American Society of Health-System Pharmacists®

ASHP Policy Analysis

Following Pharmaceutical Products Through the Supply Chain

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Electronic tracking of pharmaceutical products would improve the integrity of the supply chain, enable health care providers to more quickly identify and remove counterfeit and recalled drugs, and improve inventory management. Florida[1] and California[2] have pharmaceutical pedigree laws, with California's law inspiring federal legislation that would require an electronic pedigree and track-and-trace system for pharmaceutical products.[3] The federal bill proposes establishing a central database where the information from electronic pedigrees would be stored and accessed.[3]

Regardless of the federal legislation's fate, California's e-pedigree law and regulations are likely to have a national impact for pharmaceutical manufacturers, wholesalers, and distributors. As these companies will not know which of their products will go to California, they may consider applying California's requirements to all drug products.

The implementation of a track-and-trace system likely will be managed by drug manufacturers and wholesalers. Responsibility for tracking a drug would end when a shipment is delivered to a pharmacy or a health system's internal distributor as all health-systems and hospitals are not equipped to extend track-and-trace to the patients' bedside. However, when a hospital or health-system pharmacy provides a drug to another end user, other than the patient, track-and-trace requirements would apply to that product.

This paper will provide an overview of drug pedigrees, the tracking of pharmaceutical products, key state and federal laws and regulations, and pending federal legislation addressing these issues. It will not address the potential cost of implementing a track-and-trace system.

What Is a Pedigree, an E-Pedigree, and Track-and-Trace?

A pedigree is a record of a pharmaceutical product that typically includes information such as the name of the drug; the drug's quantity, dosage, strength, and lot number; and the names and addresses of the manufacturer, wholesaler, and purchaser. It also could include a record of every stop a drug makes as it travels through the supply chain.

Pedigrees can be recorded on paper or in electronic form (an e-pedigree). The benefit of an e-pedigree is that it would allow individuals to more quickly track medications through the supply chain and it would make it more difficult for counterfeit or recalled drugs to reach patients.

Track-and-trace is the process of electronically following a product through the supply chain using a data matrix two-dimensional (2D) bar code or a Radio Frequency Identification (RFID) tag. As a product travels through the track-and-trace process, its location is recorded in an e-pedigree. Both the 2D bar code and RFID tag contain product identifiers that allow for verifying a product at each stage in the supply chain. RFID tags are often used to more efficiently manage large inventories. For example, Wal-Mart Stores, Inc.[4] and United Parcel Service of America, Inc.[5] use this technology.

The 2D bar code and RFID tag are preferable for identifying a product because they can contain more information than a linear bar code, such as the National Drug Code (NDC), lot number, and product expiration date, according to ASHP's Statement on Bar-Code-Enabled Medication Administration Technology.[6] "ASHP believes that pharmaceutical manufacturers should be required to place machine-readable coding that includes the NDC, lot number, and expiration date

on all unit dose, unit-of-use, and injectable drug packaging, using symbologies that are readily deciphered by commonly used scanning equipment," according to the statement.[6]

Advantages of Track-and-Trace

Electronically tracking drugs offers several advantages for health systems, hospitals, pharmacies, and pharmacists.

In order to electronically track drugs, pharmaceutical manufacturers would be required to standardize drug product serialization. The Food and Drug Administration (FDA) guidance on standard numerical identifiers recommends that each prescription drug package be labeled with a serialized National Drug Code (sNDC) that contains the drug's national drug code and a unique serial number and is readable by people as well as machines.[7]

A track-and-trace system also would establish a defense against counterfeit drugs entering the supply chain because these drugs would not have the appropriate 2D bar code or RFID tag. This system also could help state boards of pharmacy. The California Board of Pharmacy expects that an e-pedigree would make it easier for its staff to investigate drug diversion and counterfeiting cases.[8]

Further, drug recall management could be easier and more effective using a track-and-trace system because a health care professional could more easily check whether a recalled product was on a facility's shelves and where that product was located. The FDA issued 42 drug recall notices in 2011.[9]

Existing Federal Pedigree Requirements

Drug pedigrees are not new, but the existing federal pedigree requirements are less stringent than California law. The Prescription Drug Marketing Act (PDMA) of 1987, as amended by the Prescription Drug Amendments of 1992, requires wholesalers that do not have an ongoing relationship with a drug manufacturer to provide a pedigree of a drug before wholesale distribution,[10] which would no longer be required under an FDA proposed rule.[11] A pedigree also is required for medical kits that contain prescription drugs and devices as well as for bulk drugs.[10] Manufacturers and authorized distributors of record (ADR) are not required to provide a pedigree for each wholesale distribution.[10] An ADR is defined as a wholesale distributor that has an ongoing relationship with a drug manufacturer.[10] However, the FDA encourages drug supply chain participants to provide pedigrees for each sale, transfer, or trade.[10] An intra-company transfer of a drug does not require a pedigree.[10]

Supply Chain Integrity Recommendation

A new chapter in the United States Pharmacopeia and The National Formulary (USP–NF) is under development that reflects the health care community's concerns for the security of medications within the supply chain.[12] The draft chapter describes 2D bar code and RFID technologies and recommends an RFID testing protocol for biopharmaceuticals.[12]

State Pedigree Laws

Some states, such as Florida and California, have gone further than the current federal pedigree requirements by establishing laws requiring that a record be kept of a drug and its owners. Florida requires a paper record, while California requires an electronic record.

Florida

Florida enacted a law in 2003 requiring a paper pedigree for legend drugs beginning July 1, 2006.[1] A legend drug is defined in this state law as any drug subject to the federal Food, Drug, and Cosmetic Act and certain Florida statutes concerning drugs.[1] The paper record must identify the change in ownership of a legend drug from the sale from a manufacturer or wholesaler through to the drug's sale to a pharmacy or whoever is administering or dispensing the drug.[1]

The pedigree must include:

- the drug's amount,
- the drug's dosage form and strength,
- lot numbers,
- the name and address of the drug's owners and their signatures,
- shipping information, and
- certification that each individual receiving the drug has authenticated the pedigree papers.[1]

The law also establishes criminal penalties for failure to maintain or deliver pedigree papers; failure to authenticate pedigree papers; forging pedigree papers; purchasing legend drugs from an unauthorized person; selling or transferring a

legend dug to an unauthorized person; selling, delivering, or possessing with the intent to deliver contraband legend drugs; and forging prescription or legend drug labels.[1]

Trafficking in contraband legend drugs valued at $25,000 or more is a crime and fines are established based on the value of the drugs.[1]

California

The California legislature passed a law in 2004 requiring the creation of an electronic pedigree for pharmaceutical products.[2] The California legislature then passed two additional laws[13,14] delaying the e-pedigree's implementation, which is now scheduled to take effect January 1, 2015, through July 1, 2017.[14] California's law requires an electronic record of the change of ownership of a "dangerous drug" until its final sale. A "dangerous drug" is defined in California Board of Pharmacy regulations as "any drug or device unsafe for self-use in humans or animals."[15] A drug is considered not to have changed ownership if it is distributed between parties that are under an exclusive contract to provide health care services.[2]

The pedigree must include:

- the drug's source (name, federal manufacturer registration number or state license number, and address);
- the drug's trade or generic name, quantity, dosage form and strength, transaction date, sales invoice number, container size, number of containers, expiration dates, and lot numbers;
- business name, address, and federal manufacturer registration number or a state license number of each owner of the drug, and drug shipping information; and
- a certification that the information in the pedigree is "true and accurate."[2]

Not all transactions must be recorded in an e-pedigree. Free samples dispensed to an authorized prescriber do not have to be recorded.[2] Neither does an injectable dangerous drug directly delivered to an authorized prescriber or other entity responsible for administering the drug.[2]

California is implementing its e-pedigree requirements over a span of three years, starting by 2015 when 50% of manufacturer's products must be in compliance with the law.[14] The remaining 50% of products must be in compliance by 2016.[14] By July 1, 2016, wholesalers and repackagers must be equipped to accept and forward products with an e-pedigree.[14] By July 1, 2017, pharmacies and pharmacy warehouses must accept and pass e-pedigrees.[14]

California's e-pedigree law is supported by the state's health-system pharmacists. The California Society of Health-System Pharmacists (CSHP) issued a policy in 2008 that called for improving the medication supply chain and supports the California State Board of Pharmacy in developing an e-pedigree system for medications.[16] As stated in its policy, "CSHP advocates for improved processes to assure the integrity of medications throughout the supply chain, specifically to eliminate or minimize the persistent and increasing threat from counterfeit, misbranded, adulterated, or diverted drugs."[16] CSHP also calls for the development of technology that would allow for tracking medications to patients' bedsides and recording this information in an e-pedigree.[16]

National E-Pedigree?

Proposed federal legislation could apply California's e-pedigree requirements nationwide. The Safeguarding America's Pharmaceuticals Act of 2011 (H.R. 3026) would require the U.S. Department of Health and Human Services to issue regulations creating a national prescription drug track-and-trace system.[3] This will not apply to drugs transferred between federal, state, and local governments that are authorized by federal law to distribute the drugs.[3]

The proposed federal regulations that would be required under the bill would set standards for electronic databases that would allow for authenticating prescription drugs at every stage in the supply chain using electronically readable, standardized, numerical identifier.[3] Proprietary information would be maintained.[3]

As with the California regulations, the federal regulations would require an identifier to be placed on a repackaged drug that would link that drug to the electronic databases.[3] Each person receiving a wholesale prescription drug would be required to authenticate its transaction history with the appropriate database.[3] The proposed regulations would require protections to ensure patient privacy.[3] Similar to the California law, the federal bill would require the regulations to apply to wholesalers and repackagers beginning July 1, 2016, and pharmacies beginning July 1, 2017.[3]

A report by the Pew Prescription Project, which promotes consumer safety through prescription drug approval, manufacturing, and marketing reforms, calls for requiring a unique

serial number for each drug package and for the creation of a federal drug pedigree system with "strong consideration" to make it an e-pedigree system.[17]

However, the Pharmaceutical Distribution Security Alliance (PDSA), which includes pharmaceutical manufacturers and distributors, as well as certain retail pharmacies, countered with a proposal to create a Global Trade Item Number that would allow for lot-level pharmaceutical product tracing but not an electronic track-and-trace system.[18] This proposal would preempt state pedigree and track-and-trace laws.[18]

ASHP Members' Bar Code Experience

Moving to a track-and-trace system that requires recording the transfer of pharmaceutical products in an e-pedigree would also address the current difficulties with linear bar codes. Reading linear bar codes can be a frustrating experience for health-system pharmacists.

In a letter to the FDA, ASHP relayed members' experiences that scanning bar codes "prevented numerous medication errors in dose compounding by capturing and preventing the use of inappropriate drug products."[19] However, catching medication errors is more difficult when manufacturers can freely change bar code data, sometimes including information other than the NDC.[19] As a result, the scanners sometimes cannot read a drug's bar code.[19] Further, ASHP reported in the letter that pharmacists are challenged by the poor quality of codes on "pharmaceutical containers using the linear symbologies, the lack of an authoritative and reliable list of NDC's, and the current requirement for manual capture of lot and expiration, which has both compliance and data quality issues."[19]

Complicating any efforts to move to an e-pedigree and track-and-trace system is that a majority of U.S. hospitals are not equipped to electronically track medications to the patient. Data from the 2011 ASHP National Survey of Pharmacy Practice in Hospital Pharmacy Practice found that half of all hospitals have a bar code medication administration system, 43% of hospitals use machine readable codes for restocking automated dispensing cabinets, and 12% of hospitals use bar code verification for preparing intravenous medications.[20]

ASHP policy encourages hospital and health-system pharmacies to track medications by scanning bar codes as part of "inventory management, dose preparation and packaging, and dispensing of medications."[21]

Opportunities, Challenges for Pharmacists

Implementing a track-and-trace system brings both opportunities and challenges for pharmacists and the hospitals and health-systems where they work, as identified by several ASHP members and staff.

Opportunities

Recording the movement of pharmaceutical products in an e-pedigree would improve patient safety by ensuring the quality of medications used. A track-and-trace system within a hospital setting would increase patient safety by increasing the security of medications. Installing a track-and-trace system would deter the introduction of counterfeit products into the supply chain and would deter the adulteration of medications because every entity handling the medications would be recorded on the e-pedigree. This becomes especially important for a hospital or health system compelled to purchase a medication from an alternate supplier. With a track-and-trace system, a hospital could be more confident of the quality of the drug product.

When a drug recall is announced, it is expected that everyone within the supply chain could more easily locate the recalled products under a track-and-trace system.

Challenges

There are several technical and staffing challenges to implementing track-and-trace.

Bar codes are not uniform across all pharmaceutical products, which makes it difficult to electronically read bar codes. Though some hospitals have invested in the technology required to implement track-and-trace, not every hospital is equipped to electronically read bar codes or RFID on pharmaceutical deliveries. Even for those hospitals that have invested in equipment to electronically read bar codes, there is a lack of interoperability between bar code reading systems established in hospitals and the bar codes used by manufacturers and wholesalers.

Technology alone is not enough to implement track-and-trace. Staff must scan bar codes or RFIDs on pharmaceutical deliveries. Further, any requirement for hospitals and health systems to document drug product transfers to other hospitals will place a burden on pharmacy staff of large health systems as well as individual hospitals.

Conclusion

Electronically marking the path medications take to their final destination is on schedule for full implementation in California by July 1, 2017. Federal legislation could extend that requirement nationwide and require the creation of a database that would contain this information. The implementation of a track-and-trace system should make medications safer by making it easier to identify counterfeit drugs and prevent medication tampering. It also would be much easier to locate recalled medications. Any implementation of a track-and-trace system would likely be driven in large part by manufacturers and wholesalers who would need to develop the technological capability to track drug products, as well as the ability of that technology to interface with various members of the supply chain.

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