
On-Dose Authentication to Safeguard Patients and Uphold Brand Integrity

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Authentication Issues

Counterfeit and falsified drugs pose a significant risk to human health and safety. They also impact the pharmaceutical industry with loss in revenue, diminished brand integrity and loss of consumer trust. Globalization, outsourcing and the increasing prevalence of online sales have resulted in complex supply chains for the manufacture of pharmaceutical products. This makes products increasingly vulnerable to counterfeiting and diversion, resulting in significant loss of revenue and reputational damage for the brand owner, and serious health risks and loss of trust for the consumer.

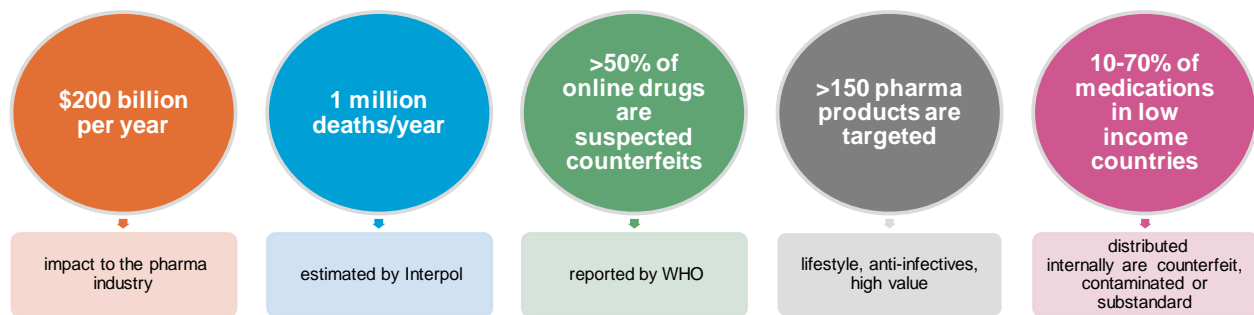
To date, the industry response has been to implement serialization in the US and Europe, which is now proving to be insufficient to fully protect patients and brands. Brand owners must develop robust strategies to protect their supply chain from external threats. More innovative solutions are now being introduced to mitigate counterfeiting and product diversion, and to help with returns monitoring, quality control and product recall.

On-dose authentication solutions offer sophisticated features that will not be susceptible to defeat within months, as is often seen with current packaging measures. In effect, the tablet becomes the barcode.

Microtags allow individual items to be tracked by product, dosage, and plant. Some microtags can now be verified by either a smartphone app – for the first-time bringing authentication to the patient level.

The Scale of the Problem

Counterfeiting of drugs is an escalating problem because the risk to the criminal is low and the potential rewards are high. A recent report focused on the scale of the problem and highlighted its continued growth, despite the implementation of serialization to try to secure the supply chain.¹



Reference: <https://www.statnews.com/2019/05/07/stopping-murder-counterfeit-medicine/>

The prescription drug market has been estimated to be worth up to \$900 billion/year worldwide, with about 85% of the world pharmaceutical market in the developed world. An estimated 10% to 30% of medical products circulating in low- and middle-income countries are either substandard or falsified, according to new research from WHO.²



WHO also reports that 16% of counterfeit drugs contain the wrong ingredients, while 17% contain the wrong level of active ingredients and more than 30% of counterfeit drugs are found to contain no active ingredients. Counterfeit products may also include toxic compounds that can endanger life.

More than half of all drugs purchased from online pharmacies may be counterfeit, according to WHO. Products targeted include those treating chronic diseases such as hypertension and diabetes, antivirals for HIV treatment, antibiotics for TB, high-value medications such as cancer treatments and products for erectile dysfunction. Low-income countries bear the biggest risk, with up to 70% of medications distributed internally suspected of being counterfeit, contaminated or substandard quality.

Parallel imports (also known as gray market imports) are genuine medicinal products manufactured under trademark, patent or copyright, which are placed into circulation in one market and then imported by an intermediary into a second market, without the authorization of the local intellectual property owner. Parallel trade exists where there are significant price differences between countries, e.g. in the EU where prices are fixed by governments. This can contaminate the supply chains of other countries and result in lost revenue and profits for the manufacturer.



A more challenging and complex problem than counterfeiting is diversion. This is the illegal distribution, or abuse of prescription drugs, or their use for purposes not intended by the prescriber. "Street" diversion is when addictive medicine is diverted without controls, resulting in dangerous use and risk of overdose. The opioid crisis in the US is an example of consumers acquiring prescriptions that are not intended for the end-users. Deaths from misuse of prescription drugs account for a significant proportion of overdose deaths.

Another form of product diversion is the unauthorized return of products when the product is often in damaged packaging or not in the original packaging. This makes it difficult to determine whether such a product is eligible for refunds. Cases have been reported of authentic pill bottles being filled with fake material and then re-sealed and returned. Many monitoring practices for returns fail to verify the contents of packages and are therefore open to this form of abuse.

Legislation

In the past decade, governments have introduced legislation to enforce serialization, requiring product identifiers to be affixed to each package to provide traceability throughout the distribution supply chain. The key drivers have been patient safety, product protection, recall improvement, supply chain visibility and efficiency, management of shipments and prevention of reimbursement fraud (in the USA),

In the EU, the Falsified Medicines Directive (FMD) was enacted July 2011; followed closely by the USA with the Drug Supply Chain Security Act (DSCSA), to be implemented by November 2017, with a one-year reprieve to 2018 for compliance. The DSCSA requires track and tracing of all Transaction Information (TI), Transaction History (TH), and Transaction Statements (TS). By the end of 2020, impacted parties will include the manufacturer, re-packagers, wholesalers, third party logistics and dispensers. By 2023, full unit-level traceability will be required.

From 9 February 2019, the FMD requires that manufacturers may only release for sale prescription drugs bearing two safety features: a unique identifier and an anti-tampering device. The unique identifier is a 2D barcode on the package that includes the product number, serial number, expiration date and batch number. Also, pharmacies may only dispense these drugs to patients following successful authentication. This works by manufacturers uploading the information contained in the unique identifier for each medicine to a central EU repository. Depending on the source of the medicine, wholesalers will also need to scan medicines at different points in the supply chain to verify their authenticity. Pharmacies and hospitals will then scan each medicine at the end of the supply chain to verify its authenticity and check it out from the repository before dispensing to patients.

Similar action has been taken in the United States, with the DSCSA road map for end-to-end traceability stretched across a period of 10 years, with requirements for all parts of the supply chain.

Addressing the Gaps of Serialization

It has become clear that traceability and security measures focused at the packaging level are not enough to protect patients. Even if a package is authentic, it may not be possible to determine if the medicine inside is real or fake, and whether it has been diverted.



- focus on the package
- barcodes can be copied
- packages are discarded and reused
- counterfeiters are increasingly sophisticated
- holograms give a false sense of security

The complexity of the pharmaceutical supply chain lends itself to entry points for adulterated or counterfeit products, which are often found in carefully counterfeited and high-quality packaging, or sometimes in authentic packaging that has either been stolen or used in a repacking operation.

There is comprehensive data contained in serialized 2D barcodes that can be used to uncover product information. Unfortunately, counterfeited products with a replicated barcode read the same and provide the same information as the legitimate item. Subsequently, when the legitimate product is later scanned, it will be recognized as “dispensed” and flagged for investigation and removal.

Another major gap is that serialization has been designed and regulated for developed geographies, focusing on track and trace, spotting when things go wrong and instigating recalls when needed. But the threat presented in those regulated regions is not particularly high. The real challenge comes when products are manufactured and distributed in lower cost and more vulnerable areas, where there are greater opportunities for diversion.



To provide more robust authentication strategies, companies have developed a range of innovative technologies that pharmaceutical manufacturers can implement to protect individual dosage forms and associated supply chains. These technologies are classified as overt or covert:

Overt technologies are features that are visible to consumers and are incorporated onto a product or its packaging. Such technologies may offer low security as counterfeiters become more sophisticated.

Covert technologies are designed to be difficult to identify and require testing to authenticate the product. If the security features are not easily seen or detected, then it will be more difficult for a counterfeiting organization to find and defeat these measures.

On-Dose Authentication Measures

To achieve true end-to-end supply chain security, on-dose authentication measures are needed. These may include coatings which are difficult to replicate, or chemical or molecular markers added to the drug formulation and/or coating or on dosage print.

Microtags or taggants are uniquely encoded materials that are virtually impossible to replicate or reverse engineer. They can be used on finished products, ingredients or materials used to make products, and on the packaging. The most useful taggants are those that can carry information or incorporate 'fingerprints' which complement packaging security and traceability systems and allow product diversion to be combated. When their presence is detected in a sample, authenticity is confirmed.

The use of taggants has been highlighted following the publication in 2011 of the US Food and Drug Administration's guidance on the use of physical-chemical identifiers (PCIDs) in solid oral dosage forms. PCIDs can include inks, pigments, flavors, and molecular taggants. The FDA recommends the use of approved food additives, Generally Recognized as Safe (GRAS) substances or excipients that have been previously used in solid oral dosage forms. In many cases, the addition of a PCID to a solid oral dosage in an approved product can be recorded as an 'Annual Reportable Post Approval Change'.

The Colorcon Solution

Through a new solution **SoteriaRx™**, On-Dose Authentication, Colorcon offers the opportunity to implement the PCID guidance. Using the 'lock and key mechanism', the coated or printed dosage form becomes the lock and the corresponding detection method (which is unique for each taggant) is the key, held by Colorcon. The taggants are customer-specific and may be used on multiple drug products or each drug product can be tagged. As the product is being used as an anti-counterfeiting measure, there is no special branding to advertise this unique feature. Many companies, especially those utilizing contract manufacturing services, may find it beneficial to maintain anonymity regarding the use of authentication measures.

Colorcon has formed technology partnerships with TruTag and Applied DNA Sciences to provide taggants for inclusion on-dosage. For drugs that are already on the market, the taggant technology can be added to an Opadry® film coating system or Opacode® printing ink formulation and applied with existing equipment. Alternatively, the technology can be included as part of a new drug development project.

The TruTag® Platform

The taggant material is safe for ingestion and resilient for application to the dosage form. To create a unique fingerprint, each taggant is etched to create a porous structure customized to create its optical signature. To provide on-dose authentication, the signature can contain information such as product, dosage and manufacturing site.

TruTag offers a range of detection options suited to meet customer needs. Each method is based on software specifically designed to identify the spectral index of the taggant. Without the special reader, only available through Colorcon/TruTag, the taggants cannot be detected and the product is not authenticated. The detection methods range from forensic, or destructive measures, to field read non-destructive types. A consumer read option will soon be available that provides detection capability through any smartphone. This option brings the solution down to the patient level – something that is not available with serialization.

ADNAS Molecular Taggants

These involve a unique molecular tag, produced by **Applied DNA Sciences**, which can be used across a wide range of applications. Tagging of inks, coatings, and other ingredients can be used in the pharmaceutical supply chain, ensuring authenticity.

The specific information to be authenticated such as company name, product and manufacturing site can be coded into the DNA sequence. The number of base pairs used is too low to be biologically active and acts like an individual barcode that cannot be broken, and which is traceable at parts per billion/trillion. A corresponding reagent is used for detection, utilizing a standard PCR (polymerase chain reaction) process. This reagent can only be used to detect the DNA to which it is coded. Without access to the specific reagent, there is no way to detect the DNA and authenticate the product. This creates a high level of security and should it be needed, the results from forensic testing are admissible in a court of law.

Choosing the Best Approach to Protect Your Product

Through **SoteriaRx™** Colorcon offers on-dose authentication to help brand owners, risk managers and senior managers in the pharmaceutical industry bridge the gaps of serialization to ensure a robust supply chain. We are building a platform of authentication technologies and detection services to provide an optimal solution based on a clients' specific needs. The lock and key approach provided by Colorcon ensures the integrity of the authentication process, as it is nearly impossible for counterfeiters to replicate. It protects patient safety and health while maintaining brand integrity and consumer trust through end to end supply chain security.

With microtags, an in-field reader can confirm the origin of the product without needing to send it back to a central laboratory for verification. This gives pharmaceutical companies the power to scan a pill, anywhere in the world, and immediately confirm its authenticity directly, without needing the product packaging. On-dose technologies provide a more robust and reliable means of identifying counterfeit pills, verifying product identity, and ensuring product traceability.

References

1. <https://www.statnews.com/2019/05/07/stopping-murder-counterfeit-medicine/>, accessed April 2020
2. WHO study on the public health and socioeconomic impact of substandard and falsified medical products, November 2017 https://www.who.int/medicines/regulation/ssffc/publications/SE-Study_EN_web.pdf?ua=1, accessed Sept 2019

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