# Where are Pharmaceutical Anti-counterfeiting Technologies Headed?

Introduction
Interpol estimates the annual turnover from pharmaceutical crime as USD 75 billion worldwide.[1] In the US alone, the number of IPR-related seizures in the pharmaceutical and personal care industries amounted to USD 72,939,399, or 6% of the market share for FY2014.[2] Improvements in technology, however, have allowed government officials, brand owners and experts in the field to curb this alarming trend. Particular focus has been placed on pharmaceutical packaging as a means to solve drug-product counterfeiting. An attempt is made to explain the constraints under which the pharmaceutical industry is working to implement anti-counterfeiting solutions (regulatory, design, and financial constraints), to describe some of the major pharmaceutical anti-counterfeiting technologies applied to packaging in use today (barcodes, RFID, invisible printing, etc.) and to offer some recommendations for the future.

## Background

The Falsified Medicines Directive (2011/62/EU) adopted in June 2011 and put into force in January 2013, calls for the obligatory application and harmonisation of safety features on the outer packaging and labelling of individual packs of medicinal products. These measures seek to reduce the sale of falsified medicines in the legal supply chain, particularly via the internet. The scope of the safety features is threefold: one, "verify the authenticity of the medicinal product"; two, "identify individual packs"; and three, verify "whether the outer packaging has been tampered with."

## EU-FMD Delegated Act

The Directive calls on the European Commission to prepare and adopt delegated acts that will lay down the technical specifications of the safety features,[4] determine the methods for the verification of the security elements,[5] and institute a repository system to store and manage them.[6] The notes published from the 74th meeting of the Pharmaceutical Committee, held on March 17, 2015, indicate that the European Commission is set to publish these acts in Q4 2015.[7] Once published, pharmaceutical companies will have exactly three years to comply with the EU-FMD, roughly by the end of Q4 2018.

The minutes also give some insights into which features were identified as the most cost-effective. The measures begin with the introduction of a 2D barcode[8] containing data such as product, serial and batch numbers. Authentication is then described as an "end-to-end verification system"[9] enabling the control of the authenticity of medicinal products at the point of dispense. Finally, the repository system should be established and managed by relevant stakeholders,[10] in other words manufacturers, distributors, and providers. As for tamper-evidence, "the choice [...] is left to the manufacturer."

## Unique Identifier

### *2D Barcode*

A matrix code or 2D barcode as a traceability solution is a valid one, as it can encode large amounts of data, such as batch number, expiry date, and national reimbursement number (as opposed to a traditional linear or one-dimensional barcode). It can also provide, with a single scan, detailed information on the current and past locations of a medicinal product. Finally, this system is noticeably cheaper than other technologies, such as radio-frequency identification or RFID systems, as the only cost involved is the ink. This said, barcodes are visible to the naked eye and are thus more vulnerable to counterfeiting. They are also subject to damage (e.g. excessive handling, exposure to chemicals, water and dirt) and therefore less reliable over time. Finally, barcodes must be scanned one by one, within line of sight, feasibly impacting the workflow process.

### *RFID*

There has been growing interest in RFID technology as a means to reduce medical errors, curb drug counterfeiting, and promote patient safety. Applied as a tag or label on pharmaceutical packaging, the unique identifier is embedded in a microchip and uses radio waves to store and transfer data from product to reader. Unlike barcode scanners, the RFID reader can detect hundreds of tags or labels at once and can be held at a distance. Because the unique identifier is embedded in a microchip, RFID tags cannot be altered and are therefore more reliable and more secure over time. Unlike barcodes, RFID tags can ultimately be applied to any type of material, withstand damage, and thus ensure a longer product lifespan.

Despite the many advantages of barcoding and RFID as traceability measures, what these two technologies fail to do is verify the authenticity of medicines. Indeed, authentication, as defined by the International Standard 12931, is the "act of establishing whether a material good is genuine or not."[12] So whereas identification is the process of making claims about the characteristics of a product, authentication is the process of actually confirming the validity of those claims. The concept of a unique identifier as means to identify an individual pack can only work if there is also a reliable authentication system in place.

## Safety Features

### *Overt (Visible) Features*

Some pharmaceutical companies have added visible security features to their packaging to prevent counterfeiting. These include holograms, kinegrams, optically variable devices or OVDs, security inks, embossing, micro printing, and moiré, to name a few. These features are prominently visible and are therefore conducive to a visual inspection of the medical pack. However, because they are visible to the naked eye, counterfeiters can also in theory create a replica virtually indistinguishable from its original counterpart, and dupe the average end user into thinking the pack is authentic. For this reason, a visible safety feature should at least be incorporated with an invisible one, if not be eliminated altogether.

### *Covert (Invisible) Features*

A covert feature is by nature more difficult or even impossible to detect and therefore copy. Indeed, the knowledge of its very existence remains within

a very small and restricted group of trusted industry specialists, an approach that restricts consumer access. Because invisible safety features typically do not require any additional consumables, they can be simple and low-cost to implement, easily added or modified, and applied in-house, without regulatory approval. Examples include invisible printing, latent images, digital watermarks, taggants, and substrates (e.g. UV fluorescent fibres, chemical reagents and even odours), among others.

There are several constraints to keep in mind when selecting a covert safety feature for pharmaceutical packaging.

**Cost-effectiveness**

Per the Falsified Medicines Directive (2011/62/EU), "When establishing the safety features due consideration shall be given to their cost-effectiveness."[12] Covert safety features can be simple and low cost to implement, if they require no additional consumables, no special reading devices, and no production changes.

For example, invisible printing, while generally achieved through the use of special inks, can be realised using regular visible inks or varnish and standard printing processes (e.g. Cryptoglyph). Integrated with prepress, this technology embeds a pseudo-random pattern of microdots (10 to 20 microns) in the imperfections of the printed material. When applying overprint varnish, this process adds a pseudo-random pattern of micro-holes (40 to 80 microns) to the coating. Non-intrusive and totally invisible, these microdots or holes cover the entire surface of the packaging or label without changing its design. Digitally encoded within the artwork, this form of invisible printing can be easily integrated into any existing packaging or label assembly process at zero production cost. Highly secure, this technology can only be deciphered with a 128-bit encryption key.

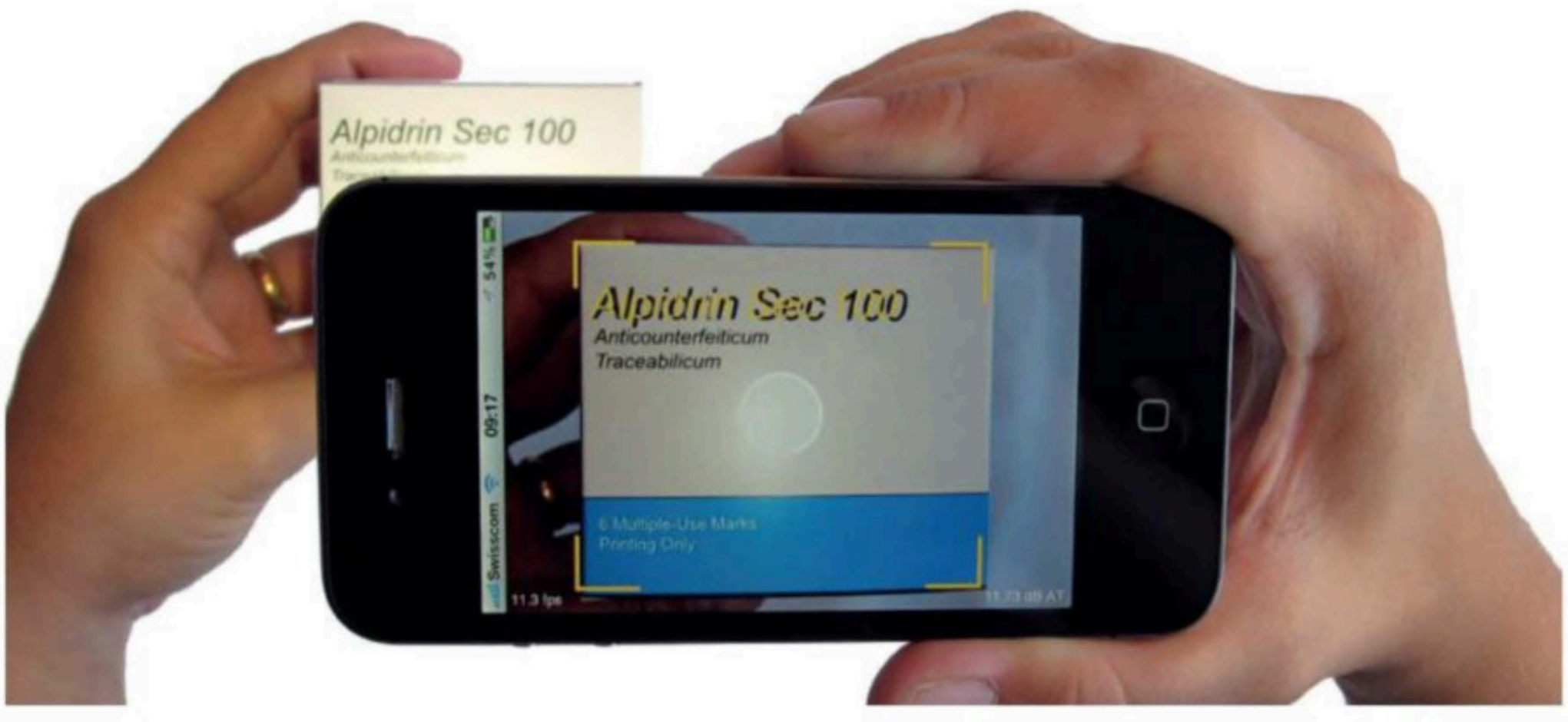
Another cost-effective authentication solution uses the concept of fingerprinting to authenticate moulded products, such as vials, containers and lids, test tubes and caps (e.g. Fingerprint). This technology leverages the surface irregularities naturally occurring in a mould and uses these unique features as the means of authentication. The process simply requires capturing a digital image of the moulded product and storing it in a database. This image is then used as a reference to perform product authentication. As with invisible printing, fingerprinting does not require any additional consumables, markings or production changes. Instead, this solution uses the object 'as is', making it economical and easy to deploy.

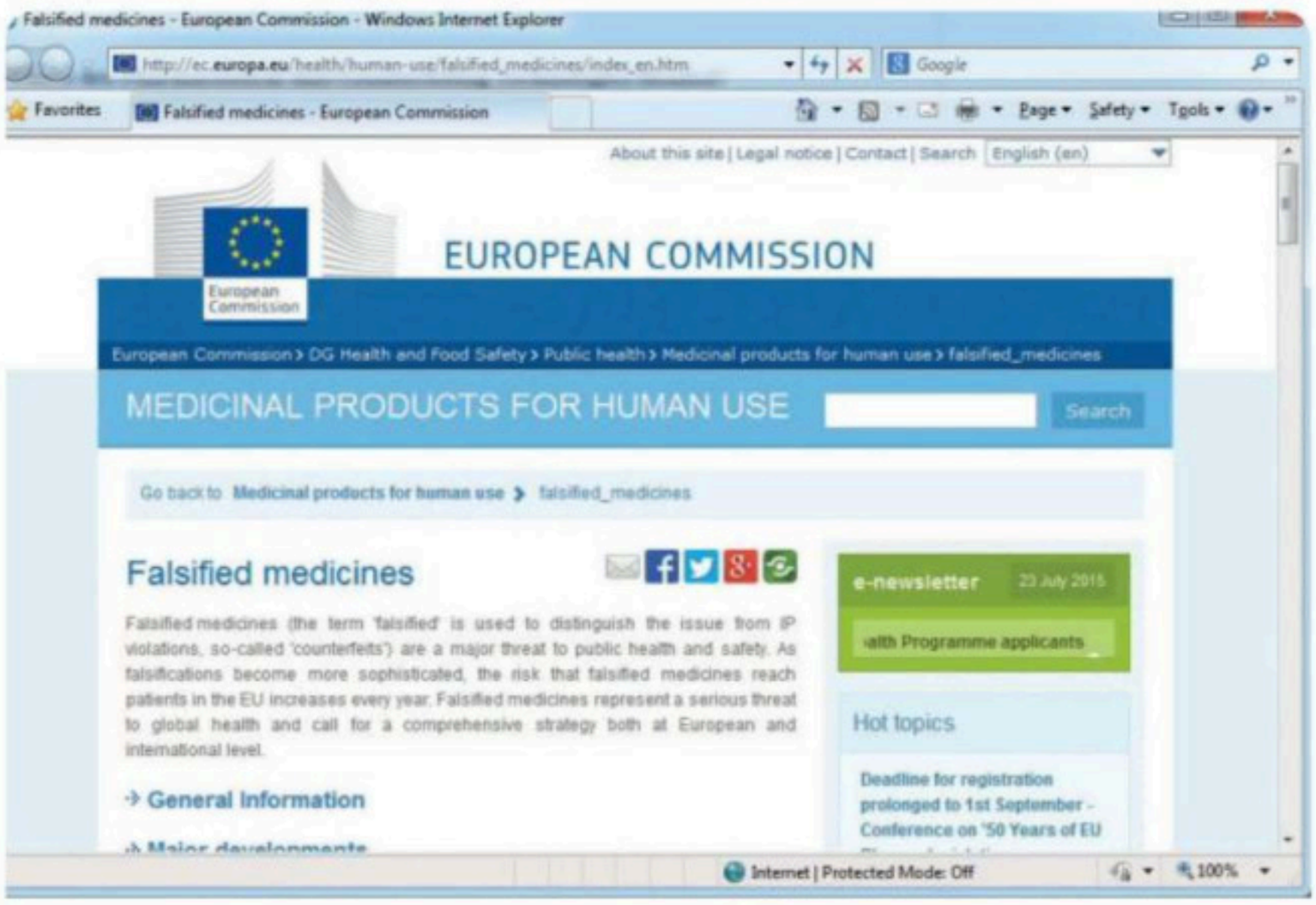
**Harmonisation**

In addition to cost, the Falsified Medicines Directive (2011/62/EU) requires that "Safety features for medicinal products should be harmonised within the Union in order to take account of new risk profiles, while ensuring the functioning of the internal market for medicinal products."[14] Taking steps towards harmonisation means establishing common standards to identify, authenticate and trace medicinal products between the Union and the member states. Good automated manufacturing practice (GAMP) is a set of guidelines for manufacturers and users of automated systems in the pharmaceutical industry that is already influential throughout Europe and recognised internationally. This set of industry best practices helps ensure that a medicinal product meets the expected qualities in all aspects of its production. Applied to pharmaceutical packaging printing, this system guarantees that the computer system will "…consistently produce results that meet its predetermined specification and quality attributes."[15] As a digitally printed covert safety feature, Cryptoglyph has performed as expected, continuously and with minimal attention for fifteen years and is developed in accordance with GAMP 5 CSV guidelines, making it an ideal candidate for pharmaceutical packaging authentication.

Another example of safety feature harmonisation is the World Customs Organization's Interface Public-Members (IPM), an online tool that provides frontline customs officers with real-time product data. Today, 85 countries have joined IPM. In 2013, AlpVision was one of the first providers of authentication solutions to become *IPM Connected*[16] in an effort to tackle pharmaceutical counterfeiting, among other forms of illicit trade.

Harmonisation also entails developing a system that can be easily used by all stakeholders—manufacturers, suppliers, distributors, pharmacists and possibly patients. Unlike most covert anti-counterfeiting features available on the market today, AlpVision's product authentication solutions do not require any highly specialised equipment to be detected. A regular smartphone






application can be used to verify the authenticity of a package. When it's time to authenticate a product, the relevant stakeholder launches a custom application, positions the smartphone over the item and if the pattern is present, receives a positive authentication message within seconds. Automated, this system eliminates interpretation and training, significantly reducing human error. It is also developed using an everyday consumer electronic, making authentication easier and more universal.

**Repositories System**

Per the Falsified Medicines Directive (2011/62/EU), "The costs of the repositories system shall be borne by the manufacturing authorisation holders of medicinal products bearing the safety features."[17] The advantages of digital covert security features are threefold: one, they can often be applied in-house or through certified printers. Two, they are web-based and hence do not require expensive hardware. And three, the server can be housed by a brand owner, a national government, or a designated body anywhere in the world, all together limiting involvement of third-party suppliers and minimising and even eliminating unnecessary costs.

**What's Next?**

Although predicting what the EU-FMD Delegated Act will bring is difficult, we can safely say that the provisions include the obligatory application of a unique identifier in the form of a 2D barcode, in combination with a safety feature for product authentication, and a device for tamper-evidence. Not only do these measures need to be interoperable EU-wide, they also need to be cost-effective. To say that this is a challenge would be an understatement. While the manufacturer has very little leeway in terms of the unique identifier, the choice of a safety feature for product authentication is broader. The manufacturer would therefore be well advised to select a digital covert security feature that would not only comply with the Directive, but also be simple to implement and deploy, highly secure against counterfeiting, instantly detectable using an everyday consumer electronic like the smartphone, and overall cost-effective.

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