Falsified Medicines Directive in European Union

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The Falsified Medicines Directive (FMD) and the Delegated Regulation (DR) impact the pharmaceutical supply chain. The European Union published the Falsified Medicines Directive, introducing a safety feature on the packages of drugs, ensuring the verification of a drug's authenticity before supplying it to the patient. The details of implementing a Europe-wide system for authentication of medicines is included in the Delegated Regulation, published in February 2016. The deadline for DR implementation was 9 February 2019, with the authentication systems required to be operational and running before this deadline. The FMD impacts the entire pharmaceutical supply chain.

Keywords: falsified medicines directive ; delegated regulation ; supply chain ; hospital

1. Impact of the Falsified Medicines Directive (FMD) on the Pharmaceutical Supply Chain

The pharmaceutical supply chain involves a series of intermediate stations, from manufacturers and wholesalers, to healthcare institutions, pharmacies, and patients.

The Falsified Medicines Directive (FMD) and respective DR impact every intervenient of this supply chain, especially in terms of the regulatory compliance that needs to be met in the nearest future [1].

1.1. Manufacturers

The main changes for pharmaceutical manufacturers are the new labelling regulatory requirements and adaptability of the production lines [2]. Medicinal products need to bear a unique identifier, a 2D bar code matrix on each medicine package compliant with ISO 16022 [1][3].

The unique identifier generated by the pharmaceutical industry needs to be reported to the European hub that identifies the code with a market authorization holding and reports the unique identifier to a national repository system that stores it until the moment of decommissioning is performed by the end user, who verifies the authenticity of the product through a scanning dispensing operation. Furthermore, each medicine package needs to contain an anti-tampering device.

1.2. Wholesalers

Wholesalers also need to implement new operations under the FMD. They need to verify medicinal products returned by other parties (community and hospital pharmacy, wholesalers, other organizations that supply medicinal products) and medicinal products supplied by wholesalers who are not the market authorization holder (MAH). Depending on what type of operations wholesalers have, if they supply only wholesalers, if they receive products only from manufacturers, it changes the verification and decommission operations they need to perform.

There is no need to verify the authenticity if the medicinal product changes ownership but remains in the physical possession of the same wholesaler or the distribution of drugs is between a wholesaler's own warehouses [1].

Wholesalers are responsible for decommissioning the unique identifier through the scanning of the 2D matrix bar code, removing the unique identifier from the national repository system. Decommission can be performed for several reasons.

Persons authorized to supply medicinal products to the public need to decommission the unique identifier at the time of supplying it to the public; this can be accommodated easily in a community pharmacy perspective. The DR gives the possibility for hospitals to verify or decommission products in their internal supply chain, so this generates some options for them depending on the institutions [1][4].

Dispensing part of a pack also impacts dispensing operations, so healthcare professionals need to decommission the package before opening it.

2. Other Implications of the FMD That Affect All the Intervenients of the Pharmaceutical Supply Chain

2.1. Verification vs. Decommission

A medicinal product can be verified or decommissioned through an authentication system. The verification process allows the serial number of the package to be queried in a national repository system and, thus, the authenticity of the product can be verified. Verification can be performed several times. A decommission scanning process removes the code from the national database. This ultimately confirms that the product was dispensed and used [1].

2.2. Products Included in the DR

The majority of drugs that bear the safety features are prescription-only medicines (POM). Non-prescription medications are excluded. Annex I and II of the DR refer to medications that do not need to bear the safety features and to this end one over-the-counter (OTC) product that needs to bear the safety features, respectively. Also, member states can adapt the respective lists if they wish to include or exclude medicinal products that are at risk of being counterfeited; Annex III and IV serve that purpose [1].

So, manufacturers who depend on the product portfolio that they have do not need to adapt all their products to bear the safety features required by the FMD. Wholesalers and healthcare institutions do not need to perform verification and/or decommission of medicinal products that do not bear the safety features. Therefore, this knowledge can ultimately influence the efficiency of the supply chain.

2.3. The Tendays' Rule

The DR introduces another important aspect that can impact the distribution and, especially, the returns for all of the supply chain: the 10-day rule from Article 13, which pertains to reverting the status of the unique identifier. From the moment the decommission is performed, the organization has 10 days to revert the unique identifier's status [1][5][6].

If that period elapses, the medicinal product can only be used in the respective physical location where it was decommissioned. In the case of wholesalers of the manufacturers decommissioning the products to supply some organizations, it is difficult to revert the status of the unique identifier from the moment the product is supplied, reach the organization, and decide to return it before the 10 days elapse. When manufacturers and wholesalers decommission medicinal products, possible returns from the organizations induced in article 23 of the DR is impossible.

This significantly impacts distribution in the entire supply chain. Furthermore, it can impact several organizations economically.

3. The Impact of FMD Implementation on the Supply Chain of a Hospital

A proposed supply chain is detailed with the relevant impact of the implementation of the FMD in operations. The support activities, regarding infrastructure for FMD implementation, and the need for extra human resources to implement automation, can be a solution and the procurement of an automated solution can be considered. Normally, companies provide automation provide scanners for the rest of the operations that cannot be done through automation. If not, procurement of 2D bar code scanners needs to be made [7][8].

Regarding human resources, if the option of automation is not pursued a recruitment process needs to be planned, and if automation is pursued, a training is normally done by the company that supplies the solution, but a possible plan for training needs to be implemented.

The IT department possibly has to adapt the dispensing software with the final interfaces of verification and decommission that are going to be delivered by the blueprint provider. If automation is implemented normally, new software comes with the solution that needs to be implemented and integrated with the dispensing software, so IT needs to liaise with the automation company if any issues arise with the dispensing operations.

The procurement of medicines can be done directly through the pharmaceutical industry that selects the products containing aggregation to reduce operational dispensing time [9][7]. Delivery to other hospitals can re-think other options

that can be pursued by accessing the costs of outsourcing or through tender processes to evaluate if there are more inexpensive ways of delivering to reduce the impact of expenditures in daily deliveries. Public tender processes for automation and possibly new scanners are needed.

The primary activities have the biggest impact in terms of adapting to the FMD regulatory requirements.

The inbound logistics continue to be done by the manufacturers. Nevertheless, change can be adapted to achieve better efficiency. Procurement can be done centrally but the dispatch of certain drugs can be done directly to the specific hospitals. Instead of being received by the case hospital centrally and then dispatched, this can transfer delivery costs to the supplier. Large infusions and medications that are recurrently used can be delivered from the industry, bypassing especially the ones included in Annex I of the DR. Also, manufacturers deliver medicinal products with the respective unique identifier in each medicine package. If automation is an option, inbound goods to the robot need to occur at this point.

In terms of operations, orders are going to be received in the same way; if automation or semi-automatic solutions are pursued, the operator needs to select the order and dispense it through the system. Decommission needs to be performed on goods outside of the solution. Other possible solutions for the dispensing operations are mobile scanners because of the pharmacy's infrastructure; the decommission of medicinal products at the dispensary eases the workflow and the distribution of medicinal products for the internal hospital and external ones [10].

To optimize the operations, there is a need to change the storage format; items that need to be authenticated should be close to the dispensary. The others included in Annex I of the DR can be stored in other locations so that the staff easily differentiate the products that need to be decommissioned or not.

Other regulatory implications for operating in a FMD environment are required. If a split pack is dispensed, the original container should not leave the dispensary until its entire content is used; the pharmacy cannot re-sell or supply other pharmacies with this product. For products sent to the wards and to external hospitals, the authentication can be done when the item is dispensed to the wards. Because this decommissions the serial code from the database, this needs to be the last step of the workflow. Manual authentication should also be performed in the last step by an accredited pharmacy technician or pharmacist [11]. Drugs manipulated in the cytotoxic clean room can also be authenticated in the dispensary before being distributed to this area.

Other recommendations in terms of operations achieved in other studies also impact the supply chain. A verification of the serial code can be done if necessary at any point of the supply chain, including in the workflow of the pharmacy. Medicines identified as falsified or recalled should be quarantined for inspection by suitably qualified professionals. Also, once a national medicines serial code repository is established and in operation, any medicine returned to the pharmacy, intended for re-use, should be verified. Authentication should be incorporated into departmental procedures. Incidents, when medicinal products leave a dispensary without authentication, should be classed as a dispensing error. If a medicine has been authenticated but is no longer required for the current dispensing process, there should be an option to return the unique identifier scanned to the national repository database [10]. Products that become non-compliant with FMD during the duration of the directive are considered in the system as unverifiable and their codes will cease to be active when the expiry dates are reached. It is the most economical solution because it is cost-free.

The outbound logistics can also be adapted. A better assessment of the resources, in terms of medicines, a hospital needs should to be made to understand if logistics can be changed. Large orders of electrolytes and high consumables can be delivered once a week by bulk, instead of being included in a daily order. The manufacturer can directly deliver medicinal products that are included in annex I of the DR to other hospitals. Orders should be done three times a week instead of daily to reduce the cost of logistic operations. The cost of possible outsourcing of logistics needs to be confirmed to investigate the impact on the overall costs of logistics. A secure supply chain to the wards and other hospitals under GDP is needed to be implemented to safeguard the authentication process [12].

Hospital wards deliver the drugs to the patients.

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