Combating Counterfeit Medicines with Technology

A novel remedy to an increasing problem

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For decades, highly branded and valuable goods have been targets for fakes. It's not the oldest profession, but counterfeiting has been around since before the Middle Ages when skilled craftsmen attempted to make and pass off fake English and Viking coins. Fast-forward to modern days, and the stories of fake designer goods abound on all continents.

In the last three decades, even pharmaceutical companies have come under increasing attack by criminal organizations that manufacture fake medicine and successfully steer substandard and dangerous goods into legitimate supply chains. Today, there are more drugs in development than ever before, and companies are continuing to bring to market new and targeted drugs to fulfill the growing demand by patients and medical providers.

Counterfeiting and the Pharmaceutical Industry

Pharmaceutical companies compete and invest in drug development for specific and growing markets including psychiatry, oncology, and general lifestyle-enhancement. These companies will often invest billions of dollars into the development of a single drug, where patent protections can be obtained and the company can recover high margins over a long period of time to recoup the development expense (and to provide an acceptable return to shareholders).

As these new products grow in distribution and pick up market share globally, they also become targets for counterfeiting enterprises that aim to produce a fake product at a fraction of the expense. Unbeknownst to the general public, these counterfeit rings then get to enjoy the same gross margins received by legitimate manufacturers while supplying product that could be lethal to the consumer.

We continue to hear stories of fake drugs being discovered worldwide, including well-known brand names in multiple markets. The amount of financial losses to the industry are estimated to be around $80 billion each year and growing. It is worth noting that there has been an extremely proactive effort on behalf of most major pharmaceutical companies to combat the counterfeiting of their own products, but even so the problem persists.

There are obvious reasons for these companies to mobilize investments to address this issue, including concern for patient safety, financial losses from missed sales, brand erosion and, of course, potential financial impacts from product liability. The larger companies with the most to lose have created entire divisions known as "brand protection groups" that are usually composed of staff with multiple disciplines and experience, including formulation, packaging, supply chain management, marketing and legal backgrounds.

These individuals tend to work across the organization to lead the effort to detect problems and move quickly to mitigate them. Moreover, since the early 2000s many companies have deployed 'security features' on their packaging, including UV and other invisible inks, holograms, special phosphorus materials and other covert and overt security measures in an attempt to stay a step ahead of the counterfeiters.

Many of these technologies have proven useful and have been effective for a time. Some are still used widely today. But with the fast-moving technology gains of recent years, criminals have access to digital printing, packaging duplication equipment, and knowledge of manufacturing through the recent globalization of the pharmaceutical industry itself. Further, materials that were once difficult to procure (UV and infrared inks, phosphor compounds, holographic labels) are now becoming widely available via the Internet and through global sourcing. Criminals now know how to create medicines with well-produced fake packaging, and quickly find points of entry to supply chains.

The rise of online pharmacies has also allowed criminals to distribute these fake and substandard medicines on a global basis with efficiency and anonymity. In the United

States, many consumers will purchase prescription drugs via the internet in search of hard-to-believe deals. The National Association of Board of Pharmacy recently conducted a study of over 10,000 Internet sites and determined that 97 percent of them were operating in conflict with pharmacy laws and practice standards, including failing to require a prescription and selling product that is not FDA approved.

Many of these sites also obscure or falsify their true physical address. In more than 50 percent of cases, medicines purchased over the internet from illegal sites that conceal their physical address have been found to be counterfeit .

The Gray Market: The Other Side of the Problem

Beyond counterfeiting, pharma manufacturers must deal with "product diversion," where product is sold into one distribution channel at a discounted price but is ultimately found in another, higher-priced distribution area. With tiered pricing structures, diversion of genuine product allows gray market operatives to profit from the arbitraging of these pricing differences, to the financial detriment of the pharma manufacturer.

By having the ability to verify the specific lot of the drug product itself, the brand owner can track back through its legitimate supply chain to discover the source of this unauthorized product diversion. In investigating criminal cases, the FDA has helped prosecute diverters for improperly obtaining drugs intended for nursing homes and selling them to other customers via gray market distributors.

They found medicine intended as physician samples being diverted into the regular drug product supply chain. In one case, a pharmacist stole drugs from a hospital for resale via the pharmacy. And cargo theft of shipments of pharmaceuticals are a common occurrence, with stolen product finding its way back into the authorized stream of commerce.

Where Does the Fake Drug Problem Stand Today?

Today, the industry keeps upping the ante by licensing new technologies and deploying them throughout their supply chains to stay a step ahead. It is a constant cycle and the folks working in these brand protection groups constantly assess risks by product and country, making investments in new technologies with the hope that counterfeiters won't find a way to mimic or spoof the system.

In many cases suspect product must be brought back to the company's own laboratories and chemical testing must be performed to know for sure whether the drug is legitimate, a process that can take days to resolve. But even when these laboratory tests prove the product meets the formulary requirements, the company still may not know for sure if it was made by them. The origin of the drug can also be difficult to discover because the packaging could be fake, reused or simply mislabeled.

Therefore there exists a battle that continues, mostly out of public view, between brand owners of high-profile pharmaceutical products and the criminal organizations that stand to profit through selling the fakes or diverting legitimate product to unintended distribution geographies.

The question that comes to mind for many is, "with all of the advances in technology and the seemingly tight controls over pharmaceutical manufacturing and sales, why is counterfeiting still such a vast and growing problem?" It's a good question and one not easily answered.

Much of the problem stems from globalization of the pharmaceutical industry itself. With the goal of cost reduction and an eye on competitiveness, many companies have outsourced supplies of excipients, APIs, and even the actual manufacturing of their final goods around the globe. This includes suppliers and contract manufacturers in lower cost countries like China, India, and many other countries where the majority of counterfeiting operations are located. Sifting through the labyrinth of the good guys and bad guys can be daunting in this new globally-outsourced ecosystem.

Given these conditions, it's not surprising that counterfeit and substandard medicine finds its way into every country and every market. In July 2014, police in Southern California broke up a crime ring from Mexico that was supplying California outlets with fake prescription medication, including Ritalin, Xanax, Adderall, antibiotics, analgesics and lifestyle drugs.

The drugs were found to have been brought in from Mexico, Pakistan and other countries, and many were fake or adulterated, including some made of shredded plastic. In May 2014, the U.S. Department of Justice announced the conviction of a U.S. resident—the third in a group of conspirators spread from Texas to Illinois—guilty of importing fake Viagra drug product from China.

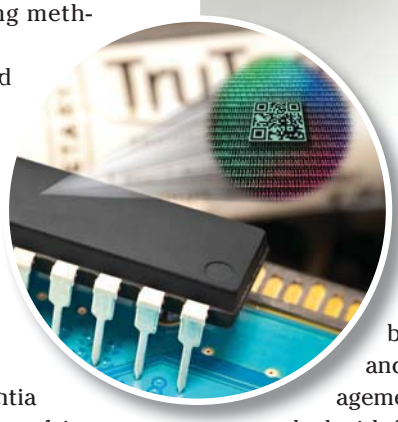
And the recent counterfeit Avastin case illustrates how complex the counterfeit supply chain can be as the fake cancer drug took a path around the world that touched Turkey, the United Kingdom, Denmark, Canada, Barbados and Switzerland, before landing in the United States. Once in the U.S., the counterfeit drug made its way to 22 states and 76 doctors across the country.

Careful examination of new technologies will be key in protecting patients against pharmaceutical counterfeiting.

Incidents around the world are too numerous to recite, but what is clear is that the counterfeit drug problem is growing and the battle between multi-billion dollar pharmaceutical companies and sophisticated criminal enterprises rages on.

Technology's Helping Pharma Combat Counterfeiters

The hologram became a de facto standard security device in the 1980s, and by the 2000s, pharmaceutical companies added to this by introducing invisible inks, color-shifting inks, and laser readable printing methods to their highest profile products. At the time, these technologies were quite advanced and sometimes difficult to copy, but not always.



In 2003, GSK readily admitted in its communications with the FDA that its overt security technologies can be compromised in just a few months. By 2013, even with other advancing printing technologies, including 2D bar codes, many of the tried-and-true security methods had become subject to compromise.

In an October 2012 industry report from Scientia Pharmaceutica, it was concluded that even counterfeit-resistant technologies must be rotated regularly as they can themselves be duplicated, often within 12-18 months. Also, it reached an additional conclusion that the overt and covert packaging technologies are rendered useless if a drug is repackaged.

It is a long-held, and usually wise, belief that a company should never just use one security technology to combat counterfeiters for the above reason. Once compromised, the entire technology is rendered potentially useless and it becomes impossible to rely on it any further. Therefore, it is most commonly the practice of pharma companies to deploy multiple "layers" of technology on their packaging and as indicated herein, routinely rotate technologies in and out to reduce the ongoing risk of compromise. However, it costs millions of dollars to bring on and phase out new technologies, and this is often frustrating to product management, operations, and partners who have to deal with frequent changes to packaging production and global coordination.

Advanced printing technologies could be key in track n' trace efforts.

The FDA and Physical-Chemical Identifiers

A long-discussed possibility has been adding unique PCIDs to products that make the tablets and pills themselves identifiable without relying on packaging. The pharmaceutical industry has welcomed the idea for years and in 2011, at the request of industry, the FDA issued its final guidance to companies entitled *Guidance for Industry Incorporation of Physical-Chemical Identifiers into Solid Oral Dosage Form Drug Products for Anti-counterfeiting*.

This guidance provided the industry with a clear line of sight on how to best go about the process of including a unique identifier inside the drug itself. Essentially, the FDA recommended that, in order to ease the regulatory filing requirements, manufacturers use PCIDs that are well studied materials, such as those that are already affirmed as "generally recognized as safe" or are on the list of materials found in the FDA Inactive Ingredient Guide.

In those cases, the regulatory disclosure could be as simple as inclusion in a year-end annual filing. As a result, companies are starting to explore various technologies for on-dose authentication that would not require major changes to the manufacturing process, be cost-effective, and be in line with the guidance issued by the FDA.

Identifying Unique Drugs, Dosages, and Lot Numbers

TruTag Technology has introduced, and is now commercializing, a micro-sized particle material that can be safely added to solid oral dosage form (SODF) drugs with-

out modifying the manufacturing process already in place. Further, once included in the medicine itself, the taggant will last indefinitely through the product's lifecycle, and can be read using one of TruTag's proprietary scanning devices.

Since TruTags are inert and made of 100 percent silicon dioxide (SiO2 or silica), which is a GRAS (generally recognized as safe) material, the solution falls squarely within the FDA's PCID Guidance requirements. Also, these tags can be engineered to go on at very trace amounts and therefore be very cost-effective to the manufacturer.

The TruTag platform is secure because it uses a highly proprietary and patented process for etching the codes into microscopic silica particles. The electro-chemical process must be accomplished using machinery that is not available on the open market, and is not otherwise possible using short cuts or less sophisticated methodology.

Further, interpreting the code using TruTag's proprietary device uses high-security encryption and custom software that makes the solution virtually impossible to spoof or copy.

TruTags contain a unique signature or 'bar code' that can only be interpreted by the TruTag scanning device in confirming the drug's authenticity and providing product intelligence. This can include the product name, dosage, manufacturing location, and even lot or batch number.

It can even show the user a picture of the product, package, and other images to confirm that the correct drug is in the correct location. Further, these codes can be changed periodically to provide incredibly high levels of security.

So what will it take for industry to adopt this cutting edge 'on product' security that will change the landscape of how pharmaceutical companies examine and police their supply chain? Could this product be able to fully confirm physical evidence of the drugs provenance and origin?

Coupled with other track and trace methods already being implemented to the packaging, this could be the ultimate audit tool that the pharma industry has been seeking.

TruTag is already being tested in pharmaceutical manufacturing locations and is forming partnerships with other contract suppliers to be able to offer the solution in short order.

The biggest challenge of incorporating the solution into the existing manufacturing process has been completed, and the company is poised to enter the market with the TruTag solution, which it hopes will become the de facto standard for identifying SODF drugs in the future. ■