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Exception Management in Pharmaceutical Industries to attain DSCSA Compliance

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Abstract

Drug Supply Chain Security Act (DSCSA) was introduced by USFDA to identify and remove the harmful drugs from the commercial distribution for patient safety. The traceability of the saleable units needs to be maintained from drug product manufacturer to dispenser by all authorized trading partners, using interoperable electronic data transmission i.e., EPCIS (Electronic Product Code Information Services) files to their downstream trading partner. EPCIS files contain overly complex data sets containing product master data, trading partner`s master data and fully aggregated serialization data for the drug product from saleable unit till case level/shipper level. Due to complexity of the EPCIS files, probability of the failure is remarkably high for unsuccessful transmission, which lead to quarantine that drug product and restrict the further distribution. Any aggregation issues or data issues from the EPCIS files need to be identified, investigated, rectified, and needs to be documented, that procedural approach handled by using exception management systems. If root cause cannot be identified and traceability of the product come into question, then it may fall in to suspect / illegitimate product and trading partner(s) need to notify USFDA, cannot sell further and need to keep that product into their possession under quarantine. If root cause identified and corrected EPCIS files received by the purchasing organization, then the product can be further commercially distributed. Ultimately its drug product manufacturer`s responsibility to have adequate exception management procedure and system in place to stay compliant.

Keywords: Exception Management, Drug Supply Chain Security Act (DSCSA), EPCIS, Serialization Data, Authorized Trading Partner, FDA Form 3911, USFDA

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1. Introduction

To keep the traceability of the prescription drug products in the US for patient`s safety by removing harmful drugs from the supply chain, FDA mandated DSCSA (Drug Supply Chain Security Act) to all the trading partners in the pharmaceutical industries including manufacturers, wholesalers, distributors, hospitals, dispensers, etc. Each saleable units must have basic four product identifiers – Lot Number, Expiration Date, Unique Serial Number and NDC (National Drug Code), known as serialization data, unless exempted due to container size or exemption received from FDA. The traceability of the saleable unit using these four-product identifiers needs to be maintained and transferred throughout the supply chain from manufacturer to dispenser using EPCIS (Electronic Product Code Information Services) files, considering virtual shipment of the electronic data of the physical shipment of the drug products. The downstream trading partner cannot sell further, until they receive the complete data in the EPCIS file, and they must quarantine the drug products, until receipt of the complete and accurate data in line with the physical shipment, which may occur due to aggregation errors. (1)

2. Data Aggregation

To facilitate and achieve the secure supply chain, selling trading partners must provide the fully aggregated data using EPCIS file to purchasing trading partner. The aggregation is known as parent-child relationship and expected to be done at least from saleable individual unit to homogeneous case level. For the other supply chain management and data management perspective, manufacturers aggregate the serialization data from individual saleable unit to homogenous case level to non-homogenous shipper level to pallet level. Aggregated data helps to provide security, enough assurance and faster receipt of the physical product to purchasing trading partner. The selling trading partner needs to ensure that this aggregation data should be accurate, complete, and in line with the physical product being shipped. Along with complete aggregation data, physical products also need to be fully secured using tamper-evident tape, shrink wrap and/or anti-counterfeiting technologies. (2,3)

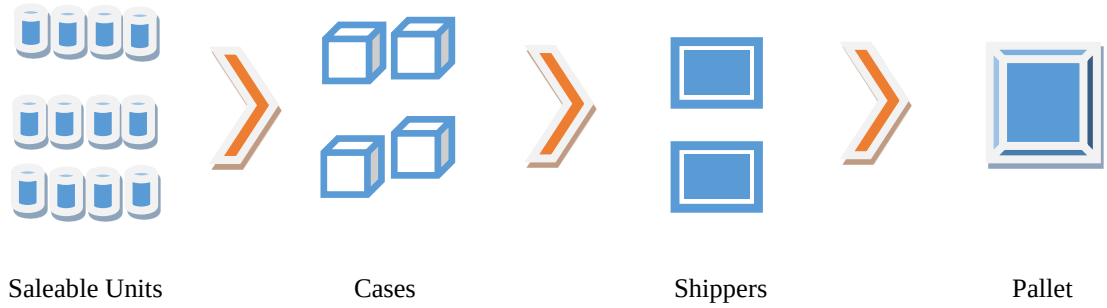

Figure 1. Aggregation Flow

The aggregation error could occur at any unit operation, from packaging operation to shipping operation and resulted due to incorrect configuration of the automation or due to manual intervention during these operations. It's very remote possibility that aggregation error occurred during packaging operation, as manufacturers of the products have a system and processes in place along with quality unit checks throughout the packaging operation. In case any aggregation error is observed, its being corrected and documented as per the current good manufacturing practices by quality unit. Most of the time aggregation errors are reported from purchasing trading to selling trading partner upon receipt of the physical product. Its purchasing trading partner`s responsibility and compliance requirement, that they must ensure that EPCIS files containing product traceability data are complete, accurate and in line with physical product that they have purchased. When any discrepancy observed for this aggregation data and physical product, selling trading partner must be notified for the nature and magnitude of this error. Aggregation errors observed, when there is physical short shipment, physical overages, incorrect product quantity, incorrect product identification, incorrect purchasing organization data, incorrect shipping organization data, duplicate data, missing data, etc. during shipping operation. These aggregation errors need to be resolved and managed, which is called DSCSA exception handling in the supply chain. (2,4)

3. Exception

There could be multiple reasons that lead to exceptions. It can happen while scanning the product identifier data from physical shipment, creating EPCIS files, posting EPCIS files, incorrect product master data, incorrect aggregation data, incorrect shipment location data, incomplete connections between trading partners, etc. If the product cannot move further into the supply chain, businesses are at risk and patients cannot get the drug product and the whole supply chain destabilize. Wholesalers/distributors needs additional space to store the quarantine products due to these exceptions. Products start losing their life. It leads to increased communications between the trading partners, until the exception is resolved, which takes more hours and costs more for the company. FDA mandated that all these exceptions need to be resolved within ten calendar days, else it needs to be returned to an upstream trading partner, and it may also fall into suspect or illegitimate drug products, which requires the manufacturer to report to FDA and further leads to investigation. (4)

The standard operating procedure needs to be placed for handling of these exceptions. Though this field is really evolving and there could be multiple reasons for this exception, trading partner should develop the process/policy based on the current knowledge and periodically needs to revise based on the experience of managing the exceptions. The written procedure should include the role and responsibilities of the downstream/upstream trading partners, defined timelines of resolution, mode of communications, responsible person(s), DSCSA compliance requirement, when to quarantine and re-release the product, logbook for the exceptions, documenting evidence, root cause analyses, corrective actions taken, if any, exception generation and exception resolution date, etc. This procedure also addresses how to handle the exception, when it arises due to 1) partial and/or incorrect EPCIS files (virtual shipments), that lack of product master data, missing product data, partial product data, incorrect shipping location data, incorrect aggregation data, incorrect version of EPCIS data, etc. and 2) partial and/or incorrect physical drug product shipments, that does match with the EPCIS data, damaged shipments, shortages, overages, incorrect shipping locations, etc. (4,5)

4. Exception Management

The exception may be reported from purchasing organization to selling organization, when transaction data containing EPCIS files content and format is not as per GS1 standard, supplier`s and/or wholesaler`s master data, i.e., GLN, SGLN, addresses are incorrect, product master data are incorrect, etc. The selling organization/ manufacturer needs to identify the error, correct the format/data elements, update the master data for product and purchasing organization and repost the EPCIS file to selling organization. (4,5)

The exception may be reported from purchasing organization to selling organization, when transaction data containing EPCIS files not received due to technical errors, missing/incorrect serial numbers as per product receipt, missing/incorrect purchase order or delivery number, incorrect distribution center address, etc. The selling organization/manufacturer needs to investigate the root cause of the error, propose corrective action for that error and repost the EPCIS file to the selling organization. (4,5)

The exception may be reported from purchasing organization to selling organization, when physical

product is not in line with the transaction data containing EPCIS files. There may be a shortage/overage of the physical product, partially/full incorrect products in the received shipment, damaged products, etc. The selling organization/manufacturer needs to investigate the product status at their own facility or with the shipping carrier, propose corrective action for that error and either ship the correct physical product in line with EPCIS file or take back the physical product from selling organization. (4,5)

The exception may be reported from purchasing organization to selling organization, when physical product is not in line with its packaging and/or labeling details, comparing to the EPCIS files, missing / illegible / incorrect 2D barcodes, Serialized Shipping Container Code (SSCC) is missing/ illegible/ damaged. The product needs to be verified for its legitimacy by selling organization/manufacturer and further course of action needs to be decided by communicating with the selling organization and adequate product disposition needs to be done with documentation. (4,5)

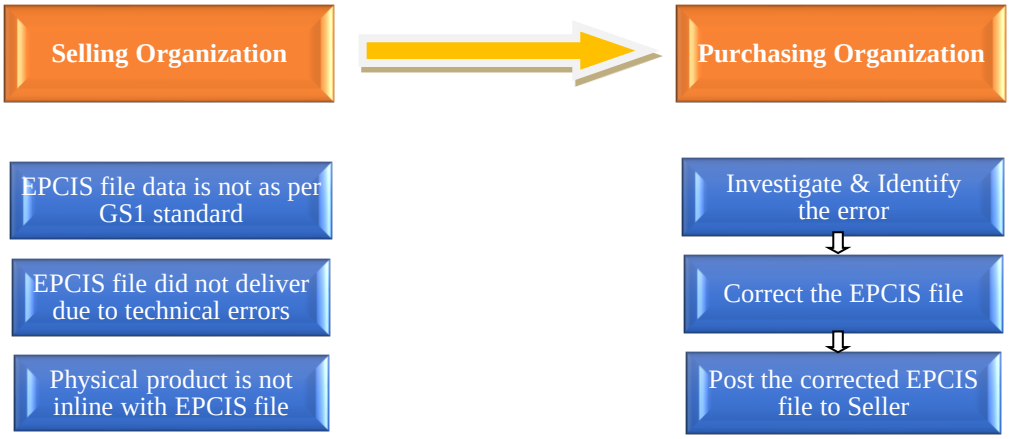

Figure 2. Exception Management

5. Suspect/Illegitimate product

The drug product may fall into the category of suspect/illegitimate product if exceptions cannot be resolved in a timely manner or cannot lead to satisfactory resolution. The exception can be reported by any of the trading partners to their upstream trading partner and that could be dispenser, distributor, or wholesaler. In those cases, its burdensome for manufacturers and as per the FDA`s DSCSA compliance, they must send the initial drug notification to FDA using FDA Form 3911 with all available information. Manufacturers must identify and archive complete traceability of that drug product from the manufacturing site till exception reporter. Manufacturers need to do thorough investigation of the exception including identification, root causes, corrective action, if any and later obliged to notify immediate trading partners of this drug notification. Manufacturers can submit follow-up communication to the FDA, when any significant information is available during the investigation. Manufacturers can submit the request for termination of the drug notification to FDA along with the investigation report. The FDA will review the investigation report and may ask for additional information, before granting the termination of the drug notification. (6-8)

6. Conclusion

The trading partners are relied upon serialization solution providers, who provide the platform to transmit, maintain and archive the serialization data. Based on the exceptions handling issues, they produce their exception solution management services, but they can help to identify the issue and cannot address or resolve the issue. When manufacturers use the 3PL (Third Party Logistic) services for their business, it becomes more complex and difficult to identify and resolve the exceptions. At the end, responsibility lies with the trading partners to identify and resolve the exception handling issue to make drug products available to sell further and make available to patients. Exception handling is part of the DSCSA compliance, which needs to be adequately managed and documented, that plays a critical role, especially for manufacturers during GMP inspection conducted by the regulatory agencies.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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