PHARMACEUTICAL SUPPLY CHAINS: ISSUES AND CHALLENGES

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ABSTRACT

Healthcare is a trillion dollar industry and well-regulated by the United States Food and Drug Administration. Maintaining pharmaceutical supply chain to hospitals and clinics is essential for patients care as well as for healthcare providers. The main objective of drug supply chains is to provide drugs to hospitals, clinics, and research organizations an uninterrupted supply of drugs, equipment, and other related items needed at hospitals, at the right time, in right quantity and quality, at the right place. We discuss healthcare supply chain processes, Drug Supply Chain Security Act (DSCSA), and issues and challenges faced by healthcare providers pertaining to their supply chains. The crucial issue is the coordination among different partners of the supply chain and it aggravates the every other issue directly or indirectly.

INTRODUCTION

Healthcare industry contributes more than a trillion dollar to the U.S. economy. Baby-boomers are joining the category of senior citizens at a fast rate. Currently, more than a quarter of U.S. population is over the age of 60 years and their healthcare needs increase exponentially as they grow older. Maintaining pharmaceutical supply chain to hospitals and clinics is not only important but essential for patientcare as well as the reputation of the organization. Pharmaceutical supply chains are of two types: Clinical Supply Chains and Clinical Supply Cold Chains. The latter one includes temperature controlled drugs, medications, and supplies. The objectives of logistics companies is to get drug products and biomarker samples to the right place, at the right time, in desired quantity, quality, and the right way, all in a cost-efficient manner while taking into consideration the increasing concern of clinical trial costs and patient safety. To achieve this objective, logistics companies face various issues and challenges pertaining to several aspects of the supply chain. In this paper, we discuss the following:

- Pharmaceutical Process
- Healthcare supply chain process
- US FDA regulations and their compliance

- Presence of counterfeit drugs in supply chains
- Issues and challenges the process faces
- Active and Passive temperature Controls

Pharmaceutical companies and their supply chain personnel will benefit from this paper.

DRUG CONTROL REGULATIONS

The U.S. FDA regulates drug products intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and intended to affect the structure or any function of the body of humans or animals. Registrar Corp provides Registration, U.S. Agent, and Compliance Assistance for U.S. and Non-U.S. Companies in the Drug Industry. Operators of all U.S. and non-U.S. drug establishments that engage in the manufacture, preparation, propagation, compounding, or processing of drugs are required to register and submit a list of every drug in commercial distribution by way of U.S. FDA's new Electronic Drug Registration and Listing System (eDRLS).

The U.S. FDA now requires that drug labels be indexed using Extensible Markup Language (XML) in Structured Product Labeling (SPL) format. Registrar Corp can help modify your drug labeling to comply with U.S. FDA regulations. Registrar Corp provides revised graphic files ready to be printed or edited, and a report that details the regulations, compliance guides, warning letters, import alerts, and other guidance documents from the U.S. FDA. A Drug Master File is a submission to the U.S. FDA that may be used in support of pre-market submissions to provide confidential, detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more drugs. Registrar Corp's team of Regulatory Specialists provide guidance as to required elements, formats, and particularities of Drug Master File submissions.

Drug Supply Chain Security Act (DSCSA)

On November 27, 2013, the Drug Quality and Security Act (DQSA) was signed into a law, and Title II of the DQSA, the Drug Supply Chain Security Act (DSCSA) sets forth new definitions and requirements related to product tracing and provides a national standard for drug security, and replaces the pre-existing patchwork of state-level pedigree regulations. The DSCSA outlines critical steps to build an electronic interoperable system by November 27, 2023 to trace certain prescription drugs as they are distributed in the United States. The new system will enhance the U.S. Food and Drug Administration’s ability to help protect U.S. consumers by improving detection and removal of potentially dangerous products from the pharmaceutical distribution supply chain.

Companies selling pharmaceutical products in U.S. markets are subjected to the requirements of the Drug Supply Chain Security Act (DSCSA), regardless of where the company is located. Drug manufacturers, wholesale distributors, re-packagers, and dispensers that work with prescription medications will have to comply with DSCSA requirements, but pharmaceutical manufacturers and their contract partners are the only ones that must meet the first serialization mandate.

Beginning in November 2017, pharma companies must:

- **Serialize products**
    - At the package level, use a 2D Data Matrix.
    - At the sealed homogeneous case level, use a 2D Data Matrix or linear barcode.
    - Data must be machine- and human-readable and include National Drug Code and serial numbers, lot number, and expiry date.
- **Verify**
    - Respond to requests for verification from authorized re-packagers, wholesale distributors, or dispensers to verify the product identifier, including the serial number, within 24 hours.
    - Verify the product at the package level, including the standardized numerical identifier, upon receiving a request from the FDA following a determination that a potentially suspect product may exist.
    - Verify serial numbers of sealed homogeneous cases or individual units for received saleable returns.
- **Store**
    - Serialization data must be stored in an active, readily available location for six years past transaction date.
    - In addition, starting in 2017, the pharmaceutical manufacturer must also send the transaction history, information, and statement (T3) electronically to all parties.

Product Tracing, Verification and Serialization Highlights

Product Tracing – By January 1, all supply chain businesses except dispensers needed to achieve lot-based traceability, which involves sharing a Transaction History with every partner to whom you sell product. For many companies, establishing the necessary infrastructure for communication with partners at the level they need for regulatory compliance is the biggest challenge. In addition, the law does not prescribe standard formats for data exchange, so companies need to be equipped to receive transaction data in many configurations. When serialization come into play, product tracking will still be required but the nature of the requirement changes. Track and trace and serialization requirements will finally converge in 2023.

Verification –In the event of a suspect product inquiry, supply chain companies must be able to produce the relevant transaction documentation within twenty-four hours (dispensers have forty-eight). The challenge is in being able to locate and access the necessary records in this tight turnaround time. Businesses need a storage and retrieval mechanism that supports these queries.

Serialization – During lot level preparation, the industry discovered that completing one transaction between two parties was challenging. When serialization with its end-to-end tracing takes effect, businesses will need to manage many transactions, involving billions of items, with tens to hundreds of partners, including outsourcing ones. So there is the supply chain communication challenge but there is also a data volume challenge as businesses generate, process, and store an unprecedented amount of data and transactions. In the US the smallest saleable unit and the sealed homogenous case need to be serialized. By law, aggregation is not required but there is speculation that it will be required at some future point.

Manufacturers must serialize by November 2017. The rest of the supply chain has more time before they need to make full use of the serial numbers, but there will be circumstances prior to that in which they need to interact with the serial number, like for product returns and suspect product investigations.

PHARMACEUTICAL SUPPLY CHAIN PROCESS

Pharmaceutical supply chain process map is depicted in Figure 1 which shows three main flows: product flows, payment flow, and rebate flow. Drugs and medications ar the product and they flow from manufacturers to wholesaler/distributor to pharmacies, both retail and mail-order, and finally to consssumers. Most patients have healthcare insurance and pay their monthly premiums and co-payments only to the parmacy. The remaining payment is made by the patient's insurance company. Payments flow from the consumers employer, plan sponsor, or health insurer and to pharmacy benefit manager, who negotiates drug costs with drug manufacturers and pays to the pharmacy. Payments are then transferred to drug manufacturers either ddirectly or through wholesalers/distributers. Drug manufacturers pay volume discount to wholesalers but rebates to rebates to the pharmacy benefit manager who transfers it to health insurer. Deamnd flows from consumers to pharmacies and to manufacturers, directly or through wholwsalers.

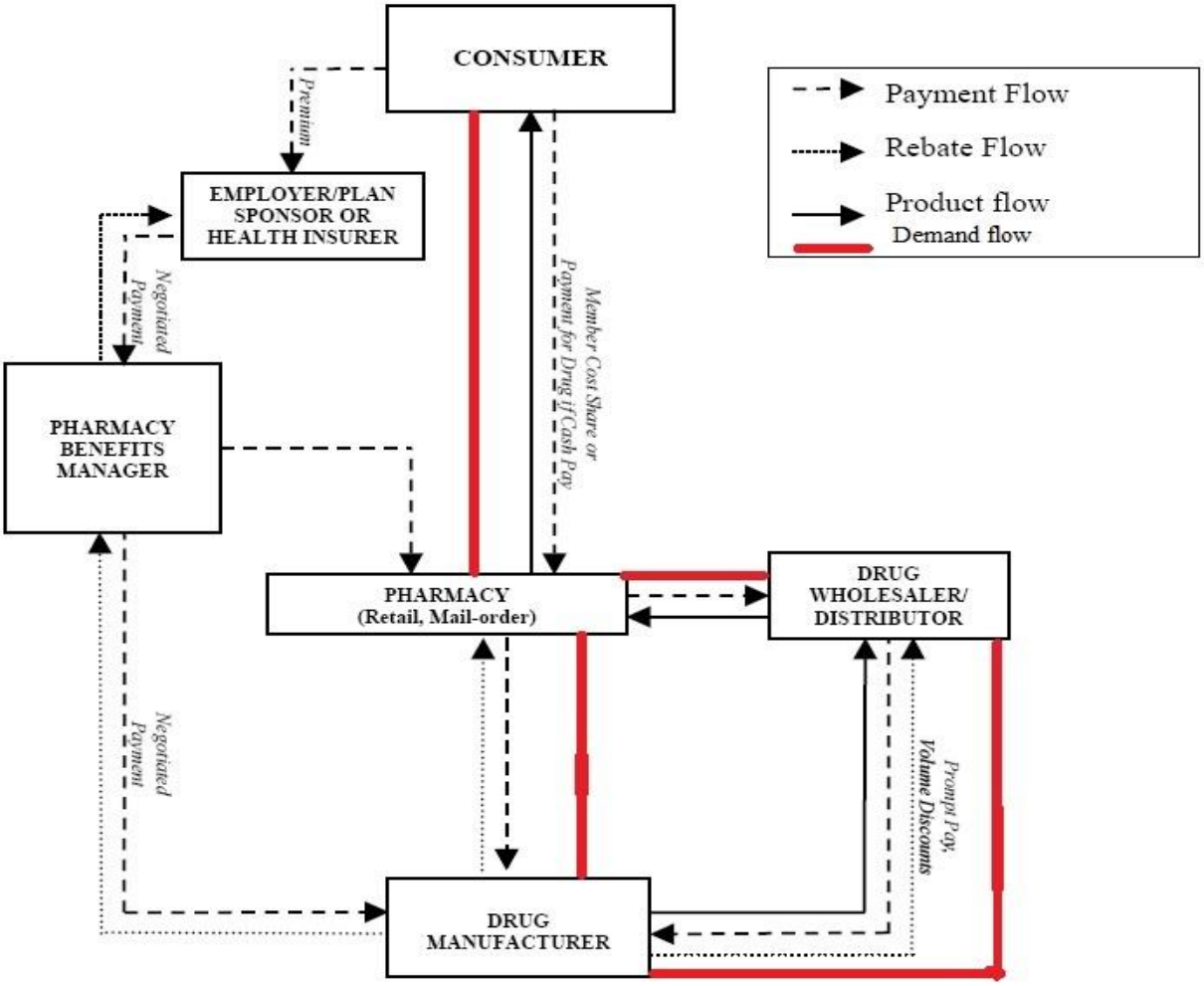

Figure 1: Pharmaceutical Supply Chain Process Map

HEALTHCARE SUPPLY CHAIN PROCESS

Healthcare supply chain process includes manufacturing planning cycle, order-to-cash cycle, information cycle, and the information chain. This depicts a wholistic approach.

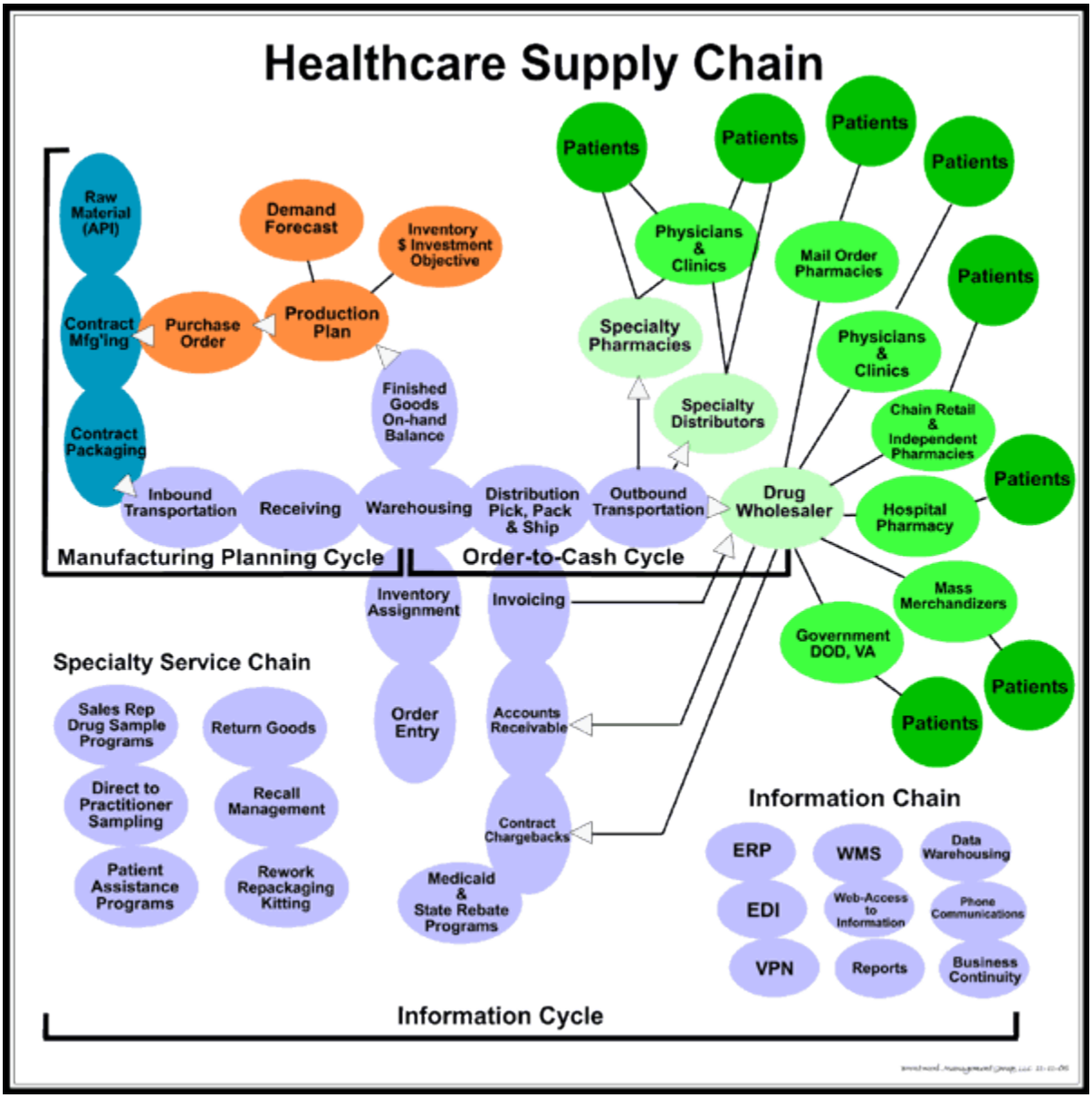

Figure 2: Healthcare Supply Chain Process Map

CLINICAL SUPPLY COLD CYCLE

Certain drugs are required to be temperature controlled and are categorized as Active Temperature Control and Passive Temperature Control. The active temperature range is -20°C to +20°C and it

is designed for temperature-sensitive commodities. Pharmaceutical Shipments are accepted in temperature controlled cool-containers which actively regulate temperature levels, irrespective of ambient conditions. Such supplies need to be transported either by refrigerated trailers or refrigerated containers. Passive temperature control range is +2°C to +20°C, and is designed for insulated shipments pre-packaged with dry ice or cold packs, which can accept minor temperature fluctuations and do not require transportation or storage in active temperature controlled

COUNTERFEIT DRUGS AND THEIR IMPLICATIONS

There are many examples now in the news about counterfeit drugs circulating in black market channels. The biggest recurring problem is in the developing world where, in Africa and parts of Asia and Latin America, the proportion of counterfeit medicines has been estimated to be as high as 30%. In 2009, the World Health Organization (WHO) reported that 34 million counterfeit tablets had been taken out of circulation in Europe in just a two-month period. I rarely think twice about the packet of pills that may be prescribed to me when I am ill. I trust it implicitly to make me feel better. I therefore expect the ingredients those pills contain to be safe and do their job effectively and, most importantly, safely. Beyond the obvious harm, counterfeit drugs can inflict on consumers. Pharmaceutical manufacturers are also concerned about the harm bogus medicine might inflict on their brand. It costs billions to develop, market and distribute drugs. The last thing manufacturers want is for that investment to go to waste as counterfeit pharmaceuticals undermine those efforts.

CHALLEGES FACING PHARMACEUTICAL SUPPLY CHAINS

Not much research is conducted pertaining to pharmaceutical supply chains. Healthcare and pharmaceutical companies have started thinking of using supply chain knowledge and gaining from it. Some drug companies are also using global supply chains to take advantage of cheap labor in developing countries. On the pretext of utilizing cheap labor, some companies or countries are manufacturing counterfeit drugs and medications. Capable supply chains will win war against disease but also they will be instrumental in winning battle against counterfeit drugs.

Pharmaceutical supply chains have to deal with several issues and face certain challenges. The following are the top ten challenges:

1. Lack of coordination
2. Inventory management
3. Absent demand information
4. Human resource dependency
5. Order management
6. Shortage avoidance
7. Expiration
8. Warehouse management
9. Temperature control
10. Shipment visibility

Lack of coordination is the root cause issue whose existence aggravates nearly every other issue directly or indirectly. Pharma companies have to manage incredibly complex supply chains and manage the operational challenges of working and interacting with a large numbers of suppliers contributing ingredients and components to drug production. And now they need to meet track and trace directives and comply with new serialization regulations that require inventory to be auditable as it moves through the supply chain.

Importance of Visibility

The first step toward achieving the directives of track and trace and serialization is to improve visibility throughout the supply chain. Until a company can see all the activity taking place among its suppliers, shippers, vendors, and partners, it will struggle to prevent leaks in supply chain and – importantly – have a hard time showing regulators they're following the rules. A cloud-based supply chain management platform offers visibility to all companies, regardless of size. For a large, multinational pharma business, access to data from all operational regions allows for greater awareness of growth areas, understanding of where hold-ups might exist in the supply chain, and insight into how these might be navigated in order to avoid impact on distribution. And crucially, this can help track and tracing via serialization.

Looking for Solutions

Companies getting to grips with serialization should consider if their existing supply chain management systems and processes provide:

1. Accurate information across the entire chain at any point and at any location
2. Instant access to real-time updates and alerts if issues are detected
3. Visibility of all handovers in the supply chain
4. Traceability back to source of all materials
5. Seamless collaboration between all parties

Traditional ERP systems do not provide a holistic and complete view of the production and movement of goods from start to finish that is now needed. With these traditional models, each link in the supply chain has its own systems that often cannot connect into each other so the level of visibility, so desperately sought, is difficult, if not impossible, to achieve. Networking suppliers, partners, and logistics providers along the supply chain can offer a more comprehensive view of activities. Organizations need a collaborative system that is equipped with reliable information throughout the supply chain.

CONCLUSION

Pharmaceutical supply chains are critical for healthcare providers, hospitals, clinics, and patients as well. Baby-boomers' requirements for healthcare and drugs has increased manifolds because they constitute more than a quarter of the United States population and have turned over the age of sixty years. Due to globalization and outsourcing, counterfeit drugs have entered the supply chain and their origins are not traceable. At the same time, pharma companies are losing revenues. The United States Food and Drug Administration (US FDA) controls and regulates the manufacturing, sales, distribution, and repackaging, etc. and Drug Supply Chain Security Act

(DSCSA) mandates several directives and requirements for pharma companies for their compliance. We have enumerated essential requirements in this paper. Additionally, two processes for pharmaceutical supply chain and healthcare supply chains are described. We have also listed issues and challenges supply chains face and need to deal with and the most crucial is the lack of coordination between various links from raw material suppliers to retail pharmacies. This is an exploratory study and needs further research, data collection, and statistical analysis.

REFERENCES will be provided on request