Life Sciences Supply Chain Security: *SNI and UDI*

In 2013, US Customs & Border Protection seized more than 2,350 parcels containing counterfeit medical devices and pharmaceutical products valued at $83 million, according a new report from the US Dept. of Homeland Security.[1] Counterfeit drugs can be contaminated or contain inactive, incorrect, sub-potent or super-potent ingredients, or improper dosages. As a result, patients may be at risk of serious adverse health consequences or even death. Counterfeit medical devices can have the same serious adverse consequences, including potentially lethal events caused by the use of devices that are non-sterile, or that may not be effective for their intended use.

FDA Legislation – Supply Chain Security Background

In the fall of 2013, the US Congress passed the Food and Drug Administration Safety and Innovation Act (FDASIA) and the bill was signed into law by President Obama. The purpose of the legislation was primarily to re-authorize user fee amendments paid by manufacturers of drugs, medical devices, and biologics for product licensure applications. The law also contains additional provisions, the most important of which are Supply Chain Provisions that empower the FDA to protect medical device and drug supply chains. Although an attempt to add a nationwide track & trace requirement to the bill failed to become law, a number of significant supply chain security elements became law with

the enactment of FDASIA. These are "Title VI —Medical Device Regulatory Improvements. Sec. 614. Unique Device Identifier" and "Title VII—Drug Supply Chain" which define changes that enhance FDA's inspection authority and the drug supply chain. Similar to the medical device UDI system, FDASIA requires FDA to create a Unique Facility Identifier (UFI) system and to maintain an electronic database containing the registration and listing information of drug facilities.[2]

Over the past several years, both industry and consumer groups have been advocating to create a national serialization regulation that eliminates the patchwork of those proposed by state laws. On November 27, 2013, President Barack Obama signed the Drug Quality and Security Act of 2013 (DQSA) into law, bringing a successful conclusion to efforts by the industry and consumer groups to establish a national serialization regulation for pharmaceuticals. Similar to the medical device UDI regulation, this national serialization regulation is federally mandated and thus has never been regulated at the state level.

In the last two years, the United States and the European Union have enacted legislation and introduced regulations that will have a profound impact on the security of these major supply chains over the next ten years.

This legislation includes:

United States

- The FDA Safety and Innovation Act (FDASIA)
- The FDA Unique Device Identification Rule (UDI)
- The Drug Supply Chain Security Act (DSCSA)

European Union

- The Falsified Medicines Act (FMA)
- The Harmonized Unique Device Identification Framework
- The anticipated 2014 Delegated Acts related to FMA related to the FMA

Most of these laws and regulations deal, at least in part, with the identification of pharmaceuticals and medical devices in a security management context – covering the two largest markets in the world for these products. By the year 2024, all of these laws will be in effect.

Serialization: The Global Perspective

Additional international requirements pose more challenges. Basically, the foundation of any tracking system is serialization, which entails affixing a unique serial number and barcode or radio-frequency identification (RFID) to finished pharmaceuticals or medical devices so they can then be verified at the point of sale. This basic step, however, is fraught with complexities and variants. Some countries may require verification at each step in the supply chain; others may only require verification when the product is distributed to the end user. While most countries are requiring serialization at the unit level for pharmaceuticals, the US is starting with serialization at the lot level. It is our opinion that serialization for pharmaceuticals at the lot level is practical; it follows the same framework as UDI for medical devices, which also serializes at the lot (or batch level, as appropriate) for the second of the two required identifiers, the unique production identifier.

UDI was the original rule to mandate serialization with unique identifiers for FDA regulated product, for tracking purposes. The UDI rule was originally proposed in the FDA Amendments Act (FDAAA) of 2007. The original intent behind the UDI rule was to improve device safety and the reporting of device-related adverse events. Lack of unique identifiers for medical devices hindered the identification of devices throughout their distribution and use, reporting and analysis of adverse event data, and timely removal of recalled devices.[3] That intent is still valid today but is exacerbated by additional data demonstrating that serious adverse health consequences, or even death, occur when counterfeit pharmaceuticals and medical device make it into the hands of patients.

We believe that those in the life sciences distribution network have to be the first to enact FDA regulations to protect the supply chain. The protection initiative has already begun, and the GS1 Drug Pedigree Messaging Standard (DPMS) is the standard used by industry today. It is interesting to note that the designers of DQSA intentionally avoided the types of requirements contained in the Florida and California pedigree laws, leading to the design of DPMS.

Note: Other than those devices requiring mandatory tracking under 21 CFR Part 821, mandatory tracking is a forced order for devices whose failure would be reasonably likely to have serious, adverse health consequences; or which are intended to be implanted in the human body for more than one year; or are life-sustaining or life-supporting devices used outside of a device user facility.

TRANS-X and the Standardization Dilemma

The first phase of the DQSA requirements begins on January 1, 2015. These requirements include the need for all US pharmaceutical supply chain trading partners to pass transaction information, transaction history, and transaction statements from seller to buyer. There are a few exclusions, which can be reviewed further in the law.

The FDA has been given only one year after enactment of DQSA to come up with standards for trading partners to exchange pedigree information – defining the terms "transaction information," "transaction history" and "transaction statement" in H.R. 3204. The real problem is that, according to the letter of the bill, companies in the supply chain would need to begin using the standards to format and exchange pedigree information on January 1, 2015.

FDA has stated that for four years after the law's enactment (i.e., January 1, 2015 until late November 2017) the trans-X information can be sent in either paper or electronic form. However, after late November 2017, it must be transmitted electronically. Downstream trading partners will have to make paper copies or scanned images of the incoming packing lists so they can send out necessary transaction histories with each shipment. Most companies will not want to store incoming and outgoing trans-X paper documents for six years, particularly if documents need to be retrieved accurately and efficiently within 48 hours. Thus, electronic archival for lot-based trans-X documents is a top priority in the industry.

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The Process of Securing the Supply Chain

Serialization

Serialization is most often the starting point to implement a Track & Trace program. Products are serialized by placing a unique identifier on each product. Serialization applies to both pharmaceuticals and medical devices. The pending requirement for pharmaceuticals is for lot level identifiers to be in place by January 1, 2015, with unit level identifiers planned for the future. Medical devices will be required to have unique device identifiers (UDI) on September 24, 2014.

Typically the identifier is a data matrix code containing at least the product related GTIN (Global Trade Identification Number) paired with a serial number. The pharmaceutical SNI system defines an SNI as a 10-digit NDC with up to 20 digits of serialization. The SNI data is stored in a database for tracking and retrieval of the lot and expiration date of the pharmaceutical. The guidelines for SNI do not specify a requirement for the use of a particular technology, so linear, 2D barcodes, or RFID can be used.

UDI

The medical device UDI system is slightly different, consisting of two identifiers: a unique device identifier and a unique production identifier. The GS1 GTIN-14 provides the unique device identifier (the manufacturer's ID and product ID). The production identifier can include a serial number, lot or batch number, a manufacturing or expiration date, or any combination of these numbers. An agency that is accredited by the FDA to issue UDIs must be utilized to obtain the first identifier. There are currently two known agencies that meet these standards: GS1 and the Health Industry Business Communication Council (HIBCC). The UDI is encoded in any standard bar code determined by HIBCC or GS1 industry standards, then entered and stored in a UDI database. This identifier must also be registered in the Global Unique Device Identification Database (GUDID) in accordance with the FDA's GUDID Guidance.

Track & Trace

By utilizing an identification system, pharmaceuticals and medical devices become vehicles for carrying the information needed for Track & Trace, and can be identified individually. [Note: the Track & Trace regulation is only applicable to pharmaceutical products at this time; but, this may soon change due to a recommendation for Track & Trace by the Global Harmonization Task Force (GHTF) now IMDMF].[4] An added benefit is that since both SNI and UDI are stored in databases via a unique identification number, additional important product related information can also be stored there.

Aggregation

Serialization is performed on the product and production lines and often requires the implementation of new printing and scanning technologies and software. After serialization is complete, aggregation is the next step. Aggregation is the process of building packaging hierarchies and storing the hierarchical relationship in a database. The packaging hierarchy can be as simple as packing all products in a carton and then loading all cartons onto a pallet. Each new packing level (e.g. primary cartons, secondary cartons, pallets) also requires a unique serialized identifier and barcode. Scanning processes are used to store packaging hierarchy into a database to show the individual serial numbers of all the units included in that bundle, shipper box, or pallet. Because aggregation stores all packaging components by identification number starting from the pallet down to the product, it can be used to meet pending track and trace requirements.

ePedigree

Another proposed tracking requirement is an ePedigree, an electronic document that moves through the supply chain with the drug, recording each sale, trade, or purchase of the product. Currently, ePedigrees are not required by the countries that have implemented tracking systems, but some, including the US, are proposing them.

Serialization Challenges Unique to Distributors

The Situation

One of the greatest challenges for companies in the US pharmaceutical and medical device supply chain is to maximize efficiency when dealing with serial numbers on each package. It is possible to read the case serial number only, trusting that the unit package-level serial numbers are correct from the unit-to-case aggregation information supplied by the upstream trading partner.

Manufacturers pack serialized unit packages into shipping cases shortly after they are produced. The shipping cases are also serialized. This allows for easy stocking in manufacturer warehouses before shipment to distribution centers. After receiving the cases from the manufacturer's distribution center, the distributors open most cases in order to fulfill their customer orders by packing smaller quantities into unit packages that are then placed in totes for delivery. At this point the case-level aggregation information is no longer needed.

The unit level serial number on each package would be recorded to update the ePedigree for the customer's order. If the orders are large and the manufacturer's case does not need to be opened, the manufacturer's aggregation information can be used to determine which unit package serial numbers are shipped to the customer, and to update the ePedigree to pass to the customer.

Given that the distributor's customer will want to receive the shipment quickly, they will probably use the aggregation information to update the ePedigrees they received from the distributor; this way, they don't have to open every case to read the serial numbers on each package.

Potential Challenges

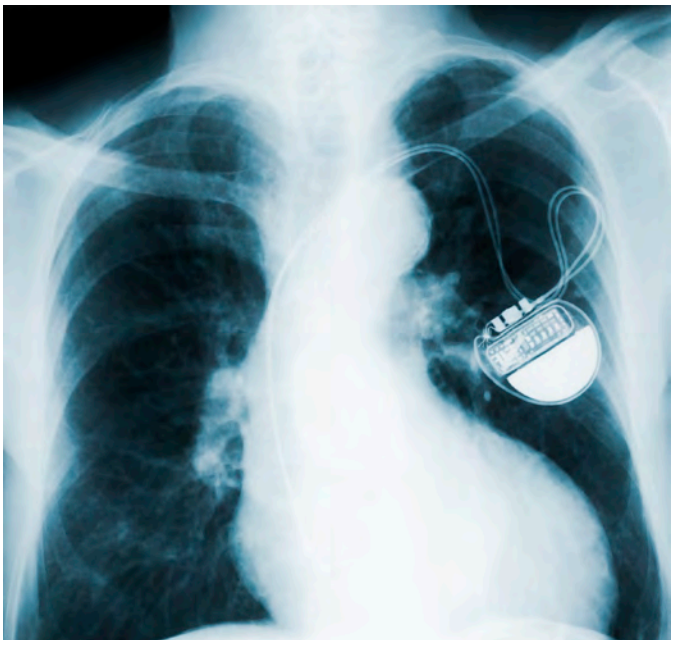
The potential problem with this scenario is that the manufacturer's distribution center, the distributor, and the customer rely on the accuracy of aggregation information captured by the manufacturer at the time of packing. If the aggregation information is perfect every time, no problems arise. But unintentional errors can occur in manufacturing that are not caught at control points. For example, if the information on two cases is inadvertently crossed, the unit package-level serial numbers will be attributed to the wrong case serial number. This error will remain throughout the supply chain.

Ultimately, the customer will open the case and see that the serial numbers on the packages do not have an accurate record – and thus an invalid ePedigree. Without a valid ePedigree, the drugs cannot be sold, returned, or dispensed. The same problem will occur with the company that received the other case involved in the error. Both will have to dig back through the supply chain to determine where the error occurred. A robust system at the distributor could solve this issue efficiently. In order to consistently generate 100% accurate aggregation information, a unique approach to the case packing operation should be implemented. The key is to read the unit-level serial numbers only after the packages are bound together in a serialized grouping (inner-pack or full case grouping) prior to customer delivery.

Track & Trace: Compliance as Supply Chain Value Proposition

The global supply chain is becoming increasingly demanding and complex. Companies need to deploy applications, services and mobile solutions to manage these complexities and demands. Ensuring compliance, product integrity, product visibility and risk reduction will secure the supply chain and keep it moving efficiently.

Product counterfeiting is an increasing problem for businesses, including those in the life sciences. Implementing compliance initiatives like serialization, unique device identification and track & trace offers businesses assurances against counterfeiting. Deciding to serialize and track products at the unit level creates a new level of value for companies, making counterfeiting more difficult and improving remediate efforts should it occur. A global distribution chain with security, transparency and traceability of supply will not only help address counterfeiting and diversion, but will also enhance preparedness for medical emergencies. Additionally, the transparency and traceability that is gained as a result of implementation can facilitate control of loss reduction and optimization of supply chain, marketing, and sales strategies.



We believe that pharmaceutical and medical device manufacturers will also realize benefits by using identification standards that are already recognized in a large portion of the world. More importantly, the ability to add extra data elements within the barcode, without rendering the regulated data elements unreadable, will allow manufacturers to provide downstream trading partners with increasingly diverse information about each product on both cases and units.

Commensurate with the original intent of designing and mandating serialization regulations, we agree that the greatest benefactors of this legislation's implementation will be patients and consumers. This includes faster detection of safety concerns associated with specific pharmaceuticals and medical devices, more efficient communication between providers and patients regarding important safety information, and independent access for patients to information about their pharmaceuticals or medical devices. Ultimately, all data, regardless of the format, can be requested by FDA or other regulators for the purpose of protecting public health, particularly for recall actions or notification of widespread safety issues.

Conclusion

The goal of the DQSA legislation and UDI requirement is to protect the supply chain, better ensuring patient safety and the integrity of the pharmaceuticals and medical devices. There are many parallels between how pharmaceuticals and medical devices are identified and distributed throughout the supply chain. DQSA lays out a roadmap for pharmaceutical companies on the timing of serialization and traceability implementations. The UDI final rule requires manufacturers to label the product with a unique identifier, and to submit the data to the FDA database.

While there is no specific requirement to electronically communicate information with their trading partners, distributors have tracking obligation per 21CFR821.30 to provide to the manufacturer information about where and to whom the product was distributed. We believe that over time, medical device manufacturers will follow the pharmaceutical model and will be required to automate the product tracking information.

When designing systems to support serialization, there is an opportunity to include UDI requirements. Therefore, if a future requirement to automate the exchange of information is enacted, the serialization structure built for drug products can also be used for medical device products. We recommend taking a holistic approach to developing your UDI system since evidence strongly suggests that supply chain security and counterfeiting will be an ongoing issue.

In summary, organizations should develop their UDI implementation strategy with the big picture in mind, designing solutions to meet the immediate requirements, but also addressing the potential track and trace requirements. Building a flexible solution may require a larger investment in the short term, but will likely generate significant savings down the road.

When developing a UDI implementation strategy, consider each of the topics below:

- When does a device need a new UDI?
- Which parts of a device need a UDI?
- Where should the UDI be placed?
- When should UDI be placed on the device (Direct Part Marking) instead of the packaging?
- Are there packaging levels that don't need a UDI?
- Are there exceptions and alternative placement issues?
- Are trading partners ready and able to exchange information electronically?
- What are the global UDI requirements? Are they different from the US requirements?
- How can the serialization architecture be leveraged for UDI?
- How will UDI impact components vs. spare parts?
- Adherence to the integration with nomenclature (GMDN)

About the Author

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