

A Business Solution for Improved Drug Supply Chain Visibility

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ABSTRACT

Global increases in supply chain regulations are creating additional burden on manufacturers, distributors and pharmacies. Drug Supply Chain Security Act (DSCSA) is the U.S.A version. It is vital for regulatory purposes to be able to see every product in the supply chain at a unit-of-sale level, but the data can be used for business gains as well. Predictive analytics provide this capability. Examples of opportunities include: what each customer is going to order next; which point in the supply chain is going to not meet SLA; where stock deficiencies or surpluses are going to occur and what can be done in advance to avoid these variations; Identify when a customer's needs are not going to be met and implement steps to attenuate concerns and losses before they happen; Know how to move any and all available products and groups of products to specific anticipated needs and groups of anticipated needs at lowest price. Predictive analytics are stronger when they are integrated analytics, using both data sources from across the industry and analytical models of various types and capabilities. On top of analytics, the best ROI is gained from making analytics results available in a usable, actionable format for each person, process and point in the system, plus receiving feedback from each in order to further refine the business, with the end result becoming a sentient enterprise.

INTRODUCTION

The United States Food & Drug Administration has implemented the Drug Quality and Security Act (DQSA) in an effort to improve the quality of pharmaceutical supplies. (U.S. GPO: Public Law 113-54) DQSA was signed into law in November, 2013. The act is intended to reduce diversion, plus minimize entry of adulterated products – and their associated morbidity, mortality and cost - in the healthcare marketplace. This act is similar to efforts occurring in parallel worldwide. A cooperative effort between U.S. federal government and industry, Title II of the Act includes the Drug Supply Chain Security Act (DSCSA), which endeavors to allow tracking of each product line's unit-of-sale from the pharmaceutical manufacturer all the way through the very complex supply chain to the final shipping location of the product (e.g., pharmacy, hospital or physician office). (U.S. F.D.A., Drug Supply Chain Security Act) This will aid in rapid location and recall by either the manufacturer or government, should a question of quality arise.

This presentation provides attendees an overview of the current pharmaceutical supply chain complexity, the top business issues with product quality being maintained throughout the supply chain, and technologies that can aid in ongoing monitoring of both seller and recipient, along with rapid identification of every location where a unit-of-sale may reside, should a recall be needed or a question of diversion occur. This article offers insights into technologies that are being considered in this cross-industry sharing of data, as well as business decisions that must be made.

A GLOBAL INITIATIVE TO INCREASE SUPPLY CHAIN VISIBILITY

As the axiom goes: where there's money, there's crime. Today's global pharmaceutical supply chain is expected to climb to almost \$1.4 Trillion by 2020. (Constantino T, 2015). This very lucrative growth rate matches the world's demand over the last few decades for improved healthcare and the willingness to spend for better care.

As healthcare has grown, and continues to grow, both in innovation bringing new treatments to market and the ability to tailor personalized medicine to a specific patient in order to improve outcomes. Along with new opportunities and strong demand comes attempts to counterfeit, defraud and adulterate medications. In addition, the ongoing risk of manufacturing error or failure of specialized storage means patients are at risk of harm, ranging from mild to deadly.

The U.S. Center for Disease Control states that "global estimates of drug counterfeiting range from 1% of sales in developed countries to >10% in developing countries. In specific regions in Africa, Asia, and Latin

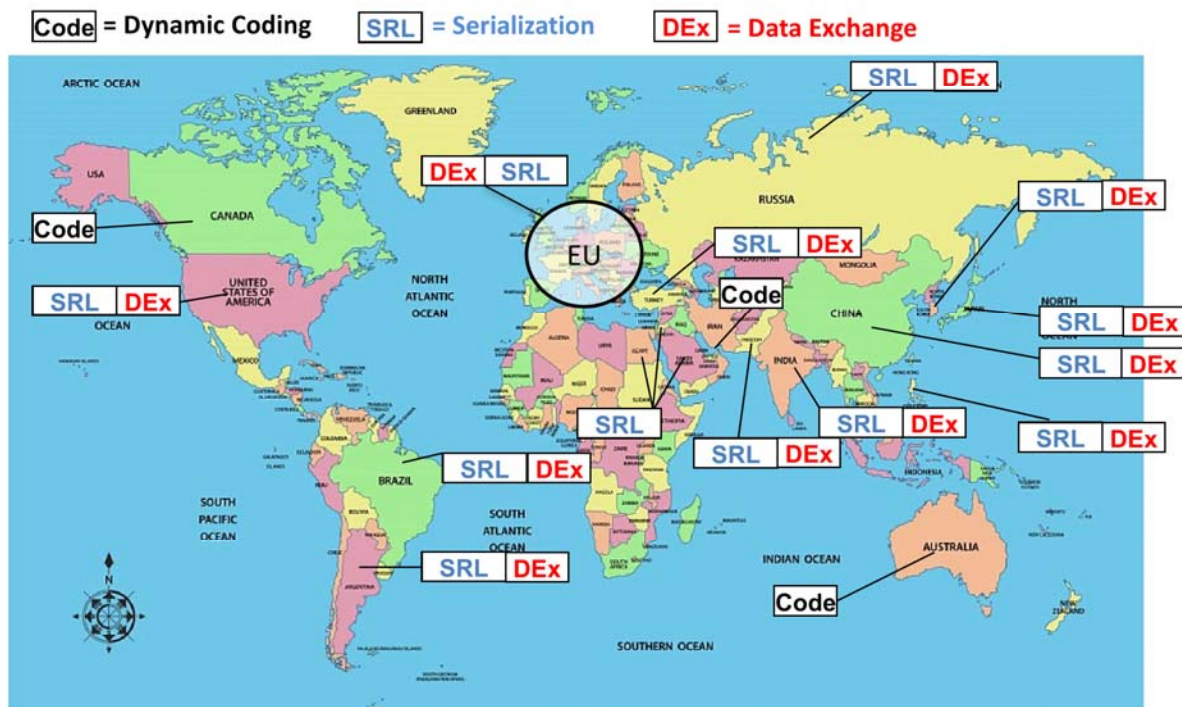
America, chances of purchasing a counterfeit drug may be >30%.” The U.S. Food and Drug Administration maintains a running list of reported failures to maintain drug quality in the current supply chain. Prior to implementation of new regulations for drug supply chain monitoring (as described below), the FDA reported over one incident a month of counterfeit, smuggling, and misbranding of drug products in the U.S. pharmaceutical supply chain.

The FDA reports describes one incident of the cancer drug Avastin that was counterfeited and entered the U.S. Supply Chain. The products were shipped with false customs declarations from Turkey. Participants involved in this supply chain ruse included a distributor from the United Kingdom and physicians from California, Tennessee, Ohio and Texas. After further investigation, they alerted over 1,500 medical practices who had purchased or received this product. The FDA also reports that this is an ongoing issue. (Sklamberg H, 2014)

But not all of the concerns are crime related. The difficulty in correctly interpreting product labelling, whether by human or machine readable means, continues to create problems with medical errors. Several years ago, the actor Dennis Quaid and family were in the news for near-tragic reasons related to a product identification error. (CBS News, March 16, 2008) He and his wife were proud parents of newborn twins. Prior to discharge from the hospital, a medication error occurred due to poor labelling and tracking of products and the children had severe bleeds that kept them in the hospital for many weeks.

As a result of public concerns about these and many other incidents of failure of drug quality controls in the supply chain, 18 countries have initiated legislation over the last two years designed to improve the ability to track pharmaceutical products from the manufacturer to the patient. Figure 1. Global Serialization Initiatives (IQPC, 2016), illustrates those initiatives and countries as identified by the International Quality Product Council as serialization initiatives.

Serialization Initiatives Around the World Through 2022



IQPC 2016

Figure 1. Global Serialization Initiatives (IQPC, 2016)

Serialization at a unit-of-sale level is considered the first step toward uniquely identifying products as they leave the manufacturer and move through the supply chain. Unfortunately, serialization of pharmaceuticals is not a standard today. Much of the difficulty lies with the need to create a cooperative serialization across both industries and participants within an industry – participants who may at times vary between being competitors, sellers and buyers. Also, many industry participants involved in these countries are concerned about how to implement many of the government guidelines effectively and efficiently. The costs to track all

products at a unit of sale level can

Figure 2. Pharmaceutical Industry Participants Perspective on Supply Chain Visibility Regulations



become daunting, as illustrated by survey results in Figure 2. Pharmaceutical Industry Participants Perspective on Supply Chain Visibility Regulations. (Goodbaum B, 2015)

One of the first initiatives scheduled to be fully implemented was in Brazil. After a strong start, the initiative has been delayed due to funding issues. India, the European Union, and China have also made progress in their efforts, each with its own approach on how to implement, but no country has achieved complete implementation. The European Union has a timeline of implementing by 2019, as illustrated in Figure 3. European Union Timeline and Purpose for Increased Supply Chain Visibility. The European Union first published its guidelines in 2016 and is currently in the midst of an aggressive roll-out schedule. (European Union, 2016) Upon completion, a centralized database will maintain all records of all items moving through the pharmaceutical supply chain, including who bought from whom and what validation is occurring to oversee accuracy and quality of the items received.

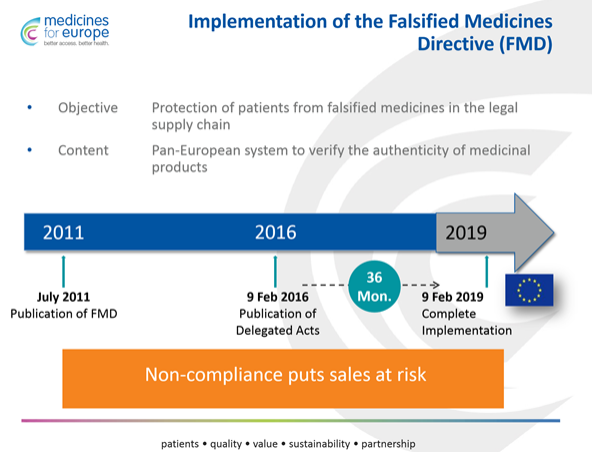


Figure 3. European Union Timeline and Purpose for Increased Supply Chain Visibility

THE U.S. DRUG SUPPLY CHAIN SECURITY ACT (DSCSA)

Several attempts to implement a “Track and Trace” system in the United States, by both the Federal Government and State Governments (e.g., California and Florida) have not been successful. Yet the need to create a functional system continued, driven on by repeated episodes of counterfeit substance appearing in the supply chain; stolen products; drug shortages; and adulterated products.

In 2013, the United States became perhaps the earlier implementer of a basic serialization system by passing Public Law 113-54: Drug Quality and Security Act (DQSA). One section of this act focused on product tracing and is known as the Drug Supply Chain Security Act (DSCSA). Congress has since updated the Act with industry guidance for Dispensers and a requirement for annual reporting of state licensing, contact information and any disciplinary actions by State or Federal Government by prescription drug wholesale distributors and third-party logistics providers. (FDA Guidance for Industry, 2015; FDA

Guidance for Industry, 2016) The U.S. Food and Drug Administration has also published the experiences of Johnson & Johnson while serving as a test case for DSCSA implementation. (FDA, 2016)

Industry Segments affected by DSCSA include:

- Manufacturers and Repackagers (referred to collectively as Manufacturers, although regulated slightly differently)
- Wholesale Distributors and Third-Party Logistics Providers (referred to collectively as Distributors, although regulated slightly differently)
- Pharmacies and other providers who dispense medications (referred to collectively as Dispensers, although regulated slightly differently)

DSCSA is being implemented over a longer time span than the European Union initiative, with completion expected by 2023. But DSCSA has broken implementation into multiple components and allows for differing timelines for participants in each segment of the industry (Manufacturers, Distributors and Dispensers. The first phase of implementation was completed in 2015 and is now in place for all three segments, but with varying expectations. These are described below:

- 2015 Requirements (Focused on creating tracing capabilities)
 - Manufacturers, Distributors and Dispensers must have processes in place to ensure:
 - Licensing as an authorized participant in the supply chain
 - Trading shall occur only with other licensed participants
 - Transaction Statements shall be created and shared with the trading partner for each transaction
 - Suspicious products shall be quarantined and investigated in a timely manner
 - Transaction statements for all participants involved in a trade must include the following (commonly known as the 3T's: TI, TH and TS):
 - Transaction Information (TI) – who was involved as seller or recipient and for what product on what date,
 - Transaction History (TH) – a record provided by the seller to the recipient of all transaction information described by these 3Ts throughout the history of the product's movement through the supply chain, and
 - Transaction Statement (TS) – a statement by the seller – provided to the recipient - that the seller believes the party from whom the seller received the product was licensed and provided true information for the 3T's, along with a statement that the product is correctly identify and the quality was maintained by the seller (and has processes in place to verify these requirements) up to acceptance (ownership) by the recipient.
- 2017 Requirements (focused on creating an electronic means of maintaining the 3T's)
 - Manufacturers must:
 - Create a machine-readable Serialized Numeric Identifier (SNI) that can be attached to packages and cases, allowing electronic data capture and record transfer
 - Develop and implement policies and procedures for recurring verification of a product and it's quality
 - Respond to requests for the 3Ts on any product in the supply chain at either a lot or unit of sale level
 - Implement electronic transfer of the 3T's to anyone capable of receiving them electronically

- Distributors must:
 - Implement the ability to receive electronic transfer of the 3Ts from all manufacturers
- Dispensers must:
 - Implement the ability to receive electronic transfer of the 3T's when purchasing from a manufacturer
- 2020 Requirements (focused on audits)
 - Distributors must:
 - Implement the ability to verify all suspicious products at a unit-of-sale level using the SNI
 - Document that they are purchasing only products that have an SNI and satisfy the 3Ts
 - Implement policies and procedures for returns that comply with the SNI requirements
 - Dispensers must:
 - Implement a process for verifying that items satisfy the SNI and 3T's requirements at the unit of sale level that ensures no greater than a 10% suspicious product rate
 - Document that they are purchasing only products that have an SNI and satisfy the 3Ts
- 2023 Requirements (focused on full implementation by all participants in the supply chain)
 - Manufacturers, Distributors and Dispensers must:
 - Use serial numbers on all products at a unit-of-sale level
 - Record the SNI electronically and be able to recover all electronic transaction data
 - Transaction history no longer has to be passed, but a mechanism for tracking a product through it's history must exist.

DSCSA also includes significant civil and criminal penalties for violations with regard to licensing or failure to meet the traceability requirements. These can be applied to entities and individuals and include:

- Imprisonment for not more than one year and a fine of not more than \$1,000
- Imprisonment for not more than three years and a fine of not more than \$10,000 for subsequent or intentional violations
- Seizure of goods or an injunction
- A general fine of up to \$250,000 for individuals and \$500,000 for entities

Since the FDA has not invoked these penalties as yet, it remains to be determined whether a penalty is for an event or for each item in an event.

DATA REQUIREMENTS

DSCA requires the ability to identify all products using a unique identification number assigned to each item. This identifies the item with a product number and associated serial number and is to be applied at every package level (i.e., bottle, case and pallet). (FDA, 2016)

When transactions occur, the data required in TI include:

- The proprietary name of the product
- The strength and dosage form
- The National Drug Code (NDC) number
- The size of the container and the number of containers
- The lot number
- The date of the transaction
- The date of the shipment, if is it longer than 24 hours after the transaction
- The business name and address of the person who is the seller (previous owner)
- The business name and address of the person who is the recipient (new owner)

For product identification, at the smallest saleable unit level, all participants must use a GS-1-compliant standardized graphic that is both machine and human readable. It will include:

- The standardized numerical identifier (SNI) – allows unique identification of each package or homogenous case and will be the NDC plus a unique alphanumeric serial number of up to 20 characters
- Lot number
- Expiration date of the product

When companies are implementing these data requirements, they will of course need to merge easily with other data in the organization. An sample DSCSA form is provided below in Figure 4 Sample DSCSA Transaction Form.

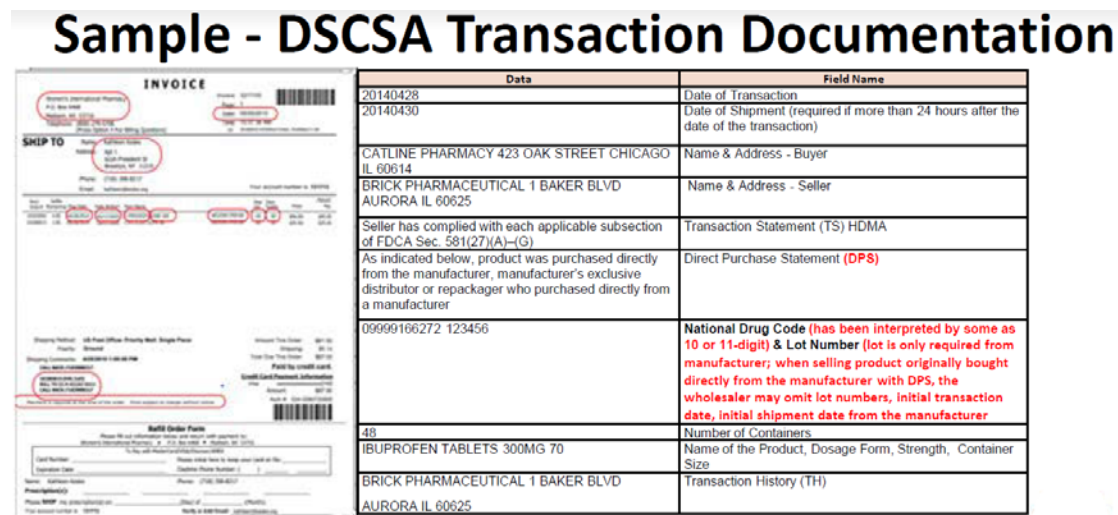


Figure 4 Sample DSCSA Transaction Form

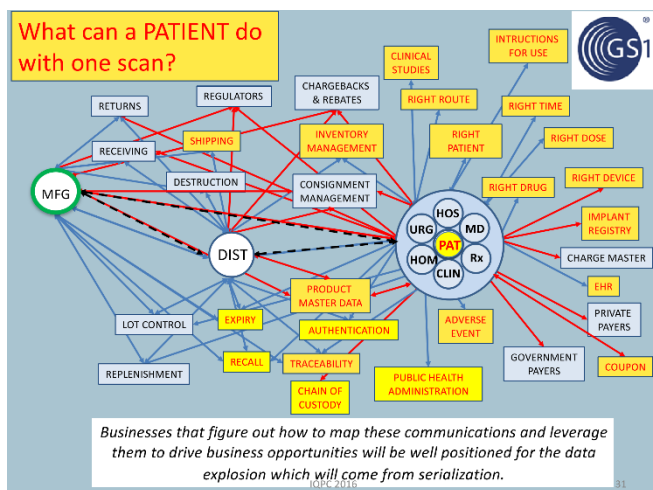
INFORMATION ARCHITECTURE AND BUSINESS NEEDS

The data will of course need to merge easily into a DSCSA participant's business. The type of data used to track a product includes:

- Manufacturer Part Number/SKU Number
- Product Description
- Proprietary Name

- NDC (10-digit code for FDA format or 11-digit code for CMS format)
- GTIN for every packaging level
- UPC for saleable units
- Dosage Form
- Strength
- Container Size
- Container Unit of Measure (UOM) for the package
- A full UOM table for every packaging level with the quantity per package

However, since only the DSCSA-specific data from the list above has to be shared with trading partners, applications will need to be written to select the correct information and exposing it to meet DSCSA queries from external parties (such as a Federal Government recall request), while also protecting all propriety information.



In addition to this data superset, business will need to consider new ways of using DSCA data for improving business and gaining new business opportunities. The ability to pinpoint the location of every unit of sale item offers all participants a new way to manage their business. GS1 has presented DSCSA participants with ideas regarding the gains to be achieved by this higher visibility into the supply chain, as illustrated in Figure 5. Examples of Business Relationships and Opportunities From DSCSA Data.

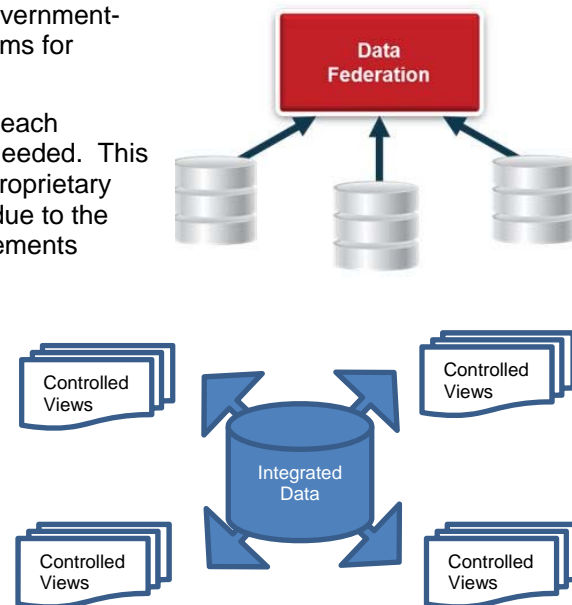
Figure 5. Examples of Business Relationships and Opportunities From DSCSA Data

One of the remaining issues to all DSCSA participants is how to best retain and share DSCSA data in such a way to make either manufacturer-issued or government-issued recall easy. A few architectures and mechanisms for achieving this have risen to the top.

One approach is a set of federated databases where each participant keeps its own data and shares from it as needed. This seems comfortable to participants concerned about proprietary data. However, this approach is rapidly losing favor due to the high human resource, storage and networking requirements involved in order to meet all potential requests.

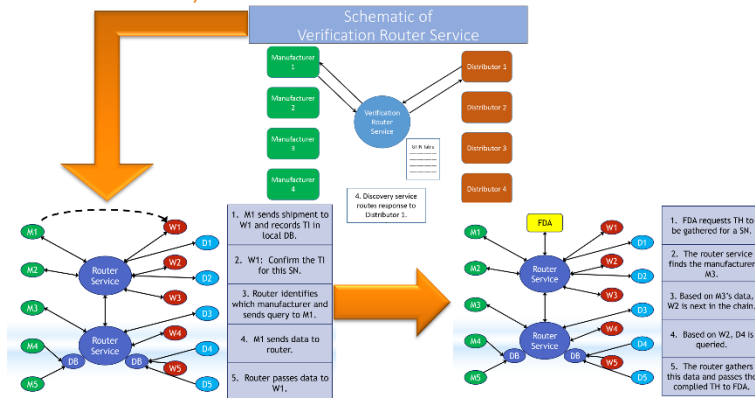
Figure 6. Federated Databases Allow Each Participant to Maintain All Their Own Records

A second is a centralized data warehouse that protects each participants proprietary information, while also allow quick retrieval of all data pertinent to satisfying DSCSA requirements or for internally initiated product recalls. This offers the easiest implementation and the highest degree of integrity of data due to there being one integrated set of data. In addition, it provides the greatest amount of control and flexibility for each participant due to the ease of creating shared, controlled views with external



participants while having more robust views internally, while always protecting proprietary information. This also allows integration of DSCSA data into other business data sources across the enterprise in order to maximize the use of the data for business purposes.

Current Industry Discussions: Router-based



A third approach is a multi-router-based approach that allow anyone in the supply chain to submit a request that is passed to all participants and those who have knowledge about the request to reply. This reduces storage requirements for each participant, but requires significant coordination on communications, plus multiple points of failure.

Figure 7. Router-Based Solution for Sharing DSCSA Data

As DSCSA participants move forward with these considerations, it is important to realize that there are likely to be additional gains from a well-architected solution that integrates DSCSA data with other operational and departmental data across an organization. For example, business opportunities that can be enhanced, refined or discovered include:

- Deeper, unit-of-sale level insight to improves monitoring and forecasting
- Shared cross-industry information that allows identification and forecasting of:
 - How each customer orders - today, tomorrow and across time
 - What each customer has on hand
 - Where each product is in the supply chain
 - Which product is going to each customer
 - Who's contracts are preferred between vendors based upon service level agreements (SLAs).
- More rapid determination and resolution of operational issues such as:
 - Why does truck X exceed SLA for product X
 - Which logistics-structure analysis can be implemented to improves efficiencies
 - What each customer is going to order next
 - Which supplier is going to not meet SLA for a specific location or set of locations
 - Where stock shortages or surpluses are going to occur
 - When a customer's needs are not going to be met
 - How to move available product to specific anticipated needs at lowest price

CONCLUSION

It is imperative to not only meet the current and upcoming deadlines of DSCSA, but to also understand the business purpose. It is also important to understand the risks from a poorly designed information architecture and the resulting data access and integrity limitations, as well as opportunities for new business gains that can be achieved by improved integration of the DSCSA data, infrastructure, and processes into the business.

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