Coding & Serialisation

Delegated Act on the Detailed Rules for a Unique Identifier for Medicinal Products for Human use, and its Verification

Concept Paper submitted for Public Consultation

Joint Response (EAEPC-EFPIA-GIRP-PGEU)

26 April 2012

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The main objective of the Delegated Act should be to lay the foundation for the development of a **harmonised system across the EEA based on international standards** that provides a **high level of security for patients** while being **cost-effective** and **integrating into existing structures** in the distribution chain.

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Summary table outlining the stakeholders' (EAEPC, EFPIA, GIRP, and PGEU) preferred option for each consultation item:

Consultation Item	EAEPC-EFPIA-GIRP-PGEU
1	Policy option n° 1/2 (harmonisation through regulation)
2	Harmonised and internationally recognized standards for the identification of products, i.e. a product code and serial number, along with batch number and expiry date
3	Add batch number and expiry date to the pack code
4	Adoption of a "third option", i.e. where the national number is required to be in the pack code, it should be integrated into the harmonised product code
5	2D Barcode (DataMatrix)
6	Policy option n° 2/1, point-of-Dispensing Verification by the pharmacist
7	Policy option n° 2/2, i.e. systematic check-out of the pack code at the dispensing point with additional random verifications at the level of wholesale distributors
8	Policy option n° 3/1 Stakeholder Governance
9	High degree of data security needed - In accordance with existing legal principles, all stakeholders having access to the system will own the product verification data they generate in interacting with the system
10	The European Stakeholder Model (ESM) envisaged will not generate, process or store any personal/patient data Equivalent level of safety features for parallel distributed products
11	All (except GIRP[1]) agree that all prescription-only products should bear safety features
12	Agree with quantified approach outlined in the EC Concept Paper
13	EAEPC, EFPIA, GIRP & PGEU strive to work with all supply chain stakeholders namely governments and/or public agencies

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Each stakeholder organisation part of this joint submission will also submit a complementary individual response to the Concept Paper.

[1] *GIRP supports the risk based assessment in terms of the scope of application of the safety features to be applied to products as set out in the Falsified Medicines Directive. Due to the additional requirement placed on wholesale distributors to record the batch number at least for products containing safety features it is obvious that this represents additional costs for wholesale distributors and if fewer batch numbers need to be recorded then the cost impact will be reduced*

A. CONSULTATION TOPIC N°1: CHARACTERISTICS AND TECHNICAL SPECIFICATIONS OF THE UNIQUE IDENTIFIER

Consultation item n°1: Please comment on points 1 and 2 (policy options n°1/1 and n°1/2). Where do you see the benefits and disadvantages of each policy option?

EAEPC, EFPIA, GIRP and PGEU (the ESM[2] stakeholders) recommend policy option **n°1/ 2**, i.e. **harmonisation through regulation.**

Given the movement of medicines across national borders, any effective coding and identification system must be able to exchange information between Member States. Option **n°1/ 2** will ensure interoperability across EU Member States and thereby protect patients against receiving falsified medicines. European wide harmonisation through regulation will also reduce overall costs by avoiding fragmentation which would be costly to integrate into verification systems.

The Delegated Act should require the use of existing and internationally recognised standards which are already used for serialisation numbers and their carriers in existing verification systems (e.g. in South Korea, Turkey and other countries).

Option **n°1/1** would give the manufacturer the greatest flexibility to use the appropriate technical solution; however, this flexibility could result in a high fragmentation due to different specifications and data carriers on the market, potentially using different standards for equipment and processes. These differing standards and processes would be costly and difficult to integrate and might compromise the effectiveness of the system in preventing patients from receiving falsified medicines. Policy option n° 1/1 should therefore be ruled out.

Consultation item n°2 to 4: Regulation of the Composition of the "Serialisation Number"

***Note**: The ESM stakeholders would like to draw the attention of the European Commission to a lack of clarity in the terminology used in the Concept Paper. When referring to a "serialisation number" it is often the "pack code" as a whole (i.e. product code, serial number, batch number and expiry date) which is being referred to in the Concept Paper. For consistency, the stakeholders use the term "pack code" for these four data elements (instead of 'serialisation number'). For technical accuracy we would stress that the "unique identifier" feature referenced in the Falsified Medicines Directive (FMD) and envisaged in this submission would equate with a "serialised product code" (i.e. serial number + product code). The ESM stakeholders*

[2] European Stakeholder Model (ESM) – see Glossary in Annex 2 for further details

suggest that the European Commission include a glossary list in the final Delegated Act in order to avoid any confusion or misunderstanding.[3]

The ESM stakeholders support the use of harmonised and internationally recognised standards for the identification of products and stress the inherent cost-effectiveness of this approach. This will ensure a smooth transition from current state-of-play across the EU and flexible implementation.

Basing the approach on established international standards – in line with systems in place in other countries - will also help ensure alignment with national healthcare cost reduction initiatives.

In contrast, if Member States select coding systems outside the internationally recognised standards, this is likely to generate a highly fragmented system. This would increase costs significantly for Manufacturing Authorisation Holders (MAHs)[4]. It would also hinder interoperability thus making it more difficult to ensure prompt verification, patient safety and alignment with other national programmes. Clearly, this situation should be avoided.

Optimum composition of the "Pack Code"

In order to function as a viable safety feature, the serial number on the pack has to be serialised randomly and should be used in conjunction with the product code to form the "serialised product code", referred to as the "unique identifier" in the FMD.

A cost-effective system will require the inclusion of batch number and expiry date in the pack code, in addition to the product code and serial number. Their inclusion would enable wholesale distributors and pharmacists to automatically read the batch number, serial number and expiry date, significantly enhancing patient safety and improving product recall procedures. It would also facilitate the provision of additional services to patients by pharmacists.

Moreover, a system incorporating batch number and expiry dates into the code would allow pharmacists and wholesalers to:

- Optimise their inventory management (according to expiry dates);
- Track materials such as narcotics, record batch numbers as required by the FMD "at least for products carrying safety features" and in some countries (e.g. France) as required by law;
- Help prevent the dispensing of expired or recalled products, and confirm the identification of products subject to recall;

[3] An indicative glossary is equally enclosed in Annex 2 of this submission

[4] For the purposes of this paper MAH means both manufacturers and parallel distributors engaged in repackaging to the exclusion of contractors and subcontractors involved in the manufacturing process but not responsible for putting pharmaceutical products on the market. For the avoidance of doubt, a manufacturer engaging contractors or subcontractors to produce on its behalf shall be considered the MAH.

- Optimise reporting on adverse events in biological and biosimilar products, which present distinctive safety challenges, through batch number recording as provided for under EU pharmacovigilance rules[5];
- Other healthcare providers, such as hospitals, would also derive value from this optimum pack code during administration of products to help prevent medical errors and administer short dated products, etc.

Not requiring the inclusion of batch number and expiry date in the pack code would represent a wasted opportunity to tackle the significant dangers for patients posed by currently sub-optimal recall processes, requiring manual checking of every pack of medicines.

The format of the expiry date inside the DataMatrix and the format of the expiry date in the human readable text next to the DataMatrix will not necessarily match.

- The expiry date in the data carrier will be YYMMDD as per existing standards, with DD being the actual Expiration Day or 00 if not specified.
- The format of the expiry date in the human readable text will follow current national labelling requirements.

In summary, to ensure the system cost-effectively delivers on its goals, all prescription-only packs should be encoded with four data elements, i.e. product code, serial number, batch number and expiry date. The additional costs of including these data elements in the pack code are discussed later in our response but are likely to be negligible.

Perceived "Cost-effectiveness" of Pre-Printed Barcodes

Some stakeholders maintain that it would be possible to reduce the cost of applying serial numbers by ordering cartons from third parties that are "pre-printed" with barcodes containing the serial number, product code and, in Member States where such exists, national number.

While pre-printing presents certain marginal benefits when handling smaller volumes, printing pack data in the packaging line provides greater benefits in terms of logistics and cost-effectiveness when handling higher volumes of products.

The suggested cost benefits for pre-printed cartons stem from simpler requirements for packaging lines. When using cartons with pre-printed serial numbers, there would be no need for a print head on the line. However, the line would still require a camera, a reject ejection mechanism and packaging line controller software. And the backend IT system would not be simplified, as it would require additional interfaces to carton manufacturers.

Furthermore, pre-printing cartons would introduce an additional risk to the security of the overall system as valid serial numbers would need to be shared with additional external partners, i.e. the carton suppliers. The security

[5] Volume 9A of the Rules Governing Medicinal Products in the European Union: Pharmacovigilance for medicinal products for human use Chapter I.4.

risk would also be increased through the time gap between producing the cartons and having them uploaded and dispensed as serial numbers would potentially be available for criminals to obtain and apply to falsified products.

Finally, pre-printed cartons would not have batch number and expiry date in machine-readable form. While these data elements could be 'looked up' by making a live connection to a central database rather than encoding them on the pack, this process is likely to require upgrades of scanning equipment to manage a live connection and will place additional load on the central database thus requiring a higher system specification and increased costs.

Wholesale distributors estimate the additional annual labour costs of capturing batch numbers by looking them up on a database rather than reading them directly from the carton to be around €13.2 million. Furthermore, were the database that holds the batch numbers to be unavailable, wholesale distributors could not comply with their legal obligation under the Falsified Medicines Directive to record batch numbers.

Taken together, the marginal cost benefits of pre-printing small volumes are outweighed by the security risks it introduces to the system and by the diseconomies of scale involved with pre-printing large volumes. Much greater cost-effectiveness is achieved when the four data elements are encoded in machine-readable form on the outer packaging.

Use and Application of Human-Readable Data

Pharmacists should be able to enter certain data manually to allow for cases where the machine-readable code cannot be read electronically.

In this respect, an issue not touched upon in the Concept Paper is the extent to which – in addition to the pack code - packs should include human-readable data.

In addition to including the four data elements in the machine-readable pack code, all products should contain at least a minimum of human-readable data (batch number and expiry date) if not a larger amount of human-readable data (including product code, batch number, expiry date, and possibly serial number). The use of human-readable data, including the serial number, should be evaluated in the light of experience with the system.
The data elements should be included in a human-readable format unless there is a pack size or other technical constraint in which case batch number and expiry date must be included.

Attention also needs to focus on the positioning of the pack code and the human readable information. We would suggest that flexibility is exercised but that the ideal target should be to have the DataMatrix code and human-readable text in close proximity. The size of the pack may mandate that the information be split across two faces of the pack.

For products containing a "Blue Box" (as required for EMA centrally registered products) the pack code should not be required to be placed inside the Blue

Box. The ESM stakeholders would prefer having the pack code placed on the end of the pack and not on the back as is often the case regarding the Blue Box.

National Reimbursement and Product Numbers

While the ESM stakeholders agree that European medicinal products should be identified through the use of a harmonised serialised product code, it is recognised that some countries already have national numbers for pharmaceutical product identification in place today. Often these are used to facilitate reimbursement and logistic processes and are embedded into IT systems, business processes and even legislation which present challenges for these countries to move to a harmonised European pack code. These national numbers are in some countries required on the product packaging in a machine readable format such as a barcode.

Replacing national numbers by new numbers would be highly complex, error prone and expensive as many business processes and IT systems at the national level are currently based on these numbers. However, a problem would arise if national numbers are not globally unique and therefore cannot be used across countries, meaning that they are not compatible with a pan-European approach to serialisation.

Regarding the consultation, neither option 1 nor 2 fully accommodate current needs. Therefore, the ESM stakeholders suggest a 'third option': where the national number is required to be in the pack code, it should be integrated into the harmonised product code. This is already the case today in a number of European countries, e.g. France, Denmark, Sweden, Finland, Austria. In these countries, a specific prefix is used in the product code indicating that the subsequent number is a national number.

Such a prefix must be provided by an issuing agency that is accredited with the ISO. This approach guarantees international uniqueness of the resulting product code even if the national number itself may not be globally unique. It ensures at the same time that the national number can be used in existing processes as it can always be easily extracted from the product code.

The ESM stakeholders would therefore favour the proposed third option where the following data elements are included in the pack code:

- Globally unique product code, that includes prefix and national number, or – where the latter is not required – another product identifier;
- Unique identification number for the pack (serial number);
- Expiry date;
- Batch number.

This information should be encoded using a coding scheme that fulfils the following principles:

- Only one ISO compliant symbology should be used for the data carrier, i.e. the DataMatrix[6]
- Standardised syntax and structure should be used for the pack code's content[7].

This third option is fully supported by existing coding schemes, like the GS1 scheme (GTIN/NTIN) and the IFA scheme (PPN-Code). The European Hub, as currently designed by the stakeholders, will also support both schemes (see Consultation Item n° 8 below).

In addition to this third option, provisions are needed which enable the handling of packs intended for sale in more than one country (multi-country packs) while meeting the different national requirements and at the same time minimising the number of codes on the pack. As this is quite a complex aspect the ESM Stakeholders are currently working on a solution.

Care should be taken in providing for the use of more than the existing coding schemes (GTIN/NTIN and PPN) in the future as this will result in additional (and unforeseen) cost at all stages of the European verification system.

Consultation item n°5: Please comment on the three concepts described under point 2.2. Where do you see the benefits and disadvantages of each of the three concepts. What are the costs for each concept? Please quantify your reply, wherever possible, by listing for example:
- costs for reading devices for the different carriers;
- costs for adapting packaging lines of medicines packaged for the EU market.

Based on current analysis, the only reasonable, cost-effective, technical solution is to adopt the 2D barcode, i.e. a DataMatrix code, as the data carrier. The DataMatrix code has technical and economic advantages in comparison to the two other concepts and in our view should be used for serialisation of pharmaceutical products in Europe.

It should be recognised that a number of costs will be incurred no matter what system is selected, including costs to adapt pharmacy and wholesaler software.

DataMatrix Code

The **DataMatrix code** is the most cost-effective carrier to hold the information relating to each single pack (product code, batch number, expiry date, a unique randomised serial number and, where necessary, the national product number) as:

- It has the ability to store the information multiple times in the same code which allows a reading even if 25% of the code is damaged;
- It is applicable to small packs;

[6] ISO/IEC 16022
[7] ISO/IEC 15459, ISO/IEC 15418 and ISO/IEC 15434

- It is widely used and thus tried-and-tested (the DataMatrix has been an ISO standard for 12 years and is widely used globally);
- Manufacturers have wide experience of its use due to existing serialisation requirements;
- It is flexible, i.e. it can adapt and respond to technical advancements/changes in the future.

Cost efficient: the costs for adapting packaging lines amount to approx. €Cent 1.6 per pack (annually and EU wide). This covers printing the DataMatrix, as well as equipment and IT-system investments.

While the requirement to purchase scanners will generate an additional cost for pharmacists, parallel distributors and wholesale distributors, the price difference between a linear code scanner and a 2D scanner is negligible. Pharmacists estimate the costs for the reading devices at €250-300. Costs for scanners in a wholesale environment are likely to be higher due to additional requirements: industrial, wireless, mobile 2D bar code scanners equipped with radio signals technology. GIRP estimates the costs for such scanners to be €1,200 per device.

Linear Barcode

The **linear barcode** is not designed or suited to holding more than 1 or 2 data elements on consumer packaging. It would be unable to carry the necessary amount of data and still fit on the majority of packs. It is not a cost-effective solution (large barcodes may mean larger packs or may require the linear barcode to be split into two or three separate linear barcodes), it would be more difficult to print and more prone to damage and could have lower read rates than the DataMatrix code.

Packs with linear barcodes could not have batch number and expiry date in machine-readable form and still fit on packs; and for some smaller packs it is possible there would be insufficient room for even the unique identifier (i.e. product code and serial number). As previously detailed, while batch number and expiry date can be 'looked up' by making a live connection to a central database rather than encoding them on the pack, this process is likely to require upgrades of scanning equipment to manage a live connection and may place additional load on the central database thus requiring a higher system performance.

Although most pharmacies are today equipped with linear readers, many of these will be replaced/upgraded over the coming years and since new 2D readers can also handle linear codes this will ensure a smooth transition.

RFID

Given the current state of RFID technology, the ESM stakeholders do not believe it is the appropriate technology for the following reasons:

- It would not detect any more falsified medicines than a DataMatrix code solution and has no benefits over a DataMatrix in a point-of-

dispensing model where the pharmacist is holding the pack when it is verified;
- RFID scanning of multiple packs in pallets at a single time is not yet robust enough[8].

While the ESM stakeholders do not rule out the future use of RFID in tandem with DataMatrix codes once the technology matures, RFID brings little benefit to patient safety and does not justify its use given its high cost (5 times higher as compared to DataMatrix codes). Additionally, implementation costs might also be higher due to the need to re-engineer some processes in laboratories, i.e. different tags are needed to work with different types of medicines, and therefore an adapted design could be necessary.

To conclude, the use of a DataMatrix code is recommended for efficiency and cost-effectiveness.

B. CONSULTATION TOPIC N° 2 - MODALITIES FOR VERIFYING THE SAFETY FEATURES

Consultation items n°6 & 7:

- √ **Item n° 6: Regarding point 1 (policy option n°2/1), are there other points of dispensation to be considered? How can these be addressed in this policy option?**
- √ **Item n°7: Please comment on the three policy options set out in points 1 to 3. Where do you see the benefits and disadvantages? Please comment on the costs of each of these policy options. Quantify your response, wherever possible. This applies in particular to the:**
  - **number of wholesale distribution plants;**
  - **costs for adapting such plants;**
  - **duration of scanning of the serialisation number;**
  - **number of pharmacies, including hospital pharmacies;**
  - **number of medicinal products dispensed by pharmacies and hospital pharmacies.**

Systematic check-out of the serialisation number at the dispensing point (Item 6)

EAEPC, EFPIA, GIRP and PGEU endorse **policy option n° 2/1, Point-of-Dispensing Verification by the pharmacist.** Systematic verification by wholesale distributors as suggested in policy option n° 2/3, is not warranted as this is more costly, disproportionate to the objectives of the Directive, and would provide no greater level of safety to patients than point of dispensing verification. In this respect, we welcome the fact that track-and-trace is at no point mentioned as a policy option in the Concept Paper.

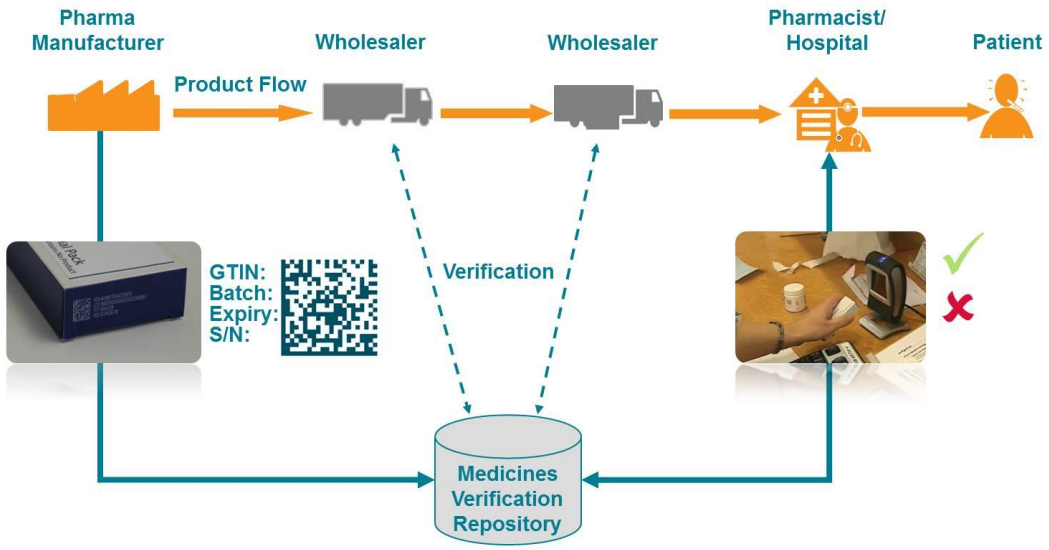
[8] As shown in a pilot developed by the Ministry of Health in Spain on traceability technologies in 2010-2011.

Pharmacy level verification at the point of dispensing with an interface for wholesalers is a robust and cost-effective way to improve patient protection.

Systems should be configured so that pharmacists and parallel distributors can undertake checks at any point after receipt of goods, as well as performing the check-out operation at point of dispensing/repackaging.

Irrespective of the model chosen, since the technical challenges of point of dispensing verification may initially vary across the EU, pharmacists should be permitted initially to check out medicines as they enter the pharmacy, until such time as any technical issues with regard to point of dispensing verification have been resolved.

The process of verification and checking out in the pharmacy should be virtually instantaneous in order to ensure efficient pharmacy workflow and avoid delays. In order to ensure that products are verified in one scanning action, verification software should be integrated with existing pharmacy software.



Point-of-Dispensing System

Other points of dispensation to consider - Check Out Rights

Once introduced into the System, products must subsequently be "checked out" (meaning that their serial numbers are decommissioned) by the relevant stakeholders. Check out rights should be provided for the following actors and scenarios:

1. By the pharmacists at the point of dispensing, including legitimate internet pharmacies, dispensing doctors, hospital pharmacies;
2. By the parallel distributor engaged in repackaging. The pack should be checked out prior to repackaging and new serialised product codes applied and checked into the system. The old and new serialised numbers must be linked at the batch level in the database to enable the product to be tracked in case of recalls or other safety issues;

3. By the MAH in the event of product returns, recalls, accidents, damaged products, the correction of uploading errors in the initial check in phase, unforeseen logistics adjustments, theft of serialisation numbers/packs;
4. By wholesalers in the event of (1) disposal due to damage or expiry, whether caused at the wholesaler's premises or returned as damaged by pharmacists, or (2) their export outside of the EEA/other participating countries.

Unless every individual serialised pack is correctly "checked out" at one of the points listed above, patients will not benefit fully from the safety features. The unique serial number can only provide protection against falsified medicines if it is systematically checked out and the status changed in the database to "dispensed" when the product is handed to the patient or processed in repackaging.

Alternatives to "Point of Dispensing" Verification

EAEPC, EFPIA, GIRP, PGEU would like to stress our opposition to the view that wholesalers could perform the final verification and check-out of products instead of pharmacists. This circumvents the security provided by the final product scan taking place as close as possible to the patient receiving the product. Moreover it would involve wholesalers breaking down pallets, cases and bundles in order to scan at the individual pack level, which would be highly impractical and very costly. Under the assumption that all prescription-only packs carry safety features and would need to be verified, the estimated annual costs for this policy option (2/3) would be around €636 million, under the assumption that every pack of prescription-only medicine is scanned once by the wholesaler.

Point-of-dispensing verification with additional random verifications at the level of wholesale distributors (Item 7)

Because it is more cost-effective, the ESM stakeholders support **policy option 2/2**, i.e. systematic check-out of the pack code at the dispensing point with additional random verifications at the level of wholesale distributors following a risk-based approach.

Wholesalers will have access for verification purposes. The process of verification should be based on the following risk considerations:

- For products obtained from either the manufacturing authorisation holder or the marketing authorisation holder or a person authorised by them, the wholesaler is deemed to have satisfied the process of verification and thereby Article 80(a)(ca) of the FMD;
- Products obtained from other authorised sources must be verified in the system by the receiving wholesale distributor;
- Similarly, if products are returned from persons authorised or entitled to supply to the public, the wholesale distributor must verify the products in the system.

In conclusion, the ESM stakeholders support both policy options 2/1 and 2/2, as the combination of these two options will ensure the highest and most cost-effective safety for patients. The ESM stakeholders oppose option 2/3 (systematic verification by wholesalers) as this is costly, disproportionate to the objectives of the Directive, and would provide no greater level of safety to patients than point of dispensing verification.

Cost-Effectiveness of Point-of-Dispensing Verification

It is important to highlight the cost-effectiveness of a Point-of-Dispensing system as opposed to systematic verification by wholesale distributors. Systematic verification by wholesale distributors will add significant costs for MAHs and wholesalers (at least two times as costly compared to a point-of-dispensing verification system) with no gain in preventing falsified medicines reaching the patient. It is also important to note that there are currently no technological solutions available which would allow wholesale distributors to maintain the speed of their operations while systematically verifying every pack of medicines. This policy option must be ruled out if the continuous and timely delivery of medicines is to be guaranteed.

Under the assumption that wholesale distributors verify medicines on a risk-based approach as described above, the annual costs for financial impact of policy option n° 2/2 would be €36 million. The impact on wholesale distributors of policy option n° 2/3 would be € 636 million annually, under the assumption that every pack of prescription-only medicine is scanned once by the wholesaler.

Significantly increased workload, such as it is associated with policy option n°2/3, would result in the need to significantly increase warehouse space, which in many cases would mean to either move to a bigger warehouse, as many warehouses cannot simply be extended (e.g. hindrance through surrounding buildings). We estimate that around 10-15% of all wholesale branches are likely to have to be moved. Given the current number of around 2,100 warehouses in Europe, this means that 200 to 300 existing warehouses would have to be abandoned and newly constructed – an investment, which is not possible under the current remuneration of wholesale distributors.

C. CONSULTATION TOPIC N°3 - PROVISIONS ON THE ESTABLISHMENT, MANAGEMENT AND ACCESSIBILITY OF THE REPOSITORIES SYSTEM

Consultation item n°8: Please comment on the three policy options set out in points 1 to 3. Where do you see the benefits and disadvantages? Please comment on the costs of each of these policy options. Please quantify your reply, wherever possible.
This applies in particular to the estimated one-off costs and running costs for a repositories system. Where possible, please provide information on past experiences with a repositories system at individual company level and at national level (taking into account the experiences of Member States and companies).

Policy Option n° **3/1 'stakeholder governance'.**

Over the past three years, the ESM Stakeholders have been actively engaged in defining the specifics of a stakeholder governed system as a cost-effective and scalable product verification system to be run on a non-profit basis at European and national levels. The organisations have reached a common understanding through an MoU bringing our vision forward. They therefore fully support policy option n° **3/1 'stakeholder governance'.**

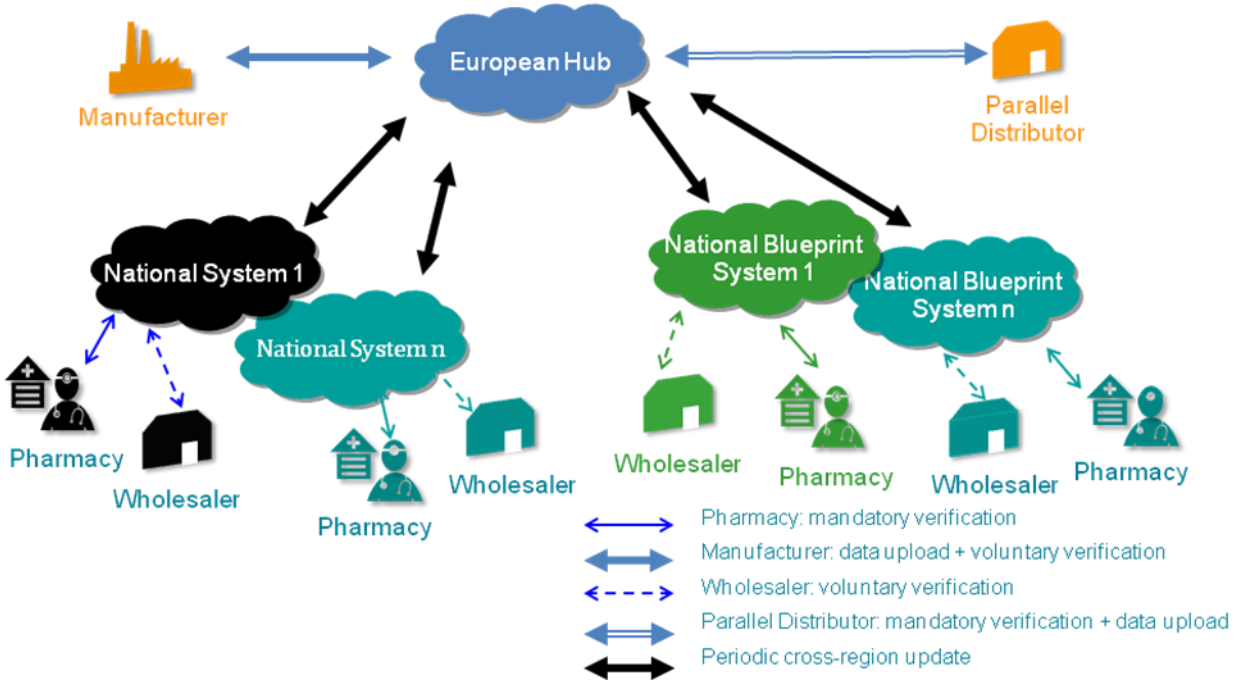
Five key reasons summarize our preference for policy option 3/1:

- Responsibility for Outcomes
    - Combining paying and governing provides a great incentive to ensure cost-effectiveness and actively discourages "gold-plating" the system to accomplish the same objective
- Expertise
    - MAHs, wholesalers, and pharmacies operate the European supply chain every day and will be forced to integrate this expertise as part of a joint governing body
- Responsiveness
    - Establishes an interoperable system across the EU while accounting for regional variations
- Consensus Achieved
    - Working level Memorandum of Understanding (MoU) establishing European-level system governance
- It has been successfully tested and works
    - EFPIA Sweden pilot (2009-2010)

In other words, a stakeholder-governed system ensures greater cost-effectiveness which is necessary in the current economic climate, it ensures that it is the people who know the system best that design and operate it, it allows for an EU-wide model integrating regional differences, and finally it has already been tested and proven to work.

The European Stakeholder Model (ESM)

The European Stakeholder Model (ESM), proposed by EAEPC, EFPIA, GIRP and PGEU, is composed of a series of national data repositories (linked via a European Hub and together forming the European Medicines Verification System, EMVS), that serve as the verification platforms which pharmacies and other registered parties can use to check a pack's authenticity. The system will be interoperable between EU Member States with flexibility to account for national needs.



European Medicines Verification System (EMVS)

ESM working in Partnership with National Governments

Importantly, and in line with the FMD, the European Stakeholder Model will be developed in partnership with governments and public agencies – as well as all other relevant actors along the supply chain. As a fundamental principle, the stakeholder governance at national level will *always* run in partnership with national public authorities.

The national system may be established by the stakeholders and procured to local specifications through a tender process. Alternatively a ready-made system will be available to implement at national level based on a standard blueprint developed together with the European Hub. This option is the "National Blueprint" (nBPS) in the diagram above and will under certain circumstances generate economies of scale and thus a more cost-effective system versus each EU Member State creating its own national repository.

The ESM's "European Hub"

The ESM stakeholders envision establishing the European Medicines Verification Organization (EMVO) as a non-profit entity that will manage the European Hub. The European Hub will constitute:

- A centralised location for the storage of product master data e.g. product description and other static details about the product;
- A single entity from which national systems can receive new/revised product serialisation data;
- A means by which multi-country packs can be systematically marked as 'unavailable' in all relevant markets once a pack has been dispensed in one market;
- A mechanism by which parallel distributed products can be reconciled at a dose level over the lifetime of a batch as they undergo any repackaging process;
- A central point from which product recall actions can be initiated (without prejudice to the ability of the responsible manufacturing entity to initiate a recall in accordance with established recall procedures at national level);
- A central point from which those alerts that cannot be handled solely at the national level can be managed (e.g. an EU-wide recall). The system design will generate alerts in case the automatic checking procedures detect an exceptional event[9];
- Serial numbers and product status details will be held at the national level not in the European Hub.

ESM: Tried & Tested

The stakeholder-governed model was tested at national level through a successful pilot project carried out in Sweden in partnership with Swedish retail pharmacy chain Apoteket AB and locally based wholesalers Tamro and Oriola KD from September 2009 to February 2010.

The following conclusions were drawn from the pilot:

- The stakeholder verification system concept works in practice and allows for effective identification of fake packs;
- The system's availability and performance allow pharmacists to work at normal pace (for 95% of transactions the system provided a response within less than 0.5 second) and without any significant additional effort;

[9] **Exceptional Event:** Any indication that gives rise to a suspicion that a given product may be falsified or that the system may be attacked or another problem that prevents normal or uninterrupted use of the system. An exceptional event would include, by way of illustration, a verification failure (because the serial number is not in the system, or is already logged as having been dispensed or decommissioned due to a batch recall for instance), attempted intrusion by an unauthorised party, or any other activity that suggests an attack on the system. Exceptional events will be assigned escalation levels, and related processes will be set out in the Foundation Documents, annexes to the ESM MoU

- The presence of more than one code on the pack causes confusion for the user and will jeopardise user acceptance;
- Pharmacists and wholesalers valued having access to expiry date and batch number in a machine-readable format.

Other Proposed Options present Disadvantages

The other two options put forward in the Concept Paper present significant weaknesses compared to the stakeholder system outlined above for the following reasons:

EU governance:

- A system run solely by one body, outside the pharmaceutical supply chain, will not be able to fully integrate and rely on the necessary expertise from key supply chain actors to maximise system benefits;
- Timely, secure and cost-effective implementation of a product verification system is best assured with a system that is designed, run by and paid for by those who will use it day-to-day, such as pharmaceutical manufacturers, parallel distributors, pharmacists, wholesalers;
- A system which operates solely above national boundaries, holding nationally sensitive data, presents serious concerns for national stakeholders including governments and is likely to face opposition from national stakeholders. This in turn reduces the acceptance of such a system and will at best slow down adoption and at worst become a complete barrier to its adoption;
- The system is likely to be much less responsive to specific regional market features such as local reimbursement practices, or pharmacovigilance needs, and local dispensing practices that may need to be accounted for in complying with the Directive;
- Experience from the Sweden pilot shows that there will be a significant number of exceptional events whose root cause needs to be analysed in order to differentiate false alarms from instances of a detected falsified pack. This analysis must rely on good knowledge of local distribution and pharmacy procedures as well as local regulation and cannot be carried out by a centralised organisation.

National governance:

A fragmented system governed by national public authorities is sub-optimal from two key perspectives:

- Cost-effectiveness – the system would be highly burdensome and expensive to run as each MAH (especially when serving multiple markets) would need to be connected to a multitude of national repositories rather than using a single European Hub that connects them to all national data bases and the national data bases to each other. There would also be more points of attack for criminals through hacking etc.
- Unless national systems are based on a single blueprint, development costs are likely to be much higher than for a set of interconnected

systems based around a single but flexible set of standards and processes.
- Unlinked national systems will not be able to ensure patient safety across the EU.

In reality, the European Stakeholder Model proposed by EAEPC, EFPIA, GIRP & PGEU is a hybrid, using the best elements of each of the three options, i.e. a single interface and high enforceability through the European Hub, as well as flexibility and adaptability to country/region needs through national repositories (either established locally or based on a central blueprint to reduce cost). The ESM seeks to be highly cost-effective, based on the expertise of the key actors of the supply chain, financially responsible for the system.

Costs of the Stakeholder Governance Model – Our Estimate

The **thorough cost estimates developed by the ESM stakeholders**, provide detailed evidence to support the cost-effectiveness of our proposed point-of-dispensing, stakeholder run system.

In 2010-11, EFPIA conducted a study to estimate the total cost of a European system for the verification of pharmaceutical products. The study was carried out with input from reputable, expert sources, i.e. structured surveys among EFPIA member companies and potential system providers with regard to manufacturer internal cost and cost of the verification system respectively. Collation and consolidation of data was performed under the supervision of legal counsel in order to avoid conflict with competition laws.

The ESM stakeholders have used the outcome of the 2010-11 study as a solid basis to further cost the ESM, revisiting and adapting the initial data to recent developments so as to better reflect the reality of the system. Indeed, having worked on the ESM for over three years, the partners have gained an increasingly in-depth knowledge and thorough understanding of the system and its various components. Consequently, this also applies to the associated costs.

The overall ESM system cost estimates are broken down into five main blocks (that again are comprised of different elements):

- Set-up costs
- Running costs (annual)
- Technical investments
- Administration fees
- Stakeholder governance (annual)

The cost estimates are based on the assumption that approximately 9.5bn coded prescription-only packs are sold in the EU annually.

The estimates below provide a general overview of the European Medicines Verification System (EMVS) costs. For further details, please see Annex 1.

Cost element	Annual cost EU wide	Cost per pack
Cost for **Pan European Verification System (ESM)**	€ 120m to € 205m (includes European Hub: € 12m)	€Cent 1.3 - 2.2

These estimates are likely to vary subject to the number of national databases in the final system. The final cost may also be lower than presented above given that the stakeholders envision a procurement process involving multiple competitive bids.

The ESM stakeholders are confident that the system could be delivered against these estimates. Indeed, the costs have been established through the use of actual real life examples rather than theoretical estimates. To our knowledge, this is not the case with any other estimate of system costs we have seen from other potential system providers. Vendors, MAHs and other stakeholders have used figures from live serialisation requirements in other jurisdictions, pilots and operation systems so that these costs represent realistic estimates and account for some of the hidden costs that can only be understood through actual deployment of live systems. Great caution should be taken when comparing these figures to estimates which are not based on actual live working deployments or from those without this critical first-hand experience.

Tamper Evidence:
The choice of tamper evidence technology has major cost implications. The ESM stakeholders support the Commission's position that the manufacturer is free to choose the appropriate technology (page 4 in the Concept Paper).

As regards replacement by parallel distributors of tamper evidence features with features having equivalent effect, EFPIA and EAEPC are developing a bilateral understanding.

MAH internal cost for applying tamper evident features (depending on the technology) is estimated at approx. €Cent 0.2 – 2.

Conclusion and Next Steps – Investing in the European Hub

Based on the above, the European Stakeholder Model is the most compelling, cost-effective solution to implement the requirements of the Directive.

EFPIA, in consultation with EAEPC, GIRP, and PGEU, launched a tender process for the development of the first elements of the system (namely the European Hub and a National Blueprint System template) in Q2 2012. The

tender process will be open and based on transparent principles. We welcome all proposals to reduce system costs while fulfilling the requirements of the Directive. Technology providers and other stakeholders that have developed cost estimates that are lower than those collated through our process will be able to enter the tender process with a view to taking an active role in developing the system.

Consultation item n°9: Please comment on point 4.1. Are there other items of information which should be taken into consideration when addressing the issue of commercially sensitive information in the delegated act?

We agree that there is a need for a very high degree of data security.

A distinction needs to be drawn between data generation, ownership, and license to use and the provision of access rights. In accordance with existing legal principles, all stakeholders having access to the system will own the product verification data they generate in interacting with the system.

That said, the patient safety objective of the FMD cannot be effectively achieved without access to certain commercially sensitive data in certain circumstances e.g. when there is a negative verification. In order to maximise patient safety benefits, it will therefore be important to ensure that the effectiveness of the system is not compromised by undue restrictions on access to data.

EAEPC, EFPIA, GIRP and PGEU recognize the sensitive nature of this type of information and propose a system that is highly secured and that permits access to data under strict and defined conditions including:

- *Negative verification*

If a negative verification occurs, i.e. a situation that may indicate the presence of a falsified pack, it will be necessary to clarify the root cause of this event. While there may be circumstances that will allow automatic checks to identify the case as a false alarm, there will be other cases in which this analysis requires the involvement of the affected manufacturer. The manufacturer will then require access to data to help track down the source of the problem, and potentially the source of illicit product insertion.

The design of the system will ensure that only the agreed and relevant data are made available under these conditions and the European Hub will be responsible for requesting and receiving such data from the relevant national system(s) in order to allow MAHs to fulfil their obligations vis-à-vis the regulators. If the analysis provides substantial evidence that a falsified product is detected the local regulatory authorities will naturally be involved subject to national regulation.

- *Product recalls*

Using the status information relating to individual packs, the system would provide near real time identification of information for impacted batches and

allow recalls to be more effectively managed. In a product recall scenario, relevant stakeholders would require access to the status of all impacted serial numbers, including details of which impacted serial numbers have been dispensed or re-packed in accordance with the agreed processes on the handling of exceptional events and in line with relevant data protection laws.

For repacked parallel distributed products, the original manufacturers' and the new batch numbers being applied by the parallel distributor must be linked in the system to permit rapid and efficient recalls. Again, the European Hub will allow for the appropriate level of data abstraction in terms of what data can be obtained from national/regional repositories and made available to individual manufacturers.

- *System maintenance*

When running the ICT system, occasionally it will be necessary to check whether a transaction(s) has taken place or has been successfully completed. In these circumstances, the ability to run a report or at least to access data will be required. Access in these circumstances would be limited to authorised ICT contractors subject to appropriate safeguards.

Consultation item n°10: Please comment on points 4.2 and 4.3. What aspects should be taken into consideration in the delegated act?

EAEPC, EFPIA, GIRP and PGEU appreciate many of the sensitivities surrounding data access. The European Stakeholder Model envisaged will not generate, process or store any **personal/patient data**.

As regards the obligations on the **parallel distributor** to replace mandatory safety features, the original pack's serial number must be checked out in the database by the parallel distributor and a new number checked in. The new serial numbers must be linked to the original product number at batch level in the database to enable the product to be tracked in case of recalls or other safety issues.

The system will improve recall efficiency by informing the parallel distributor that the originator's batch is being recalled. It will then be the responsibility of the parallel distributor to proceed with any necessary action in relation to the repackaged products as required by the recall. The recall function within the system is considered to be an 'add-on' (and not a substitute) to existing recall processes and related standard operating procedures as it can send an early warning to all supply chain stakeholders that a specific batch is under recall. The recall functionality will not result in an original manufacturer being able to prevent the dispensing of all packs in a recalled batch.

Other safety features, including mandatory tamper-evident packaging should be replaced with similar features guaranteeing an equivalent level of protection (by effect).

D. CONSULTATION TOPIC N°4 - LISTS CONTAINING THE MEDICINAL PRODUCTS OR PRODUCT CATEGORIES WHICH, IN THE CASE OF PRESCRIPTION MEDICINES SHALL NOT BEAR THE SAFETY FEATURES, AND IN THE CASE OF NON-PRESCRIPTION MEDICINES SHALL BEAR THE SAFETY FEATURES

Consultation item n°11: Which approach seems the most plausible from your view? Can you think of arguments other than those set out above? Can you think of other identification criteria to be considered?

To reach the objectives of the Directive, all prescription-only medicines must be subject to the same level of security[10]. Introducing safety features only on some prescription-only medicines will simply move the threat to those not protected, shifting rather than eliminating the problem. Also, it is logistically easier for industry from a manufacturing perspective to put the unique identifier on all products, and more straightforward for the pharmacist to scan all products.

The fixed costs for pharmacists of implementing the system will be identical whatever scope is applied, and this should be taken into account when considering the overall cost efficiency of the system. There will however be an additional cost to adapting the system in order to identify White List products.

If there are to be exceptions, EAEPC, EFPIA and PGEU strongly recommend that the risk assessment takes a precautionary approach and that any exception be extremely limited. Realistic phase-in times for manufacturers to respond to changes to the White List (a minimum of 18 months) will also be needed to allow MAHs to install the required equipment and for existing products to flow through the supply chain.

We agree with the proposed classification criteria and support the identification using a flexible approach. This must not circumvent the purpose of the Directive by excluding large numbers of prescription-only medicines from bearing safety features.

Identification of Non-serialised Products

A key security concern is that even after implementation of the Falsified Medicines Directive and the Delegated Act, products will exist that only bear a linear barcode (e.g. OTC products that are not black-listed and any white-listed prescription-only medicines). An easy way to bring falsified medicines into the supply chain would therefore be to just print linear barcodes on packs that should bear serialised DataMatrix codes. In this case, the pharmacy point-of-dispensing system would not make any verification request to the

[10] *GIRP supports the risk based assessment in terms of the scope of application of the safety features to be applied to products as set out in the Directive. Due to the additional requirement placed on wholesale distributors to record the batch number at least for products containing safety feature it is obvious that this represents additional costs for wholesale distributors and if fewer batch numbers need to be recorded then the costs impact will be reduced*

medicines verification repository. As noted above, the most cost-effective and robust way of countering this threat would be to mandate that all prescription-only medicines should carry safety features and should be verified at the point of dispensing.

Safety features and the "White List"

The "no optional scope" position set out in article 85 of the Concept Paper adds unnecessary complexity for all supply chain actors and may result in a greater level of errors in the application of serial numbers than would be the case if all products were covered. Therefore, if the application of safety features to all prescription-only medicines is not mandated, then a more flexible approach to the use of the safety features should be permitted. Specifically, the application of safety features (including serial numbers) should be left to the discretion of MAHs, including parallel distributors.

Parallel distributors and the "White list"

When safety features are applied on medicines falling outside the scope of the FMD, the parallel distributor will as a rule stick to the principle of "discretion of the MAH to apply safety features or not".

Consultation item n°12: Please comment on the quantified approach set out above.

EAEPC, EFPIA and PGEU agree with the quantified approach set out in the concept paper. Exceptions should be very exceptional (difficult to get 6/10 points or less/more). For prescription-only medicines we believe the criteria strike the right balance.

In particular, the price criterion should reflect the cost of producing falsified medicines and likely sales price in order to identify a point at which counterfeiting becomes economically unattractive.

The criteria used in the proposed approach might need some adjustments as criterion number 1 might need to be split up and criterion 5 needs more details to be useable. It is crucial to note that the price of a medicinal product does not need to be high in order for it to be a potential target for counterfeiters. The cost of manufacturing falsified medicines is close to zero, hence any medicinal product, no matter its price, is likely to generate a profit for the counterfeiter.

E. CONSULTATION TOPIC N°5 - OTHER ISSUES

Consultation item n°13: Please raise any other issue or comment you would wish to make which has not been addressed in the consultation items above.

Finally, the ESM stakeholders welcome the involvement of other relevant stakeholder organisations which play an active role in the pharmaceutical supply chain in the further elaboration of the product verification system at point of dispensing.

In this respect, we would in particular like to stress the opportunities for enhanced partnerships and cooperation with governments and public agencies in implementing the European Stakeholder Model for greater patient safety.

Annexes:

1. Cost estimates
2. Glossary

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Annex 1

Cost Estimates

I. European Medicines Verification – Cost Estimates

The overall cost to enable the verification of medicines in Europe is comprised of a number of different categories. These include costs that are incurred by the need (a) to install and run equipment and information technology to apply safety features on the packs, (b) to install and run equipment and information technology to verify safety features throughout the distribution chain, and (c) to provide data repositories that will hold the data relating to the safety features. The joint stakeholders' estimates for the respective cost categories are listed in the table below.

Cost element	Annual cost EU wide	Cost per pack
Manufacturer internal cost: Serialisation	m€ 125	€Cent 1.6
Manufacturer internal cost: Tamper Evidence (depending on technology)	N/A	€Cent 0.2 - 2
Pharmacist internal cost: software extension & scanners	Software: €0 to m€616[11] Median cost of m€308 - if pharmacy software extension costs €2.000 on average for each European community pharmacy Scanners: m€192.5 (average of 5 scanners per pharmacy)	Software: €0 – 4000 per pharmacy Scanners: €250-300 per device

[11] This estimate is based on the assumption that pharmacies are equipped with necessary hardware and already operate pharmacy software

Wholesaler internal cost: warehouse management system and scanners	Annual costs warehouse management system upgrades m€10.3	Number of additional scanners for policy option 2/2: 500 Number of additional scanners for policy option 2/3: 11,000 Scanner cost €1,200 per device
Cost for **Pan European Medicines Verification System (EMVS)**	€ 120m to € 205m (includes European Hub: 12 m€)	€Cent 1.3 - 2.2

The above estimates are based on the assumption of 9.5bn prescription-only packs dispensed per year within the EU.

<u>The cost estimate for the EMVS includes:</u>

Set-up cost for national systems and European Hub

- Core system development (incl. interfaces to European Hub and pharmacy/wholesaler systems)
- Deployment of pharmacy/wholesaler interfaces
- Testing and Quality Assurance
- User Training
- Project Management

Technical running cost

- Licences
- Information technology infrastructure
- System & application maintenance
- Help-desk

Administrative running cost

- User administration
- Management of system provider(s)
- Provision of reports
- Analysis of exceptional events, i.e. analysing events that may indicate that there is a falsified product in the market

Governance cost

→ Total running cost for all national systems amount to 70% of total cost
→ Governance cost lies between 1% and 3% of total cost

II. Risks associated with not using a stakeholder-led model

- 27 different systems which are not interoperable through a hub-and-spoke system will require direct connections between each and every system. This, in turn, will be highly complex and costly.

- Full Track-and-Trace system. This will at least double the manufacturer internal cost (aggregation cost, i.e. packaging line equipment, investment in IT, additional product handling effort) compared to pure serialisation. Also, it will lead to much higher complexity in the supply chain as;
  - Each supply chain partner would be required to install goods receipt/dispatch monitoring equipment to ensure that 'the system' knows where the goods are at any time;
  - Each wholesale partner entity would have to install goods receipt, dispatch and de-aggregate/re-aggregate equipment.
    - Financial impact for Option 2/3 (which does not even meet the requirements of full track-and-trace) estimated at €636 million annually (€36 million annually in pure serialisation with random verification by wholesalers).

- Inappropriate governance structure. A system in which the party incurring the costs (i.e. 'making the rules') is not bearing the costs introduces the risk of 'gold-plating' as there is no clear incentive for cost-effectiveness.

Annex 2

Glossary

EAEPC - European Association of Euro-Pharmaceutical Companies representing Europe's licensed parallel distribution industry comprising licensed wholesalers who supply ("export") and/or purchase ("import") and repackage legitimate European medicines in free circulation.

EFPIA – European Federation of Pharmaceutical Industries and Associations.

EMVO – European Medicines Verification Organisation – an international not-for-profit association established by stakeholders to manage a European Hub that will connect to a series of national or regional data repositories that will serve as the verification platforms to allow the authenticity of medicines anywhere in the supply chain in the EEA to be checked. Collectively, the European Hub and the national/regional repositories may be referred to as the "European Medicines Verification System" or the "System".

EMVS – European Medicines Verification System – the technical components of the overall European Stakeholder Model (ESM), i.e. the actual operational system.

ESM – European Stakeholder Model – the overall vision of the stakeholders. This term covers the underlying principles of the joint proposal put forward and is based on both the joint '10 Core Principles', the Memorandum of Understanding (MoU) and the technical specifications contained in the Foundation Documents in annex to the MoU.

Exceptional Event – any indication that gives rise to a suspicion that a given product may be counterfeit or that the System may be attacked or another problem that prevents normal or uninterrupted use of the System. An Exceptional Event would include, by way of illustration, a verification failure (because the serial number is not in the System, or is already logged as having been dispensed or decommissioned due to a batch recall for instance), attempted intrusion by an unauthorised party, or any other activity that suggests an attack on the system. Exceptional events will be assigned escalation levels, and related processes will be set out in the Foundation Documents in annex to the MoU.

GIRP – European Association of Pharmaceutical Full-Line Wholesalers.

MAH – Manufacturing Authorisation Holder(s) which term, for the purposes of this submission, includes both manufacturers and parallel distributors engaged in repackaging to the exclusion of contractors and subcontractors involved in the manufacturing process but not responsible for putting pharmaceutical products on the market. For the avoidance of doubt, a manufacturer engaging contractors or subcontractors to produce on its behalf shall be considered the MAH.

Master Data – data related to a sales article that is the same for all packs of this article (e.g. name, article number, dose form, dose count, pack type) that shall be registered in the System.

Medicines – those products required bearing safety features in accordance with the Directive on Falsified Medicines[12] and the related Delegated Acts adopted there under.

PGEU - Pharmaceutical Group of the European Union representing community pharmacists.

* * *

[12] Directive 2011/62 of 8 June 2011 amending Directive 2001/83/EC on 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 (OJ 2011 L 174/74)