European Medicines Verification System data

GIRP reflections on potential use of data contained in the EMVS for shortages monitoring

Introduction

GIRP, the European Healthcare Distribution Association, is the umbrella organisation for pharmaceutical full-line wholesalers and distributors of healthcare products and services in Europe. It represents the national associations of over 750 pharmaceutical full-line wholesalers serving 33 European countries, as well as major international and pan-European healthcare distribution companies.

EMVO, the European Medicines Verification Organisation, of which GIRP is a founding member, is a Belgian non-profit organisation representing stakeholders united in securing the legal supply chain from falsified medicines. It has taken responsibility for advancing the formation of the European Medicines Verification System (EMVS) which has been set-up and managed in accordance with the Falsified Medicines Directive (FMD) and the Delegated Regulation (DR) laying down detailed rules on safety features. It ensures the implementation of a functioning, secure, interoperable and cost-effective system across Europe.

Even prior to the EMVS' inception and during more recent announcements from stakeholders and National Competent Authorities (NCAs) alike, the idea to use the EMVS for shortages monitoring is frequently mooted. Despite our continued efforts to highlight the limitations of the system for shortages monitoring, calls continue to be made that the system can be used for the purposes of monitoring medicines shortages.

FMD and DR provisions

Directive 2011/62/EC of the Parliament and the Council of 8 June 2011 amending Directive 2001/83/EC of the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products (Directive 2011/62/EC) and European Commission Delegated Regulation 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (Delegated Regulation) are the main legal instruments underpinning the establishment of the EMVS system.

During the process of reflecting on the potential use of data contained in the EMVS for purposes other than those defined in the legal framework, it is important to take full account of a number of important provisions of the Delegated Regulation (DR) - namely DR Art. 35 (h)[1] and Article 38[2] (see below).

---

[1] Characteristics of the repository system:
"In accordance with Article 38, its structure shall be such as to guarantee the protection of personal data and information of a commercially confidential nature and the ownership and confidentiality of the data generated when manufacturers, marketing authorisation holders, wholesalers and persons authorised or entitled to supply medicinal products to the public interact with it;"

[2] Data protection and data ownership:
"*1.Manufacturers, marketing authorisation holders, wholesalers and persons authorized to supply medicinal products to the public shall be responsible for any data generated when they interact with the repositories system and stored in the audit trail. They shall only have ownership of and access to those data, with the exception of the information referred to in Article 33(2) and the information on the status of a unique identifier.*

It should be noted that there are legal limitations to data access even for NCAs as set out the in the legislation. NCAs of the Member States can only access data contained in the repository systems for the following purposes: (a) supervising the functioning of the repositories and investigating potential incidents of falsification; (b) reimbursement; (c) pharmacovigilance or pharmacoepidemiology. Despite the legal limitations concerning data access even for authorities, which foresee full data access only investigating potential incidents of falsification, our analysis of the suitability of data included in the EMVS for shortages monitoring is based on the assumption of full access to all available data in the EMVS.

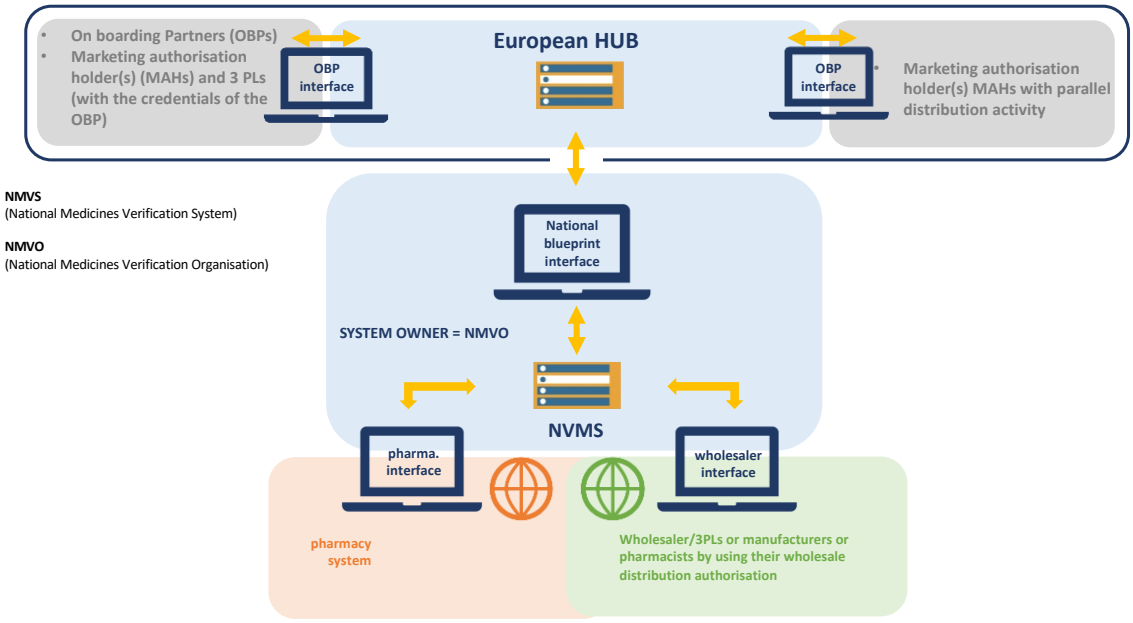
Background:

The following users are accredited to interact with the different elements of the EMVS (European Hub and National Medicines Verification Systems (NMVSs)):

- On-Boarding Partners (OBPs) for Marketing Authorisation Holders (MAHs) only interact with the European Hub.
- Manufacturers either interact with the system(s) through their MAHs and OBPs connections with the European Hub or in some cases in their capacity as a holder of a wholesale distribution authorization for their own products - they can interact with the respective NMVS.
- Third Party Logistic Providers (3PLs) or Pre-wholesalers interact either through the credentials of their OBP with the European Hub or in their capacity as holders of a wholesale distribution authorization. In the latter case they interact with the respective NMVS.
- Wholesale distribution authorization holders only interact with the NMVS.
- Pharmacies and persons authorised to supply medicinal products to the public only interact with the NMVS.
- National Competent Authorities (NCAs) interact with the EMVS within the context of their right to access data as established in Article 39 of the DR and the framework of the reports established for this purpose.

2. The legal entity managing the repository where the audit trail is stored shall not access the audit trail and the data contained therein without the written agreement of the legitimate data owners except for the purpose of investigating potential incidents of falsification flagged in the system in accordance with Article 36(b).”

Accredited EMVS users



The interactions of the above-mentioned operators generate the following data:

- OBPs upload Master Data, a combination of product data and pack data (i.e. serial numbers, product identification numbers, batch numbers, expiry dates, etc…), for their packs which also include an indication of whether it is a single or multi-market pack with an indication of the markets. In case of multi-market packs all countries in which the product can be marketed have to be included in order to root the data down to all the national repositories where the pack can potentially be dispensed.
- MAHs check upon batch release whether the safety features are operational (i.e. by checking one pack per batch).
- 3PLs or pre-wholesalers are required by MAHs to check one pack per batch upon receipt.
- Wholesale distributors will verify within the limits of their obligations packs upon receipt and may perform an additional verification on a voluntary basis (as recommended by EMVO) one pack per batch as a preventative measure to ensure that products delivered to pharmacies do not raise alerts at the point of dispense. Furthermore, wholesale distributors fulfil their obligation to verify packs, which are returned to them from their customers.
- Pharmacies, hospitals and other persons authorised to supply medicines to the public will verify and decommission the products at the point of dispense (unless exempted in accordance with DR Article 23);
- Member States can exempt a list of entities (Article 23 actors) from verifying and decommissioning the safety features and oblige wholesalers to do this on their behalf;
- The various reason for decommissioning (sub-states) will be visible in the system if either the pack is in hand or the serial number known (EMVO and NMVO stakeholders can only access this information for verification purposes – so the pack must be "in hand").
- National Competent Authorities (NCAs) have access to the system according to the pre-defined reports and will leave a trace in the system when running them, unless investigating a potential case of falsification.

System interactions of different stakeholders

Use Case	Initiator				
	Manufacturer	*Par. Distributor*	*Pharmacist*	*Wholesaler*	*Administrator*
Upload product master data	X	X			
Upload product pack data	X	X			
Recall batch	X	X			
Verify pack	X	X	X	X	
Dispense pack	X	X	X	X	
Decommission pack		X			
Export pack from EU	X	X		X	
Request report	X	X	X	X	X
Withdraw Product	X	X			
Mark pack as Stolen	X	X		X	
Mark pack as Destroyed	X	X	X	X	
Mark pack as Free Sample	X	X		X	
Mark pack as Sample	X	X	X	X	
Mark pack as Locked	X	X		X	

Assessment

During recent discussions amongst stakeholders and NCAs alike, the idea to use the EMVS for shortages monitoring is still frequently mooted.

Furthermore, in the 2018 European Commission "Summary of Responses to the Questionnaire on the Measures implemented in the Member States territories in the context of Article 81 of Directive 2001/83/EC" a high number of respondent Member States (17 in total) indicated that they are considering the use of the system for the monitoring of shortages.

In our view however, there are several noteworthy limitations / obstacles to this ambition:

<u>In relation to the OBPs:</u>

- Presently, not all packs are authenticated. Assuming that 97% of all packs are authenticated (at present, we are still very far from this scenario), and that products have a 3-years shelf life, this would mean that after 3 years we will have a volume representing 9% of a years consumption in the system implied as an inventory. This effect will remain until several years after when having achieved a "100% level" of authentication.
- Multi-market packs are uploaded in all potential destination markets and therefore counted multiple times without being available in these markets. Currently 9.5 %[3] of the uploaded packs are multi-

[3] Status July 2019

market packs and they on average target 2.43 countries. This would mean (once the system is fully populated) that medicines available on the European market would be over-estimated by about 2 billion packs.

- OBPs upload Master Data upon batch-release, regardless of whether the products have arrived in the destination market(s). OBPs may centrally stock serialized packs with uploaded batch numbers and decide at a later stage to send them to the destination market (for example based on assumptions on local markets' demand and quotas) or eventually decommission the packs and repackage them for another market.
- Some products are removed from supply for testing purposes – serial numbers are uploaded but the actual product will not or was never destined to reach the market. If we assume this is the case for only 1% of all packs, product availability in the market would be overestimated by 150 million packs.
- **In summary, the EMVS cannot provide a clear overview of national stock levels as the data contained therein will always be significantly higher than the number of packs actually shipped to the national markets.**

In relation to the wholesale distributors:

- Wholesale distributors only verify products when purchased from sources other than the MAHs, manufacturers, or designated wholesalers or when returned to them, or decommission products on behalf of Article 23 entities, when they either send medicines to destruction, or export them to third countries.
- The EMVS has not been set-up as a track and trace system and therefore no stock level data are available as a result of scanning. Introducing a track and trace system would have, as shown during the impact assessment prior to the remittal of the Delegated Regulation, a huge and largely disrupting impact on the business processes of pharmaceutical wholesalers and is therefore practically unfeasible.
- Not every pack will be scanned out of the system. Assuming that 97% of all packs get scanned and have a 3-year shelf life, the inventory level in the supply chain will be overstated by 33 days.

In relation to pharmacies/hospitals/persons authorised to supply medicinal products to the public:

- While the number of dispensed packs as well as the number of products decommissioned in total in their territory are available to the relevant NCA, the amounts are not representative of the national demand, especially in situations where the product is short in supply.
- If the level of authentication was to be used as indicator, this indicator would be very late in time and would not alert about problems of increased demand (as bird flu).
- National demand could only be evaluated through the number of prescriptions.

The current EMVS has not been built for the collection and publication of information on shortages. Without specific features of the information system for that purpose, the EMVS does not allow to identify the genuine reasons of supply difficulties that have a negative impact to patient care.

GIRP

European Healthcare Distribution Association
Brussels, September 2019