MULTIPLE STRATEGIES AND TECHNOLOGIES TO COMBAT COUNTERFEIT DRUGS

ABSTRACT

Keywords: Anti-counterfeit, Drug Supply, Biomarkers, Nanotechnology, Radio Frequency Identification Devices (RFID), ePedigree, Supply Chain, Brand Erosion, Brand Labeling.

An anti-counterfeiting strategy helps to effectively detect counterfeit products, increase audit compliance, enhance supply chain management capabilities, prevent brand erosion, and eliminate supply chain routing leakage (e.g., misplaced inventory and drug expirations). This strategy can identify multiple best-fit solutions for meeting a company's requirements via Radio Frequency Identification Devices (RFID), ePedigrees, label security, dosage unit level security, nanotechnology, and other capable solutions to combat counterfeiting of drug products. Government regulation will play a future role in the coming years in determining the strategies companies will use. A recent trend is the push for covert strategies such as nanotechnology and biomarkers to safeguard the supply chain to protect high revenue drugs. These are safe for human consumption and are added to the labels or pills directly. They are confirmed for authenticity via an external reader based on spectral properties or receptor binding assays. One item alone will not protect the companies from counterfeit drugs, but a strategy with a multi-level approach will lead to safeguarding the supply chain and increasing revenues. This will result in decreasing the number of counterfeit products in the marketplace and improving patient safety and enhancing product authenticity and identification.

The U.S. Food and Drug Administration (FDA) has seen a rise of counterfeit drug cases since 2000 when there were only six. In 2006, the number of cases rose dramatically to 54 (Bernstein, 2007). The market for counterfeit drug is approximately $40 billion (WHO, 2006). According to the Center for Medicines in the Public Interest, counterfeit drug sales globally will reach $75 billion by 2010. This represents an increase of 90 percent from 2005 (WHO, 2006) and will represent 14 percent of the total drug market (Pitts, 2005). Furthermore, it is estimated that 10 percent of the global medicines are counterfeit. Approximately 60 percent of counterfeit drug cases occur in less developed countries in which 25 percent of their drug supply is counterfeit (Morris, 2006). The largest producers of these drugs are Southeast Asia, Nigeria, Russia, Mexico, Brazil, and Latin America (U.S. Immigration and Customs Enforcement, 2006).
Counterfeit drugs are an increasing threat in the marketplace. These substandard drugs affect human lives as the quality and/or type of drug is harmful to the patient. These products may not cure the targeted diseases and could possibly even kill patients. Also, they affect the profits of the companies which manufacture the drugs. Pharmaceutical companies invest large amounts of resources to create drugs. They spend up to 12 years and $1.2 billion on clinical development for drugs (Archarya, 2006). However, only 30 percent of drugs which are approved and marketed produce revenues that match or exceed initial costs (DiMasi, 2002). Therefore, any counterfeit drugs sold as legitimate drugs reduce the companies’ revenues and lead to lower profits.

There are five different types of counterfeit mechanisms in which drugs are manufactured or distributed without proper regulatory approval and do not meet the determined standards of safety, quality, and efficacy (WHO, 2007):

- No active ingredient (43 percent)
- Low levels of active ingredient (21 percent)
- Poor quality drugs (24 percent)
- Wrong ingredients (2 percent)
- Wrong packaging or source (7 percent)

Counterfeiting can apply to both branded and generic products. In wealthy developed countries, expensive drugs such as hormones, steroids, and antihistamines are frequently counterfeited due to lifestyle preferences. While in developing countries, those used to treat life threatening conditions such as malaria, TB, and HIV/AIDS are chosen to be imitated due to their relatively high costs. As this trend continues, other drugs such as anti-cancer and anti-virals might be next on the list due to the high costs of these drugs and the lucrative returns by the counterfeiters.

SOURCES OF COUNTERFEIT MEDICINES

Counterfeit drugs can be diverted and sold from various channels within the drug distribution system due to its complexity. There is no enforced government mandate to track the drugs efficiently within the system which allows for openings for counterfeiters throughout the system. Drugs can be diverted from their original purpose and sold outside the regulated distributed channels. For example, free samples to doctors may be sold illegally within the system. Patients may, in turn, sell their prescription drugs for a profit. Also, drugs sold for lower prices in various countries can be sold to other markets where the price is higher. These drugs are not regulated through safeguards as they are sold outside the normal distribution channels.

The 1988 Prescription Drug Marketing Act (PDMA) introduced a need for paper drug pedigree to track the drug from manufacturer to end user. However, it has yet to be fully implemented throughout the industry and supply chain due to the high recordkeeping effort needed to maintain this type of system. Incomplete paper pedigrees lead to increasing the risk of counterfeit drugs in the marketplace as the ingredients or products are not tracked within the supply chain. On the other hand, complete paper pedigrees help validate the authenticity of the drug but counterfeiters are finding ways around this paper-based process. For example, illegitimate secondary wholesalers can prepare fake paper pedigree documents
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which pharmacies detect as valid. An increasing trend is to use tools and processes to copy drug labels and packages. This makes it difficult to identify the real drug from the fake copy due to the striking similarities between the two. Repackaging is another way to bring expired or compromised drugs into the distribution system and mix them with genuine drugs. Finally, the lack of tamper-evident packaging allows the original packaging to be reused for unregulated drugs (HHS, 2004).

The differences between counterfeit and authentic drugs can be difficult to detect unless one looks closely at the bottle or packaging. These can be minor changes in the product container, label, or the individual pill that can be hard to visually detect by the human eye. For example, a change in the type of font, border type, or logo color is difficult to detect unless someone knows how they are packaged by the manufacturer (Palmer, 2004; Genentech, 2001).

Therefore, counterfeit drugs are passed as real drugs due to the counterfeiter's abilities to reproduce items. As a result of illegal medical drugs within the system, the companies that manufacture and sell the authentic products incur large losses of revenue. This decreases sales and profit margins due to other unauthenticated "substitute" products that people are buying in place of the authenticated drug product. Large inventory losses and write-offs are placed on the balance sheets due to routing leakages and medicines which were not purchased legally. As noted earlier, these drugs threaten patient safety leading to possible deaths. There are audit and regulatory compliance issues with counterfeit drugs as they do not follow the regulated channels. Furthermore, the supply chain for the drugs is complicated due to higher inventory carryover leading to increased costs. The supply chain issues push for an efficient and reliable tracking mechanism which has yet to be mandated by the industry or regulators due to high initial costs and lack of industry standards.

ANTICOUNTERFEIT STRATEGIES

An anti-counterfeiting strategy helps to effectively detect counterfeit products, increase audit compliance, and enhance supply chain management capabilities. This strategy can identify the multiple best-fit solutions for meeting a company’s requirements via Radio Frequency Identification Devices (RFID), ePedigrees, label security, dosage unit level security, nanotechnology, and other capable solutions to combat counterfeiting of drug products. One item alone will not protect the companies from counterfeit drugs, but one with a multi-level approach will lead to
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safeguarding the supply chain, prevent erosion of the brand image, and increase revenues. This will result in decreasing the number of counterfeit products in the marketplace and improving patient safety and enhancing product authenticity and identification. It also meets the necessary increased audit compliance by reducing the supply chain issues such as time to account and inventory tracking. Therefore, this leads to an increased bottom-line by effectively locating its products within the supply chain from manufacturer to patients. This enables the drug manufacturer to capture higher revenues for legitimate drugs in the marketplace.

RFID
New trends in the industry are creating unique opportunities within the anti-counterfeiting market. The FDA has also recommended that pharmaceutical companies start using RFID as a means of better tracking drugs. These are radio transmitters that can be attached to drug packages, medicine bottles, or active ingredient containers and scanned to emit an electronic product code. Individual packages of drugs or their respective ingredients can be monitored throughout the supply chain from manufacturers to distributors and wholesalers to pharmacies (Wyatt, 2006). As a result of enhanced inventory management practices, RFID can decrease revenue losses as a result of stock-outs and drug expirations and create cost savings of $2 billion worldwide (Paddison, 2005).

One major obstacle for RFID tags is the costs associated with the system. As RFID tags become more of a commodity, the prices for tags and readers will be significantly lower and lead to more cost savings. Each passive tag costs $0.25 – $1.00 while the each reader costs $500 – $3000. Furthermore, there is the need for other resources such as computers, networks, databases, and additional training for the end users. A study by A.T. Kearney believes implementation of a RFID system for a manufacturer with $10 billion in prescription sales will receive annual benefits of $20 – $55 million with the system excluding initial and recurring costs. A large distributor with $40 billion in prescription product sales will have an annual benefit of $12 – $24 million (Paddison, 2005).

In 2005, Pfizer announced it would use RFID tags on its Viagra® bottles which are sold in the United States. GlaxoSmithKline took the initiative by planning to implement RFID tags on one of its anti-HIV drugs within the next 18 months. Furthermore, Purdue Pharma utilized RFID tags on Oxycotin® bottles to better track and authenticate the medications (FDA, 2004). RFID tags can be embedded into the label of the medicine bottle or within the blister pack to prevent easy removal.
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This is very similar to airline initiatives to utilize RFID tags rather than traditional barcodes to track the baggage location in real-time. The tags have a read rate of 99 percent, whereas bar codes have a read rate of 85-90 percent. This higher read rate leads to less manual sorting due to unreadable bar codes. This also decreases the time and costs in getting the bags to the customers. The current cost for bag retrieval is estimated to be $2.5 billion a year by The International Air Transport Association (Demerjian, 2005).

<table>
<thead>
<tr>
<th>Type</th>
<th>Benefits</th>
<th>Costs</th>
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<tbody>
<tr>
<td></td>
<td>Intangible Benefits</td>
<td>One-time</td>
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<tr>
<td>Large Manufacturer</td>
<td>1. Protect Overall Supply Chain</td>
<td>$15 – $20</td>
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<tr>
<td></td>
<td>2. Prevent Stolen and Lost Products</td>
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<tr>
<td>Large Distributor</td>
<td>3. Decrease Recovery Costs</td>
<td>$9 – $20</td>
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<td></td>
<td>4. Protect Brand Loyalty</td>
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- Large Manufacturer — $10 billion in prescription product sales
- Large Distributor — $40 billion in prescription product sales

Source: Paddison, 2005
Another development is the focus on ePedigrees to create a more efficient supply chain in a secure environment. The PDMA states that pedigrees are required for all non-Authorized Distributor of Record wholesale distributions (SupplyScape, 2006). In 2006, ePedigrees were implemented in only 200 million medicine bottles and blister packs. In comparison, the number of prescriptions dispensed in 2006 was 3.7 billion (Lamb, 2007). As drug shipments arrive within the various elements of the supply chain, ePedigrees are matched and signed to confirm and validate the authenticity of the drugs. Software programs show the detailed information of the validated drugs within the supply chain and their specific location at various time periods. ePedigree will be utilized within all steps of the supply chain from manufacturer to retailer and customer.

This will provide information on the “chain of custody” of the drug and decrease counterfeit drugs in the supply chain. As the drug flows through the supply chain from manufacturer to wholesaler(s) to pharmacy, each step is tracked via an Internet portal. In the ePedigree system, the medical product’s information is verified and documented during each step within a secure environment. Therefore, a product’s path is followed in real-time via the portal to ensure it is coming into the system from a valid source. A new data management infrastructure to store and share the data has to be implemented within the company. A few vendors are already providing services for the new system in order to easily transition into this environment.

The ePedigree shows detailed real-time information regarding the product and its distribution within the supply chain. It provides general product information along with a tracking number for easier identification. As it travels from one location to another, it will provide the transaction details including names, addresses, and drug license numbers. It will also have the receiving person’s name and electronic signature. In addition, it will include details such as the production number and...
expiration date so it can easily be traced back in the future for recalls or quality checks (Bernstein, 2007).

OVERT STRATEGIES
Pharmaceutical companies are experimenting with overt strategies such as optically variable devices (OVDs) that can help track/authenticate drugs. Some companies are testing holograms, color-shifting inks and watermarks that can help them authenticate medicine bottles and packages. Similar techniques are currently utilized in safeguarding the U.S. currency. The currency utilizes multiple safeguards which makes it difficult, time-intensive, and costly for counterfeiters. It utilizes a dual color-shifting ink, watermark, security thread within the paper, and new symbols on the bill. In 2004, the pharmaceutical companies started using color-shifting ink that changed color depending on the viewing angle so counterfeits can be easily recognized by members downstream within the supply (Palmer, 2004). Others are experimenting with using inks or dyes and some are already using tamper-resistant packaging tape on some of their products. Also, there is a change to raised printing in which letters are raised above the paper for easy inspection and detection for counterfeits.

Figure 5: Color Shifting Logo — Changing the Viewing Angle Shifts the Color
COVERT STRATEGIES

A. Markers Emit Light at Specific Wavelength

B. Receptor Binding Test

Figure 6: Nanotechnology Markers Emit Light at Specific Wavelengths and Bind to Specific Receptor Binding Liquid (Weinberg, 2007)
Companies are also shifting to covert strategies which utilize special devices to authenticate the drugs. Authentix utilizes a new method incorporating nanotechnology markers (50 nM to 5000 nM in size) which are mixed into the drug packaging and individual pills. They can be specifically added to the inks, labels, and pill ingredients for easy detection. These markers have spectral properties that “light up” when a light with a specific wavelength is placed on the packaging. For the highest level of security, the markers can be added to the individual pills in order to identify if the drug is counterfeit. The markers are odorless, tasteless, and approved for human consumption. A quick test kit, similar to a pregnancy test, can be performed in the field to determine the authenticity. The pill is put into a special receptor-binding liquid, and a test strip is placed into the liquid. If the specified marker is in the pill, the strip turns a specific color (Weinberg, 2007). Also, Kodak’s Traceless® technology incorporates an odorless and colorless powder within the medicine packaging label or within the drug ingredients. The package is read in real-time with a patented handheld reader to authenticate the drugs. For medicine packaging labels, this method works with conventional printing methods and can be utilized during the manufacturing process (Kodak, 2007).

BENEFITS
Pharmaceutical companies are more concerned about brand image and reputation these days than ever before. This is one of the key reasons to protect the supply chain by utilizing the latest technologies. Counterfeit drugs can lead to drug recall and liability suits which can cost the company millions and billions of dollars. Fen-Phen was recalled in 1997 and led to 50,000 liability lawsuits. The total costs for the recall and lawsuits were estimated at $14 billion (Gilchrist, 2005). In addition, brand loyalty is compromised as consumers perceive additional risk when using a company’s products. It might take several months or years for a product to regain its market share depending on the severity of the initial damage. This will result in lost sales and revenue along with the high costs of marketing and public relations to bring the drug back to the market (Paddison, 2005).

Figure 7: Pharma Value Chain — Shifting Strategies and Technologies from Overt to Covert Results in Increased level of Security at Higher Costs
An anti-counterfeiting strategy can better analyze how these methods benefit the client most effectively depending on business needs, requirements, desired level of security, and geographic location. However, for this strategy to work properly, a multi-step approach has to be implemented because an individual strategy alone has not worked in the past. A multi-level strategy uses complementing technologies that can provide the most protection for a company’s brand and the highest level of security. This will also result in additional costs as the technologies become more sophisticated and the quantity of products becomes marked or tagged. A basic foundation for protecting the Pharma Value Chain focuses on tracking methods such as RFID and ePedigrees. The next step is to protect the medicine bottles and blister packs with overt technologies by increasing safeguards such as raised fonts, color-shifting inks and logos, holograms, and watermarks so they can’t be reproduced by other sources. The final step utilizes covert technologies to protect the individual pills, medicine bottles, and blister packs by incorporating nanotechnology markers and patented ink markers and readers for authentication. By using multiple safeguards into a specific product, it makes it expensive and time-consuming for the counterfeiters. Furthermore, higher risk geographic areas for counterfeit drugs require enhanced security levels and increased layers of protection in order to protect the Pharma Value Chain.

All of these items will lead to better-guarded supply chain and costs savings. This will result in decreasing the number of counterfeit products in the marketplace, improving patient safety, and enhancing product authenticity. It also meets the necessary increased audit and regulatory compliance by reducing the supply chain issues. Therefore, this complementing strategy based on client’s needs leads to an increased bottom-line by effectively locating its products within the supply chain from manufacturer to patient and reducing leakage during the routing process. This enables the drug manufacturer to capture higher revenues for legitimate drugs in the marketplace and protecting the brand reputation.

Figure 8: Implementation of Multiple Strategies for Protecting the Supply Chain, Maintaining Brand Reputation, Increasing Revenue and Profits, and Enhancing Patient and Drug Safety
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