Guidance for Industry

Bar Code Label Requirements

Questions and Answers

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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I. INTRODUCTION

FDA regulations require that certain human drug and biological product labels contain a bar code consisting of, at a minimum, the National Drug Code (NDC) number (21 CFR 201.25). This guidance provides questions and answers relating to how the bar code label requirements apply to specific products or circumstances. The questions are based on those posed to the Agency since the final rule published in February 2004. This guidance, which is a revision of the April 2006 version, contains input from the Center for Biologics Evaluation and Research.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

In the *Federal Register* of February 26, 2004 (69 FR 9120), we published a final rule requiring certain human drug and biological products to have on their labels a linear bar code that contains, at a minimum, the drug's NDC number (21 CFR 201.25). The rule also requires the use of machine-readable information on blood and blood component labels (21 CFR 606.121(c)(13)).[2]

[1] This guidance has been prepared by the Office of Regulatory Policy in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration, in conjunction with the Agency's Bar-Code Working Group. The Agency may revise this guidance as we receive additional questions.

[2] Section 606.121 requires the container label of a blood or blood component to bear encoded information in a machine-readable format and approved for use by the Director, Center for Biologics Evaluation and Research (CBER).

Bar codes will allow health care professionals to use bar code scanning equipment to verify that the right drug (in the right dose and right route of administration) is being given to the right patient at the right time. This new system is intended to help reduce the number of medication errors that occur in hospitals and health care settings.

III. QUESTIONS AND ANSWERS

WHO IS SUBJECT TO THE BAR CODE RULE?

Q1: Is a firm subject to the bar code rule if it sells its drugs to distributors, and the distributor then sells it to others (including hospitals)?

A1: Yes. Under § 201.25, manufacturers, repackers, relabelers, and private label distributors of human prescription drug products, biological products, and over-the-counter (OTC) drug products that are dispensed pursuant to an order and are commonly used in hospitals are subject to the bar code requirement, regardless of the method they use to distribute their drug products.

Q2: If a distributor merely distributes a product and does nothing to the drug itself, is the distributor subject to the bar code requirements?

A2: No. Under § 201.25, manufacturers, repackers, relabelers, and private label distributors of drug products covered by the bar code rule who are subject to the establishment registration and drug listing requirements in section 510 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360) are responsible for placing the appropriate bar code on the product. A distributor who does nothing to the drug itself is not subject to registration and listing requirements and thus is not required to place a bar code on the product. However, any drug that requires a bar code and does not have one is misbranded under section 502 of the Act (21 U.S.C. 352).

Q3: Are all OTC drug products required to bear a bar code?

A3: No. As discussed at length in the preamble to the final rule, 69 FR 9120 at 9124-9126, as well as the codified regulation, OTC drug products must bear a bar code if commonly used in hospitals and dispensed pursuant to an order.

Q4: If an OTC product is commonly used in a nursing home, is it "commonly used in hospitals" for the purposes of the rule (21 CFR 201.25(b))?

A4: Not necessarily. The preamble to the final rule, 69 FR 9120 at 9124-9126, explained that FDA did not intend to imply that the rule would cover OTC drug products that were commonly used in "institutions" other than hospitals, and revised proposed § 201.25(b) to replace "institutional use" with "hospital use." The preamble also explained that determining whether a facility is a "hospital" depends on whether the

facility "provides medical, diagnostic, and treatment services that include physician, nursing and other health services to inpatients and the specialized accommodation services required by inpatients" (69 FR 9120 at 9125). If an OTC drug product is commonly used in a nursing home that meets the definition of a hospital (and the product is dispensed pursuant to an order), then the OTC drug product should bear a bar code.

EXEMPTIONS

Q5: Are OTC drugs that are packaged in LDPE (low-density polyethylene) containers and are commonly used in hospitals and dispensed pursuant to an order exempt from the bar code rule?

A5: No. However, effective immediately, in the exercise of our enforcement discretion, we do not intend to object if OTC drug products in LDPE form fill and seal containers that are not packaged with an overwrap do not bear a bar code. We responded to a comment on LDPE containers in the preamble to the final rule (response to comment 22, 69 FR 9120 at 9129). Because the comment was presented in the context of prescription drugs, our response addressed prescription drugs. The technical issue (potential leaching), however, affects any drug packaged in this manner. We will also consider amending the regulation to extend the exemption for prescription drugs in § 201.25(b)(1)(i)(F) to OTC drugs.

Q6: Can a firm whose products have a very low rate of medication errors obtain exemptions for those products?

A6: No. The low frequency of error is not considered a justification for an exemption. As we explained in the preamble to the final rule, if the type of medication error is serious, such as an error that results in death, it would be difficult to justify an exemption on the grounds that few deaths occur. We also have no basis to establish a threshold or baseline number of medication errors that would determine whether a drug should or should not be subject to the bar code requirement. Even if we could establish such a threshold or baseline figure, that figure may not be reliable because health care professionals are not required to submit adverse event reports to us. In other words, the adverse event reporting system can signal the possible existence of a problem, but it cannot reliably predict the frequency with which such problems may occur (response to comment 17, 69 FR 9120 at 9128).

Q7: Can drugs such as suppositories be exempt from the bar code requirements because of their small container size or their container material (including foil wrap)?

A7: No. The final rule does not provide a blanket exemption for suppositories or small containers. As discussed in the preamble to the final rule, we declined to exclude suppositories from the bar code requirement (response to comment 25, 69 FR 9120 at 9130). Furthermore, we declined to exempt small vials or containers (including suppositories, prefilled syringes, and other small products) and stated that firms may,

alternatively, modify the drug's immediate container to accommodate a label bearing a bar code (response to comment 27, 69 FR 9120 at 9131). A firm may apply for an exemption from the bar code requirement under § 201.25(d) if it can document that putting a bar code on its particular suppository product would adversely affect the product's safety, effectiveness, purity, or potency or is otherwise technologically not feasible ***and*** the problem cannot be solved by a package redesign or overwrap.

Q8: Does the bar code rule require hospitals to affix bar codes on drugs?

A8: No. The rule applies to drug manufacturers, repackers, relabelers, and private label distributors who are subject to the establishment registration requirements under the Act. Hospitals, clinics, and public health agencies that only "maintain establishments in conformance with any applicable laws regulating the practice of pharmacy or medicine and that regularly engage in dispensing prescription drugs . . . upon prescription of practitioners licensed by law to administer these drugs to patients under their professional care" are exempt from the establishment registration requirements (21 CFR 207.10(b)) and, by extension, are exempt from the bar code rule (response to comment 2, 69 FR 9120 at 9123).

IMPLEMENTATION DATES

Q9: How is the 2-year implementation date intended to work?

A9: Drugs approved on or after April 26, 2004, have 60 days from their approval date to comply with the bar code requirement (21 CFR 201.25 and response to comment 71, 69 FR at 9147). All other drugs subject to the bar code requirement, including drugs with applications approved before April 26, 2004, and drugs marketed without an application, whether prescription or OTC, must implement the requirements within 2 years of the effective date (i.e., no later than April 26, 2006) (21 CFR 201.25 and response to comment 71, 69 FR at 9147). As explained in the preamble to the final rule, FDA settled on this 2-year period to give industry sufficient time to make the labeling changes necessary to comply with the rule and to enable firms to exhaust existing stock. The following considerations will affect whether a drug complies with the rule by April 26, 2006:

- A drug manufactured on or after April 26, 2006, must bear a bar code (21 CFR 201.25 and response to comment 71, 69 FR at 9147).
- We will not require a drug manufactured and distributed by the manufacturer before April 26, 2006, to be recalled or repacked to bear a bar code.
- We intend to exercise enforcement discretion, as described in the next paragraph, for a drug manufactured before April 26, 2006, that has not left the manufacturer's control by April 26, 2006.

For products packaged and labeled without bar codes before April 26, 2006, in the exercise of our enforcement discretion, we do not intend to object if those drugs are distributed and sold after April 26, 2006, until the existing supply is exhausted. Although we would consider subsequent distribution of those drug products to be a violation of the bar code rule and a misbranding under section 502 of the Act, we will allow distribution and sale of the drug products until the existing supply is exhausted, rather than requiring the products to be relabeled or destroyed.

Given that firms had 2 years to comply with the bar code rule, and the rule provides an exemption mechanism where compliance is not technologically feasible, we believe that the quantities of drug products packaged and labeled without bar codes before April 26, 2006, but not yet in distribution on that date, will be minimal. We also expect that the brief period of enforcement discretion will not apply to many firms because of prior contractual obligations to supply bar coded products or other reasons. Therefore, we anticipate that existing stocks of drug products packaged without bar codes will be exhausted and replaced with bar coded products within a relatively short time period.

Q10: Does the product expiration date have any bearing on the bar code requirements?

A10. No. The expiration date of a product has no bearing on the bar code requirements.

Q11: If a drug was approved before the effective date of the final rule, but a supplement is still pending as of the effective date, what date is used to determine when the product needs to meet the bar code requirements?

Should companies use the original new drug application (NDA) or biological license application (BLA) approval date (getting 2 years to comply), or does FDA intend to apply the supplement's approval date (triggering compliance within 60 days)?

A11: The original application approval date is the applicable date for determining when a product would need to meet the bar code requirements. As discussed in the preamble to the final rule, we expect drugs approved before the effective date of this rule to comply with the bar code requirements within 2 years of the effective date, i.e., on or before April 26, 2006. Drugs approved on or after April 26, 2004, the effective date of this rule, must comply within 60 days after the drug's approval date. (See response to comment 71, 69 FR 9120 at 9147.) For circumstances in which a drug is approved before April 26, 2004, and a supplement for a new potency or other change subject to the approval of a supplement is approved after April 26, 2004, the application's original approval date controls; therefore, we would expect the product subject to the supplement to comply with the bar code requirements on or before April 26, 2006.

QUALITY, APPEARANCE, AND PLACEMENT OF THE BAR CODE

Q12: Can a firm use another automatic identification technology, such as a radio frequency identification chip or a two-dimensional symbology, instead of a linear bar code?

A12: No. The final rule requires the use of a linear bar code to encode the NDC number on most prescription drug products and certain OTC drug products. However, we do not intend to object if firms voluntarily encode lot number and expiration date information, and we recognize that some firms might use other technologies to encode that additional information (response to comment 35, 69 FR 9120 at 9134-9135).

In addition, we stated in the preamble to the final rule that we will consider revising the rule to accommodate new technologies and may begin examining other automatic identification technologies by April 2006 (69 FR 9120 at 9138).

Q13: What should be used in lieu of an asterisk in an NDC number?

A13: Nothing should be put in place of the asterisk in an NDC number in a bar code.

Under 21 CFR 207.35(b)(2), the Agency uses the National Drug Code (NDC) numbering system in assigning an NDC number. The number is a 10-character code that uses only numerals.

The NDC number is divided into three segments. The first segment, the labeler code, identifies the manufacturer or distributor and is four or five characters long. The second segment, the product code, identifies the drug product and is three or four characters long. The third segment, the package code, identifies the trade package size and type and is one or two characters long. The 10-character NDC number can be in the following three configurations of labeler code–product code–package code: 4–4–2, 5–4–1, or 5–3–2.

The asterisk is for FDA's internal use only. For entries into our database, the asterisk is a dummy character used to differentiate between the three different configurations. A zero cannot be used in place of the asterisk because a zero is a real numeric character in an NDC number. An NDC number that contains a non-numeric character (an asterisk) reverts to a 10-numeric character code when used on the labeling of a drug product or included in a bar code. For example, if the NDC number for a firm's product is in a 5–3–2 configuration, the Agency, potentially, assigns a dummy asterisk as follows: 12345–*542–12. When a bar code is placed on the product, the asterisk is dropped, and the number included in the bar code is 1234554212.

Q14: If a drug product has a bar code on the immediate container and the outer container is an overwrap through which the bar code is human-readable but not machine-readable,

does the overwrap also have to contain the bar code if the drug product is administered without the overwrap?

A14: Yes. The Agency intends for bar codes to be on the drug's outside container or wrapper as well as on the immediate container, unless the bar code is readily visible ***and*** machine-readable through the outside container or wrapper (section II.E in the preamble to the final rule, 69 FR 9120 at 9140). When the bar code is not easily machine-readable through the overwrap, the overwrap should contain the bar code. The fact that the overwrap is removed before administration does not change the answer; to prevent medication errors, hospital personnel may need to scan the bar code during the dispensing process before the overwrap is removed.

Q15: For a product packaged in blister cells divided by perforations that enable the cells to be separated, should there be one bar code for the entire package or does each cell need a bar code?

A15: Assuming that each cell has a label, the bar code should go on each cell because the final rule requires that the bar code be on the drug's label. Furthermore, the bar code must remain intact under normal conditions of use; thus it should not be printed across the perforations of a blister pack (response to comment 43, 69 FR 9120 at 9140).

Q16: Does FDA intend to issue guidance regarding bar code quality, such as size, symbol quality, symbol grade, reflectance?

A16: No. We believe there are sufficient documents and standards issued by third parties to address such bar code quality and standard matters (response to comment 56, 69 FR 9120 at 9144).

MACHINE-READABLE LABEL REQUIREMENTS FOR BLOOD AND BLOOD COMPONENTS

Q17: Must blood and blood component container labels include specific machine-readable information?

A17: Yes. Products subject to the bar code rule, including blood and blood components intended for transfusion, must be in compliance by April 26, 2006 (21 CFR 606.121(c)(13)).

Q18: What machine-readable information is required for blood and blood components?

A18: Under 21 CFR 606.121(c)(13)(ii-iii) the container label must bear encoded information in a format that is machine-readable and approved for use by the Director, Center for Biologics Evaluation and Research. Currently, two types of machine-readable information are recognized by FDA.

- In 1985, FDA recognized the use of Codabar (a specific bar code symbology).
- In 2000, FDA recognized the use of ISBT 128.[3]

Each label must have, at a minimum, the following information:

(A) A unique facility identifier;
(B) Lot number relating to the donor;
(C) Product code; and,
(D) ABO and Rh of the donor.

Q19: We are a transfusion service and very infrequently prepare split units, pediatric units, and pooled cryoprecipitate units; do we need machine-readable labels for these units?

A19: Yes. This situation was described in the preamble to the proposed rule (68 FR 12500 at 12513):

> The unit of blood or blood component label would contain the machine-readable information if the blood or blood component has any possibility of being transfused to a patient, whether or not the unit is actually transfused. Additionally, the phrase, "from which the blood or blood component can be taken and transfused to a patient" would include the circumstance where blood or a blood component is extracted or aspirated with a syringe from the container of blood or blood component in order to transfuse to a patient. This technique might be used when transfusing neonates or under other medically necessitated circumstances. In this case, the blood or blood component from which the aspirate is taken must have affixed to it a label containing the required machine-readable information. This would be consistent with the pre-existing requirement at § 606.121(c)(8)(iii) that requires specific statements if a product is intended for transfusion.

Q20: How do we encode facility identifiers and product codes for pooled and aliquoted units for Codabar or ISBT 128? Where do we get information about these issues?

A20: Please contact CBER's Manufacturers Assistance and Technical Training Branch (MATTB) at matt@cber.fda.gov for additional information. The regulation requires a unique facility identifier.

Q21: How will FDA evaluate compliance with the rule?

A21: Our investigators will evaluate compliance with these regulations during routine inspections of blood establishments.

[3] See CBER's website for the currently acceptable version(s) of ISBT 128 (http://www.fda.gov/cber/blood/bldguid.htm).

Q22: May I request an exception or alternative under 21 CFR 640.120 for this requirement of the blood and blood component container label regulations?

A22: Yes. However, the purpose of the bar code rule is to reduce transfusion errors and increase patient safety. CBER will carefully review any request for an exception or alternative. The bar code regulation for drug products recognizes that exemptions may be warranted when compliance would adversely affect the drug's safety, effectiveness, purity, or potency, or when compliance would not be technologically feasible. In the preamble to the rule, FDA noted that almost all drug products are capable of bearing a bar code. FDA also noted that we would not consider written requests based on factors such as financial reasons, a claimed low rate of medication errors, or a claim that the product is unique and medication errors do not occur or rarely occur. In assessing requests for exemptions for blood and blood components, FDA would follow the same approach described in the drug regulations (21 CFR 201.25(d)).

Q23: Do the bar code regulations apply to routine intraoperative or postoperative blood collection from surgical drains ("salvaged blood") followed by reinfusion on the nursing unit or other location within the hospital?

A23: No. In a 1989 memorandum to all registered blood establishments, CBER delineated its policies on autologous blood. That memorandum stated that the quarantine, storage, recordkeeping, and labeling requirements of 21 CFR part 606 are generally not applicable to salvaged blood collected for proximate transfusion to the patient as part of the patient's treatment (http://www.fda.gov/cber/bldmem/031589.txt).[4] Because bar code requirements fall under the category of label requirements contained in 21 CFR part 606, the requirements would not be applicable to salvaged blood.

However, the intent of FDA's bar code rule is to reduce medication errors, including transfusion errors. To help reduce transfusion errors for salvaged blood, some hospitals may voluntarily implement the use of machine-readable information, including bar codes, blood bank computer systems, and bedside readers.

MISCELLANEOUS

Q24: Does FDA intend to buy bar code scanning equipment to promote bar code use in hospitals?

A24*:* No. We have no intention to buy or distribute bar code equipment.

[4] If salvaged blood is stored in the hospital blood bank, the requirements under 21 CFR 606.121(c)(13) apply.