New Pharmaceutical Marking Guidelines and Opportunities

Tips, techniques and technologies for implementing unit-of-use bar code, anti-counterfeiting and RFID labeling to improve patient safety, satisfy new FDA rules and business partner requirements

APPLICATION WHITE PAPER
Executive Summary

Events of February 2004 will have a far-reaching and lasting impact on patient safety and pharmaceutical labeling. The U.S. Food and Drug Administration (FDA) released its long-anticipated rule that requires nearly all prescription drugs and select over-the-counter medications to be identified with a bar code at the unit-of-use packaging level by April 2006. In a separate action, an FDA task force released an important report on security labeling techniques to protect against drug counterfeiting. It recommends full implementation of radio frequency identification (RFID) in the pharmaceutical supply chain by 2007. Many pharmaceutical manufacturers and distributors can’t wait that long to get involved with RFID, because the U.S. Department of Defense, Wal-Mart, Target, Albertson’s and other organizations have announced RFID pallet tagging requirements for their suppliers, some taking effect as early as 2005.

It is very plausible that many pharmaceutical makers will need to institute separate labeling systems for unit-of-use bar coding, brand protection/anti-counterfeiting and RFID marking in the next two or three years.

In many cases, a single labeling system can satisfy all three requirements. Bar code, anti-counterfeiting and RFID technologies are complementary and can be combined successfully to fulfill responsibilities at all points in the pharmaceutical supply chain and provide business benefits to the labeler.

Each of the new requirements creates opportunities to update and improve operations. By clearly understanding the requirements, options for compliance, and capabilities of bar code, authentication technology and RFID, companies can plan new labeling systems that can meet current needs, accommodate future requirements, and improve the security and efficiency of pharmaceutical labeling.

This white paper will provide an overview of the current state of labeling requirements in the pharmaceutical industry. The paper will:

• Present the final FDA unit-of-use bar coding rule and options for compliance;

• Describe the available technologies for unit-of-use identification and how to choose the method that best suits specific application needs;

• Identify important anti-counterfeiting and RFID labeling initiatives;

• Provide an overview of secure media solutions suitable for brand protection;

• Explain the basics of smart label RFID technology and how it can be used to meet pharmaceutical industry requirements;

• Describe how bar code, anti-counterfeiting and RFID technologies can be integrated into flexible and powerful labeling systems.

Zebra’s white paper *Track and Trace Solutions for the Life Sciences Supply Chain* provides further information on the uses and benefits of the technologies and programs referenced in this paper.
The FDA created its unit-of-use bar code rule to spur the adoption of automated systems to prevent medication errors. Medication errors represent one of the most persistent and enduring dangers of the healthcare system. Every segment of the industry—pharmaceutical manufacturers, distributors, insurers, hospitals, pharmacists, doctors, and nurses—is developing safeguards, yet deadly mistakes are still common and widespread. Preventable medical errors cause an estimated 770,000 adverse events and up to 98,000 deaths—including 7,000 from medication errors—in the United States each year, according to “To Error is Human: Building a Safer Health System,” a study by the Institute of Medicine (IOM). A September 2002 study by the Archives of Internal Medicine found nearly one in five medication doses is given in error.

The Institute of Medicine made another chilling finding: Up to 77 percent of all medication errors are preventable. Entities in the healthcare industry have put numerous controls in place, but the problem has gone largely unsolved.

Early adopters among hospitals and pharmaceutical manufacturers have proven unit-of-use bar coding is highly effective for improving patient safety but a “Catch 22” situation has held up implementation of point-of-care bar code scanning systems to prevent medication administration errors. Most hospitals have not put such systems in place, in large part because they consider it cost prohibitive to apply their own unit-of-use bar codes to make the system effective. Many drug makers have noted the lack of adoption and concluded it is not worthwhile to print bar codes because hospitals don’t scan them.

The FDA’s intent is to break the gridlock. The FDA estimates that when implemented, the bar code rule will prevent 500,000 adverse drug events over the next 20 years. The FDA also predicts medication errors will be reduced by 50 percent, although results from early adopters have shown the improvement percentage may be much higher. For example, the Veteran’s Administration (VA) hospital system, which operates the most widespread and best-known point-of-care medication scanning system, reduced medication errors by 86.2 percent with bar code scanning. The IOM estimates the practice could prevent up to 95 percent of errors.

**FDA Anti-Counterfeiting Task Force Highlights**

- The FDA formed a task force to investigate counterfeit pharmaceutical threats and potential protections, which issued its final report in February 2004.
- The report acknowledged that various authentication technologies are effective deterrents to counterfeiting, and singled out RFID’s potential to improve security.
- The task force issued recommendations and suggested practices but not proposed rules; participation is voluntary.
- The report also includes recommended steps leading to full implementation of RFID systems throughout the pharmaceutical supply chain by 2007.
- See the FDA's announcement and links to related resources at: www.hhs.gov/news/press/2004pres/20040218.html

The FDA is also taking action to safeguard the flow of pharmaceuticals from the manufacturer to the patient. An estimated eight to 10 percent of all pharmaceuticals worldwide are counterfeit, and in the U.S. investigations of
pharmaceutical counterfeiting have quadrupled since 2000. The FDA has formed an anti-counterfeiting task force to combat pharmaceutical counterfeiting and diversion. The task force issued a major report in February 2004 whose conclusions suggest additional pharmaceutical labeling and packaging regulations or guidelines may be forthcoming. The report summary includes the following statements:

The adoption and common use of reliable track and trace technology is feasible by 2007, and 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.

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.

Despite the FDA’s highly favorable view of RFID as an authentication technology, there is no proposed RFID security rule on the horizon. In comments announcing the anti-counterfeiting task force’s findings, the FDA said it would not likely specify a single technology for authentication, so that potential counterfeiters could not concentrate on defeating a single approach.

<table>
<thead>
<tr>
<th>RFID Initiatives at a Glance</th>
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<tr>
<td>• There is no FDA requirement for RFID use.</td>
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<td>• The FDA has acknowledged the potential value of RFID in its comments released with the unit of use pharmaceutical marking rule and through statements from its anti-counterfeiting task force.</td>
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<td>• The task force concluded that RFID implementation throughout the supply chain is feasible by 2007, and encouraged stakeholders to begin a series of steps to make this a reality.</td>
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<td>• The U.S. Department of Defense is requiring suppliers to apply RFID tags to shipments as early as 2005.</td>
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<tr>
<td>• Wal-Mart, Target, Metro GROUP and other leading retailers have also announced RFID supplier tagging programs.</td>
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<tr>
<td>• Visit <a href="http://www.rfid.zebra.com">www.rfid.zebra.com</a> for more information and links to additional RFID resources.</td>
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Independent of any FDA action, many pharmaceutical manufacturers and distributors may need to implement RFID labeling systems to satisfy customer requests. RFID is a powerful tool for improving supply chain performance, which has led some large organizations to mandate their suppliers apply RFID labels to shipments. The U.S. Department of Defense, Wal-Mart, Target and METRO Group are among the organizations who have announced programs that require at least some RFID tagging by 2005. Other supply chain RFID marking programs are also in the works.

Organizations must find a balance between meeting current requirements and positioning themselves to succeed in future initiatives. By taking a big-picture view of unit-of-use labeling, brand protection and RFID marking initiatives, pharmaceutical manufacturers can provide unprecedented protection to patients while protecting their labeling system investments from premature replacement.
The FDA requirements are clear – essentially stating that drugs must have their NDC number encoded in a linear bar code by April 2006. The final rule is flexible, which means pharmaceutical manufacturers will need to make choices about the information included in the bar code, the type of symbol to use, and the standards (e.g. EAN.UCC or HIBCC) to follow.

FDA Unit-of-Use Bar Code Labeling Rule at a Glance

- The rule requires human drug products and biological products, including prescription drugs and over-the-counter medications that may be sold to patients, be identified with a bar code at the unit-of-use packaging level. There are very few exemptions.
- The effective date of the rule is April 24, 2004. Current products must be bar coded by April 24, 2006. Drugs approved for use by the FDA after the rule’s effective date must be bar coded within 60 days of their approval.
- The National Drug Code (NDC) number must be encoded in the bar code symbol. The product’s lot number and expiration date may be encoded but are not required.
- Any linear symbology, including Reduced Space Symbology (RSS), can be used for the bar code.
- Two-dimensional (2D) bar code symbologies are not permissible. This includes Data Matrix, which is already in use in the pharmaceutical industry.
- RFID is not an acceptable substitute for the bar code.
- EAN.UCC or HIBCC standards may be used, but neither is required.
- View the complete rule at: www.fda.gov/OHRMS/DOCKETS/98fr/04-4249.htm

Specifically, the rule states the NDC must be encoded in a linear bar code, and that the drug’s lot number and/or expiration date may also be encoded. The rule makes no requirement or recommendation as to which linear bar code symbology can be used. The final rule is even somewhat ambiguous as to the definition of a “linear” symbology, suggesting that some stacked codes, which are generally considered two-dimensional (2-D) symbologies, could qualify. To qualify as a linear symbology and thus be allowable for unit-of-use marking, the FDA requires: “...that stacked code must be capable of being read clearly by scanning or reading equipment in the same manner as conventional linear bar codes to fall within Sec. 201.25(c).” Data Matrix, a 2-D symbology already in use in the pharmaceutical industry, is specifically disallowed for unit-of-use marking. PDF417, another popular 2-D symbology, is not mentioned. It could conceivably pass the FDA’s scanning requirement, but would be difficult to read with a conventional linear scanner and may not be an acceptable choice. The FDA noted that the Reduced Space Symbology (RSS) family, which includes a stacked version, is acceptable.

Labelers are left with several hundred symbologies to choose from. The choice is simplified when companies first determine the information content they will encode and settle on a standard data format.
There are many potential advantages to going beyond the minimum marking requirement and including the lot number and expiration date in the bar code. Encoding this information creates the foundation for automating return and recall operations, more efficient stock rotation, production tracking, sample management, compliance with the Electronic Signatures Rule (21 CRF Part 11) and the Prescription Drug Marketing Act, and meeting other traceability needs. The FDA also recognized in its ruling that variable information encoding could play a role in improving patient safety. Lot codes and expiration dates were not required in the final rule because they are thought to be more useful for supply chain applications, and the focus of the FDA initiative is to improve patient safety.

The National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP), whose members include the American Pharmaceutical Association, American Medical Association, Healthcare Distribution Management Association (HDMA), Generic Pharmaceutical Association, Institute for Safe Medical Practices, Pharmaceutical Research and Manufacturers of America (PhRMA) and United States Pharmacopeia, all recommend that lot or batch control number and expiration date be encoded in the unit-of-use label in addition to the NDC.

Putting lot numbers and expiration dates in a bar code makes 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 needed to record and transcribe the 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 according to a 1997 study on Efficient Healthcare Consumer Response (EHCR). Manufacturers and distributors can help drive these costs out of the supply chain, rather than shifting them to downstream partners, by using automated systems for data capture and communication. These applications and benefits are described in detail in Zebra’s white paper Beyond Point of Care: Benefiting from Unit-of-Use Bar Code Traceability in the Life Sciences Supply Chain.

One shouldn’t assume that there is not enough space available to encode the optional information. The RSS symbologies enable the NDC, lot number and expiration date to be encoded in less space than the more commonly used Code 128 and Code 39 symbologies require to encode the NDC alone. Some brand protection media has security features that enable variable information to be encoded. The security codes may be invisible and overprinted with text, graphics and bar codes, which overcomes many physical space limitations. Alternatively, lot codes and expiration dates can be included at other packaging levels. RFID tags used for case, carton and pallet marking can easily accommodate optional data.

**Symbology Considerations**

There are more than 200 bar code symbologies, but only a few are being considered for unit-of-use identification. The leading candidates are favored because of their proven performance, suitability for the task, and support by international and industry standards. The three leading symbologies for unit-of-use labeling are Code 128, Code 39 and the Reduced Space Symbology (RSS) family. Each is profiled below.

**Code 128 and Code 39**

Many packaging engineers already have experience using Code 128 and Code 39 symbologies for outer pack labels. Neither Code 128 nor Code 39 scales well, making them unsuitable for small-item identification. For example, encoding an NDC number would require a Code 39 symbol of approximately 1.5 inches wide by 0.25
inch tall, or a Code 128 symbol of 1.25 inches by 0.25 inch. Adding the lot number or expiration date would significantly increase the symbol size. Most unit-level packaging doesn’t accommodate these minimum symbol sizes, making Code 128 and Code 39 poor choices for the application.

**RSS**

The RSS family of symbologies was created specifically to help identify the 10 percent of pharmaceutical products an EAN.UCC study found are unsuitable for marking with traditional symbologies. RSS is an all-numeric bar code symbology that can encode a National Drug Code (NDC) in a fraction of the space required for a traditional UPC symbol. RSS Stacked is an alphanumeric symbology that enables an ID code, lot number and expiration date to be encoded in a symbol less than an inch wide. Other symbologies in the RSS family, including RSS Truncated and RSS Composite, provide options for additional space savings and data capacity. Legacy, low-cost scanners used throughout the supply chain can easily process RSS symbols, which gives RSS cost and adoption-time advantages over other symbologies.

**Standards and Data Structures**

The symbologies referenced above are used in multiple standards and data structures in the life sciences supply chain. The most commonly used standards include the EAN.UCC system that is administered by the International Article Numbering Association (EAN) and the Uniform Code Council (UCC), and various standards from the Health Industry Business Communications Council (HIBCC), which manages the Universal Product Number (UPN) system for identifying healthcare products at each packaging level. EAN.UCC and HIBCC systems both support the use of bar coded NDC numbers. The final FDA rule states either standard may be used for unit-of-use labeling, and while commenting on each, does not endorse the use of one over the other.

**The EAN.UCC Approach**

UCC and EAN International are separate, not-for-profit trade associations with joint coordinating bodies in 104 countries. More than 200,000 companies are members, including an estimated 20,000 in the pharmaceutical and healthcare industries. Best known for creating and maintaining the UPC system for bar code identification of consumer goods, the UCC and EAN support 22 industries with bar code and electronic commerce standards. Their joint set of internationally accepted standards and guidelines is known collectively as the EAN.UCC system. In 2003, the organizations gained responsibility for developing standards for and commercializing EPC RFID technology, which is managed by an EAN-UCC subsidiary, EPCglobal. The EPC system will be discussed further in the RFID section.

The foundation of all EAN.UCC systems is the 14-digit GTIN (Global Trade Item Number) data structure, which is used by manufacturers to identify their products down to the packaging level for use anywhere in the world. The EAN.UCC systems support many bar code symbologies and other data carriers that use the GTIN data structure. NDCs can be encoded using the GTIN structure.

The AMA and the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) have endorsed RSS, and it is currently used by many early adopters of unit-of-use coding, including Alcon Laboratories, Abbott Laboratories, Baxter International, Pfizer and St. Alexius Medical Center. Profiles of successful healthcare RSS users, technical specifications, and other background information is available on the UCC and EAN Web sites [www.uc-council.org](http://www.uc-council.org) and [www.ean-int.org](http://www.ean-int.org).
The HIBCC Approach

HIBCC is a U.S.-based nonprofit trade association with five international affiliates. Its members include medical industry associations, distributors, and providers. HIBCC maintains the Healthcare Identification Number (HIN) system and Labeler Identification Codes (LIC) used to identify trading partners in electronic transactions, and has undertaken a variety of bar code and e-commerce standards efforts. HIBCC promotes the UPN number as a method to identify medical and surgical products similar to the way that NDC is used to identify drugs.

UPNs uniquely identify manufacturers and products to the packaging level. The UPN data structure supports both LIC (which is alphanumeric) and EAN.UCC (all numeric) data structures. For expressing UPNs in a bar code, HIBCC recommends different symbologies depending on the application. The HIBCC recommends Code 128 or Code 39 symbologies. The organization previously recommended Data Matrix or PDF417 for unit-dose coding, but the FDA rule does not allow the use of 2-D symbologies.

The U.S. Department of Defense requires that its suppliers mark their medical and surgical products with a UPN encoded in a bar code. The Defense Logistics Agency, HDMA, Health Industry Distributors Association (HIDA), and several large health plans, hospital chains, and manufacturers have endorsed UPN identification. The UPN Repository, a master database of UPN-identified items maintained by HIBCC, includes more than 250,000 items. More information about UPN and related systems is available on the HIBCC Web site, www.hibcc.org.

Printing Unit-of-Use Bar Codes

Unit-of-use bar codes can be created using a variety of printing methods. The most common printing technologies are traditional packaging presses, ink jet, laser coders, and compact thermal printers. Preprinted labels may also be purchased and applied. The methods vary significantly in speed, flexibility to process variable data, label formats supported, printer size and cost.

The multiple symbologies, content and standards allowed in the FDA rule will likely result in pharmaceutical manufacturers, packagers and relabelers being required by different customers to support their own preferences. Therefore, it is extremely important for these organizations to develop flexible printing systems that can easily handle all the possible symbology and data encoding options.

The most common technologies currently used for pharmaceutical printing may not be the most effective options for fulfilling emerging labeling challenges. Current print systems are optimized for high-speed, high-volume printing of non-customized packaging without bar codes or variable information. They may lack the adaptability required for shorter print runs that include specific variable data produced for specific customer orders. The high-speed printing capability will be rendered useless if the equipment requires excessive changeover time to accommodate different label formats.

The following factors must be considered when evaluating different print technologies and specific equipment:

- **What effect does variable data have on performance?** If lot codes and expiration dates are to be included in the bar code symbol, the marking method must be able to process variable data. Variable data output slows some printers considerably, while others process variable data at their top print speeds.

- **Does standard equipment produce enough resolution?** Readable bar codes require sharp, clear edges. Requirements become more exacting as symbols get smaller. Users must pay particular attention to edge definition, which refers to the clarity and contrast of the dark and light edges within the symbol. Packaging presses, ink jet and laser marking methods apply ink, which spreads after it is applied to material. This spread
may be imperceptible to the human eye but is apparent to the bar code reader and may cause misreads. Printing bar codes, especially small unit-of-use symbols, with these technologies often requires higher quality printers. Existing equipment may require an upgrade. Thermal printers are known for producing outstanding edge definition. Standard, 200 dpi thermal printers typically provide greater quality than higher-resolution laser and ink jet equipment.

• **Are special inks or label materials required?** Legacy printing systems may require different supplies to produce unit-of-use codes. For example, ink jet systems may need higher quality ink to provide the quality and durability required for the bar code to remain readable at the point of care. The heat produced in the laser printing process can degrade label adhesives, necessitating the use of more expensive media or another print method to ensure labels will stay on until the medication is administered.

• **Is the desired symbology supported?** Some print technologies can only output symbologies commonly used for retail packaging. RSS support can be especially hard to find. Another factor to consider is the effort required to modify existing equipment to support required symbologies. Questions to consider include: Can symbols be downloaded from software? Is new firmware required? Can users install it themselves or is a service call needed? Will the new symbologies strain system memory and performance? Is new equipment required?

The following section provides a brief overview of the technologies commonly used for pharmaceutical packaging and the unit-of-use printing considerations specific to each.

**Packaging presses**

Flexographic, Letterpress, platen, and other web-printing, packaging-grade technologies commonly used by pharmaceutical manufacturers and packagers can be adapted to produce bar codes. Printing bar codes does not slow line speeds, but throughput does decrease because more frequent changeovers are required if lot numbers, expiration dates, or other variable data is included in the code. Film masters must be obtained to produce bar codes on web presses. The film master serves as a template for accurately reproducing bars and spaces within exact tolerances on the packaging material. Separate film masters must be used for each unique product and bar code. Therefore, if manufacturers need to encode lot codes and expiration dates, they must order film masters for each drug/lot/expiration date combination, which can lead to inventory management challenges. This can cause inventory management and quality problems, as companies must ensure they have necessary film masters and that the correct version is used to prevent mislabeling. Platen and other demand-printing technologies used with packaging machinery eliminate the need for film masters, but only a few can produce the required bar code symbologies.

**Ink jet**

Ink jet is widely used for printing variable text on packaging but is not an ideal technology for printing bar codes. Few ink jet systems support the bar code symbologies used for unit-of-use coding. Ink jet coders work by spraying dots of ink onto the subject being marked. The process can be messy and does not always provide the print quality necessary to create small codes that must remain readable for weeks or months.

**Laser**

Laser imagers and laser printers can each produce bar codes, but only one technology is suitable for unit-of-use coding. Office-style laser printers are not intended for labeling, tend to get jammed by adhesive label materials, and frequently don’t provide the edge definition required for readable bar codes.
Industrial laser imagers burn a permanent image into the item being marked, work on a variety of materials, and are fast enough for integration in packaging lines. Laser imagers can produce high-quality small images and two-dimensional bar codes, although symbology support may be limited. Users must make sure there is enough print contrast between light and dark bars to produce a readable symbol.

If print contrast performance is satisfactory, the only drawbacks to laser imagers are the purchase and maintenance costs. The purchase price of a laser imager is many times higher than the cost of a new thermal printer. Operation and maintenance costs are also high relative to other technologies.

**Thermal**

Thermal is the dominant technology for producing bar code labels in all industries. Thermal printers excel at producing high-quality, variable information labels on demand and are commonly used to create compact bar codes for specimen vials, electronic components, sample containers and other small items. Although they are not widely used in packaging, thermal printers can often meet the suggested print speed guidelines for bar code printing in packaging lines.

Thermal printers are the smallest devices capable of creating unit-dose codes, with models that fit easily on a desktop. One of the most popular and effective configurations for pharmaceutical labeling is to use a thermal print engine in an automated printer/applicator system. These machines print labels and use one of a variety of techniques to apply them to objects with great precision. Thermal printers are manufactured in a variety of other form factors, including mobile units that can be carried in one hand or worn on a belt, small desktop models, and industrial strength printers capable of 24-hour operation.

The range of sizes makes thermal printers a convenient option for use in pharmacies, nursing stations, and other healthcare settings. Many distributors already use thermal printers for shipping and receiving applications and are familiar with the performance and convenience the technology provides. Manufacturers can use integrated, print-and-apply applicators with thermal printing engines for accurate, automatic label placement on production lines. Thermal printers are also the least expensive option for creating unit-of-use bar codes. Their space-efficient design, integrated bar code support, and affordability make thermal printers the most suitable choice for use at all levels in the supply chain.

Zebra Technologies is one of the world’s leading providers of thermal bar code printers, print engines, and labels. Zebra supports all the bar code symbologies used in healthcare, including RSS, and works closely with standards bodies to ensure future compliance.

**Preprinted labels**

A final option is not to print bar codes on demand at all, but to order and apply labels that have been preprinted with a bar code. Preprinted labels offer excellent quality and are available in all symbologies and a wide range of materials. However, as with film masters, labels must be printed in shorter runs for variable lot and expiration information. This can lead to frequent changeovers and requires stringent quality practices to ensure labels are applied to the correct items. Preprinted labels have no flexibility for variable data and can’t be created on demand.

A summary of the relative advantages and disadvantages of each marking method is included in the table on the following page.
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<thead>
<tr>
<th>Technology</th>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>Packaging presses</td>
<td>Top print speeds; existing infrastructure for manufacturers and packagers.</td>
<td>Requires use of film masters; not well suited for encoding variable data; requires changeovers for variable data printing.</td>
</tr>
<tr>
<td>Ink jet</td>
<td>Fast; used in existing packaging printers.</td>
<td>Limited symbology support; quality concerns for small bar codes.</td>
</tr>
<tr>
<td>Laser</td>
<td>Fast; encodes variable data.</td>
<td>Limited bar code support; expensive to own and operate.</td>
</tr>
<tr>
<td>Thermal</td>
<td>Excellent for producing variable information bar codes; all symbologies supported; compact; least expensive option; can print labels in batches.</td>
<td>Somewhat slower than web and ink jet.</td>
</tr>
<tr>
<td>Preprinted labels</td>
<td>Excellent quality; no printing system required.</td>
<td>Manual application needed; requires short print runs and management of multiple label inventories.</td>
</tr>
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</table>

**Brand Protection and Anti Counterfeiting**

Although it is intended mainly to improve medication administration, unit-of-use labeling can also play a role in safeguarding pharmaceuticals against counterfeiting and diversion. Brand protection specialists and pharmaceutical security experts agree that layering several forms of protection into product packaging is the best approach to protect integrity. Technologies that can be layered to provide brand protection and product authentication include secure label stock and laminates, taggants that hold encoded information, patterned adhesives, RFID tags and more. Unit-of-use bar codes, particularly if lot numbers and expiration dates are encoded, can provide one layer of security. The FDA advocates going further, to include additional forms of protection.

The Pharmaceutical Research Manufacturers of America (PhRMA), Healthcare Distribution Management Association (HDMA) and other industry groups support the FDA stance and have created their own guidelines and initiatives for improving security. There is broad consensus that the industry needs “track-and-trace” systems to protect product and distribution channel integrity. Track-and-trace systems provide a convenient and accurate way to identify products and their chain of custody. According to comments submitted to the FDA by the HDMA’s Product Safety Task Force (PSTF):

*... 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 unto itself as certain information is not carried on the package itself but rather in a controlled database...*
Fortunately, many of the recommendations are compatible for convenient use with unit-of-use bar code labeling systems. For example, the FDA has identified security taggants and RFID chips as effective deterrents to counterfeiting. Thermal printers can combine these technologies in a single label that also carries the unit-of-use bar code. The following section provides a brief overview of authentication technologies and how they can be used in the pharmaceutical industry.

**Authentication Technologies**

The ideal authentication solution is extremely difficult for counterfeiters to copy, is cost-effective to include on all products, detects and deters fraud, and is convenient enough to be checked at all levels of the supply chain. Traditionally, verifying product authenticity required lengthy, specialized laboratory techniques. Today however, secure media allows for end-to-end tracking through the supply chain, instant field verification, and seamless integration with product tracking systems. At the same time, these sophisticated new technologies impose unprecedented new hurdles for would-be counterfeiters.

Here’s an example of how new secure media could help ensure patient safety. The 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-of-use bar code labels could be produced on material with hidden security features that require a specialized reader for authentication. Medication packages would then be packed into a cardboard carton for shipping, which receives 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.

Distributors would authenticate incoming shipments with low-cost portable readers to ensure no piracy or substitution occurred while the shipment was in transit. Random samples of individual packages could also be tested if desired. 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 at the pharmacy. For added security, pharmacists or nurses could check authenticity prior to dispensing any drugs.

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.

Authentication materials have recently been developed for use with thermal printers, which are commonly used for printing small labels and bar codes. Here is a guide to secure thermal media.

**Invisible Taggants**

Invisible taggants are engineered materials with specific optical qualities that make them invisible to the naked eye, providing a covert layer of security that is difficult for counterfeiters to detect or reproduce while preserving the desirable appearance of the finished tag or label. Varnishes, adhesives and ink can all carry taggants. Invisible materials do not interfere with label readability, bar code scanning, or packaging appearance. Information can often be printed on top of the taggant, so no changes to label size or format are required. Some invisible taggants can even be detected through several layers of packaging material, so authenticity can be verified without opening the packaging.
**Pattern Adhesives**

Combining particularly aggressive adhesives with areas of less permanent adhesive or specially die-cut substrates allows a label to self-destruct if it is removed after application, leaving a visible mark and prohibiting the label from being reused. These overt features prevent stolen labels from being applied to unauthorized goods, and enable inventory or retail clerks to easily detect potentially diverted goods.

**Magnetic Threads**

Magnetic thread technology uses magnetic strands that are woven into the paper substrate before it is converted into tags or labels. Because the threads are visible but woven into the paper itself, the physical appearance is extremely difficult to reproduce and a significant deterrence to counterfeiters. Threads can’t be removed without destroying the paper.

Magnetic threads carry a unique identification number that only be read with specialized equipment and cannot be erased. The identification number may be constant or expressed incrementally for each individual tag or label.

Zebra’s white paper *Brand Protection in the Supply Chain: Protecting Products and Profits with Secure Media Solutions.* provides a thorough overview of security taggant varieties and capabilities for use with thermal printers.

**RFID**

Although it is usually used for item identification, RFID technology, in which information is securely encoded on a computer chip and accessed wirelessly, is also highly suitable as an authentication technology. In fact, the FDA anti-counterfeiting task force report said RFID is the “most promising” track-and-trace technology. The HDMA has voiced its endorsement of the FDA task force recommendation that pharmaceutical manufacturers begin applying RFID at the case and pallet level by 2005 and at the item level by 2007.

A smart label is an adhesive label with an RFID chip and antenna embedded within the material. Data can be securely encoded in the chip, with bar codes, text or graphics printed on the label material. Smart labels therefore are excellent for authentication, because they offer at least two layers (authentication media can also be used for the smart label) of security that are each capable of encoding variable information. RFID readers use radio waves to read data from chips. No line of sight between the chip and reader is necessary, and data can be accessed even if the RFID tag is covered by several layers of packaging.

These robust reading capabilities enable many time- and labor-saving storage, handling, inventory control and distribution processes to be developed. The business benefits of these highly efficient new processes are what’s driving companies to require their suppliers to apply RFID tags to pallets, cases and other packaging.

**RFID Initiatives**

There are no current or proposed FDA requirements for using RFID. The FDA considered RFID as an option for unit-of-use labeling, but instead required bar coding. The anti-counterfeiting task force has made clear and specific recommendations on how to use RFID, but the recommendations are voluntary. However, the U.S. Department of Defense is requiring its suppliers to apply RFID tags to shipments, and several private-sector businesses have announced similar marking requirements.

Announcements of new supplier marking requirements seem to come out every month and are expected to continue as retailers, logistics providers and manufacturers develop their RFID plans. This white paper cannot
provide details for each program, but will provide some background information about compliance RFID tagging initiatives and their general implications for pharmaceutical manufacturers. For more detailed information about meeting the labeling requirements of these programs, see Zebra’s white paper *Zebra’s RFID Readiness Guide: Complying with RFID Tagging Mandates.*

The compliance marking requirements announced thus far generally specify that RFID labels be applied at the pallet, case or carton level, to facilitate automated supply chain operations. Therefore, there should be no conflict in meeting RFID and unit-of-use bar code marking requirements. There has been considerable speculation that retailers some day may require RFID for item-level identification, and some technology promoters aggressively advance this view. However, RFID was considered impractical and cost-prohibitive for wide scale item-level marking in the near-to mid-term when the FDA issued its final rule in 2004. RFID technology will continue to evolve and could become practical for item-level tagging on pharmaceuticals and consumer goods in the future. The technology specifications and standards currently called for in compliance tagging programs could support item-level marking.

Just as there are many bar code symbologies, there are multiple forms of RFID, which vary by frequency, data format, memory capacity and other characteristics. The Electronic Product Code (EPC) system is one of the best-known forms of RFID. Many of the compliance marking programs require that suppliers mark their shipments with tags that conform to EPC specifications. Standards and specifications managed by the International Organization for Standardization (ISO), including ISO 15693 and the ISO 18000 series, are other popular types of RFID.

Smart label printers are able to encode these and other types of RFID chips. For more information about smart label printing and RFID technology, visit [www.rfid.zebra.com](http://www.rfid.zebra.com).

**Conclusion**

Whatever their effect on safety and security, unit-of-use bar code labeling, anti-counterfeiting and RFID marking initiatives will have a huge impact on pharmaceutical labeling. By understanding the different requirements and options for satisfying them, pharmaceutical manufacturers can create integrated labeling systems that meet the needs efficiently, without requiring continuous changes, upgrades or additional equipment purchases. By considering all the applicable marking requirements and suggested practices, labelers can prepare systems that will provide a smooth, secure migration path to embrace future marking and identification methods utilizing multiple technologies.

Zebra Technologies is a world leader in bar code printing with an installed base of nearly 4 million units, including systems for unit-of-use bar coding, brand protection and RFID smart labeling. Together with our partners we have the experience, industry knowledge and specialized products needed for successful implementation pharmaceutical labeling systems. Zebra is also a leader in bar code and RFID standards development who actively participates in the work of life sciences industry associations so that we will be prepared to meet the emerging needs of our customers. Contact Zebra at +1 800 423 0442 or visit our Web site at [www.lifesciences.zebra.com](http://www.lifesciences.zebra.com) for more information about bar code printing solutions.