Background information on EVMS

The European Commission's approach regarding extended uses of EMVS for monitoring shortages

According to the European Commission, there are legal concern regarding the use of the EMVS to monitor shortages.

The Commission claims the EMVS does not receive all the information necessary to deal with shortages and that the system is not robust enough to provide all the data.

At the same time, EMA is working on a system, the European Shortages Monitoring Platform (ESMP), which should be able to provide this data in the future.

EFPIA statement

EFPIA questions the Commission statements that there are legal barriers to prevent the use of EMVS to monitor shortages.

There are inconsistencies in the Commission approach to the EMVS. While raising legal concerns for monitoring shortages, the Commission proposes the use of the EMVS for monitoring the implementation of the regulatory data protection prolongation for market launch provision - Article 67 (6) of the Medicines Directive. In so doing, the Commission indicates that the EMVS includes all data needed to check if medicinal products have been "released and continuously supplied into the supply chain in a sufficient quantity and in the presentations necessary to cover the needs of the patients in the Member States in which the marketing authorization is valid", Article 82 (1) of the Medicines Directive.

The 'pharmacoepidemiology' purpose referred to in the FMD Directive and Regulation includes the supply and use of medicines on a given territory. The extract of the data sets that MAHs regularly upload in the EMVS corresponding to the volume of prescription medicines placed on the various EU-27/EEA, fully meets the pharmacoepidemiology purpose referred to in Article 39 of Delegated Regulation 2016/161, enabling the monitoring of supply of medicines on the various EU markets. The extraction of end users' data, i.e. data generated by wholesalers, pharmacists and hospitals through their interaction with EMVS, would provide additional insights but would require an amendment of the legislation in order to include the monitoring of drug shortages among the explicit purposes for which Member States can use the information contained in the national medicines verification repositories.

Why EFPIA believes EMVS is a legally viable tool to monitor shortages

The EMVS was established under the EU Falsified Medicines Directive and its Delegated Regulation[1].

The EMVS contains unique identifiers (i.e., product code, serial number, batch number, expiry date, and where applicable, national reimbursement number) for all prescription medicines sold in the EU/EEA. The EMVS provides useful intelligence regarding the number of packs for all prescription products being supplied by manufacturers on the various EU markets, number of packs dispensed in national pharmacies, number of packs exported (and/or imported), as well as on the level of stocks present in the supply chain at country level. The real time information in the repositories can be analysed according to very granular time frames (per day, per week, per month etc.) as well as per region (postal codes).

1 https://eur-lex.europa.eu/eli/reg_del/2016/161/oj

That wealth of data would supplement information already provided by Marketing Authorisation Holders on manufacturing and quality related supply disruption to NCAs, and in providing information on causes and extent of shortages beyond manufacturing related issues, would greatly facilitate the detection and mitigation of genuine shortages. This is all the data required to correctly measure the supply of each medicine presentation on all EU markets and therefore monitor shortages.

EFPIA and Medicines for Europe are aligned on the use of EMVS for monitoring shortages.

That is why EFPIA proposes the following amendments to the Commission proposal:

Article 67 (6): Member States may, for the purposes of reimbursement, pharmacovigilance, pharmacoepidemiology, **shortages prevention and monitoring, electronic product information support or for the monitoring of marketing authorization holders and wholesale distributors supply obligations** ~~or for data protection prolongation for market launch~~ use the information contained in the repositories system referred to paragraph 2, second subparagraph, point (e).

EFPIA position on the European Shortages Monitoring Platform (ESMP)

We are committed to work constructively with EMA, EU and national competent authorities and relevant stakeholders to enable EMA to deliver on its reinforced role in crisis preparedness and management for medicines. EU Regulation 2022/123 of 25 January 2022 entrusts the European Medicines Agency (EMA) to set up an IT platform, known as European Shortages Monitoring Platform (ESMP), to facilitate the collection of information on shortages, supply and demand for medicinal products, to be operational on 2 February 2025. Article 9.1.c of the Regulation requires EMA to "*develop streamlined IT monitoring and reporting systems, in coordination with the relevant national competent authorities, that facilitate* ***interoperability with other existing IT systems*** *and IT systems under development until the ESMP is fully functional, on the basis of data fields that* ***are harmonized across Member State*****s**" (emphasis added).

The legislation, specifically Article 9.1.(c) and Recitals 19 and 20 of EU Regulation 2022/123, define that a significant amount of data will be required directly from each and every MAH. Most of this data is already provided by member companies to the EMVS as part of the business-as-usual processes involved with FMD and European serialisation. In addition, because of the nature of the EMVS as a common European platform for serialisation data across Europe, the EMVS can provide the market share information stipulated in Article 9.1.c of the above Regulation (see attached EFPIA & Medicines for Europe letter to DG SANTE/DG HERA/EMA of 25 January 2023 and DG SANTE response of 23 February 2023).

The EMVS data sets relating to the volume of prescription medicines placed on the various EU-27/EEA markets are uploaded **and fully owned by Marketing Authorisation Holders**, in accordance with Article 38 of Delegated Regulation 2016/161 of 2 October 2015. **In line with the Better Regulation Agenda**, EFPIA and Medicines for Europe will continue to advocate for the use of the fully owned, standardized and already trialed MAHs data contained in the EMVS to be used as input to the ESMP.
Any new IT system that EMA would impose on MAHs without having fully exploited the information and interoperability with existing systems would be entirely disproportionate from a technical and legal perspective, as well as run contrary to the Better Regulation framework and ethos.

Further information

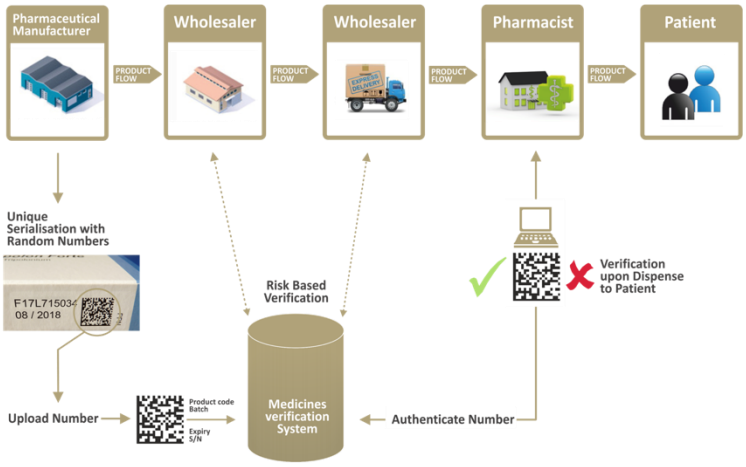
How the medicines verification system work in practice

In the interest of patient safety, the European Union (EU) adopted the Falsified Medicines Directive[2] (FMD) in 2011 to protect the legal medicines supply chain from the entry of falsified medicines. The FMD 2011/62/EU mandates the supply chain stakeholders to develop, implement and run a medicines verification system, to allow the verification of the authenticity of medicinal products.

How the medicines verification system work in practice

1. Manufacturers place a *unique* identifier on each individual prescription medicinal pack.
2. Manufacturers, prior to release of product into the market, upload the information contained in the Unique Identifier into the European Medicines Verification System (EMVS), the repository database (see further below).
3. Pharmacists are legally required to systematically verify – via the repository system – the authenticity of the unique identifier for each pack, before dispensation to the patient. Pharmacies will therefore only dispense a product if this product is verified (i.e. information is included in the EMVS and all data elements of the unique identifier correspond to the correct information uploaded by the legitimate manufacturer).
4. With a risk-based approach, additional verification will be carried by wholesalers along the supply chain. For example, returns or products received from other wholesalers historically represented a higher risk of falsification, therefore the legislation mandates wholesalers to systematically verify these two product categories.

Figure 1: The verification flow along the supply chain



Data availability in the European Medicines Verification System

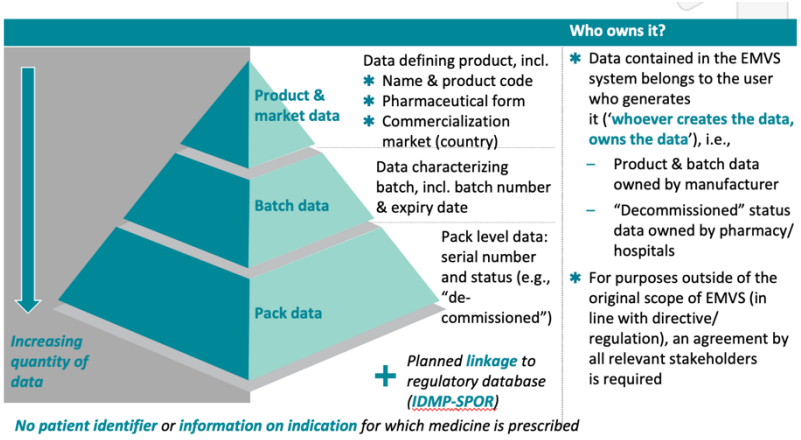
The **EMVS** was established by manufacturing/ marketing authorization holders in Europe, with the contribution of distributors and pharmacies (i.e. a stakeholder model). It is a **single-point-of-data entry**, with strict and robust technical requirements in place to make sure that only legitimate manufacturers (i.e. marketing authorization holders in Europe) can connect and upload data into the system and only pharmacies/persons authorized to dispense medicine to the public can decommission data for each pack. This means the **EMVS is also an end-to-end verification system, recording and reconciling the supply of each prescription medicine placed on the market with its respective dispensation to patients** (or subsequent removal from the supply chain: exported, destroyed, withdrawn etc.)

EU National Competent Authorities (NCAs) supervise the system and have access to all data contained in this repository.
The EMVS holds the following information (see also Figure 2):

[2] https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2011_62/dir_2011_62_en.pdf

• Product Code (plus national reimbursement number if appropriate)
• Batch number
• Expiry date
• Serial number
• Product Master Data
• Marketing Authorisation Holder
• Manufacturer details (the assigned manufacturer of the batch)
• Current status of the unique serial number, i.e., active or de-commissioned—in case of "de-commissioned" also the detail, e.g., dispensed, recalled, stolen, etc.;
• By whom/where a change of status has happened
• Time and date of preceding changes.

Figure 2: Data available in the EMVS



The requirement of recording the status of the unique identifier (when decommissioned by persons authorized to dispense medicines to the public) is equivalent to the generation of sales data on a continued basis (this requirement for decommissioning also applies to parallel traders and to wholesalers under some circumstances).

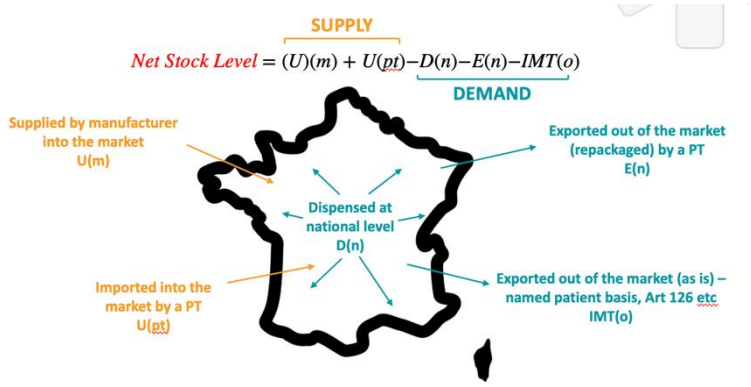
Where EMVS data meets supply chain reality

Considering all of the above, we believe that the data stored in the interoperable network of national repositories being set up in the context of the Falsified Medicines Directive and its Delegated Regulation on safety features can be used to provide additional intelligence to monitoring shortages.

This data could provide useful intelligence regarding the number of packs for all prescription products being supplied by manufacturers on the various EU markets, number of packs dispensed in national pharmacies, number of packs exported (and/or imported), as well as on the level of stocks present in the supply chain at country level. The real time information in the repositories can be analysed according to very granular time frames (per day, per week, per month etc.) as well as per region (postal codes). That wealth of data would supplement information already provided by Marketing Authorisation Holders on manufacturing and quality related supply disruption to NCAs, and in providing information on causes and extent of shortages beyond manufacturing related issues, would greatly facilitate the detection and mitigation of genuine shortages.

Figure 3 shows how a NCA can identify the Net Stock Level of available medicinal packs in its territory at any given moment.

Figure 3: Net Stock Level calculations



NS(n) = net stock level at national level

U(m) = number of unique identifiers uploaded into the national market by the original manufacturer (corresponding to the number of physical packs released on the market)

U(pt) = number of unique identifiers uploaded into the national market by parallel trader(s) (corresponding to the number of physical packs imported in the national market)

D(n) = number of unique identifiers decommissioned at national level by persons authorized or entitled to supply medicinal products to the public, typically community pharmacists, hospital pharmacists or in some cases wholesalers (on behalf of Article 23 actors) (corresponding to the number of physical packs which have been dispensed to patients within the territory)

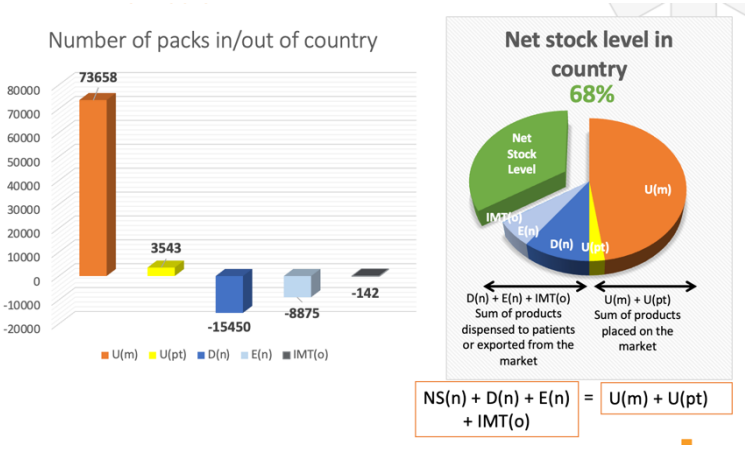
E(n) = number of unique identifiers decommissioned for export at national level by parallel traders (corresponding to the number of physical packs exported from the national market)

IMT(o) = number of unique identifiers destined for the national market but decommissioned in other markets via the Inter Market Functionality of the system.

Proposal for Collaboration Between National Competent Authorities and Manufacturers in Order to Proactively Monitor Country Stock Levels

Continuously monitoring the Net Stock Level of a medicinal product in a Member State allows for proactive measures to be taken both by NCAs and by manufacturers to avoid the national Net Stock Level to fall in negative territory. For this purpose, we propose the creation of a "dashboard" type early-warning mechanism (see Figure 4 for an example of such dashboard) whereas a NCA would notify the manufacturers once a certain minimum threshold is reached at national level (for example, Net Stock Level reaches 20%) so that the manufacturer can take actions to pre-emptively re-supply the respective market. As the data access rules within the system are strict, this early warning notification system can only be triggered by NCAs (as they have access to the full data) and be exchanged only at aggregate level. Depending on the type of product different thresholds can be set for different medicines, in collaboration with the original manufacturer (depending on manufacturing lead time, availability of stock in other markets, etc.).

Figure 4: Dashboard for monitoring net stock level



Issue of Multimarket Packs

Some medicinal products are released for sale in multiple markets at the same time (and are packaged according to the packaging requirements—for example the language of the patient information leaflet—of multiple countries). In such cases, a manufacturer will upload the unique identifiers of the

batch released for sale into the repository systems of the countries in the multi-market pack cluster. When a medicinal pack is decommissioned for dispense in one market then the unique identifier is automatically decommissioned in all markets. Therefore, there is a need for collaboration and data exchange between the NCAs in the respective markets of the cluster so that the data can be interrogated and aggregated for all markets of the cluster. The formula outlined above still holds but will show the net stock level across the markets in the cluster.

Issue of Multi-Source Products

Currently the data in the system can only be identified according to Product Code (corresponding to a physical Stock Keeping Unit). While this is straightforward for single source products (typically on-patent medicines) the analysis is further complicated in the case of multi-source products (typically off-patent medicines) as NCAs need to analyse the net stock level in parallel for multiple medicinal products which are deemed interchangeable for the treatment of a specific condition in order to identify the risk of shortage. Currently this can be done in a manual way by running and aggregating multiple reports, however, once the connection with the EMA IDMP/SPOR database, NCAs will have the possibility to run reports on an ATC class level. Such reports would automatically assembly the required data for multiple products in a specific class.