

PROGRESS IN PHARMACEUTICAL PRODUCT IDENTIFICATION

New coding and marking technologies can help pharmaceutical companies comply with new FDA regulations, combat counterfeiting, enhance patient safety and increase profits

By

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Table of Contents

ABSTRACT	2
ADDRESSING THE CHALLENGES	2
BAR CODE REGULATION – PREVENTING DISPENSING ERRORS	3
COUNTERFEIT PREVENTION	5
OTHER BENEFITS OF CODING	6
MAXIMIZING THE INVESTMENT, INCREASING PROFIT	6
Updating Ink Jet Technology	7
Ink Options	7
Switching to Laser	7
Switching to Thermal Transfer	8
RSS: A Smaller Coding Option	8
The New Solution: RFID	8
CONCLUSION	8
ABOUT THE AUTHORS	9
REFERENCES	9
APPENDIX: CODING AND MARKING SOLUTIONS FROM VIDEOJET TECHNOLOGIES	10

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New coding and marking technologies can help pharmaceutical companies comply with new FDA regulations, combat counterfeiting, enhance patient safety and increase profits

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ABSTRACT

As pharmaceutical product coding regulations change, and as the threat of counterfeiting increases, drug companies are looking for better methods of product identification. Coding and marking are keys to accurate, reliable product identification, which can combat counterfeiting and prevent errors in administering drugs to patients. The latest coding and marking technologies have the added benefits of helping to provide flexible coding methods, streamline production, improve productivity, reduce costs and increase profits.

ADDRESSING THE CHALLENGES

New and updated regulations on drug product coding, driven by security issues and emerging technologies, have left pharmaceutical manufacturers, repackers, relabelers and distributors searching for cost-effective options to comply.

Medication dispensing errors have become a big concern in the healthcare industry.

Drug companies, regulators, insurers, caregivers and patients face tremendous challenges due to the growth in drug counterfeiting and need better ways to protect the integrity of the healthcare delivery system, the drug products and patient safeguards.

These are critical challenges to pharmaceutical companies. Product coding and marking strategies and technologies form an important part of the solutions. Control of the drug product begins with the manufacturer. The solutions required to thwart counterfeiting and enhance the control of drug dispensing are best applied before the products leave the control of the manufacturer. Significant emphasis is placed on designing difficult-to-duplicate, unique drug dose shapes and colors, and on using secure, robust drug product package coding and marking technologies. Providers of these technologies are rising to the occasion.

Coding and marking technologies and their application are constantly evolving. The latest advances include:

- Improvements in ink jet printers and lasers that make coding easier, faster, more reliable and more efficient than ever before.
- Scannable coding that is applied directly to oral dosage forms.
- The development of unique code formats that comply with Federal regulations and are readable on standard equipment, including reduced space symbology (RSS) coding and invisible fluorescent inks. These allow for the addition of more information in less space.
- Radio frequency identification (RFID) is poised to become the ultimate solution as a secure, robust, and highly functional drug product package coding technology, with instantaneous information updating and tracking.

Drug companies will inevitably make product line changes to meet regulations, combat counterfeiting, enhance patient safety, and address other industry concerns. Companies that adopt the latest coding and marking technologies can improve productivity, reduce costs, comply with the latest regulations and substantially enhance their competitive position.

BAR CODE REGULATION – PREVENTING DISPENSING ERRORS

Patient safety is the key driver for the development and use of better product coding and marking technologies, and it is the primary goal of new drug coding regulations.

A properly implemented coding system for pharmaceutical products can save human lives. This alone is sufficient justification for broader use of coding technologies on drug products, but there are added benefits, including reduced manual tracking costs, improved tracking functionality, reduced costs of insurance and litigation, and reduced costs of remedial treatments and lost work time for adversely affected patients. When drugs are coded at the unit-of-use level, and when healthcare providers can easily compare product codes with codes from patient profiles, medication errors can be reduced significantly.

By reducing mistakes in drug dispensing, healthcare providers face less risk of lawsuits. That means fewer payouts for punitive damage awards and a stop to increasing malpractice liability insurance rates. This leads to a reduction in overall health care costs, benefiting every individual and company.

Historically, drug manufacturers have used bar codes to various degrees and in various formats for their own benefit to facilitate the identification, verification and tracking of their products. Although industrywide standardization efforts were initiated, true standardization and cross-functionality were elusive. The different formats in use were often not always functional at all points in the distribution and dispensing systems, and the lack of a legal requirement for bar coding allowed many products to enter the healthcare distribution system with no scannable identifications at all. This situation led to complexity, continued manual intervention and, ultimately, errors and inefficiencies. The FDA responded by designing, with industry and public input, a regulation that requires drug packages entering the hospital environment to be bar coded.

In February 2004, the United States Food and Drug Administration (FDA) issued a final rule amending 21 CFR Part 201, Subpart A, to add Section 201.25, "Bar Code Label Requirements." This section stipulates that a bar code must be on most drug products, including certain prescription drugs sold into hospitals or intended for hospital use (typically unit-of-use packs), all biologicals and certain over-the-counter drugs commonly used in hospitals. A scannable bar code in linear format that identifies the National Drug Code (NDC) number for the product in the package must be on each hospital-destined package and unit-of-use. The regulation requires that most previously approved drugs must comply within two years; new drugs must comply within 60 days of their approval. The two-year grace period for existing drug products is allowed in recognition of the enormity and complexity of the task of implementing this regulation. Drug manufacturers are allowed this time to evaluate, fund, install and validate the coding technologies of their choice, and coding system providers have this time to develop the capacity, technology and current Good Manufacturing Practice designs required to support the industry's needs.

The ruling was made to protect patients from preventable medication errors and to reduce healthcare costs. Bar codes on drugs can help doctors, nurses and other healthcare providers verify that they are giving patients the right drugs at the correct dosages.

"By giving healthcare providers a way to check medications and dosages quickly, we can create an opportunity to reduce the risks of medication errors that can seriously harm patients," said Tommy Thompson, secretary for the United States Department of Health and Human Services (HHS).¹

In a 1999 report, the Institute of Medicine (IOM) estimated that 44,000 to 98,000 Americans die each year from preventable medical errors. IOM estimates that medical mistakes cause half of adverse reactions to medicines.²

While the FDA rule requires each bar code to contain at least the drug's NDC number, many companies are considering including other information, such as lot numbers and expiration dates.

The setup involves a bar coding operation at the manufacturer's plant and a bar code scanning system and computerized database throughout the supply chain and in the hospital. Each package and unit-of-use dose is coded with identifying information by the drug product manufacturer, usually during the packaging operation. This code is scanned during manufacturing, during distribution and upon arrival at the hospital to identify each product.

When admitted to a hospital, a patient would receive a bar coded identification bracelet that links the patient to his or her electronic medical record. Before administering a medication, the healthcare provider would first scan the patient's bar code, then scan the bar code on the medication. The computerized system would compare the patient's record to the drug to confirm a match. In case of an error, the system would indicate a problem: an incorrect medication, a wrong dosage, wrong timing for administering the drug, a patient's allergy or diet restriction, a drug interaction issue, potentially an outdated or recalled lot (if lot code/expiration date are included in the bar code), or an indication that a patient's chart has been updated and prescribed medications have changed.

In a study conducted at a Veterans Affairs Medical Center that employed a bar code-scanning system, 5.7 million doses of medication were administered to patients without a single medication error.³ According to FDA estimates, the bar code rule, when fully implemented, is expected to help prevent nearly 500,000 adverse events and transfusion errors over 20 years. Over the same time period, the economic benefits of reduced health care costs, reduced patient pain and suffering, and reduced lost work time due to adverse events is estimated to be \$93 billion.⁴

The National Coordinating Council for Medication Error Reporting and Prevention has recommended that bar codes be included on all immediate unit-of-use packaging that may include single-use, single-dose, unit-dose, unit-of-use, multiple-unit and multiple-dose containers.⁵

COUNTERFEIT PREVENTION

Another major concern in the pharmaceutical industry is counterfeiting. Besides eroding profits, counterfeiting can potentially damage a company's reputation. Most importantly, it can cause serious harm or death to patients.

According to the World Health Organization (WHO), counterfeiting can apply to any branded or generic product that is deliberately and fraudulently mislabeled for its identity and origin. Counterfeits may include products with the correct ingredients but fake packaging, with wrong ingredients, with insufficient or too much active ingredient, or with no active ingredients at all.

The FDA has seen growing evidence of well-organized counterfeiters backed by sophisticated technologies and criminal operations set up to profit from drug counterfeiting.⁶ Counterfeiting can also be performed by terrorist organizations that aim to harm groups of people for political or social reasons. In either case, the result is that innocent patients are harmed for the gain of others. FDA counterfeit drug investigations conducted per year have increased by 400 percent between 2000 and the late 1990s.⁷

Counterfeiting is even more prevalent outside the United States. The FDA estimates that counterfeits make up 10 percent of the global medicines market. Up to 25 percent of medicines consumed in poor countries are counterfeit or substandard. The annual earnings from the sale of counterfeit and substandard medicines is estimated at more than \$32 billion USD globally.⁸

The Russian Association of Pharmaceutical Manufacturers reports that more than one out of every 10 prescription drugs, over the counter medicines, vitamins and other pharmaceutical products in Russia could be counterfeit.⁹

The real-life consequences of counterfeit activity are startling:

- In Niger in 1995, more than 50,000 people were inoculated with counterfeit meningitis vaccines, resulting in 2,500 deaths.¹⁰
- Fake cough syrup containing diethylene glycol (a toxic chemical used in automotive antifreeze) was responsible for 89 deaths in Haiti in 1995 and 30 infant deaths in India in 1998.¹¹
- In 1999, at least 30 Cambodians died after taking counterfeit anti-malarials.¹²

The application of a well-selected drug product coding scheme can combat counterfeiting by providing unique serial numbers for marking and tracking. Along the supply chain, if a serial number is identified as not coming from a legitimate source, then its progress to the end user is halted. For example, when a drug bar code is scanned at a distribution center, that unique information (such as lot number) is compared to records within the manufacturer's system. If the destination is incorrect or if a lot code is invalid, it will notify the system that the product is counterfeit. The more information included within a code, the more difficult it is to counterfeit. Because of their capacity for large quantities of information, RSS codes and RFID tagging are ideal for use against counterfeiting.

OTHER BENEFITS OF CODING

Prevention of dispensing errors and counterfeiting are only two benefits of pharmaceutical coding and marking. The technologies also help reduce costs in inventory control and billing for drug manufacturers, repackers and healthcare providers alike. With a simple scan, drug companies and hospitals can determine immediate inventory needs to prevent overstocking or understocking a product.

In addition, computerized billing systems can invoice in real time — whether it's a manufacturer billing a hospital, or a hospital billing a patient. This prevents billing errors, reduces paperwork, ensures complete charge capture, and cuts down on accidental overbilling for insurance and Medicare.

Drug coding also helps with electronic pedigree compliance (21 CFR Part 211, Section 211.150, "Distribution Procedures," and Section 211.196, "Distribution Records"). As drug manufacturing and distributing companies move away from the cumbersome paper pedigree system and move to electronic pedigree, coding and data capturing technologies will eliminate manual record keeping and human error, making the process faster and more accurate.

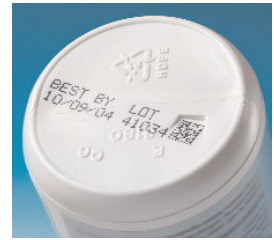
MAXIMIZING THE INVESTMENT, INCREASING PROFIT

Implementing a new coding system requires a financial and time investment for drug makers, repackers and relabelers. It may involve a redesign of packaging, as well as adjustments to the production line. Such changes often require validation of the system to meet FDA requirements, which can be time-intensive. To better support the industry, some providers of coding systems offer design consultation, custom engineered systems, installation and validation assistance.

During such a changeover, a company can maximize its investment by further investigating updated coding technologies that can reduce costs, increase efficiency and productivity, and improve profits. These technologies include the latest advancements in ink jet printing, laser coding, thermal transfer overprinting, RSS, invisible fluorescent inks and RFID. By making such process improvements to the line, companies can see returns on investment almost instantly.

Updating Ink Jet Technology

Ink jet coding machines today are more efficient than those from only a couple of years ago. Small character, continuous ink jet printers use less fluids and require less maintenance than their predecessors. For example, some newer ink jet printers have automated nozzle cleaning for maintenance-free start-ups. Plus, auto-flushing printheads eliminate the need for manual cleaning.



Ink jet coding

Modifications in printhead designs have increased ink throw distances and improved drop placement for better character generation and print quality. Ink jet machines have significantly increased speeds, often achieving 1,200 feet per minute or faster.

Binary array technology further enhances the coding process by providing a high-resolution image at fast drying times with no smearing. This technology also allows for a wider variety of fonts and typestyles to be used.

Ink Options

A variety of inks are available in the industry to simplify coding needs. For example, invisible fluorescent inks that are visible only under ultraviolet lights (also known as blacklight) can allow for more coding on a package without cluttering the customer-targeted graphics on the package. If space limitations are also an issue, manufacturers can add manufacturing codes in invisible fluorescent ink and not interfere with customer-oriented codes and information.



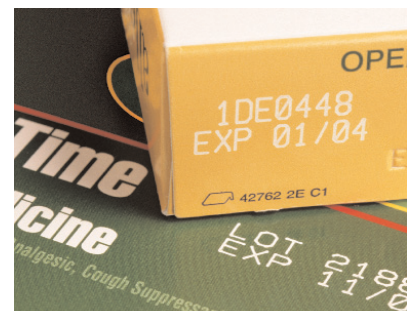
Coding with invisible fluorescent ink

Multiple codes on a package can also confuse or unnecessarily scare a consumer (Which one is the expiration date? What do all these codes mean?). Printing detailed manufacturing data (production line, ingredient batch code, etc.) in invisible ultraviolet ink reduces such concerns.

In addition, invisible codes improve the security of tracking and tracing shipments from point-of-origin, through the supply chain and to the point of sale.

Switching to Laser

Companies that currently use ink jet technology for coding may want to consider laser coding. Compared to ink jet printing, laser coding significantly increases productivity by up to five percent because it requires virtually no maintenance. Laser coding requires no ink, so there is no mess, no downtime to replace fluids and no fluid costs. Plus, it makes permanent, non-smearing marks and can print smaller characters, which is particularly important when printing 1-D and 2-D linear bar codes such as RSS codes. For applications that require higher resolution, a steered beam laser coding system is recommended over a dot matrix laser coding system.



Steered beam laser coding

Switching to Thermal Transfer

Instead of printing and applying labels to flexible packaging, such as foil or medical-grade paper, thermal transfer overprinting has the ability to print directly onto substrate in roll-stock form. Direct thermal transfer increases productivity while reducing costs associated with downtime because it requires very little maintenance, and ribbon changes take less than 30 seconds. This system also eliminates the need and cost of fluids.

RSS: A Smaller Coding Option

The use of RSS instead of standard bar codes allows a great deal more information to fit in 1/15 of the space. Instead of just including an NDC number, manufacturers can include proprietary, possibly encrypted, SKU identifiers, lot and date codes, time stamp, drug interaction or other precautionary information, storage requirements, or other information important for the control and tracking of the drug through distribution, storage and use.



RSS code

Considering the new regulatory requirements related to bar coding at the single dose level, particularly unit-of-use blister packaging and other small format packages, the space efficient RSS code format may be the only viable option for compliance.

The New Solution: RFID

In a 2004 report, "Combating Counterfeit Drugs," the FDA stated that track-and-trace technologies and product authentication technologies should provide greater drug security. The FDA also said that this is a more reliable solution for ensuring drug legitimacy than current paper record keeping (pedigree) requirements.



RFID tag

The FDA concluded that RFID tagging is the most promising technology for marking and tracing drugs, and that RFID is feasible for use by 2007.¹³

RFID will further increase the efficiency of coding and marking systems because it eliminates manual scanning. When an RFID tag is within the vicinity of an RFID scanner, the information will be automatically transferred. For example, when a pallet of a drug leaves or enters a warehouse, the system will scan and log that transaction, making inventory updates instantaneous. With RFID systems installed in hospitals, a healthcare worker entering a patient's room will instantly know if a prescription is allowed to be administered without having to scan the drug and patient bracelet manually.

CONCLUSION

As the pharmaceutical industry encounters challenges such as new coding regulations and counterfeits, coding and marking technologies will continuously develop to address those demands. Now is the time for drug companies to take advantage of these opportunities by adopting new technologies to further improve production lines, comply with current regulations, support downstream systems designed to enhance patient safety, and provide for secure distribution of drug products, which will ultimately lead to increased profits.

ABOUT THE AUTHORS

Richard Jushchyshyn, BS/MBA, has provided engineering and validation services to the food and pharmaceutical industries for over 29 years. He currently manages JM Hyde Consulting, Inc.'s office in North Wales, Pa., which provides compliance, engineering and validation services to pharmaceutical and biopharmaceutical manufacturers (www.JMHyde.com).

Rich Holzchuh specializes in sales and service of Videojet marking and coding solutions for pharmaceutical companies. He has been in the pharmaceutical and medical device industry for eight years.

Based in France, Xavier Chaveton provides market-specific support and direction for Videojet's pharmaceutical customers in Europe, the Middle East and Asia. Xavier has held a variety of sales and marketing positions with Videojet for over 16 years.

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APPENDIX: CODING AND MARKING SOLUTIONS FROM VIDEOJET TECHNOLOGIES

Videojet Technologies Inc. offers a comprehensive range of product identification technologies to help provide the perfect solution to coding and marking challenges.

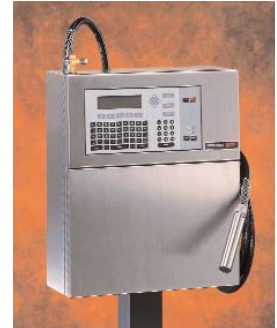
Small Character Ink Jet

Videojet offers a complete line of industrial printers able to produce reliable codes at today's production line speeds — up to 1,333 ft/min. (406 m/min.) — with code heights ranging from 1/32" (0.8 mm) to more than 1/2" (13.7 mm). With features such as WYSIWYG displays and self-cleaning printheads, Videojet continuous ink jet (CIJ) printers provide optimum efficiency and versatility, increasing throughput and minimizing downtime.

Videojet Excel® 2000

The Videojet Excel® 2000 and 2000 Opaque ink jet printers deliver the highest degree of reliability and print quality at the speeds you need. They will code reliably in a variety of applications where speed, quality of code and flexibility are key factors.

- Enhanced standard features provide coding flexibility
- Opaque capability allows for bright codes on dark surfaces
- Up to 4 lines of print



Videojet Excel 2000

Videojet® 46s

The Videojet® 46s ink jet printer provides the highest reliability and lowest running costs available from an airless printer.

- No need for factory air
- 4 line printing for maximum flexibility
- Single line print speed up to 1,066 feet per minute (5.4 m/sec.)
- Push button stop/start with automatic printhead flushing
- Stainless steel IP54 cabinet



Videojet 46s

FLUIDS

Videojet inks and fluids are designed, tested and manufactured together, to function together at optimum performance levels, no matter what your application or production environment.

From food grade and ultraviolet inks to thermochromic inks formulated to change color when heated, and from water-based "environmentally friendly" to the most aggressive inks possible, Videojet's premier fluids deliver premium images because they are premium quality products.

Laser Coding

The Videojet Focus series laser coding systems deliver affordable, steered-beam laser coding to a wide variety of applications. These laser coders offer permanent, superior quality codes at high production speeds. The Focus series features small footprints, high-speed printing, and rugged reliability in a wide variety of production environments.

Videojet Focus® S10

The Videojet Focus® S10 series laser coder delivers affordable, steered-beam laser coding to a wide variety of applications. This laser printer offers clean, permanent, superior quality codes on a variety of materials. The Videojet Focus S10 series laser system features a small footprint and rugged reliability in a wide variety of production environments.

- High-speed, permanent laser coding
- Small footprint, easy on-line integration
- Clean, high-resolution coding
- Reliable, easy to use



Videojet Focus S10

Alltec CS10

The ALLPRINT CS laser coding system meets the highest demands for permanent, clean, reliable, flexible, and economic product marking. With a small footprint and easy-to-position laser head, the ALLPRINT CS system is ideal for printing text, numbers, logos, graphics and codes on a range of products, including cartons, electronics and automotive goods. The ALLPRINT CS is the compact solution to your marking requirements.

- Easy integration for flexible installs
- High-end graphics, logos, codes
- Superior character formation (vision readable)
- Large print window (multi-lane print)



Alltec ALLPRINT CS

Thermal Transfer Overprinting

The Videojet DataFlex™ thermal transfer overprinter (TTO) represents a breakthrough in thermal transfer coding on flexible packaging. A full generation beyond any other TTO, this new system is capable of intermittent or continuous operation, making it flexible enough to handle your changing application needs.

Videojet DataFlex™ Thermal Transfer Overprinter

The Videojet DataFlex™ thermal transfer overprinter (TTO) represents a breakthrough in thermal transfer coding on flexible packaging. A full generation beyond any other TTO, this new system is capable of intermittent or continuous operation, making it flexible enough to handle your changing application needs. The clutchless ribbon drive increases



Videojet DataFlex

mechanical reliability with less required maintenance, and the graphical user interface offers easy operation.

- Digital, thermal transfer technology provides flexible, high-quality images
- Intermittent and continuous motion — from the same system
- Reduced downtime, increased reliability and superior cost efficiency
- Intuitive touch screen user interface
- Easy to learn and use

Label Application

Labeljet modular labeling systems offer the latest microprocessor-controlled technology for fast and accurate label placement in a wide range of applications.

Labeljet 210

The Labeljet 210 is a modern, microprocessor-controlled, industrial label applicator. The integral stepper motor drives the label web at up to 98.4 feet per minute (30 m/min.). A shaft encoder input (for speed compensation) is standard, and optional application methods include tamp and blow modules

- Fast, accurate and simple operation
- Low maintenance
- High speed
- Stepper motor with microprocessor control
- Storage of multiple production settings
- Airjet, non-contact application
- Touch and tamp modules with various strokes



Labeljet 210

RFID

Videojet Broadcast System™ RFID Tag applicator

The Videojet Broadcast System™ automatically dispenses and applies self-adhesive RFID Tags from a roll. The basic machine is a simple touch (wipe) applicator that can be synchronized to the production line speed to ensure optimum performance. The configuration can be changed by the addition of optional modules.

- Portable, flexible, affordable
- System supports Class 0 or Class 1 tags
- EPC Global Standard upgradable
- Simple touch screen display
- Low maintenance
- High speed
- Microprocessor control
- Stepper motor
- Storage of multiple production settings
- FAST-Tag™ ready



Videojet Broadcast System

For more information about Videojet products, or to locate a dealer in your area, visit www.videojet.com or call 800-843-3610.

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