

# GMPs and Pharmaceutical Labeling

*FDA labeling regulations protect consumers and ensure product identity*

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**M**islabeled drug products can pose a threat to public health and, according to FDA rulings, lead to costly product recalls with significant product liability. To help prevent mislabeling (and thereby protect consumers) manufacturers of pharmaceutical packaging components conform to good manufacturing processes (GMPs) designed to maintain product identity and ensure product quality.

Requirements for label inspection and identity control have become increasingly stringent. Those same requirements have been passed on to packaging component suppliers. To maintain product identity when printing packaging components, manufacturers increasingly rely on electronic verification of the printed product.

## Electronic Verification

Several methods of electronic verification are available to assure that the packaging component produced is exactly what the customer ordered. Most printed packaging components come in either sheets or rolls. Each method presents unique challenges for maintaining product integrity.

**Sheet items.** For sheet items at the printer, packaging components — such as folding cartons, patient information literature, and cut labels — are laid out so that the maximum sheet size is used. The goal is to get the most individual images of the same item on the press sheet. Putting multiple items on the same press sheet is strongly discouraged because it increases the risk of a product mix-up.

**Bar codes and IC marks.** Electronic detection devices can scan a number of different bar codes or identity control (IC) marks on individual sheets or pieces. Many components incorporate bar codes into the artwork, but codes and IC marks can be added in the waste area of the sheet when necessary. This unique form of identification is particularly helpful when common sheet sizes are used for similar items.

After printing, the sheets are cut into individual pieces. Item-specific bar codes are then scanned on these pieces at the final folding or gluing operation for further identification and control. In addition, IC

marks can be used for visual confirmation of the product identity. It is recommended that a unique item- or revision-specific bar code be used, rather than a universal product code (UPC) because the same UPC may be used on different revisions of the same packaging. That can cause the electronic scanner to fail to detect a mix-up of a different revision of the same item.

To further assure compliance, bar codes and part numbers should be used (and recorded) for each product batch. Bar coding on both front and back sides allows a manufacturer to verify that a product is correct and that copy exists on both sides if necessary to comply with the product specifications. Bar code verification traditionally includes examining print contrasts, magnifications, bar heights, light margins, and bar width. It can also give an assessment of overall print quality.

**Roll products**, such as labels and patient information literature, present different inspection and identity detection challenges. Like sheet producers, roll product producers maximize the capabilities of their equipment by putting as many images as possible on a press repeat. With the amount of information required on the label, sometimes there just isn't enough space for bar codes. This makes full electronic inspection using bar codes impossible. Although bar codes can be added to the outer edge of roll stock, that can get quite expensive, especially if producers have to special order a roll width just to accommodate the bar code. In addition, every label might not need scanning — just every repeated label.

Electronic inspection and detection of all the copy on a label is often accomplished with vision inspection equipment. Such equipment uses a camera that photographs the "truth copy" and compares it to the product's set specifications and guidelines. Although only a handful of companies use "100% vision inspection," it provides many advantages for compliance with various GMP interpretations. For example, copy-specific controls can be set to allow precise verification of key label components. In addition, suppliers and their customers can determine critical pieces, then

check only those items, while still remaining in compliance.

**High-level vision inspection equipment** is a combination of inspection hardware and software that uses patented algorithms to view the labels in question. One hundred percent vision inspection systems allow standard print variations, yet can still identify critical defects. In contrast to other systems that view only a portion of each label, 100% vision inspection verifies everything on each label. In addition, a line-scan camera and pipeline vision are used to process the labels, even when labels are on a moving web at full production speeds. The process can also be used to identify marks and imperfections on the printing stock surface.

Stricter enforcement by FDA has encouraged the adoption of vision inspection technology, and the increased emphasis drug companies place on quality and efficiency may increase its use by manufacturers of printed packaging components. Leaders in quality control use vision inspection equipment despite its higher cost.

Several GMPs cover distribution and storage of pharmaceutical labels, and manufacturers have taken steps to promote the traceability of their products. Work-in-progress tags should indicate job, part, purchase order (PO), and lot numbers. Records with this level of detail allow traceability from packaged product back to the raw materials.

FDA's pharmaceutical labeling requirements were enacted to reduce public health and safety risks stemming from drug labeling mix-ups. In response, printers and manufacturers of these products have enacted policies and purchased the equipment necessary to comply with the requirements — and defect-free labels are the intended end result. **AA**

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