Understanding the financial implications of the upcoming falsified medicines regulations

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The Directive on Falsified Medicines (FMD or Directive 2011/62/EU amending Directive 2001/83/EC) and its supplementing Delegated Regulation (DR 2016/161) aim at improving patient safety by preventing falsified medicines from entering the legal supply chain. One of the measures that is being undertaken to obtain this goal is to mandate marketing authorisation holders and manufacturers of medicinal products (for human use) to apply safety features to the outer packaging of the medicinal product. These safety aspects comprise an anti-tampering device and a unique identifier (UI) which will allow the product to be identified as authentic at the point of dispense.

To enable manufacturers to become compliant with the FMD's requirements (focussing on the verification of the UI) the European Federation of Pharmaceutical Industries and Associations (EFPIA – representing the research-based pharmaceutical industry), Medicines for Europe (representing the generic, biosimilar and value-added medicines industries) and the European Association of Euro-Pharmaceutical Companies (EAEPC – representing the parallel distribution industry) together with the Pharmaceutical Group of the European Union (PGEU – representing community pharmacists) and the umbrella organisation of pharmaceutical full-line wholesalers in Europe (GIRP) have established the European Medicines Verification Organisation (EMVO).

EMVO has taken responsibility for advancing the formation of the European Medicines Verifications System (EMVS) in order to achieve

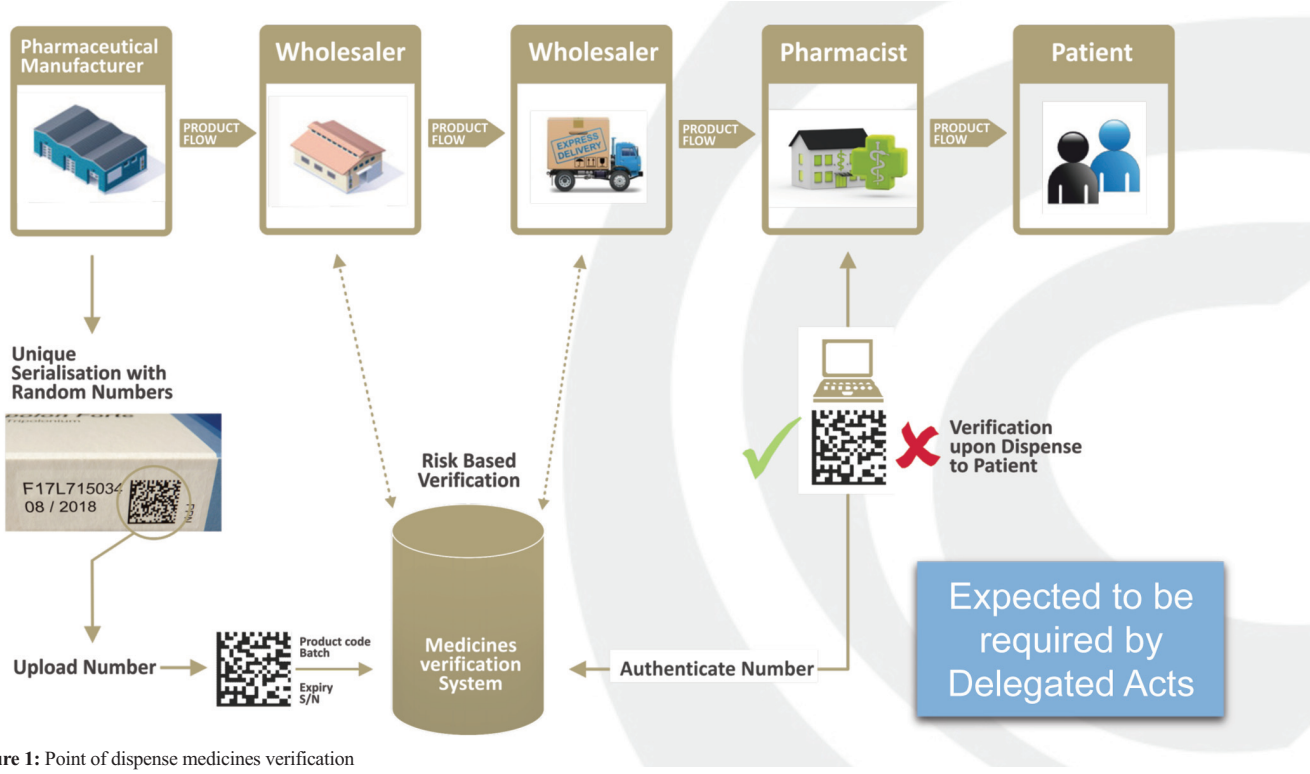

Figure 1: Point of dispense medicines verification

the implementation of a functioning, secure, interoperable and cost-effective system across Europe by February 2019. This will, as mentioned, allow the point of dispense verification of the UI in accordance with the FMD and its DR (see **Figure 1**).

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Practicalities

In practice, manufacturers will be required to print a data matrix code, which incorporates a UI, and apply an anti-tampering device on the outer packaging of all medicines for each individual sales package. At the point of dispense the medicine will be scanned and verified for authenticity against a national (or supranational) repository (see **Figure 2**; page 25). If the UI on the pack matches the information in the repository, the UI is 'de-commissioned' and the pack can be supplied to the patient. If there is a warning related to this UI, the system will highlight this as an exceptional event and the pack will not be supplied to the patient. An investigation needs to determine whether the pack has been falsified or not.

Manufacturers will need to apply an anti-tampering device on outer packaging

The FMD states that the manufacturers shall bear the costs and the DR stipulates that the system has to be set up and managed by the manufacturers and the marketing authorisation holders. To finance the system, therefore, the stakeholders representing the manufacturers – namely EFPIA, EAEPC and Medicines for Europe – have agreed on a model that will charge annual upfront usage fees based on a single flat fee per marketing authorisation holder or parallel distributor. The stakeholders see many good reasons for this approach, the most important being that, ultimately, the marketing authorisation holders and parallel distributors are the entities responsible for putting the products on the markets and therefore rely on the repository system for their products to be supplied to the patients.

Medicines for Europe (and also the EMVO) would like to notify all the manufacturing and marketing authorisation holders of the practical implications of the agreed cost allocation model and encourage them to have the necessary contractual agreements in place so that fees are paid in a timely manner, thereby ensuring that the repositories system is fully effective from the outset. Where the marketing authorisation holder for any given product is not the same legal entity as the manufacturing authorisation holder, both parties shall be required to contractually agree on how to attribute the usage fees between them, in compliance with the FMD.

Implementation stages

The founding members of EMVO have been officially collaborating since 13th February 2015 (founding date of EMVO) to establish the EMVS. The EMVS will comprise a European hub that interacts with national verification systems. Stakeholders at national level can opt for a standalone national system or can avail of efficiencies by using the 'blueprint approach'. The blueprint approach builds on the legal, technical, financial and IT architecture employed by the EMVO.

EMVO currently bears the hub development costs

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Transitional Phase – founding NMVOs and establishing NMVSs

EMVO currently bears the hub development costs, in addition to the costs for the related legal and technical support provided to the national stakeholders who choose to incorporate a repository according to the blueprint approach.

The funding of EMVO takes two aspects into account: governance costs and system development costs. Membership fees, of a total of approximately €400,000 per annum, cover the governance costs and this represents approximately 10% of the total annual costs of the EMVO. The stakeholders have agreed that the remaining costs will be financed through loans which are provided by (or via) the three manufacturer associations (EFPIA, EAEPC and Medicines for Europe). These loans are interest-bearing and will be repaid three years after the EMVS has been fully operational (that is, 2022), thus allowing for the ramp-up costs to be financed and repaid when the system is up and running.

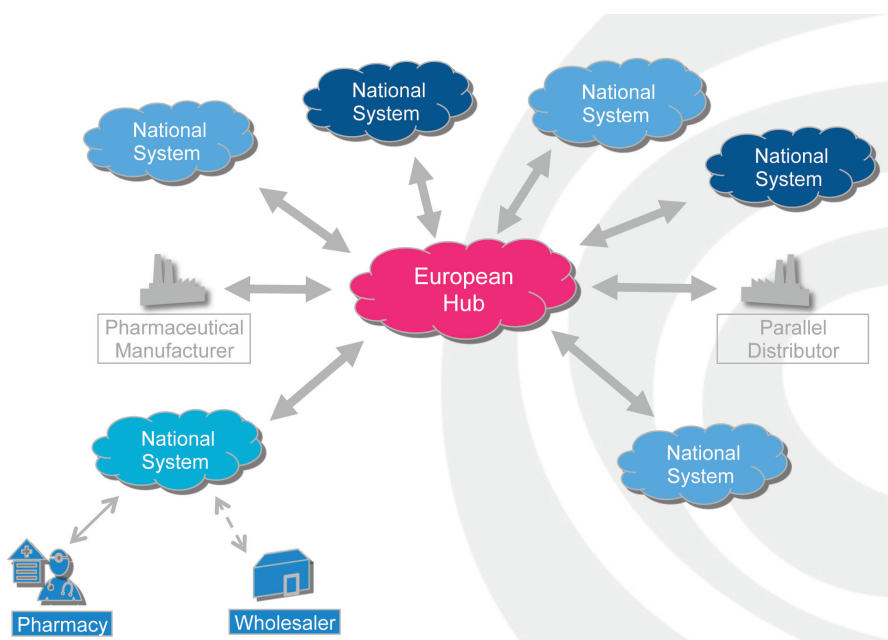

Figure 2: European Medicines Verification System

Operational Phase – Launched on 9th February 2016

This revenue stream will only begin to flow after the date of mandatory application of the rules on safety features, i.e., after 9th February 2019. For this phase, the stakeholders representing manufacturers have agreed on a flat fee financing model to cover the costs involved in designing, establishing and running the EMVS. The flat fee model is designed to be transparent, non-discriminatory and proportionate in relation to the services rendered.

The mechanisms of the flat fee model

By virtue of Article 54a (2)e, the costs of the repositories system shall be borne by the manufacturing authorisation holders.

The term 'manufacturing authorisation holder' covers pharmaceutical manufacturers as well as parallel distributors who repackage and, for that purpose, require a manufacturing license or equivalent good manufacturing practice authorisation. However, as a rule, manufacturing authorisation holders do not operate directly on the markets that their products serve, unless they are also the marketing authorisation holder. In all national markets that are part of the EMVS, it is the marketing authorisation holders or parallel distribution license holders that have the legal right to place products on each national market.

> "Larger manufacturing companies that have contracts with multiple marketing authorisation holders per market will pay multiple fees, compared with small companies"

The legal entity responsible for placing the product on the market where it is verified shall enter into an agreement with the entity managing the repositories system in a given market and shall be liable for the upfront payment of the service fees on an annual basis to the entity in charge of this repository. Any marketing authorisation holder or parallel distributor that fails to pay the flat fee will not have its medicines verified.

The cost allocation model calculates a single fixed fee based on the number of users of the national (or supra-national) repositories (i.e., all marketing authorisation holders and parallel distributors requiring the verification services of any given repository). The fee payable is equal for all users. A single flat fee model has significant advantages in terms of ease of administration in the invoicing process, as well as offering users predictability and transparency and consequently contributes to the cost effectiveness of the system.

Larger manufacturing companies that have contracts with multiple marketing authorisation holders per market will pay multiple fees, compared with small companies with fewer marketing authorisations. The level of the fees payable in any given market is estimated at between €4,000 and €21,000 depending on the market size and the number of active marketing authorisation holders and parallel distributors active in that market. This fee level is comparable to the maintenance fee of some DCP marketing authorisations and is regarded as proportionate and non-discriminatory. For these reasons, the EMVS access principles foresee that only those entities holding marketing authorisations (or parallel distribution licenses) can establish a legitimate connection to the EU Hub for the uploading of product data. This is expressly intended to protect the system against unauthorised and uncontrollable data upload, and to impose clear responsibility on the marketing authorisation holders for the proper implementation of the EMVS. This is in line with the *acquis communautaire*[1].

This means that, in the event of the manufacturing authorisation holder and the marketing authorisation holder not being one and the same legal entity, these parties should agree that fees payable for the use of the EMVS shall be made by the marketing authorisation holders and on the terms upon which those costs may be passed on to the relevant manufacturing authorisation holders.

It is incumbent upon marketing authorisation holders (and parallel distributors) to ensure they are ready to pay the fee for verification services by the EMVS, including through their contractual relations put in place with manufacturing authorisation holders, where appropriate.

About Medicines for Europe

Medicines for Europe (formerly EGA) represents the generic, biosimilar and value-added medicines industries across Europe. Its vision is to provide sustainable access to high quality medicines for Europe, based on five important pillars: patients, quality, value, sustainability and partnership. Its members employ 160,000 people at over 350 manufacturing and R&D sites in Europe, and invest up to 17% of their turnover in medical innovation.

Medicines for Europe member companies across Europe are both increasing access to medicines and driving improved health outcomes. They play a key role in creating sustainable European healthcare systems by continuing to provide high quality, effective generic medicines, whilst also innovating to create new biosimilar medicines and bringing to market value added medicines, which deliver better health outcomes, greater efficiency and/or improved safety in the hospital setting for patients.

The objective of the Market Access team is to shape a dynamic and sustainable market situation in the EU that enables fast and fair pricing and reimbursement for generic, biosimilar and value-added medicines. We thereby aim to improve and increase access to medicines for patients. For more information please follow us at www.medicinesforeurope.com and on Twitter @medicinesforEU.

Maarten Van Baelen joined Medicines for Europe in 2011 as Medical Affairs Manager with responsibilities in the areas of Falsified Medicines and Pharmacovigilance. Under his lead, Medicines for Europe negotiated the membership of the association with the European Medicines Verification Organisation 'EMVO' (a project costing approximately €100 million/year) who obtained agreement from the European Medicines Agency and National Competent Authorities on fees to be charged for pharmacovigilance services. Before joining Medicines for Europe, Maarten was active in the pharmaceutical industry, consulting on pharmacovigilance, and in the medical device industry, liaising with Key Opinion Leaders. He combined these roles while working over weekends in a community pharmacy. In addition to his scientific knowledge as a pharmacist, Maarten is now completing an MBA degree from the Solvay Brussels School of Economics and Management and the École des Ponts Business School.

Johan Verhaeghe joined Medicines for Europe (formerly EGA) in January 2015 as the Falsified Medicines Directive Project Manager. As part of the Market Access team, he provides support to member companies and national associations with regard to the implementation process of complying with this European Directive, in line with Medicines for Europe's commitment in this field: to help create a safer medicines supply chain to protect European citizens by bringing various stakeholders together and uniting them in a win-win spirit to achieve this aim. With an educational background in philosophy, Johan approaches projects with pragmatism and excels in maintaining focus on the goals to be achieved.

Footnote

1. The obligation to affix safety features onto medicines packages, as in Article 54(o) of the Directive 2001/83 as amended, is addressed to marketing authorisation holders, and it is an obligation of the QP of the manufacturing authorisation holder to ensure that these features are indeed affixed in accordance to the marketing authorisation of the product concerned (Article 51/1/a). The Human Medicines Directive holds the marketing authorisation holder legally responsible for a medicinal product on a given market and all related obligations, such as pharmacovigilance (see Article 6, paragraph 1a, of Directive 2001/83). These obligations are also imposed on parallel distributors, even if the EU legislation does not recognise them as marketing authorisation holders in the formal sense. In case a marketing authorisation holder delegates certain GMP related functions to a holder of the manufacturing authorisation, the scope and responsibilities of such delegation are set out in a GMP compliant Technical Agreement, but the responsibility for the compliance of the medicinal product with its marketing authorisation remains with the holder of said authorisation.