The European Medicines Verification System Explained

Revision History

Version Date	Version	Reason For Changes
O4-APR-23	1.0	Initial Document

The European Medicines Verification System (EMVS) explained:

The European Medicines Verification Organisation (EMVO)

emvo • European Medicines Verification Organisation

Rue du Commerce 123, 3rd floor, box 2 • B-1000 Brussels • +32 (0) 2 657 51 71 • www.emvo-medicines.eu • VAT BE0638 801 022

Table of Contents

1. Introduction to the EMVS

The European Medicines Verification System (EMVS) is an end-to-end verification of medicines, designed to ensure patient safety. This is done by preventing falsified medicines from entering the legal supply chain.

The EMVS is the first initiative of its kind that is stakeholder-driven. It is a multi-stakeholder undertaking; devised, funded and governed by the stakeholders of the pharmaceutical sector. The stakeholders of the pharmaceutical sector have been mandated by the European Commission to establish the EMVS based on the Falsified Medicines Directive (Directive 2011/62/EU) (FMD) and the associated Delegated Regulation (EU/2016/161) on safety features. The legislation dictates that a new system of verification for medicines be implemented; and thus introduced requirements for two new safety features on medicinal product packs. These features "allow the verification of the authenticity and the identification of each individual pack" in the supply chain of medicinal products in Europe. It is important to note that the EMVS covers mainly prescription medicines for human use. For more information on the FMD and the associated Delegated Regulation, please consult information released by the European Commission. A link to the FMD can be found here and one to the Delegated Regulation can be found here. The European Commission also maintains a Q&A document on the Safety Features for Medicinal Products for Human Use which is found here. This document is regularly updated by the European Commission.

According to the legislation, pharmaceutical manufacturers and parallel importers are required to print a Data Matrix code on the medicine pack. The code incorporates a Unique Identifier (UI). Pharmaceutical companies and parallel importers must also apply an anti-tampering device to the outer packaging for each individual sales package.

The UI consists of a random serial number unique to each pack and a product code. The Data Matrix carries the UI, which also includes information about the batch number and expiry date, and in some countries, the national reimbursement number.

At the point of dispense the medicine will be scanned, checked and verified for authenticity against a national (or supranational) repository. The UI may also have been checked at other points during the supply chain. Wholesale distributors following a risk-based approach are required to carry out verification checks of the UI when they receive packs from sources other than the marketing authorisation holders, manufacturers, or designated wholesalers. If the UI on the pack matches the UI in the repository, the pack is decommissioned and supplied to the patient. Otherwise, if there is a warning related to this pack, then the system will highlight this as an exceptional event and the package will

not be supplied to the patient[1]. An investigation then needs to be carried out to determine whether the pack has been tampered with.

1.1 Structure and compliance

The structure of the EMVS is divided into the European level, represented by the European Medicines Verification Organisation (EMVO), and the national level, represented by each National Medicines Verification Organisation (NMVO). Each Member State of the EU[2], EEA countries and Switzerland have their own NMVO. EMVO is responsible for setting up and running of the European Hub (EU Hub), the governance of the EU Hub and for assisting pharmaceutical companies in establishing their connection to the Hub.

The main purpose of the European Hub is to serve as the principle location for the storage of master data and as a gateway for the transmission of pack-related data to the national systems. Furthermore, data reconciliation on repackaging activities, i.e. maintaining a link between original and repackaged product batches, is exclusively performed on the EU Hub.

The NMVOs are responsible for establishing and operating a national system in their territory, which will connect to the EU Hub on one end, and to all the end-users (pharmacies, hospitals etc.) on the other end.

All actors among the pharmaceutical supply chain have duties and responsibilities under the European legislation. Marketing Authorisation Holders (MAH), also referred to as On-boarding Partners (OBPs) (this distinction will be clarified later on in this text) have to proceed with an On-boarding process to the EMVO and develop their connection to the European Hub in order to be compliant with the FMD. MAHs are also requested to conclude a contract at national level for the countries (markets) in which they are commercializing their products.

[1]To allow a smooth transition to the FMD, some countries have opted to enter a "stabilisation" period, during which packs triggering alerts can still be dispensed to the patients, at the discretion of the pharmacists.
[2] Italy and Greece have been granted an optional 6-year implementation period from the 9 February 2019 and are thus making make use of the longer implementation period.

2. Entities within the EMVS

2.1 European Medicines Verification Organisation (EMVO)

EMVO is responsible for the European Medicines Verifications System (EMVS) in accordance with the Falsified Medicines Directive (Directive 2011/62/EU) and the delegated Regulation (EU) 2016/161. EMVO's task is to ensure the implementation of a functioning, secure, interoperable and cost-effective medicines verification system across Europe.

EMVO is the manifestation of the legislation which references to the stakeholder led model and which requires industry to set up and finance the system. Its founding members are EFPIA (the European Federation of Pharmaceutical Industries and Associations), Medicines for Europe (the European Generic and Biosimilar Medicines Association), PGEU (the Pharmaceutical Group of the European Union), GIRP (the European Healthcare Distribution Association) and Affordable Medicines Europe (the European parallel distribution industry). HOPE (European Hospital and Healthcare Federation) and EAHP (European Association of Hospital Pharmacists) are also affiliate EMVO stakeholders.

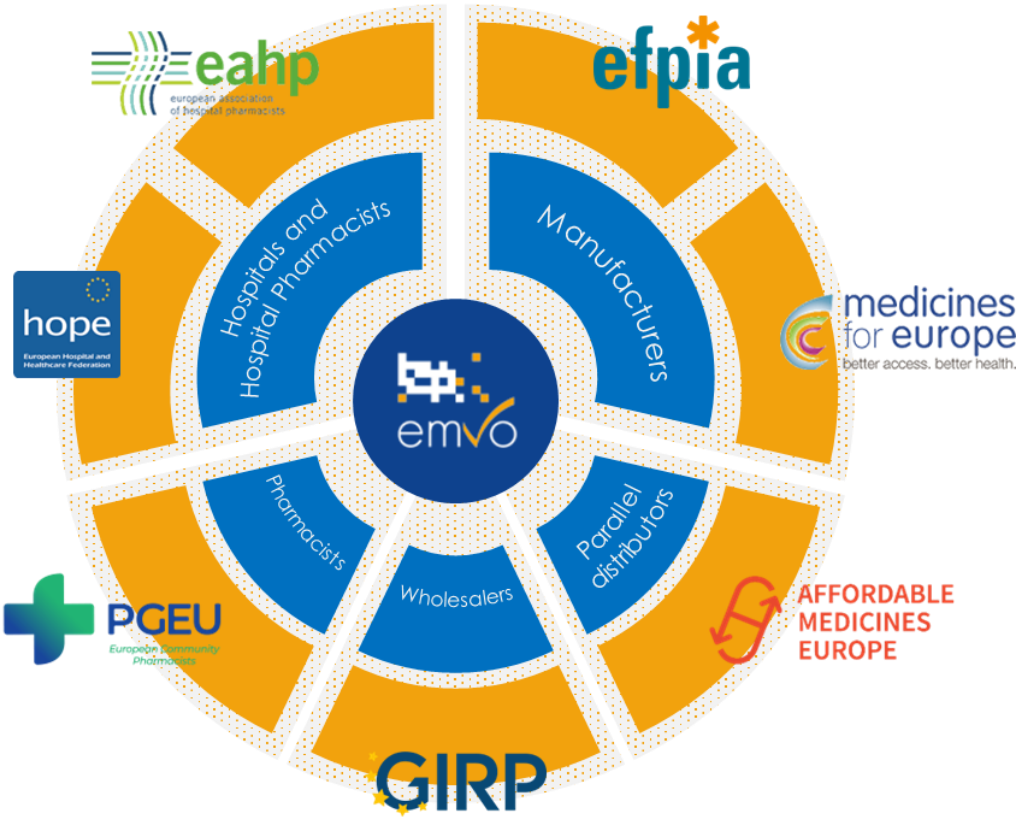

Figure 1 – Overview of the EMVO Stakeholders

EMVO is primarily responsible for setting up, running and governing the EU Hub, as well as supporting the establishment of NMVOs and NMVSs. In addition, EMVO provides a user-friendly web-based "EMVO On-boarding Partner Portal (OBP Portal)" to assist the On-Boarding Partners to connect to the European Hub (see section 2.3)

2.2 National Medicines Verification Organisations (NMVOs)

Each country must implement its own National Medicines Verification System, set up and managed by the NMVO. Likewise EMVO, and as foreseen in the DR, the NVMO should follow the same governance and financing model: the stakeholder led model and industry financed.

Article 31 of the DR requests that the national repository system shall be set up and managed by a non-profit legal entity which is established by manufacturers and marketing authorisation holders. Wholesalers and pharmacists are entitled to participate in the NMVO on a voluntary basis. National Systems can be implemented and operated as a

"Blueprint system" supported by harmonized standards and benefiting from efficiencies based on the documents listed below:

- the template of national Memorandum of Understanding (MoU).
- the template statutes of an NMVO, which notably provides for the inclusion of all stakeholders who are willing to participate and for a fair and balanced voting rights between them.
- the EMVO User Requirement specifications (URS) defining all the technical functionalities.
- the requirements for the European Medicines Verification System (URS litet), including the cost allocation model which set out the rules how Marketing Authorisation Holders and Parallel distributors will be invoiced for using the system.

A full list of NMVOs can be found here.

2.3 On-Boarding Partners (OBPs) and Marketing Authorisation Holders (MAHs)

Each pharmaceutical company, whether they be a manufacturer or a parallel distributor, is ultimately responsible for complying with the conditions set out by the FMD and Delegated Regulation. The EMVS provides a system under which each pharmaceutical company can be compliant with the legislation, however any failure to do so is the sole responsibility of that company.

An OBP provides a single entity from which national systems can obtain revised/new product serialisation data. In order to on-board to the EU Hub, OBPs are requested to sign the mandatory Participation Agreement (PA) with EMVO as well as to pay an entrance fee directly to EMVO. It is very important to note that a single OBP is allowed to upload data on behalf of one or more than one MAHs only if they entities are affiliated, as per EMVO's definition[3].

In terms of the legal relationship that exists between EMVO and a pharmaceutical company, it is the OBP which is the contracting party and it is the OBPs who conclude an agreement with EMVO (the Participation Agreement). The OBP should be legally authorised to do this on behalf of the MAH(s) it represents.

Before starting the technical on-boarding process to set up their connection to the EU Hub, each OBP must complete the contractual on-boarding, in which a legitimacy check is performed on the company to ensure only legitimate parties

[3] As defined in the Participation Agreement, Affiliate means, in relation to a Party, any other entity Controlling, Controlled or under common Control with the Party. "Control" and its derivatives mean either the holding, directly or indirectly, of 50 % or more than 50% ownership interest or the statutory or de facto authority to exercise a decisive influence on the appointment of the majority of directors or managers or the orientation of policy provided it is, at EMVO's own absolute discretion, sufficiently proven.

are connected and upload data to the EU Hub. It is also during the contractual on-boarding that the OBP must pay the one-off fee to EMVO depending on the number of MAHs they will represent. Once this has been completed, then an OBP is able to upload the required data from its UIs to the European Hub.

It is important to note the difference between a Marketing Authorisation Holder (MAH) and an OBP. Under the architecture of the EMVS, a Marketing Authorisation Holder (MAH), or a group of MAHs can connect to the European Hub via an OBP. An OBP is a legal entity, set up in order to connect with and upload data to the European Hub, on behalf of a single/ more than one MAH(s).

Alongside completing the on-boarding process with EMVO, MAHs must conclude a contract at national level with the relevant NMVO(s) and pay an entry and an annual fee. The fee model depends on each NMVO. Therefore, EMVO recommends consulting our most up to date Fee Models Presentation and Fee Models Table to identify the applicable fees. These can be found on EMVO's Knowledge Database, under "*Documents Overview*" > *"National Medicines Verification Organisation (NMVO)*". Any further details on this point must be taken up directly with the relevant NMVO(s).

2.4 End-users

End-users are any wholesaler, pharmacy or other person authorized or entitled to supply medicinal products to the public as foreseen under the EU Directive on Falsified Medicines and the Delegated Regulation or as otherwise foreseen under applicable law. End-users are connected to the European Hub through the National Systems.

As mentioned in section 1, end-users at the point of dispense will scan the medicine to check and verify its authenticity against a national (or supranational) repository. If the UI on the pack matches the UI in the repository, the pack is decommissioned and supplied to the patient. Otherwise, if there is a warning related to this pack, then the system will highlight this as an exceptional event and the package will not be supplied to the patient.

The UI may also have been checked at other points during the supply chain. Wholesale distributors following a risk-based approach are required to carry out verification checks of the UI when they receive packs from sources other than the marketing authorisation holders, manufacturers, or designated wholesalers. If you are interested in learning more about designated wholesalers, please refer to EMVO's Knowledge Database and the dedicated webinar here.

3. Processes of the EMVS

3.1 How does the process of the EMVS work? What steps are taken to ensure a pharmaceutical product is not falsified?

As was explained in the overview of the EMVS, the new features of the EMVS fall into two categories; safety features and the establishment of the EU Hub, where the Unique Identifier (UI) of each pack is uploaded and stored. The EMVS enables the operation of the Point-of-Dispense (PoD) verification concept. The EMVS has two major components as shown in Figure 2:

1. **European Hub (operated by EMVO)**:
   - Single entity for transmitting product serialization data from manufacturing organizations, including parallel distributors.
   - Centralized source for national systems to obtain revised or new product serialization data.
   - Storage of manufacturing master data and master data related to connected national systems.
   - Systematic marking of multi-market packs as "decommissioned" in all affected markets after being sold in one market.
   - Capability for manufacturers and parallel distributors to decommission packs.
   - Verification gateway for parallel distributors to access source market repositories for authenticity verification.
   - Central point for transmitting product recall information in addition to established recall procedures.
   - Mechanism for reconciling exported and imported products at a dose level when repackaging or relabeling by parallel distributors.
   - Central point for managing alerts that cannot be handled solely at the national level, such as issues with multi-market packs in different countries, including appropriate responses to manufacturers or regulatory authorities.

2. **National Blueprint Systems (operated by the NMVOs):**
   - Holding the relevant product serialization data for the national market.
   - Receiving revised/new product serialization data from the EU-Hub.
   - Serving as the verification platform for pharmacies or other registered parties such as wholesalers and hospitals to certify the authenticity of a product.
   - Serving as the platform for wholesalers in the case of member states application of Art. 23 DR, to mark a product pack as decommissioned prior to handing it over the patient.

• Serving as the platform for wholesalers to mark a product pack as “decommissioned” e.g. ‘exported out of EU’

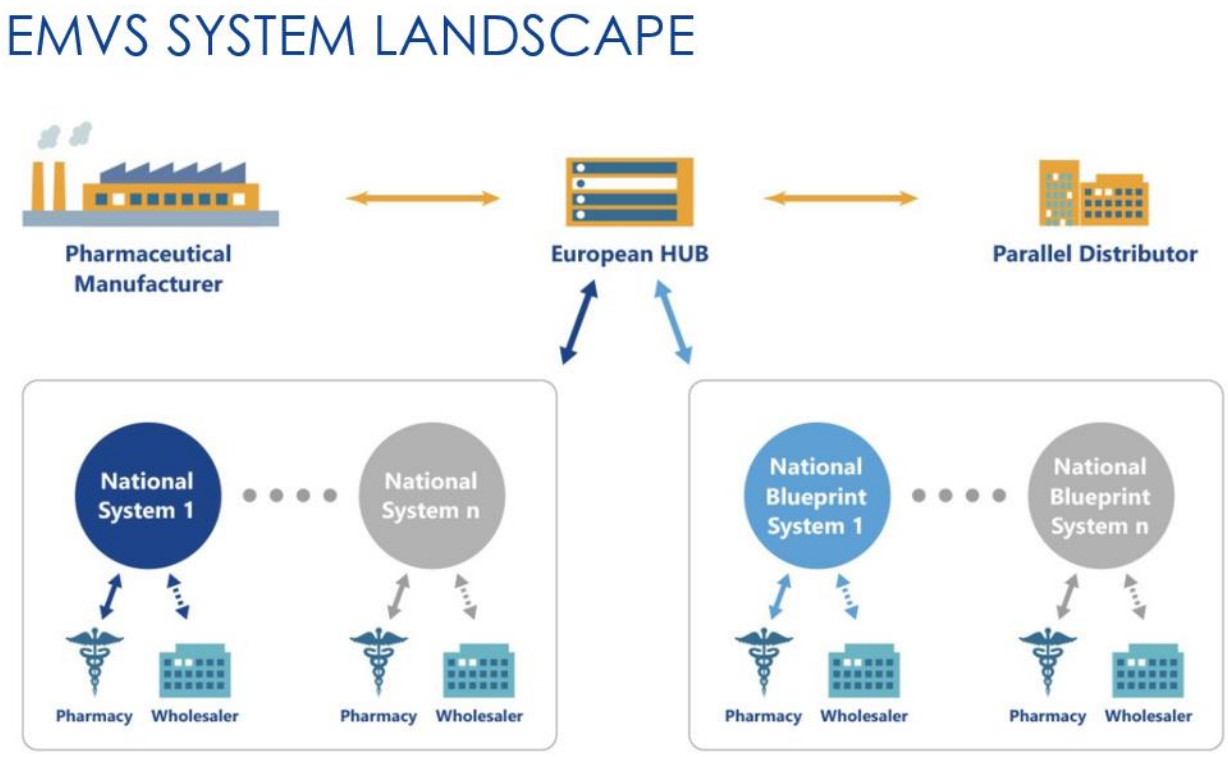

Figure 2: EMVS landscape

3.2 What does the end-user (pharmacist, hospital, wholesaler) do?

The pack is scanned by the end-user at the point of dispense. When a pack is dispensed at a pharmacy, the pharmacist scans the data matrix on the pack. The scanned information is then compared to information held in the national system.

If the information taken from the UI code matches the information held in the system, and additional criteria such as “product not decommissioned” are fulfilled, then the pack is dispensed to the patient. Simultaneously, the status of the serial number of the pack is set to “decommissioned/supplied”. This means that a record of the dispense of the pack to the patient will be kept; to check against potential future falsifications.

Should the information on the code differ from that in the repository (in particular “serial number does not exist in repository”) or the status of the serial number is already “Decommissioned”, the pack authenticity cannot be verified

and an alert will be raised. Therefore, the pack must not be dispensed to the patient. This may be due to a process error in the supply chain; but it may also mean that there has been a falsification.

An investigation for the reason of the alert will be conducted involving different actors in the supply chain. Wholesale distributors following a risk-based approach as laid down in the legislation carry out verification checks of the UI when they receive packs from sources other than the marketing authorisation holders, manufacturer, or designated wholesalers. In some countries, wholesaler distributors are required by national legislation to decommission packs which they supply to dispensing entities which are not operating within a healthcare-institution(s) e.g. research institutions, prisons, dental practices, etc.

3.3 Status of packs prior 9th February 2019

Packs put into circulation prior to 9th February 2019 can remain on the market until the end of their expiry date. These medicines are still safe and have been produced under a regulatory framework ensuring the safety of patients.

4. Alerts within the EMVS

4.1 What is an alert? At what point is an alert triggered?

An error describes a situation where the normal operation of the EMVS is interrupted with every error being noticed by the system. Within the EMVS there are 5 levels of error; going from level 1, in which the system can handle the situation by itself, to level 5, in which system administrators and external stakeholders are informed of the situation. Please refer to the document "EMVS Alerts and Notifications" here which further describes the alerts and notifications provided by the EMVS to stakeholders, including the NMVOs, EMVO and the OBPs. The document describes the alerting requirements specified by the European Stakeholders for systems that operate as part of the EMVS.

An **error** is the term to describe the actual problem within the system. An **exception** describes the informing of the actor interacting with the system that there has been an error. An **alert** describes the process of informing actors other than the one who was interacting with the system when the error was detected. Thus, every alert is an error, but not every error causes an alert.

The external stakeholders who are informed in the event of a level 5 alert are the NMVO, the OBP (MAH), EMVO and the National Competent Authority (NCA).

4.2 What are some examples of an alert? What happens when a single alert is triggered?

- **End-user scans a pack. The pack has already been dispensed in another pharmacy:**

As a first example, the end-user (pharmacy, hospital or wholesaler) scans a pack. The pack has already been dispensed by another end-user (pharmacy, hospital or wholesaler). This causes an exception to be raised by the national system to the end-user. The national system then raises an alert to the end-user, the NMVO of that country, and the EU Hub. The EU Hub then processes the alert and raises its own alert to the OBP, and to EMVO.

- **Another example of an alert is in relation to an Inter-Market Transaction (IMT)**:

The end-user scans a pack, the information from the pack is then sent to the respective national system for verification. This particular pack is not recognised by the national system, which then raises the error with the Hub to verify if the product exists in another national system and is available to sell. The EU Hub will then conduct the Inter-market Transaction and will check if the pack has been registered with another NMVS and can be dispensed to the patient. Depending on the answer that is given back, the product is dispensed or not dispensed by the end-user. However, if the EU Hub receives a response from an NMVS that the pack has already been dispensed in its market, this NMVS will raise its own alert, and not the initial alert.

4.3 Harmonization of alerts

The harmonisation of alert handling requires perseverance and resilience from the National Competent Authorities. Harmonisation of alerts handling is not only vital for the timely handling and reduction of alerts, but it will also ensure that no patients are left without their medicine due to a raised alert – a challenge recognised and faced by the end-users.

To support all the users in this task, EMVO together with the support of the NMVOs, prepared a "Best Practice on Alert Handling" guide which aims to minimise alerts due to technical, data or procedural errors generated in the EMVS. Please consult the document here.

It is important to highlight that current practice in relation to alert handling in some countries may differ to what appears in the guideline due to national legislation or NCA requirements (whether FMD-specific requirements or requirements encompassing FMD and non-FMD aspects of medicines safety) or stakeholder agreement, for example, responsibilities for investigating alerts, quarantine periods for packs under investigation, etc.; in these cases, the relevant national requirements must be followed by end-users, MAHs and the NMVO.

Notwithstanding that national variations currently exist, the aspiration is that this document will provide a basis for progressing dialogue with NCAs and stakeholders in each country towards harmonisation of requirements across Europe. It is also hoped that it will be useful for countries that have not yet defined national procedures for alert handling.

4.4 European Alert Management System (EAMS)

The EAMS went live on 9th February 2023, and it is an EMVS project which involves representatives from all EMVS stakeholders. The EAMS is composed of an AMS Hub and National AMSs. The ultimate goal of the EAMS is to maximise the efficiency of alert management in the EMVS by supporting EMVS users (end-users/OBPs/MAHs/NMVOs) to follow-up on alert investigation. It offers users the capability to:

1. Manage, track and document their own alerts. It provides real-time updates, available 24/7, on the status of alerts based on information entered by the end-user, MAH/OBP and/or the NMVO;
2. Quickly communicate with other parties (involved in an alert) about an alert, while preserving end-user anonymity vis-à-vis the MAH/OBP, a core principle of the EMVS. This removes the need for rounds of emails or phone calls;
3. Request (MAHs/OBPs) and upload (end-users) pack photos when needed for the MAHs/OBPs investigation.
4. Maintain a record of their own actions in relation to any given alert, suitable for internal auditing and NCA queries and inspections.

Currently, interested OBPs and NMVOs are able to connect and start using the system. The use of the system is free of charge and does not include any additional fees.

If you are interested in learning more about the EAMS, please refer to EMVO's Self Service Portal here which includes more information about the project.

5. Governance

5.1 European Change Control Board (EU CCB)

The EU CCB was established on 1st April 2020 and it serves as the central governance body within the EMVS framework. The EU CCB:

- Joint governance and decision making process involving all the different parties (EMVO and NMVOs);
- Ensures changes are implemented in a controlled manner;
- Assures interoperability, security and business continuity of the entire EMVS;
- Supports national functionalities covered by existing contracts that are specific to some NMVSs.

The EU CCB consists of the following members:

Representative	Role
NMVO representative	Chair
2 senior representatives from the EMVO Customer Group	Member
2 senior representatives from the Arvato Customer Group	Member
2 senior representatives from the SolidSoft Customer Group	Member
2 EMVO stakeholder representatives	Observer

6. EMVS key facts

- 9th February 2019 – the EMVS entered its operational phase.
- 30 European countries are participating in the EMVS. This number comprises all Member States of the European Union, the EEA and Switzerland. Italy and Greece have been granted an optional 6 year implementation period from the 9th February 2019 and are making use of the longer implementation period.
- 2.8000 pharmaceutical companies are represented in the EU Hub.
- 120.000+ dispending end-users are connected to the system:
    - 110.000+ pharmacies
    - 4.000+ wholesalers
    - 6.000+ hospitals pharmacies
- 9th February 2023 –the EAMS went "live"

7. Glossary of key terms:

OBP – On-boarding partner. This is the legal entity, representing one or several MAHs from the same corporation which enters into a contract with EMVO and connects to the European Hub.

MAH – Marketing Authorisation Holder. This is the entity which holds a license for the selling of a pharmaceutical product in a country. Parallel importers are considered MAHs in the context of EMVO based on their parallel import licenses.

EMVO – European Medicines Verification Organisation. EMVO run the European Hub and assists pharmaceutical companies in on-boarding to it.

NMVO – National Medicines Verification Organisation. Each Member State of the European Union (EU), European Economic Area (EEA) and Switzerland has its own NMVO**.** NMVOs are responsible for end-user on-boarding and for the operation of the national systems.

End-user – This describes a pharmacy, hospital or wholesaler.

European Hub – The centralised database and router holding the information from all Unique Identifiers across the EMVS and to which the national systems are connected.

EAMS – European Alert Management System

EU CCB – European Change Control Board

FMD – The Falsified Medicines Directive (Directive 2011/62/EU) (FMD) and the associated Delegated Regulation (EU/2016/161) on safety features dictate that a new system of verification for pharmaceutical products was needed and introduced requirements for two new safety features on product packs.

NCA – National Competent Authority

For more information on any of the points found here, please consult the Knowledge Database on our website. This includes all information that we release into the public domain and is regularly updated.