcome these obstacles. The Task Force organized a public meeting in Bethesda, Md., in early 2006 to address issues regarding the adoption of electronic track and trace technologies such as RFID. The Task Force is preparing a report scheduled to be made public in May. One area the Task Force has indicated it will comment is on whether or not to extend the current stay on the PDMA pedigree requirement, which ends in December 2006. (For more information go to www.fda.gov/counterfeit)

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. California has 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 following map provided by the Healthcare Distribution Management Association (HDMA) shows 11 states with pedigree laws on the books.



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:

- Initiation of the pedigree as the original owner of the pedigree with specific source and product information
- 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 is pedigreed, and confirmation that only pedigreed product is made available to be shipped to customers
- Association of pedigree information to outbound shipments
- Confirmation that shipped products have complete and accurate pedigrees

Managing chain of custody data within an enterprise creates various technology challenges. At a high level, the following is a list of some of challenges supply chain players face:

- **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 these technology challenges.

Beyond Pedigree – From Compliance to Strategic Value

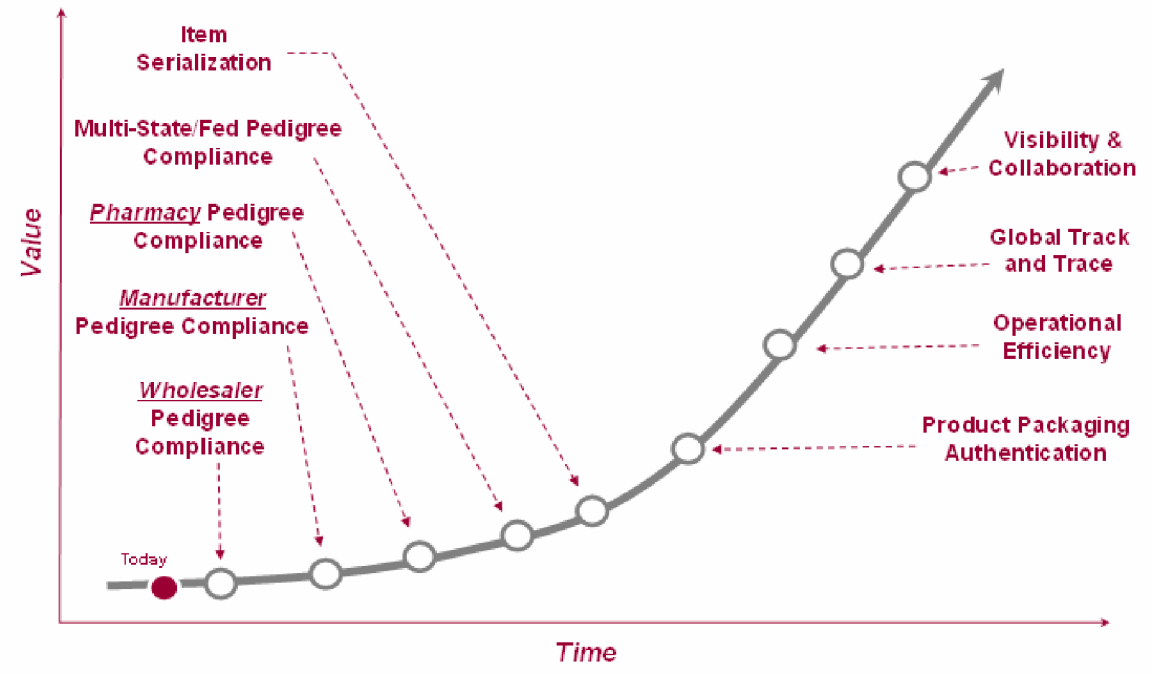
Investing in pedigree related infrastructure goes beyond compliance. It should be considered as an overall strategy of supply chain safety, security, efficiency and, potentially, collaboration. The only reason pedigree is front and center is because of the deadlines established by the FDA and by state laws. There are a number of other significant opportunities pharmaceutical companies are looking into for related technology. Patient safety is the primary concern in the industry.

Enabling better pedigree compliance is only one area where this technology can be applied. Product packaging authentication, where a unique number on a products package is authenticated against a database is another way this technology can be used. This is the model promoted by the Pharmaceutical Research and Manufacturers of America (PhRMA) in its May 2005 position

paper. This technology could also be used to help reduce the thousands of cases of drug dispensing and administering exceptions that occur in our healthcare system each year.

While safety is a primary concern, cost of delivering pharmaceuticals is also a major concern. Ensuring the right product is at the right place at the right time is the holy grail of all supply chains and the pharmaceutical supply chain is no different. The difference in the pharmaceutical supply chain is that the cost and consequences of not achieving this goal is considerably higher than in most industries. Chain of custody technology can be the platform for improving customer service and satisfaction.

At VeriSign, we believe that organizations should pursue a strategy and make investments that accomplish regulatory compliance but also establish a foundation for strategic value. The following is a possible roadmap for the industry (the order and value of each opportunity will vary depending on your vantage point).

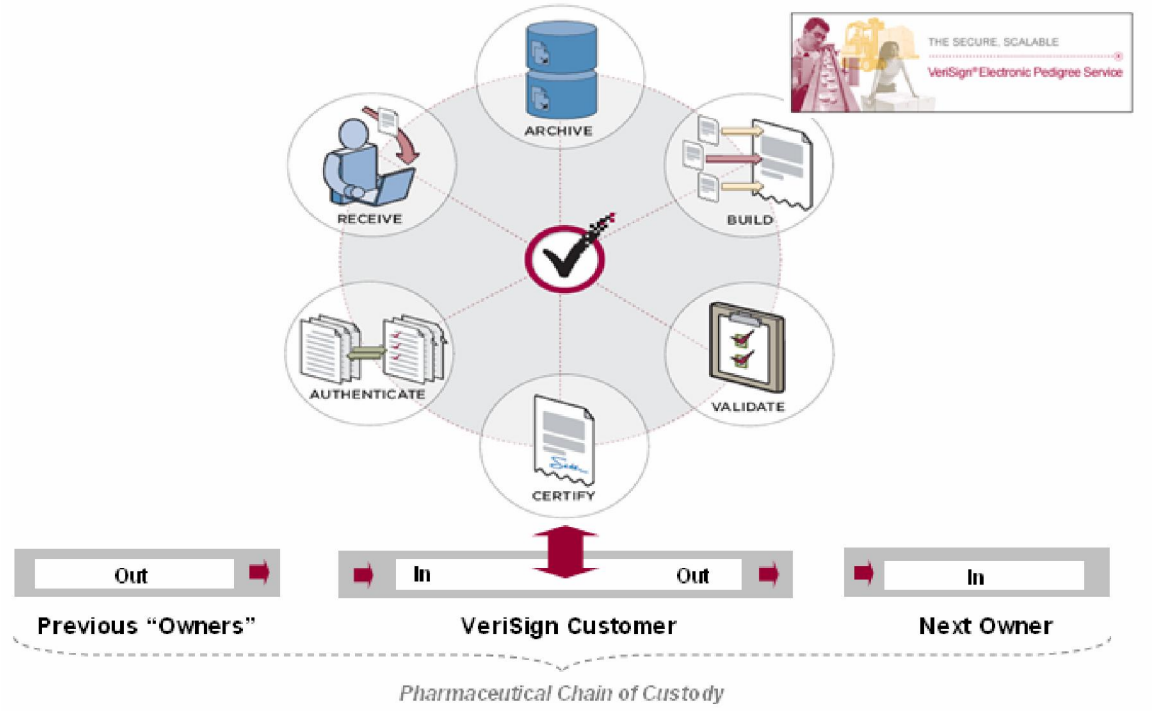


VeriSign – Your Trusted Partner

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. All of VeriSign's services leverage the security expertise and experience gained from providing encryption and authentication services for nine out of 10 Fortune 500 companies.

VeriSign is bringing that expertise in authenticating entities and protecting online information exchange to bear on the challenge of recording and sharing the pedigree of products as they move through an increasingly complex supply chain. VeriSign's Electronic Pedigree Service is the service of choice to manage pedigree data starting in 2006 for companies with combined sales of over $158 billion dollars. As depicted below, the VeriSign Electronic Pedigree Service can be used at any point in the supply chain to receive, build, authentication, validate, certify and archive pedigree information.



Pharmaceutical Chain of Custody

VeriSign's Electronic Pedigree Service enables distributors, manufacturers and pharmacies to implement their compliance strategies. Our clients leverage our infrastructure to support their compliance strategies with secure, reliable and scaleable solutions that leverage their existing information technology. To learn more about how VeriSign can enhance your pedigree systems, send an email requesting more information to epedigree@verisign.com.