Track-And-Trace Solutions for the Pharmaceutical Supply Chain

How bar codes and RFID can improve traceability, safety and business performance

A ZEBRA WHITE PAPER

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Executive Summary

Industry concern about counterfeiting, diversion, mishandling, mislabeling, and unintended or mistaken administration of prescription drugs is mounting at an unprecedented pace. Stakeholders at all junctures of the pharmaceutical supply chain – from point of production to point of care – recognize the vital importance of traceability. Not only does traceability contribute to product safety and security, but it can also support manufacturers' efforts to improve productivity and profitability.

Interest in, and adoption of, automated track-and-trace systems like bar coding and radio frequency identification (RFID) have grown swiftly. This growth was in part driven by regulations. The United States and countries around the globe are reviewing and passing legislation to enhance safety with respect to pharmaceuticals. As the Food and Drug Administration (FDA) set forth in the 1987 Prescription Drug Marketing Act, which went into effect in 2006, bar code identification is required on all unit-dose medication packaging in addition to at least two forms of anti-counterfeiting protection on the packaging. Both houses of the U.S. Congress are examining issues around medication product security and, as of late 2007, 23 states had passed laws requiring an electronic pedigree (e-pedigree).

As policy-makers move toward e-pedigree adoption, the industry is progressing closer to that goal. Early experiences with bar coding and RFID across various stakeholder groups demonstrate the opportunities and challenges inherent to securing the pharmaceutical supply chain.

This white paper provides an overview of the capabilities of track-and-trace technologies and applications. This understanding will allow pharmaceutical manufacturers to leverage identification and tracking systems to provide internal benefits, as well as to satisfy regulatory and customer requirements and improve patient safety.

Introduction

A perfect storm is driving the development of track-and-trace solutions within the pharmaceutical supply chain:

- Governmental and regulatory agencies are exerting pressure in order to ensure medication product security;
- Providers are becoming increasing concerned about quality of care and patient safety, including secure administration of correctly bar code labeled medications to patients; and
- Suppliers are seeking economical and effective methods to support manufacturing operations, control inventory and manage recalls/returns.

These forces are converging and have thrust issues related to both security and operational efficiency into the national spotlight. Consider these recent statistics:

- Counterfeit drug sales will likely total $75 billion worldwide in 2010, an increase of more than 90% over 2005 levels. Source: The Centre for Medicines in the Public Interest.
- The pharmaceutical industry handles $2 billion worth of returns annually. Source: Health Distribution Management Association (HMA).

- Preventable adverse drug events occur in up to 10% of hospital admissions. 770,000 patients are injured and 7,000 patients die each year due to medication errors. Source: Institute of Medicine (IOM).
- The additional cost associated with treating medical errors is high—estimated at $4,700 per patient. Source: The Joint Commission.

In response, industry thought leaders and regulators are implementing policies and procedures to address these issues. The Joint Commission, for example, has emphasized the need to "improve the safety of using medications" in its 2008 National Patient Safety Goals, specifically mentioning that providers should adopt targeted methods to prevent medication errors (http://www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/08_hap_npsgs.htm; accessed Feb. 15, 2008). Likewise, other groups advocate that all providers need to adopt the "five rights" to prevent medication errors: the right patient, the right drug, the right dose, the right route and the right time" (http://www.psqh.com/sepoct05/barcodingrfid1.html, accessed Feb. 15, 2008).

Industry concern about counterfeiting, diversion, mishandling, mislabeling, and unintended or mistaken administration of prescription drugs is mounting at an unprecedented pace. Stakeholders at all junctures of the pharmaceutical supply chain – from point of production to point of care—recognize the vital need for failsafe track-and-trace methodology. Traceability not only contributes to product safety and security, but it can also support manufacturer efforts to improve productivity and profitability.

The Rise of Counterfeiting

Counterfeiting is top-of-mind with healthcare and pharmaceutical industry leaders. The World Health Organization (WHO) estimates that up to 10% of medications on the market worldwide are counterfeit. In recognition of this disturbing fact, the FDA has quadrupled its level of investigation into the problem since 2000.

Industry groups representing manufacturers, distributors, retailers and pharmacies are active in efforts to prevent pharmaceutical counterfeiting and diversion. Many of these organizations took part in initiatives to identify processes and technologies to safeguard drug products. Tamper-evident packaging, authentication media, stricter pedigrees, improved physical security and increased criminal penalties are among the tactics recommended.

The concept of track-and-trace systems – built around automatic identification technologies—is being championed as the most valuable asset to protect against counterfeiting and diversion. A report from the FDA Anti-Counterfeiting Task Force noted that, "The adoption and common use of reliable track and trace technology…would help secure the integrity of the drug supply chain by providing an accurate drug 'pedigree' which is a secure record documenting the drug was manufactured and distributed under safe and secure conditions."

The Product Safety Task Force (PSTF) of the Healthcare Distribution Management Association (HDMA) confirmed this stance with similar sentiments:

> *"…The key component of track and trace is the ability to uniquely identify individual items. It is this core system element that, in the opinion of the PSTF, makes track and trace the most powerful single strategy currently known for reducing the threat of counterfeiting. When products can be uniquely identified, with a serialized number that serves as a 'fingerprint' for only that item, it creates a very high barrier for entry to counterfeit product.*

…The unique identifier simply points to a record in a database which contains other information about that particular item (e.g., lot number, expiration date, manufacturing location, etc.). This serves as a security feature onto itself as certain information is not carried on the package itself but rather in a controlled database…"

Recent industry reports recommend that drug packaging contain a combination of authentication technologies. A unit-dose bar code encoded with lot and serial numbers is one possibility, while radio frequency identification (RFID) labels on outer packs or cartons is another option. RFID is being considered at the item, outer pack, case, tote, and pallet level. Both bar code and RFID labels can be created on secure media that includes taggants and other identification features, providing an additional layer of protection. While numerous options exist for combining track-and-trace authentication methods, consensus is building within the industry that RFID should be part of the mix. The FDA Task Force states, "Authentication technologies for pharmaceuticals have been sufficiently perfected that they can now serve as a critical component of any strategy to protect products against counterfeiting …Radiofrequency [sic] Identification (RFID) tagging of products appears to be the most promising approach to reliable product tracking and tracing."

FDA: The Driving Force Behind Bar Coding

Because of the economic impact counterfeiting has on manufacturers, distributors and providers, increasing attention has been directed at how to best track the path of individual medications along the pharmaceutical supply chain.

The FDA focused a spotlight on these efforts and recommended a solution in 2004 when it introduced its bar code rule to improve tracking for recall and inventory management. At the same time, the bar code requirement provided much needed protection against counterfeiting and spurred manufacturers to implement track-and-trace solutions across the enterprise.

Since the FDA rule took effect in 2006, manufacturers have marked thousands of drug and human biologic products with a bar code on the unit-dose packaging. New drugs must carry unit-dose bar codes within 60 days of their FDA approval date. The complete rule and summary information are posted on the FDA website at http://www.fda.gov/oc/initiatives/bar code-sadr.

The FDA requires the National Drug Code (NDC) number to be printed as a linear bar code. Two-dimensional (2-D) bar codes and RFID tags cannot be used in place of the linear bar code. The FDA acknowledges that encoding lot numbers and expiration dates could improve recall management and it permits—but does not require – this information on the bar code. The National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) – whose members include the American Pharmaceutical Association, American Medical Association, HDMA, Generic Pharmaceutical Association, Institute for Safe Medical Practices, Pharmaceutical Research and Manufacturers of America (PhRMA) and United States Pharmacopeia—recommends that lot or batch control number and expiration date be encoded in the unit-dose label in addition to the NDC.

Bar codes with lot numbers and expiration dates make it easy to record the information accurately and automatically at any point in the supply chain. This capability improves data accuracy, while reducing the effort to record and transcribe information. The healthcare industry spends $23 billion annually on order management, distribution, transportation and inventory management. Approximately $11 billion of these costs are unnecessary—caused by redundant, non-value-added activities. Manufacturers and distributors can

eliminate these costs from the supply chain by using automated systems for data capture and communication. Without an automated system these costs are shifted to downstream partners.

In formulating the bar code rule, the FDA effectively removed existing industry barriers. Manufacturers argued that few provider organizations used bar codes and that there was little justification for the added cost. At the same time, hospitals were reluctant because unit-doses were not pre-labeled with bar codes. Prior to 2004, in fact, only 30 to 40% of medications in unit-dose packaging were available with bar codes. This figure has increased significantly since then. The FDA accelerated adoption by pointing out that the wide-spread benefits of bar coding would be realized across the supply chain. In 2004, the agency estimated that 478,000 adverse drug events could be prevented and $93 billion could be saved in medical costs over 20 years as a result of bar coding.

Federal and State Mandates

Federal and state governments have begun to move forward with legislation related to the issues addressed in the 1987 Prescription Drug Marketing Act. By fall of 2007, both houses of the U.S. Congress started examining issues with medication product security and 23 states passed laws requiring an electronic pedigree (e-pedigree), according to a September 2007 report in Pharmaceutical Commerce (http://www.pharmaceuticalcommerce.com/frontEnd/main.php?idSeccion=696).

The California Assembly passed a law that is the most far-reaching to date. With a compliance deadline of January 1, 2011, the regulation requires that:

- an electronic pedigree be produced whenever a change in ownership occurs from the sale by a drug manufacturer through to a pharmacy;
- electronic pedigrees be created by interoperable electronic systems;
- each prescription drug be tracked at the level of the smallest package or the intermediate container ("item level");
- a unique serial number be used for each item; and
- Certification/verification is true for every e-pedigree.

It is noteworthy that California's legislation mandates an electronic-pedigree-only program involving manufacturers as well as wholesalers. These rules could strongly influence pending legislation in other states as California's product-handling and/or consumer-protection mandates often establish de facto nationwide minimum standards for manufacturers in a variety of industries.

Bar Coding and RFID

The development of track-and-trace technology has kept pace with the growing body of legislation and regulation. Automatic identification technologies such as bar coding and RFID have been championed as the most valuable asset to implementing effective track-and-trace systems. The FDA, in fact, recommends RFID as a reliable option for carrying e-pedigree information.

How RFID works

The healthcare industry is hearing more and more about how bar coding and, most recently, RFID increase supply chain security and enhance inventory management. Moreover, RFID can help protect against medication errors – like tracking expiration dates so patients are not inadvertently injured. But how precisely does RFID work? Here is an example, excerpted from material presented by RFID Switchboard (http://www.rfidsb.com/index.php?page=rfidsb&c_ID=141; accessed Feb. 20, 2008).

1. The manufacturer places a tag on the product packaging. A number of vendors have created unique tags for pharmaceuticals that can be read only by authenticated readers. The tag contains electronic product codes with unique serial numbers, allowing a pedigree to be created and associated with each individual item (item level tagging). It combines international RFID standards with Public Key Infrastructure (PKI) technology, digital signatures and data encryption. These extra layers protect the core product.
2. The pharmaceutical product goes through a series of check points along the supply chain. Data is verified and updated at various junctures before its final destination. As the tagged pharmaceutical good moves through the supply chain, secure RFID readers record additional events to the tag (e.g., date and time the drug reaches a particular point en route), stored as "markers."
3. Approved parties monitor the event data written to the tag and compare it to corresponding event data stored in a distributed data network. To further decrease the risk of falsifying data, a reader may also be designed to digitally sign each event as it transpires, assuring supply chain managers that the planned event took place.
4. When the product reaches its destination, readers may decrypt the data, and verify its unique tag and ID number. By reading RFID tags and querying the EPCglobal Network, healthcare staff can verify the product's authenticity, as well as its precise expiration date.

Within the RFID sphere, the electronic product code™, or EPC, is an enabling technology. EPC is a numbering system for identifying a specific object in the supply chain. An EPC tag employs the EPC numbering system and utilizes RFID technology. The EPC tag attached to an object contains a unique identifier/serial number for the specific item and may contain other information similar to that found on a bar code.

Experts debate if pharmaceutical tracking needs (as well as a hospital's need to monitor items other than drugs) can be satisfied by basic or 2-D bar code technologies as opposed to RFID technologies. RFID costs significantly more per tagged item than bar coding and there is not consensus that RFID technology is necessary for medication management alone. On the other hand, RFID offers specific advantages over bar coding. For instance, many hospitals are investing in RFID to track medical equipment—and sometimes even patients. Executives and managers from those hospitals often would prefer not to invest in multiple tagging systems (bar coding and RFID) for different purposes.

It is difficult even to make simple, clear-cut calculations to compare the cost of implementing RFID versus bar coding. Costs are dependent on the volume purchased, the type of RFID tag or bar code involved, as well as their associated scanners. In general, however, RFID systems are more costly than bar code systems. Active RFID tags are more expensive than are passive RFID tags, and 2-D bar codes are more expensive than traditional linear bar codes.

Bar codes tend to be simpler; however it is becoming apparent that some of the less costly and more mature forms of RFID are more flexible in terms of purpose and reusability. Because bar code scanning is inherently line-of-sight, manufacturers and wholesalers have long sought a solution that eliminates—or at least reduces—the need for bar codes to be exposed for effective identification. Consider the work required when a

receiving department takes delivery of case containing 40 items—and that one case is one of 40 on a pallet—and that pallet is one of 40 on a truck. RFID allows even the innermost item to be tracked.

This discussion reinforces the argument that some combination in the use of bar coding and RFID will ultimately prevail as a working standard with regard to cost-effectiveness, time savings, accuracy and patient safety. Fortunately, innovations in technology continue to evolve quickly with regard to both categories of technology.

Debates concerning RFID frequencies also exist. While HF (high frequency) is the generally preferred option for item-level tagging, UHF (ultra high frequency) offers a more practical route for pallet-level tagging. Recent developments with UHF are making it a potential contender for item-level tagging. Until further advancements are made, this issue will remain an obstacle to widespread RFID adoption.

Supply Chain Operations

Many professionals are equally enthusiastic about the benefits RFID can bring to inventory management and supply chain operations. Since RFID improves both security and product handling, RFID may quickly find a permanent place in pharmaceutical packaging. RFID labels can be read through multiple layers of packaging without operator intervention, which can reduce the labor and time required for product handling in the supply chain. The EPC RFID system (managed by EPCglobal Inc.) creates a unique serial number for each RFID chip, which can be used as a digital birth certificate to uniquely identify otherwise identical units of the same product.

A report by A. T. Kearney, which focused on over-the-counter (OTC) drug makers, estimated RFID systems could reduce manufacturer distribution labor requirements by 9% and inventory holding costs by 6%, in addition to the 18% reduction in diversion. The Kearney report, "RFID/EPC: Managing the Transition (2004-2007)" is available at www.atkearney.com. A series of studies by the developers of the EPC system predicted additional inventory and cost reduction benefits.

Belief in these benefits led the FDA to encourage adoption of RFID in the pharmaceutical supply chain, including pallet and case labeling. The National Association of Chain Drug Stores (NACDS) and HDMA are among the industry groups who have endorsed this action. Nine leading pharmaceutical manufacturers, distributors and retailers formed a new group led by Accenture (www.accenture.com/) to study the potential for RFID to improve manufacturing, distribution and retailing in the industry.

The U.S. Department of Defense, Wal-Mart, Target and other large pharmaceutical purchasers are providing an additional catalyst to RFID use by requiring their suppliers to place RFID tags on shipments. Several RFID programs set—and achieved—a deadline of 2005 for tagging pallets and cases. These compliance tagging programs are creating a de facto RFID requirement for pharmaceutical manufacturers and distributors. More information about the programs and what is needed for compliance is presented in Zebra's *RFID Readiness Guide: Complying with RFID Tagging Mandates,* available on Zebra's Web site at www.zebra.com.

As a result of meeting the multiple impending labeling requirements, there will be new process capabilities that will provide unprecedented control and efficiency for recalls, returns processing and inventory control. Reading unit-dose codes, RFID tags and security marks can offer increased visibility and a higher quality of information. Many benefits can be gained through insight from information available on unit, case and pallet labels, which can drive further process redesigns in the supply chain.

Early Experiences with RFID

Dublin, Ohio-based Cardinal Health implemented a pilot project designed to assess the suitability of using UHF RFID technology for tracking and e-pedigrees in 2006. Executives at Cardinal Health, an $81 billion global provider of products and services to the health care industry, were largely encouraged by the results of the pilot.

As reported in detail in a recent issue of RFID Update (http://www.rfidupdate.com/articles/index.php?id=1246), Cardinal tracked thousands of individually labeled pharmaceutical products in totes, cases and pallets through a variety of picking, shipping and receiving processes at Cardinal's distribution center in Ohio and at one specific pharmacy location. Two different products were labeled and tracked for the pilot. Cardinal inserted blank EPCglobal Gen2-compliant RFID inlays into labels applied and encoded at the end of the production line during packaging. Cardinal reported 97.7% of labels were successfully encoded for one product and 94.8% for the other while operating at regular packaging speeds. At the pharmacy-receiving level, item-level read rates were relatively low (85.8%), indicating some operational improvements needed to be made. Cardinal's pilot project experience highlights the potential for tracking regimens that begin at the manufacturer level.

In a similar vein, Pfizer announced the results of its pilot project involving the tagging of all Viagra units in May 2007. The pilot, which ran through the end of 2005, tested both UHF and HF tags, and involved several million units of Viagra. When Pfizer announced the results, Viagra was one of only two major pharmaceutical products whose entire product line had been tagged for the United States. (For full details on the results of the project, as reported in RFID Update, see www.rfidupdate.com/articles/index.php?id=1366).

Applications

For many pharmaceutical manufacturers, the batch or lot level visibility is lost as products proceed through the supply chain. Production management, enterprise resource planning, environmental health and safety monitoring, and other systems frequently provide or require lot-level traceability. Extending batch-level traceability to the final product at the unit-dose would maximize quality management and safety benefits. RFID makes it practical to provide traceability at whatever packaging levels can be accessed throughout the supply chain.

In regulated environments where traceability is required, entering data with automated data capture (ADC) technology, such as bar code or RFID, is highly advantageous because it creates 100% accurate electronic records. Studies have found skilled typists make an error once every 300 keystrokes, while the error rate for bar code scanning is estimated at one in one million characters. Data can be entered in much less time with bar code or RFID than by manual recording, and scanned data can be transferred to any database or software application without further manual data entry. Industry experts anticipate that, in the near future, paper pedigrees will be bypassed altogether in favor of electronic records.

The following examples describe potential benefits from using bar code and RFID technologies to automatically capture and provide traceability information for supply chain operations.

Recall Management

While the pharmaceutical industry strives to ensure that recalls are rare and isolated events, they are in fact a common and costly occurrence. Recalls create extensive administrative and logistics burdens that have an immediate impact on operations. The long-term cost—measured by reduced consumer and physician confidence, lost sales, and impact on share prices—depends in part on how quickly and efficiently the recall is handled.

The effectiveness of recall management is a direct result of product information visibility in the supply chain. The amount of information included on pallet, case, carton and unit-dose packaging can eliminate the general, mass recall with notices going out in newspapers and TV news, in favor of a highly targeted, limited recall where consumers may receive notification by a phone call from their own pharmacist or doctor. Encoding lot numbers and expiration dates in bar codes on the unit-dose packaging enables manufacturers and distributors to trace specific products to specific customers. The labels could be scanned as the products are packaged into larger containers (e.g., cartons or cases) to produce an electronic record that could also be encoded in an RFID tag or 2-D bar code on the outer pack, with the process being repeated as materials are aggregated into larger containers.

By marrying lot codes on unit-dose labels with electronic records created by production control software systems, manufacturers could conduct a recall like this: "We are recalling 50mg tablets of Ourdrugicol, lot number 0123456789, made on March 19, 2007, between 8 a.m. and 1 p.m. on production line 2 at our Anytown, NJ, facility. These products were shipped to Acme Drug Distributors warehouses in Memphis, TN, and Columbus, OH. No other products are affected." When the information is available in an RFID tag, affected products can be found with automated methods that minimize the labor and time required to search for and identify the items, while increasing the ability to find a higher percentage of the affected products.

Production control systems and auditing procedures enable manufacturers to isolate quality or compliance problems during production, at the batch level. By enabling batch-level traceability throughout the supply chain, specific quantities and shipments can be recalled. This degree of traceability limits the logistics handling costs and administrative burden, so recalls can be resolved more quickly. The audit trail would also limit liability exposure and prevent lawsuits from unaffected individuals. When returned products are received, lot codes can be efficiently checked with a bar code scan, so unaffected products can quickly be redistributed.

Returns Management

Variable information unit-dose printing could have similar effects on everyday business such as returns management. The pharmaceutical industry handles $2 billion worth of returns annually, according to a study by the HDMA. Poor recordkeeping and the inability to provide audit trails in reverse logistics create inefficiencies and generate losses from otherwise acceptable products that can not be redistributed. The scope of the returns management task is one reason the HDMA position paper on bar coding includes the following recommendation: "*Use bar codes internally wherever possible. Use of bar codes to identify healthcare products has been shown to reduce labor costs in distribution and dispensing while, at the same time, reducing errors.*"

Pharmaceutical returns may be subject to regulations from the FDA, DEA, EPA, OSHA and the U.S. Department of Transportation, plus state and local transportation and biohazard laws. One of the best ways to collect the information and create the audit trail required by these regulations is to record information with bar code or RFID readers, which can easily be programmed to attach a date-and-time record to every transaction. Lot-level scanning with the automatic time-and-date stamp creates traceability, and produces tremendous time and labor savings for data recording. Scanning expiration dates will enable companies to quickly determine if products are eligible for return and if returned products can be redistributed or require disposal or special handling.

By setting shipping or database systems to record shipments to customers by specific lot number, manufacturers and distributors can quickly verify authorized returns by scanning an item label. This practice also helps detect unauthorized or counterfeit products, which would be aided greatly by using some form of brand-protection media. These topics will be explained further in the Product Authentication section (following).

Manufacturing Operations

Enterprise resource planning (ERP), manufacturing execution systems (MES), and compliance and reporting systems all need accurate, timely data. Many production facilities already use bar codes to track work in process, provide electronic signatures, batch records and other documentation. However, if lot numbers are not included on the final product, the link to the electronic record is broken and many traceability benefits are not realized.

Encoding lot numbers in the unit-dose packaging and marrying the information with electronic production records can satisfy 21 CRF Part 11 (Electronic Signatures Rule) reporting requirements and provide traceability to raw material batch, manufacturing equipment, time of production, and equipment operator for example. This data is helpful for recalls, and can also be used for process analysis and quality control. By expressing track production by lot or batch in a bar code or RFID tag, manufacturers are able to extend their audit trail, realize the full value of their enterprise applications and enable new applications throughout the supply chain.

Inventory Management

Modifying pharmaceutical distribution processes that already use bar coding to capture expiration dates in product packaging can produce meaningful improvements. For example, two improvements may be compliance with first-in/first-out (FIFO) handling practices and reduced losses from expired products. Introducing RFID can lead to new automated processes that improve visibility and significantly lower inventory levels.

Improving customer service and creating new sales opportunities can be created by capturing expiration dates automatically with bar code or RFID and marrying them in a database with sales records. A software application could automatically send notification to customers when products near the expiration date. The message, or a follow-up contact by a salesperson, could also ask if the customer needs to reorder to cover potential shortfalls caused by expiration. The program could help customers manage their own inventories, increase sales and reduce the need for rush orders.

RFID tagging enables unattended high-speed reading with significantly less labor than what is required for other inventory control methods. Items can be tracked automatically whenever they are moved, using RFID readers on lift trucks, conveyors, dock doors and other portals. These methods require no operator intervention, which reduces labor expenses. Inventory records are accurate and updated in real time, providing companies the confidence needed to reduce safety stocks. Less warehouse space and capital equipment are likewise needed for management of reduced inventory.

Strong expectations of inventory reductions and improved visibility are driving RFID adoption across industries including retail, consumer goods and defense. A study produced by the MIT Auto-ID Center, which developed the EPC system, projected that manufacturers could reduce inventory levels 10 to 30% by implementing RFID to improve visibility. The benefits of improved visibility, reduced storage and minimal handling can be attained at every segment of the pharmaceutical supply chain. An Accenture study found that improved visibility from RFID could allow manufacturers to reduce their safety stock by up to 30%. In addition, an A.T. Kearney suggests that OTC manufacturers can recoup and produce a sustainable return on capital investments in RFID in slightly more than one year by using the technology for internal inventory control and distribution operational improvements. (AT Kearney report “Meeting the Retail RFID Mandate”)

Product Authentication

The FDA recommends at least two forms of security be used on packaging. Many of the available technologies are complementary, so unit-dose bar codes and RFID identification labels can also provide anti-counterfeiting protection, especially when they are produced on secure media.

Secure packaging and encoding at the unit-dose level aids efforts by pharmaceutical manufacturers and law enforcement agencies to protect legitimate distribution channels and detect diverted or counterfeit products. For example, in July 2003, Pfizer recalled Lipitor after counterfeit pills were found mixed in packages with authentic ones. The subsequent investigation found that the manufacturer's authentic packaging and required labeling had not been used, and that expiration dates had been mislabeled. Printing the unit-dose bar code label on secure, brand-protection media, and authenticating it throughout the supply chain would reduce and potentially eliminate this type of substitution fraud.

The combinations of authentication methods along the supply chain are numerous and offer a wide variety of benefits. For example:

- A pharmaceutical manufacturer could use a pattern adhesive to seal individual packages of medication that would leave a tell-tale mark if the package was opened.
- Unit-dose bar code labels could be produced on material with hidden security features that require a specialized reader for authentication.
- Medication packages could be packed into a cardboard carton for shipping, displaying a seemingly innocent bar code shipping label. The label, however, would have a covert serial number encoded in invisible material for authentication in the field.
- The label could also contain an encrypted RFID chip. Relabelers, wholesalers and distributors would authenticate incoming shipments with low-cost portable readers to ensure no piracy or substitution occurred while the shipment was in transit.
- Before redistributing products to hospitals, distributors could use secure media to produce their own shipping labels, using the same authentication technology or a different one to increase the complexity of protection.
- Hospitals could verify incoming shipments at receiving, or check individual packages as they are placed into inventory or dispensed from the pharmacy.
- Manufacturers, using portable authentication devices, could conduct surprise audits of distribution facilities and hospitals to determine if and where counterfeit goods enter the supply chain. Manufacturers could also authenticate all returns.
- Using bar code or RFID to record lot numbers in supply chain operations could also deter return fraud and diversion. When items are presented for return, they would be scanned to record the lot number. A database lookup would verify whether or not the product was sold to the customer, so the return could be authorized or refused.
- Using bar code or RFID to record lot numbers in supply chain operations could help detect diverted products. When diverted products are recovered, authorities could check database records and follow the audit trail to see who last had possession of them.

Track-and-trace systems are considered the leading defense against pharmaceutical counterfeiting and diversion, but they are not the only tool. More effective use of pedigrees is frequently advocated as a potential solution. Pedigrees can be produced efficiently and provide protection by integrating the operation with identification labeling and authentication systems.

Pedigree Management

Pedigrees are essentially a record-keeping requirement set forth in the 1987 Prescription Drug Marketing Act. They are subject to all the limitations and vulnerabilities of paper-based reporting unless they are produced electronically. Perhaps because of these limitations, the FDA has repeatedly delayed full implementation of pedigree requirements set forth in the Act. With automated data capture and validation technologies emerging as practical tools for the pharmaceutical industry, there is renewed interest in pedigrees as a safety tool.

RFID technology could be especially effective as pedigree records because it can provide unique item identification and is difficult to counterfeit. The FDA Task Force reported: "*RFID technology, which would provide a de facto electronic pedigree, could surpass the intent of the PDMA and do so at a lower cost. In light of the rapid progress toward more effective electronic pedigrees that can be implemented within several years, FDA intends to continue to stay its regulations regarding certain existing pedigree requirements to allow suppliers to focus on implementing modern effective pedigrees as soon as possible.*"

An RFID-based electronic pedigree system would affix an RFID label to pallets or cases. The chip would be encoded with a serial number that uniquely identifies the item, as well as a customer number or other details about the recipient of the shipment. As the RFID tag is read during shipping operations, the shipper's inventory records would update and associate with a specific customer order. A date-and-time stamp would be applied to the scan to create a chain-of-custody record that is accurate to the minute.

The receiving organization could read the RFID label to record receipt and update its own inventory records. A date-and-time stamp could be applied. Organizations could compare the shipped-time to the received-time to see if there were any unusual delays in the process that could suggest the shipment was diverted or tampered with en route. If the receiving organization redistributes the product, it could use outbound shipment scanning operations as previously described.

The combination of a unique ID and automated data capture creates an accurate, timely and secure pedigree record with minimal labor. The system can be completely paperless, with no manual data entry or processing requirements.

Sample Management

Samples, which are usually dispensed in physicians' offices, were excluded from the FDA unit-dose bar coding requirement as they were considered an unlikely source of medication administration errors. Nevertheless sample distribution, inventory management and reporting operations could be conducted more efficiently with bar coding. The Prescription Drug Marketing Act (PDMA) requires sample distribution to be tracked and recorded, and The Joint Commission requires hospitals to track samples by lot and expiration date. Encoding relevant information could simplify compliance.

U.S. pharmaceutical companies spend billions each year managing sample distribution, record keeping and other administrative tasks. Not reflected in these figures, however, is lost sales time. Pharmaceutical representatives spend an average of 2.5 days a month on related administrative paperwork, according to research published by ZS Associates. Despite the time and money spent on sample management, a vast majoring of representatives noted their information regarding samples distribution was often inaccurate.

Companies could improve the quality of their data, limit risk non-compliance with the PDMA, and reduce data entry administrative requirements by instituting bar code scanning or RFID reading as part of sample distribution procedures. Sales representatives with scanner-equipped PDAs or laptops could automatically record the

receipt and disbursement of all samples. The PDA could also be used to record the signature of the physician receiving the sample. The scanning process would save considerable data entry time and the captured information would satisfy PDMA compliance requirements.

Conclusion

Combining encoded lot numbers, expiration dates and other variable data on different packaging levels creates a secure foundation for a variety of track-and-trace applications. Coding and reading techniques can connect the information required for enterprise systems, supply chain operations and compliance responsibilities, while providing complete traceability from production to patient. Building track-and-trace systems with secure bar code and RFID labeling techniques enables companies to benefit from their marking efforts.

Thermal printers are compelling tools for successfully meeting increased traceability and labeling requirements. They are the only print technology capable of producing variable information unit-level bar code and RFID labels on demand, and can output these labels on a range of authentication media. Thermal is the dominant print technology in industries that rely on bar codes for business-critical production control, distribution and inventory management applications. Thermal printers are able to:

- use secure media;
- process variable data;
- maintain quality in high-speed, small-symbol production environments;
- produce multiple bar code symbologies; and
- encode RFID chips.

This range of functionality gives users the flexibility to mix and match identification and security labeling methods without having to invest in dedicated equipment for each technology. Zebra's white paper *New Pharmaceutical Marking Guidelines and Opportunities* describes labeling requirements and printing considerations in detail.

Zebra Technologies is a world leader in bar code printing with an installed base of nearly four million units, including systems for unit-dose bar coding, brand protection and RFID smart labeling. Together with its partners, Zebra has the experience, industry knowledge and specialized products needed for successful implementation of pharmaceutical labeling systems. Zebra is also a leader in bar code and RFID standards development who actively participates in the work of pharmaceutical industry associations so that it will be prepared to meet the emerging needs of its customers. Contact Zebra at 800-423-0442 or visit http://www.zebra.com/id/zebra/na/en/index/industry_solutions/industries/manufacturing/pharmaceutical.html for more information.

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