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Beating the Scammers with On-Dose Authentication

The only reliable way to verify that medicines are authentic is the use of on-dose microtaggants.

Pharmaceutical companies are accountable for ensuring that their medicines are safe when they are delivered to patients. The COVID-19 pandemic has led to a dramatic increase in the number of online pharmacies and the supply of counterfeit drugs, prompting the World Health Organization to designate improved pharma supply chain security an 'urgent health challenge of the next decade'.[1] As scammers become more sophisticated, track and trace is no longer sufficient to secure the supply chain, and the only reliable way to verify that medicines are authentic is the use of on-dose microtaggants which can easily be incorporated into individual tablets or capsules. The inclusion of taggants is simple and cost-effective, providing a digital security layer to safeguard patients and uphold brand integrity. A unique advantage is a positive impact on the speed of decision making and action by enabling suspected counterfeit tablets to be verified in real-time, rather than waiting days or weeks for test results.

Smarter medicines incorporating microtaggants have the potential to improve health outcomes by engaging directly with patients and helping to ensure that they take the right medicine at the right time. The technology could also to reduce the use of package inserts, allowing vital information and patient support materials to be easily accessed in electronic format—something that has long been favored by the FDA.

THE THREAT OF ILLEGAL ONLINE PHARMACIES

Globalization and outsourcing have led to complex supply chains for many pharmaceutical products. This increases the risk of counterfeiting and diversion, which can result in health risks and loss of trust for the consumer, with reputational damage and reduced revenue for the brand owner. Many countries have introduced serialization legislation that requires product identifiers to be used on each package to provide traceability throughout the distribution supply chain, but even if a package is authentic, serialization cannot verify whether the medicine inside is real or fake or if it has been diverted. At the same time, counterfeiters are becoming more adept at copying many aspects of a medicine, in-

cluding the package, label, and even the appearance of the tablet itself. Moreover, counterfeit and diverted medicines can also find their way into legitimate supply chains.

Recently Gilead, a leading provider of medicines to treat HIV, issued a warning that genuine bottles had been tampered with using a counterfeit foil induction seal and that some authentic bottles contained fake antiretroviral tablets.[2] These drugs are expensive and considered specialty products; they are distributed by a small number of authorized wholesalers in the USA, and the FDA requires them to be dispensed in their original packaging. The packaging appeared legitimate and there was no easy way for patients, or people in the supply chain, to quickly determine if the actual tablets were real. Not only can counterfeit medicines potentially contain dangerous ingredients, but they often have no therapeutic effect. HIV is a life-threatening disease and a patient's viral load can quickly go out of control if they stop taking genuine medication. More and more, counterfeiters are targeting valuable medicines like this because of high demand from patients—and the high monetary rewards.

Since the start of the COVID-19 pandemic, there has been a massive increase in online drug sales as criminals were quick to take advantage of the crisis. Over the past two years, it has been reported that 100% of online searches for medicines return links for illegal pharmacies,[3] over 90% of online pharmacies operate illegally and around 62% of medicines purchased online are fake or substandard.[4] Worryingly, over 90% of incidents were in the highest risk category, potentially endangering life.[5] In May 2020, a record number of fake online pharmacies were shut down as Interpol led a global crackdown that saw more than 100,000 online marketplaces offering illicit drugs removed.[6] Unfortunately, these valiant efforts have only had a minor impact on the illegal marketplace, as over 600 new illegal pharmacies are coming online each month.

FIGHTING BACK WITH ON-DOSE TAGGANTS

Patient demand for purchasing medications online will likely continue to grow. There is increasing recognition that package security measures cannot provide a safeguard against counterfeit medicines, with many internet pharmacies routinely repackaging and separating the medicine from its original secondary packaging. Appropriate security measures for drug products will be determined by the risks associated with each product and by different stakeholders (*Figure 1*). For low-risk products, serialization on the secondary packaging may provide adequate protection but for the highest risk products, on-dose security, whereby each tablet or capsule is tagged, is the only workable solution to provide the enhanced protection with fast authentication at dosage level.

On-dose authentication is achieved with the direct inclusion of either molecular taggants or microtaggants to the dosage level—uniquely encoded materials that are virtually impossible to replicate or reverse engineer. These can be incorporated into coatings or inks used on tablets and capsules and detected in the lab or the field using a desktop or mobile reader.

THE TECHNOLOGY

Molecular taggants

These taggants are developed from non-biologic, inert DNA. Different versions of the same molecule can be produced, so it can be made regional, product, or company specific. The taggant is simply added to the standard tablet film coating or capsule printing process in extremely small quantities (parts per billion) and is easy to detect using appropriate reagents. Molecular taggants are not damaged by exposure to heat and pressure during manufacturing, so they can easily be incorporated and the integrity of the taggants remains consistent throughout the shelf-life of the product.

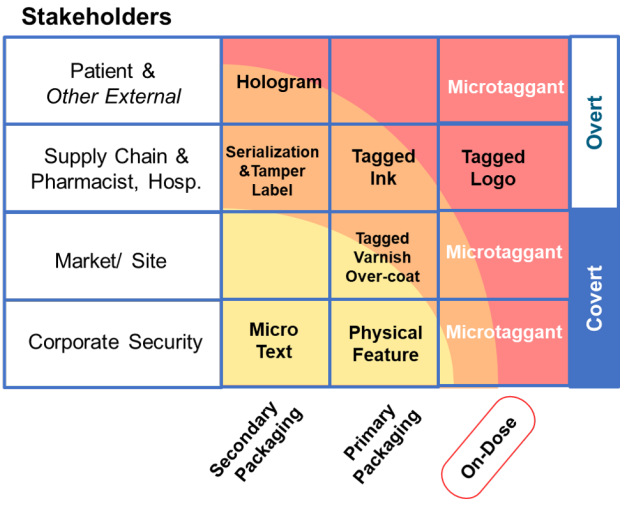

Figure 1: Stakeholder security measures for pharmaceutical products.

Silica microtaggants

Silica is already present in virtually all tablet and capsule formulations, making it an easy material to use. The microtaggants are spectrally encoded materials that are customized with unique information for product verification and traceability. They can be incorporated into the film coating or printing ink manufacturing process and are detected by how they reflect light. Proof of concept shows that it is possible to identify the on-dose microtaggants using lab readers, as well as smartphone technology, which is now being further developed to enable direct patient interaction.

SECURING PRODUCTS

These on-dose technologies represent an innovative step-change in the ability of companies to combat counterfeit and diverted medicines, providing opportunities to better protect medicines by exploiting film coatings already commonly used on solid oral dosage forms.

1. Ease and speed of verification

Smarter medicines with on-dose molecular taggants or microtaggants can be authenticated at any stage of the supply chain. A major advantage of the approach is that it allows pharma companies to determine if the product is real or fake in real-time, regardless of whether they have access to the packaging. Machine reading of security features is also faster and more reliable than manual inspections and will be suitable for high volume applications. The technology equips product quality teams with a faster way to identify rogue batches and make more informed decisions

as to whether a batch needs to be held pending further investigation or immediately recalled.

2. Cost-effective and reliable
Expensive package security measures are often susceptible to defeat within weeks or months, but on-dose technology is almost impossible to replicate. The quantities of taggants added to film coatings or inks are so small their use has no impact on how coatings are applied, and they will not affect product stability, disintegration or dissolution. The cost per tablet is negligible relative to other manufacturing costs as the taggants are simply included in the standard film coating or tablet printing process.

3. Overt or covert options
The technology can be used as a covert or overt solution based on the needs of the brand. Molecular taggants are ideal for companies that want a covert solution where very few individuals are aware that it is being used; while silica microtaggants have the option to be included as either covert or overt markers.

PROMOTE PATIENT ENGAGEMENT

But this technology doesn't just help deter counterfeiters; it can also be used to better engage with patients. Some pharma customers want to use the on-dose technology in a very covert way, so only a small number of people within the company would know about the presence of the taggants. Others are interested in a more overt approach, including consumer participation, given that an increased number of people are buying medicines online.

The evolution of this technology is now towards options that allow companies to engage with their patients and confirm the authenticity of medicines using a smartphone. So, when a patient scans a tablet to check authenticity, companies can also provide access to support materials, such as the product leaflet, information that explains the benefits of the medicine, the importance of adherence, what to do if there are side effects, and even the ability to opt into reminders to take the medicine at the right time. In other words, such "smart" medicine not only brings authentication closer to the patient but also helps them feel more comfortable with how and why they need to take their medicine.

Improve adherence and achieve better outcomes for patients
It is easy for someone who is sick or confused to take the wrong drugs or miss doses. The app could remind patients when it is time to take their medication and which tablets to take. For many conditions, for example, following an organ transplant or for the treatment of certain cancers, adherence to the correct medication regime is vital. Scanning each tablet before it is taken would reassure the patient, and results could also be relayed to a caregiver or medical team, alerting them if the patient has failed to scan the medication at the correct time.

Promote patient trust and brand loyalty
Reports of patients with extremely serious conditions failing to take their medication due to concerns over side effects, is another cause for concern. The app could alert and actively assist patients to recognize certain side effects, provide reassurance that they are not unusual, and help manage these initial challenges to ensure they stay compliant with their regimen. There could also be updates as new information becomes available. This type of engagement could give the patient a sense that the drug manufacturer is doing all it can to support them.

Improve the robustness of clinical trials
Smartphone apps have the potential to verify that patients are taking the right medicines at the right time during decentralized clinical trials, reducing the opportunity for error and providing validated patient engagement at any stage in the trial, without impacting the blinding process.

MOVING TOWARDS A SMARTER, SAFER FUTURE

Incorporating taggants directly into a product's film coating or primary packaging provides a unique opportunity for brands to secure their product. Using a smartphone app extends this technology to interact with patients to improve outcomes. Through real-time data collection and analysis, patient-focused product teams will be able to provide more personalized support resources when needed.

The introduction of a smartphone app means that patients can play a part in verifying their medication, and that interaction could be leveraged to add value through patient engagement and brand loyalty. Software development kits allow for customization by individual companies for specific medications or target patient groups.

Smart medicine is an increasingly important topic for the pharma industry as companies look for better ways to engage more with patients and encourage them to take their medicines as prescribed. There are many factors that contribute to making a medicine smart, including the packaging, the dosage form itself, and how the patient may engage with the medicine. All patients can benefit from greater information and support that ultimately improves safety and adherence. **CP**

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GARY POND has over 25 years of life science expertise and eight years in healthcare technology. He has held sales and marketing leadership positions at Sanofi, Merck and Abraxis Bioscience. Immediately prior to joining Colorcon, Gary led the Brand & Marketing Center of Excellence at IQVIA. He currently leads the commercialization efforts for authentication solutions at Colorcon, a major provider of pharmaceutical film coatings and excipients.