IHE Pharmacy (PHARM)

Educational Article

Falsified Medicines Directive -

Supply chain interoperability in support of safer medication usage

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This work is a collective initiative under the initiative of IHE Pharmacy.

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References:

Directive 2011/62/EU
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http://www.eahp.eu/news/EU-monitor/eahp-eu-monitor-25-august-2015

Draft Commission Delegated Regulation supplementing Directive 2001/83/EC
http://ec.europa.eu/growth/tools-databases/tbt/en/search/?tbtaction=search.detail&num=306&Country_ID=EU&dspLang=EN&BASDATEDEB=&basdatedeb=&basdatefin=&baspays=EU&basnotifnum=306&basnotifnum2=306&bastypepays=EU&baskeywords

Full text of the draft Delegated Act
http://ec.europa.eu/growth/tools-databases/tbt/en/search/?tbtaction=search.detail&num=306&Country_ID=EU&dspLang=EN&BASDATEDEB=&basdatedeb=&basdatefin=&baspays=EU&basnotifnum=306&basnotifnum2=306&bastypepays=EU&baskeywords

Commission Delegated Regulation (EU)
http://ec.europa.eu/growth/tools-databases/tbt/en/search/?tbtaction=get.project&Country_ID=EU&num=306&dspLang=EN&basdatedeb=,&basdatefin=&baspays=EU&baspays2=EU&basnotifnum=306&basnotifnum2=306&bastypepays=EU&baskeywords=&project_type_num=1&project_type_id=1&lang_id=EN

ANNEXES I to IV to the Commission Delegated Regulation (EU)
http://ec.europa.eu/growth/tools-databases/tbt/en/search/?tbtaction=get.project&Country_ID=EU&num=306&dspLang=EN&basdatedeb=,&basdatefin=&baspays=EU&baspays2=EU&basnotifnum=306&basnotifnum2=306&bastypepays=EU&baskeywords=&project_type_num=2&project_type_id=1&lang_id=EN

World Health Organization – Media Center
Substandard, spurious, falsely labelled, falsified and counterfeit (SSFFC) medical products
http://www.who.int/mediacentre/factsheets/fs275/en/

1 Summary

This document is an initiative of IHE Pharmacy to describe how interoperability can support the effort against falsified medicines, as laid out in the Falsified Medicines Directive - EU Regulation 2016/161.

Background: Falsified medicines are a growing economical and health problem, and it deserves the attention of organizations at highest level. Monitoring the supply chain of medicinal products can help ensure that these falsified products do not enter the circuit. IHE provides a standard interoperability architecture for the supply of healthcare products. This effort covers traceability, barcode scanning, message exchange, etc. All of these matters help monitor the supply chain and thus support the enforcement of the Falsified Medicines Directive.

This paper explains that the requirements of the Falsified Medicines Directive constitute in identifying the medicinal products along the supply chain, and reporting that to a central data hub. Using publicly available message structures helps software solution providers benefit of IHE's testing opportunities and support a truly interoperable tracking mechanism.

Scanning the products poses an operational challenge for users: even for easy barcode scanning, for normal volumes it becomes burdensome. In a medium hospital, the effort of identifying all the received primary packages upon reception would exceed one dedicated professional. For this, it is essential to use standardized AIDC (Automatic Identification and Data Capture) technologies: standard media (e.g. Datamatrix barcodes) and standardized content.

Standardized interoperability mechanisms also play a role in this: By providing a standard electronic shipment list, the supplier can inform about the content and unique identification numbers included in each shipped carton so that the users may scan the outside package, and the contents of the package are automatically filled into the necessary systems.

This document explains how these mechanisms - reporting and shipment content - can enable proper tracing of medicinal products, and when standardized they enable the different actors to do so with reduced effort.

2 Falsified Medicines

The World Health Organization addresses “Substandard, spurious, falsely labelled, falsified and counterfeit (SSFFC) medical products” as an important global concern.

The European Medicines Agency describes Falsified Medicines “fake medicines that pass themselves off as real, authorised medicines”. This goes beyond counterfeit medicines, which pose a violation of Intellectual Property rights.

Besides affecting patients’ health, they also affect also the confidence in medicines, in healthcare providers and the health systems in general.

Concerningly, these falsified products can be found in all types of products, and in all supply channels – from online purchases to pharmacies and hospitals.

The World Health Organization provides important information and guidance on how to prevent the use of falsified medicines – from awareness about the point of purchase to inspection of the physical product.

While it is important to inspect and check the medication and the purchase conditions, there are technical mechanisms that can be introduced to increase safety – namely the integral control of the supply chain.

The Falsified Medicines introduces two additional mechanisms that help evaluate a medicinal product for safety. They are described in this document, and one of them – the control of the supply chain and traceability – is supported by IHE.

Using an IHE-compatible supply chain enables:

- the global traceability of medicinal products;
- the operational aspects of the control of Falsified Medicines.

3 The EU Falsified Medicines Directive

The following is an adaptation of the FMD[1] Regulation 2016/161 of 2 October 2015:

The European Commission establishes the need and mechanisms for "measures to **prevent the entry into the legal supply chain of falsified medicinal products** by requiring the placing of safety features consisting of a unique identifier and an anti-tampering device on the packaging of certain medicinal products for human use for the purposes of allowing their identification and authentication."

Diverging authentication mechanisms and traceability requirements for medicinal products may limit the circulation of medicinal products and increase costs for all players in the supply chain. Therefore it is necessary to establish Union-wide rules for the implementation of the safety features for medicinal products, in particular the characteristics and technical specifications of the unique identifier, the modalities for the verification of the safety features, and the establishment and management of the repository of information on the safety features.

(…) The policy options identified as the most cost-effective have been introduced as core elements of this Regulation by the European Commission.

This Regulation sets out a system where the identification and the authentication of medicinal products is guaranteed by an end-to-end verification of all medicinal products bearing the safety features, supplemented by the verification by wholesalers of certain medicinal products at higher risk of falsification.

In practice, the authenticity and integrity of the safety features placed on the packaging of a medicinal product at the beginning of the supply chain should be verified at the time the medicinal product is supplied (dispensed) to the public, although certain derogations may apply. However, medicinal products at higher risk of falsification should be additionally verified by wholesalers throughout the supply chain, to minimise the risk of falsified medicinal products circulating undetected for lengthy periods of time. The verification of the authenticity of a unique identifier should be performed by comparing that unique identifier with the legitimate unique identifiers stored in a repositories system. When the pack is supplied to the public, or is distributed outside the Union, or in other specific situations, the unique identifier on that pack should be decommissioned in the repositories system so any other pack bearing the same unique identifier could not be successfully verified.

To support verifying the authenticity of an individual pack of a medicinal product for the entire lifecycle of the product, it is expected the unique number not be re-used at all.

[1] http://ec.europa.eu/health/files/eudralex/vol-1/reg_2016_161/reg_2016_161_en.pdf

4 Supply chain and traceability as applied to the FMD

For the Directive to be effective, the items must be tracked, and the tracking information must be accessible in order to cross-check the tracked items to check the integrity of the supply chain - track the flow of items, detect untraced origins, duplicate serial numbers, etc.

This requires that a few mechanisms to be functioning:

- The medicinal products packages must bear safety features and should be supplied with tracking data that enables better identification.
- The tracking information must be captured at least at the time they are supplied to the public.
    - For most products, the FMD does not mandate the tracking information to be captured at each inventory movement; rather that it is captured at least once.
    - This means retailers, pharmacies, hospital pharmacies
- Once captured, the tracking information must be exchanged to the repository.

The first mechanism is handled by measures of serialization and standardization in the production process as well as by using overt and/or covert features.

The second is made possible by the use of Datamatrix (one form of Automatic Identification and Data Capture (AIDC)).

The use standardized AIDC (Automatic Identification and Data Capture) technologies ensures that

- the information can be properly acquired (using standard barcodes that can be read by every party)
- the content of the barcode is standardized and can be correctly parsed and used.

The data captured - usually by scanning the barcodes - should then be transmitted to the parties using it. This means that upon the scan of a barcode, the information about that product is then reported to a shared data pool - a hub.

This tracking of the items and providing the tracking data to a central hub is useful for detecting possible issues, etc., as preconized in the Falsified Medicines Directive. Each Member State will implement the local hub –connected to the central hub, and there are companies providing integration services.

The exchange of information is thus an essential mechanism in preventing or detecting the introduction of illegitimate products in the healthcare supply chain.

To facilitate the integration of the hospital with other systems, and to improve the implementation of the data submission between the hospital and the hub, this interoperability should be done in a standardized manner.

Every institution should have one standard way of reporting FMD information to its local repository.

The repositories are conceived to be able to share and cross information among them in a standard manner to ensure continuity of the information.

The data must be captured from one Datamatrix. This is intensive work, as it could require scanning each barcode of each sales unit. But since the data captured is also conveyed by standard interoperability mechanisms, this can be facilitated:

When a supplier packs items for shipment, this is captured at the supplier side, and each shipment is individually labelled with a barcode that identifies that unique shipment container. The content of that container unit is tracked and can be made available by a dispatch advice - a detailed list of what is shipped.

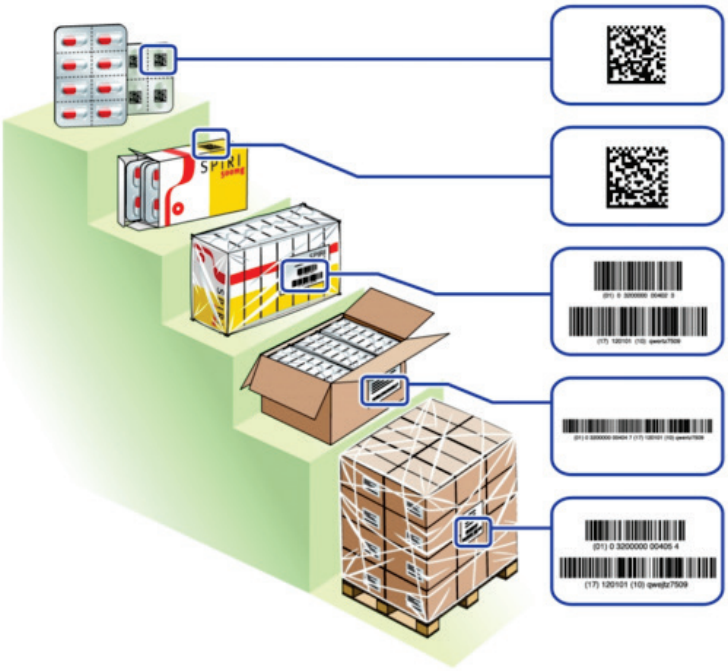

Figure 1 - Levels of Packaging (Source: GS1)

The levels of packaging may vary - what is important is that several items with an identifying barcode can be packed in a container that is itself identified with a barcode.

The dispatch advice is a declaration of the items that are contained within each shipment. If this information is transmitted electronically, it can be used to inform the consumer, and the consumer can simply scan the container identifier label to know the content, and does not have to scan each individual package label. This is of course assuming that there is a level of confidence that gives assurance that the content of the container matches the declaration of the vendor.

In terms of interoperability, this means the following requirement:

A standardized dispatch advice should be in place so that the supplier and customers can simplify, automate and control the delivery of items and the tracking of the delivered items. This information will be used to:

- Scan the shipment labels to track the shipments;
- Scan the shipment container label and electronically match the shipment notice with its content, avoiding having to open and scan every retail pack upon reception.

5 Example: Product reception

A pioneer hospital with 500 beds scans their items and is piloting of a program to detect and avoid falsified medicines. The hospital must be ready for submitting the data to a regional hub. This requires interoperability to be implemented.

If the hospital consumes about 1’400’000 boxes (secondary packaging) of medicinal products each year, this means that about 6’000 items would have to be scanned per working day, which corresponds to about 13 units to be scanned per minute. As is evident, only the scanning of the secondary packaging (boxes) is more than a full time job.

In addition to this, there are other operational issues like displacing the items for scanning, data entry in the software applications, etc. This makes such barcode scanning impractical. Especially considering that the Directive establishes that such reporting is to be done within 10 days of reception.

An interoperable supply chain can improve this:

For sake of example, a vendor, GoodSource Pharmaceuticals, produces Medication GoodRest Tabs. It packages it in boxes of 20 tablets.

The hospital has an agreement with a GoodSource Pharmaceuticals for the purchase of Medication GoodRest.

Besides presenting the lot number and expiry date in the package, as is common practice, the manufacturer has –according to the Falsified Medicines Directive - to include this information, the product code and the serial component, into one single Datamatrix.:

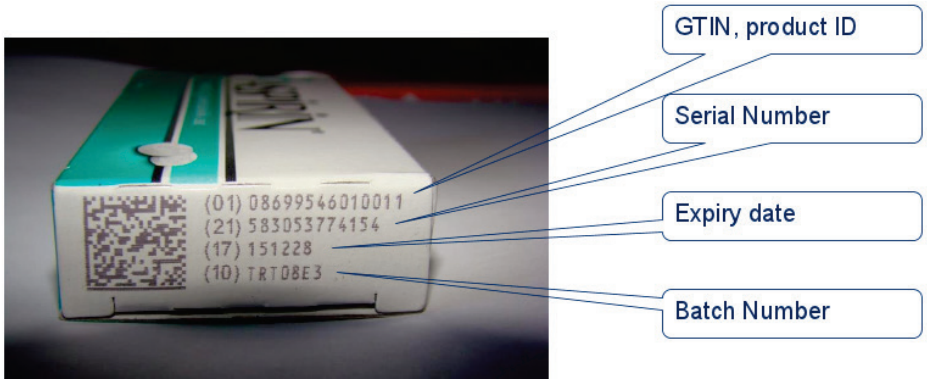

Figure 2 - Datamatrix with serialization (Source: GS1)

During normal operation, the hospital issues an order for Medication GoodRest Tabs - 100 boxes (Step 1 in Figure 4). The hospital specifies the product by using the manufacturer's code - GTIN 01234567890123.

The vendor assigns 100 boxes of Medication GoodRest Tabs from stock to prepare a shipment to the hospital (Step 2 in Figure 4). All of these 100 boxes are of the same production batch - the lot number of all primary packages is 00ABC. The expiry date is also the same - 02/05/2017.

Each box has a serial number; since the serial numbers of the 100 boxes are not sequential, but pseudo-randomized, it is impossible to anticipate which numbers will be included in the shipment.

These are the items reserved to be shipped to the hospital:

(box #)	Product ID	LOT	Expiry date	Serial
1	01234567890123	00123	02.05.2017	s0xxxxx71
2	01234567890123	00123	02.05.2017	s0xyxyxyx72
3	01234567890123	00123	02.05.2017	sababab70
4	01234567890123	00123	02.05.2017	sisisisi4
	…	…		
100	…	00123	02.05.2017	szozozoz0

The 100 boxes are contained in a bigger box (tertiary package) as illustrated here:

Figure 3 - Box with barcode

This information is submitted to the hub for enabling posterior verification and tracing (Step 3 in Figure 4).

At the end of this document there is a simplified example of the dispatch advice document that contains the data in the table above.

When the vendor ships the items to the hospital (Step 4 in Figure 4), the receiving department (usually the Pharmacy) could be expected to acknowledge the reception of the 100 items. This

is the burdensome situation described before: For each of the primary packages received, the hospital must scan and submit to the hub (Step 7 in Figure 4).

This operation contributes to drastically increasing protection against falsification: checking that the items that are dispensed have been correctly declared in a clear supply chain is a final step in a controlled chain of data and materials.

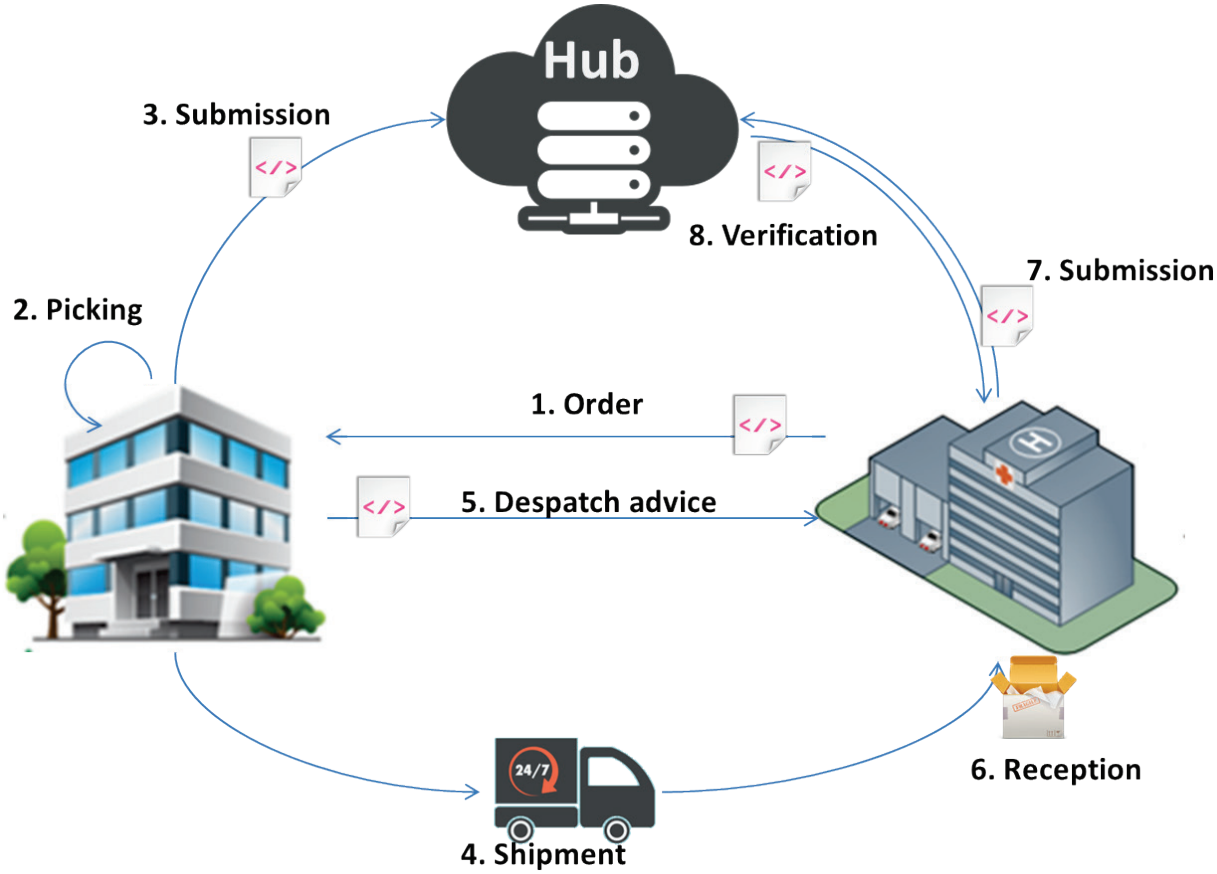

Figure 4 - Example process: ordering, shipment and verification

With an interoperable supply chain, however, when the vendor sends the items, they notify the hospital that the items have been sent - and indicate, via dispatch advice (Step 5 in Figure 4). , not only the quantity, batch / expiry date, but the detailed list of the unique numbers included in the shipment.

The shipment is itself identified with a unique identifier. The tertiary package is also identified with a unique identifier, although this is not mandated by the Falsified Medicines Directive. Since the manufacturer declared the content of the shipment and the content of the carton in the dispatch advice, then the warehouse management system at the pharmacy is capable of receiving this information.

If such interoperability exists, then the pharmacy simply needs to scan the shipment identifier, and the tertiary package identifier. **Upon scanning the shipment ID, the Warehouse Management System (WMS) looks up the content of the shipment notice and since there is a match, the ERP gets updated with the received items, including their traceability data (lot/batch number, expiry date and serial numbers). This way, with one scan of the outside container, the WMS in the hospital can acknowledge the reception of the 100 items shipped without scanning them individually.**

It is left to the discretion of the customer to decide if individual secondary packs should be scanned in addition for conformance testing.

Other example:

Verifying internal stock in October, if there is an item that is already in stock since January and signalled to be "suspected of falsification" in May (from the outside hub). Normally this situation would go undetected, but by best practices and integration of information during the lifecycle this can be checked: At the time of inventory count in October, the hospital checks the scanned items against the hub data, and the internal inventory platform identifies one of the items as being "suspect of falsification" thus notifying the competent entity in the hospital to decide further action (e.g. holding the product or investigating the product origin) and document the regional hub accordingly.

Proper interoperability should support continuous control of the items, not only at the point of reception but anywhere in the complete supply and delivery chain.

6 Sample Dispatch advice

Legend: **Sender data** **Consumer Data** **Shipment Data** **Content Data**

```
<?xml version="1.0" encoding="UTF-8"?>
<dispatch_advice><sh:StandardBusinessDocumentHeader><sh:HeaderVersion>1.0</sh:HeaderVersion>
      <sh:Sender><sh:Identifier Authority="GS1">4098765000010</sh:Identifier><sh:ContactInformation>
            <sh:Contact>GoodSource Pharmaceuticals</sh:Contact> <sh:EmailAddress>sales@goodsource.com</sh:EmailAddress>
            <sh:FaxNumber>+1-121-555-1213</sh:FaxNumber> <sh:TelephoneNumber>+1-212-555-2122</sh:TelephoneNumber>
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      </sh:Sender>
      <sh:Receiver> <sh:Identifier Authority="GS1">5412345000013</sh:Identifier>
         <sh:ContactInformation>
            <sh:Contact>Mary Smith</sh:Contact> <sh:EmailAddress>Mary_Smith@HealthyHospital.com</sh:EmailAddress>
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