Use of existing IT data systems to monitor and provide transparency of the supply chain

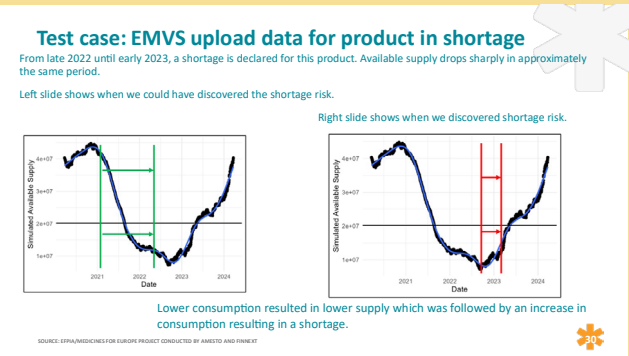
Medicines for Europe believes that to **monitor and predict medicine shortages, the Council should include in the revision of the pharmaceutical legislation the use of existing data**, and especially real-time data of the **European Medicines Verification System (EMVS), which:**

* **is an EU wide system, already allowed to be used in the Directive on art 82.1** for monitoring the supply status of products for data protection prolongation for market launch.
* Needs to be linked with the **European shortages monitoring platform (ESMP)**, where 70-80% of the information required from MAHs is readily available from EMVS.
* Includes data with the potential to follow when and how various medicinal products/INNs are placed on which markets and in which quantities, to **constantly monitor** manufacturers' market shares as well as the rate of their consumption at national level, as mentioned by the Norwegian study on "Investigation into prescription drug shortage prediction using the European Medicine Verification System database" (attached to this paper).
* ***"Will help authorities in Europe,*** *by using extensive logistics data, to better monitor supply chains for high-demand medications,* ***to stave off supply bottlenecks*** *when distributors coordinate the delivery of remainder stock, and intervene early on to make these chains more resilient*", "Our model would … also work with the extensive product data collected by the European Medicines Verification Organization and stored in the European Medicines Verification System," as described in the ETH Zurich researchers.

PRACTICAL CASE - SHORTAGES OF ANTIBIOTICS COULD BE PREVENTED IN NOVEMBER 2022

Looking at the European supply for certain antibiotics during the period 2021-2024, with the availability of only the manufacturers data (supply data) we could have predicted those shortages much earlier. It is important to consider that:

* By adding the decommissioning data of the EMVS (consumption data) there would have been close to 100% accuracy of the data. Even so, the supply data provides a very accurate picture of the situation.
* The graphs show very clearly the decline in supply (and demand) throughout 2021 and early 2022 and a sudden increase in demand at the end of 2022/early 2023. The slide on the right with the red bars shows when shortages were formally detected. The slide on the left with the green bars shows how much earlier the shortage could have been detected. These few months could have enabled supply chains to ramp up production to prevent shortages or significantly reduce them.
* The advantages of using this digital, automated data are massive compared to the current approach of compiling manual excel sheets which will lead to errors and compatibility problems. EMVS is live with up to the minute supply and demand data. It can be consolidated per manufacturer or country. The use of artificial intelligence algorithms could be used to provide even more precise data to predict and mitigate shortage risks. This data already exists, is paid for by the industry and could feed directly into the future EMA/HMA ESMP.



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Today the EMA and national regulatory authorities could already increase the visibility and transparency of the supply chain by using the data of existing IT systems, such as the data stored in the interoperable network of national repositories being set up in the context of the **European Medicines Verification System (EMVS),** introduced by the Falsified Medicines Directive (2011/62). The data stored in the interoperable network of national repositories being set up in the context of the Falsified Medicines Directive (Directive 2011/62/EU) and its Delegated Regulation 2016/161/EU on safety features can be used to provide additional intelligence to monitor 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, the number of packs dispensed in national pharmacies, the 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).

This wealth of data would supplement information already provided by Marketing Authorisation Holders on manufacturing and quality-related supply disruption to National Competent Authorities, and in providing information on the causes and extent of shortages beyond manufacturing-related issues, would facilitate the detection and mitigation of genuine shortages. This system would also facilitate cooperation and solidarity between Member States when a shortage occurs by giving visibility to the availability of stocks across the Member States.

As well as the letters and workshops that Medicines for Europe and EFPIA are sharing with the European Commission, it is important to highlight the compelling benefits of implementing this system in the context of shortage prevention which are:

* harmonised information collected across Member States.
* 70% / 80% of the data required in the European Shortages Monitoring Platform required by the EMA extended mandate Regulation are already available in the EMVS.
* EMVS data has the potential to follow when and how various medicinal products/INNs are placed on which markets and in which quantities, to constantly monitor manufacturers' market shares as well as the rate of their consumption at national level.
* Authorities can easily extrapolate the market share of the product: the market share will be a calculated value based on the percentage provided to the market by a given manufacturer's product from a total provision of the same product across all manufacturers. The ATC codes will give us the 'like product' relationship and the dose form, strength and pack size will enable us to drill down on the market share to specific forms/strengths or pack presentation.
* More details on how EMVS will work to prevent medicine shortages can be found in the following article: "Medicine Shortages: From Assumption to Evidence to Action - A Proposal for Using the FMD Data Repositories for Shortages Monitoring".
* The Norwegian study on "Investigation into prescription drug shortage prediction using the European Medicine Verification System database" conducted to assess whether the types of data available in the European Medicine Verification System (EMVS) database allow for automatic detection and/or prediction of drug shortages.

> *"We found that it is possible to detect an impending shortage based on the currently known numbers of active packs and manufacturer uploads of new batch information." "The shortage*

detection, which, when extrapolating consumption, will cross the shortage threshold and no new uploads of batch information have been made. Although our analyses of the predictive potential were somewhat hindered by the small sample data, we found that the data types should allow for prediction of future consumption as well as times of uploads by manufacturers. Together, these would allow for drug shortage prediction further into the future rather than only a detection regime to permit improved patient supportive stock management regimes to be developed."

Finally, it is important to stress some additional points:

- **Multi country packs**: The European Medicines Verification System could provide a proxy to address the problem of multi-country packs, notably by looking at historical check out patterns.

- **National pharmacy systems:** In several EU countries, systems exist at retail pharmacy level. However, these systems have several limitations.
    - 1) They primarily identify supply chain problems related to logistics, rather than actual shortages
    - 2) There does not seem to be any wish to have a common, interoperable EU-wide system
    - 3) Hospital pharmacies are not connected, therefore they give a very limited picture of the supply chain and, consequently of medicine shortages.
    - In this regard, Medicines for Europe has analysed the Spanish CISMED systems, more detailed information can be found in the Annex below.

- **Volume and complexity of the data in question**

We note a misunderstanding in discussions with the EU institutions regarding shortage reporting primarily because they seek information on this from the European medicines agency (EMA) and not from the national medicine agencies. The EMA historically only monitors centrally approved medicines which is a very small share of the total medicines on the market. In addition, the products have only one European licence whereas most medicines have multiple national licences. Here are some numbers which indicate the complexity of the issue:

- 10 000 000 000 (10 billion) prescription packs are dispensed every year across the EU according to EMVO. The current shortage reporting requirements are based on manual excel sheets supplied from marketing authorisation holders to national medicine agencies and the EMA. This is incredibly inefficient in relation to number of packs dispensed. Moreover, in practice there is no way to understand a shortage or to ensure EU solidarity (re-allocation of stock from a country or a company with excess stock to a country in shortage.) without a digital analysis of such large stock flows. This is impossible. The EMVS is a digital system which contains all this stock flow information per member state. The information can easily be extracted or formatted for the purpose of shortage prevention and shortage mitigation. The use of these data would give national authorities more visibility when needed during health emergencies and for EU solidarity. The European Commission has granted national authorities the right to restrict trading in a shortage. However, Member states

are prevented from exercising this right because they cannot in practice monitor these legally restricted activities.

- 400 000 licences (marketing authorisations) are regulated by EMA and mainly by national medicine agencies. This explains why it is so difficult, without digital data, to understand the number of shortages per member state in the EU. Once again, the EMVS solves this dilemma because the uploaded medicines data include the marketing authorisation and individual ID (number) of the medicine. It is therefore possible to read the data across member states and the Union. This data could also be linked to a future EMA database (IDMP-SPOR) which will contain information regarding each licenced medicine in the Union. This would in practice link the two data systems so that national authorities and EMA could access the data directly for shortage purposes rather than through a GUI (a webportal) or through EMVO reports. This would make shortage monitoring and mitigation an automated process based on actual batch releases to the market and real consumption data. This would mean a perfect picture of supply and demand on both national and EU markets.

Annex - EXAMPLE – CISMED SYSTEM (ES)

CISMED (Information Center on the Supply of Medicines) was established in 2014 by the Spanish General Pharmaceutical Council. A **community pharmacy generates information that will allow the Provincial Pharmacists' Chamber to have data on the supply of medicines in its province** and, once the data is sent to the General Pharmaceutical Council of Spain, **consolidates it at national level and makes it available to the Regulatory Bodies** so that they can detect and mitigate future shortages in advance.

Information is registered in the system when an order for goods has been denied by all wholesalers that the pharmacy works with and the pharmacy receives the response "there is no stock."

The main weaknesses are the following:

- **The medicines flagged as having supply problems can relate more to logistical shortages than to actual shortages**

Information contained in the system is: the national product number; the number of units of each medicine within an order that has not been supplied to a pharmacy; name of wholesalers that have not been able to serve the orders; any other information about the activity of the pharmacy. Because the pharmacists are the only source of data, it is not clear where the problems are originating and how to address them (all authorities could do would be to contact the wholesalers to identify the source of the problem)

- **There does not seem to be any wish to have a common system**

The EU, through Digital Health Europe, funded a "Twinning" programme to explore the feasibility and usefulness of exchanging comparable information on shortages generated by pharmacies across borders. France, Portugal, Italy, and Spain participated.

However, the conclusion from this pilot was that "the exchange based on common standards is possible and useful to do at a supranational level **based on existing pharmacy reporting systems in place**." -> this means that there would be multiple systems across the EU.

- The database is not connected to the Spanish Agency of Medicines

The role of NCAs, which receive EMVS reports should be leveraged.

- In 2020, **9101 pharmacies participated (around 1/3 of pharmacies)**
- **Hospital pharmacies do not seem to participate**

This gives a very limited picture of shortages.