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The Falsified Medicines Directive: How to secure your supply chain

G Smith[1], JA Smith[2,3] and DA Brindley[2,3,4,5,6,7]

With new EU-wide legislation being introduced to protect patients from falsified medicines, how can the existing supply chain adapt and thrive in this new, safer environment?

Falsified medicines, and supply chain security in general, are a global issue gaining great political and consumer attention.[1] Although no formal study has been carried out on a global scale, it is known that the issue affects both developing and developed nations, across the entire spectrum of available drugs.[2]

According to the World Health Organisation, a variety of factors contribute to the problem. These include high drug prices, demand in excess of supply and, critically, a lack of appropriately enforced legislation. The rise in illegal online retail of pharmaceuticals has greatly augmented the threat of falsified medicines from outside of the legal supply chain,[3] though they may also reach patients via the legal supply chain.[4]

When properly formulated and enforced, government legislation helps keep people safe in the realest terms. Consider Scotland's recent lowering of the drink-driving limit, which resulted in an early 30% drop in the number of drivers found over the limit.[5]

Mandatory fitting and use of seatbelts in cars have saved untold thousands of lives across Europe and electrical safety laws have reduced accidents and injuries in homes and workplaces. When you consider that, in 2009, France's inability to efficiently recall the diabetes drug, Mediator (Benfluorex; Servier Laboratories, Surenes, France) resulted in as many as 2,000 deaths,[6] the same principles must apply to the pharmaceutical industry.

What is the Falsified Medicines Directive (FMD)?

In July 2011, the European-wide FMD was passed into law, requiring all 28 European countries to have a system in place to detect falsified medicines.[3] The FMD will require many medicines to be uniquely serialised, protected by tamper-proof seals and their authenticity verified before being dispensed to patients.

This will be achieved through scanning a barcode on the pack of medicine and a check being completed against a database, identified in the legislation as a Repository System. Whilst the legislation required the adoption of the FMD into member states' national legislation by January 2013, the practical instructions on how to implement the legislation are being handled by a different instrument, that of a Delegated Act.

The use of a Delegated Act was chosen because, under normal circumstances, when European law is adopted into national law in individual member states, there is room for selectivity of which elements actually make it into local law.

A Delegated Act is different. It requires that each member state implements the entire content of the Delegated Act in the same way, to the same time line given in the original legislation. This ensures the approach to patient safety remains consistent across all member states.

What does the FMD mean for stakeholders?

The scale of the challenge is both considerable and now mandated by law. Over 6,000 pharmaceutical manufacturers must serialise and make tamper proof roughly 10 billion packs of prescription medicines that are dispensed every year across Europe.

On top of this, some 175,000 retail pharmacies and thousands of other dispensing points in all 28 member states must have a system to verify the authenticity of medicines. Wholesalers must also have a system in place to check medicines on a risk-based approach.

Both pharmacies and wholesalers will require a system to be fully integrated into their existing workflow that is secure, fast and reliable. Some 500 million

[1]Aegate Ltd, H9 The Courtyard, Melbourn Science Park, Herts, UK
[2]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK
[3]The Oxford – UCL Centre for the Advancement of Sustainable Medical Innovation (CASMI), The University of Oxford, Oxford, UK
[4]Said Business School, University of Oxford, Oxford, UK
[5]Centre for Behavioural Medicine, UCL School of Pharmacy, University College London, London, UK
[6]Harvard Stem Cell Institute, Cambridge, USA
[7]USCF-Stanford Center of Excellence in Regulatory Science and Innovation (CERSI), San Francisco, USA

Corresponding author:
G Smith, Aegate Ltd, H9 The Courtyard, Melbourn Science Park, Herts SG8 6HB, UK.
Email: Graham.Smith@aegate.com

Europeans will need to be educated and confident that their medicines are genuine and safe. This all has to be achieved and fully operational before the end of 2018.

The current economic challenges in Europe have impacted everyone in the chain. Ethical (branded) manufacturers are facing the combined challenges of the patent cliff,[7] mandated generic medicines in some markets, as in Belgium with anti-fungals, and squeezed healthcare spending overall.

Aggregate profits among the top pharmaceuticals in Europe are expected to fall, with Europe being the worst performing region according to the European Federation of Pharmaceutical Industry Associations (EFPIA). The comparative inefficiencies in the European pharmaceutical supply chain have also led to a thriving, competitive parallel trade in Europe which EFPIA estimates to be worth €5bn per year.

For branded manufacturers, new drug discovery and ultimate financial success will have to come from proving the effectiveness of the medicine, which requires knowledge of patient compliance and patient outcomes. As you might expect, the squeeze is passing through to wholesalers.

Pharmacists, used to fixed margin contracts, are under pressure too. Healthcare systems are squeezing contracts and the threat of chains and internet pharmacies are increasing.

Reduction in medicine prices and forced generic substitution are reducing pharmacy revenues. Belgium has seen a 5% drop in pharmacy numbers in the past four years. With this pressure, pharmacists are becoming more commercial and competitive in their approach, offering improved patient services and education to set themselves and their pharmacy apart from the crowd.

In the European Union there are around 175,000 pharmacies. National law and historic ways of working mean that the pharmacy concentration and profile are substantially different around European countries. In jurisdictions like Germany, pharmacy chains are not permitted and each pharmacy operates as a sole trader. Equally, the ratio of pharmacies per capita also varies wildly with 5,800 people per pharmacy in the UK through to 1,200 per pharmacy in Greece. Pharmacy in Europe serves some 500 m Europeans and is highly fragmented and sub-scale.

What opportunities will the FMD bring?

Patient safety is high on the health and political agenda, and an approach to effectively handing recalls from patients is at the top. Today, European nations have diverse and largely ineffective means of recalling medicines, ranging from advertisements in national newspapers through to notifications in pharmacy journals.

Pharmaceutical companies bear the responsibility of paying for recalls. Costs, whether stock, litigation or brand-related, can be significant and unplanned. As a result, in real terms, pack recovery rates can be as low as single digit percentages.

Recalls can also be triggered by packaging errors or changes to the Product Information Leaflet. A push towards electronic information leaflets should reduce this and further increase the value of the networks that provide access to a centralised, accurate database of current medicines.

As you might expect from EU-wide legislation, this also comes as a relief to those travelling. Making information available electronically allows patients to read it in their own languages in cases where their medicines are prescribed and dispensed abroad.

From the perspective of drug development, R&D investment may be further protected by the FMD, as the need to serialise and make tamper proof packaging may reduce the practice of parallel import and prevent associated losses of revenue.

How and where to authenticate medicines?

A system to verify the authenticity of every prescription medicine pack in Europe is a colossal task for all stakeholders. What is required is a multi-stage process which links manufacturers to pharmacies, and ultimately to patients, using multiple national databases.

The solution, unsurprisingly, would appear to be digital. Electronic verification of medicines from manufacture to distribution ensures that customers are safe by reducing the margin for human error.

An example is the Aegate system (Aegate Ltd, Melbourn, UK), which has seen use in Belgium and Italy since 2007, and is now available to around 18,000 dispensing points. In this time, the system has scanned over three billion medicine packs and flagged up over 2.4 million potential issues to safeguard patients. The Aegate system is also the first to be implemented in secondary care through a pilot scheme underway in Oxford, UK. Other medicines authentication providers may emerge in due course; however, at the time of writing, no other systems demonstrating a fully 'end-to-end system', as mandated by existing guidance from the EU Commission[8] are available.

Digital systems begin their job at the point of manufacture, with unique barcodes being printed onto every packet, each linked to the main database. This secure database is kept constantly updated with the latest information. Therefore, while pharmacists will no doubt be keeping up to speed on relevant issues as part of the job, their doing so is now no longer the final line of defence to patients receiving the wrong medicines.

Box 1. Case study of benefit of digital repository and verification system

In one case, a particularly expensive pack of medicine was sold by a pharmacist. Unfortunately, the patient died before the pack was opened, and their family returned the product in good faith to a different pharmacist.

Seeing all was well with the pack, the second pharmacist returned it to their wholesaler without warning that it had already been sold elsewhere. It was put back into circulation and sold to a third pharmacist.

Due to the pharmacist's use of a digital repository and verification system, an immediate warning that the pack had already been dispensed in another pharmacy was received. Reading this warning, the pharmacist returned the pack to his wholesaler.

Had the pharmacist ignored the warning, the sick fund most likely would not have reimbursed him as they had already reimbursed another pharmacist for the same pack.

While the second pharmacy may have acted in good faith by accepting the returned medicine in these circumstances, the impact on the third could have been significant, given how expensive this medicine was. Digital systems can keep everyone in the complex process of medicinal product distribution informed and updated.

Pharmacists can now simply scan the barcodes at the point of dispense to verify each individual pack. The database then flags up any potential problems in real time, within a quarter of a second to be exact, before patients even leave the pharmacy.

Through unique serialisation and scanning, digital data will be created, affording new insight into the pharmaceutical supply chain, pharmacy and, ultimately, the patient.

This approach can benefit all actors involved in the chain (Box 1). Manufacturers know that their products are going to the right people and can be distributed with confidence. Pharmacists benefit from their patient's added trust which comes with the extra level of oversight. Patients themselves, of course, are safer overall.

By 2018, this new method of secure distribution will have over a decade of successful testing and refinement.

There are, however, challenges in implementing such a digital system.[9] For example, there are risks of code harvesting – the collection of undispensed codes for use with falsified medicines – that need to be addressed by providers of verification systems and that may need to be addressed in the Delegated Acts. Similarly, the criteria for medicinal products to require serialisation and authentication have yet to be made explicit, and there may be difficulties associated with classification of new medicines entering the market and changing attributes of existing products. The new regulations could impact parallel trade of pharmaceuticals, which frequently require repackaging as they are distributed across borders. Further, there may be difficulties associated with points of dispensing medicines outside of wholesalers and pharmacies, such as prisons, hospitals or by healthcare professionals; these might also require systems and accompanying training to ensure that medicines are verified at the point they are dispensed to the consumer. All of these issues could increase the cost of medicines to the public.

Despite these concerns, all 28 countries have now made submissions to the EU, specifically to Directorate General for Health and Consumer Affairs (DG SANCO), which will likely lead to the adoption of the Delegated Acts by the end of 2015's second quarter. Though potentially costly and challenging to implement, the FMD will improve patient safety and decrease the risk of falsified medicines circulating in the EU, and can therefore only be viewed in a positive light. It now falls to actors in the supply chain to take note as the Directive passes into national law.

There is mounting evidence that digital verification is the solution to the incoming FMD. By adopting this approach early as in Belgium and Italy, it is possible to integrate the system with existing records and steal a march on any potential issues. The result, quite simply, is a better protected R&D pipeline, more intelligent supply chain, and safer, healthier patients.

Disclosures

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Conflict of interest

See disclosures.

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