

Aventis Pharmaceuticals



July 8, 2002

Via Fax and UPS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 02N-0204
Bar Code Label Requirements for Human Drug Products; Notice of Public Meeting; 67 Fed Reg 41360 (June 18, 2002)

Dear Sir/Madam:

Aventis Pharmaceuticals Inc. is pleased to provide the following comments on the above-referenced Notice of Public Meeting entitled, "Bar Code Label Requirements for Human Drug Products". In support to the initiative of the Secretary of Health and Human Services to reduce medication errors, the FDA is holding a public meeting to solicit comments for the development of a regulation on bar code labeling for human drug products, including biologic products, as well as medical devices.

A. General Questions Related to Drugs and Biologics

1. Which medical products should carry a bar code? For example, should all prescription and over-the-counter (OTC) drugs be bar coded? Should blood products and vaccines carry a barcode?

For the purposes of preventing medication errors, all prescription drug products should utilize bar-coding to allow automated verification that the proper product and dose are dispensed. Product packaging at all levels, down to unit-of-use, should include bar codes. Note that product bar-coding is only useful when the institutions have barcode scanning equipment available to make proper use of the codes, most notably at the point of use (i.e. the patient bedside). Therefore, any regulation should also require hospitals and institutions to purchase and install proper scanning equipment to make full use of bar codes.

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2. What information should be contained in the bar code? What do you consider to be critical bar code information that will reduce medical product errors? If data exists, please provide it for the record. What information would be helpful but not necessarily critical, for reducing medication errors? Provide data.

The most critical piece of information that should be included in a product barcode is a unique and standardized identification number for the product name, dosage, and strength (i.e. the product NDC number).

Secondary information, such as Lot Number and Expiry Date, may be helpful, but should not be required.

3. Considering current scanners and their ability to read certain symbologies, should the rule adopt a specific bar code symbology (e.g., reduced space symbology (RSS) and 2-dimensional symbology)? Should we adopt one symbology over another, or should we allow for “machine readable” formats? What are the pros and cons of each approach?

In order to promote standardization throughout industry, Aventis recommends that FDA adopt a standardized numbering system for bar-coding of drug product packaging. It is recommended that the Uniform Code Council (UCC) numbering system, based on the Global Trade Identification Number (GTIN) be adopted. The UCC system is compatible with the existing National Drug Code (NDC) and allows for differentiation between levels of packaging using “Package Indicator” digits within a barcode. This system eliminates the need for assigning a new NDC code for each level of packaging. If no system or standard is specified, dispensing institutions may create different standards. Drug product manufacturers could conceivably have to print different bar codes for each of their customers, which would lead to excessive cost and complications. Standardization of coding technology will give dispensing institutions clear and concise direction when purchasing barcode scanning equipment for use in their facilities.

Aventis does not recommend the adoption of any specific barcode symbology, as symbology requirements are primarily driven by the amount and type of data encoded, as well as the available space for printing on a given packaging component.

The UCC numbering system is compatible with most common existing barcode symbologies (including UPC, UCC/EAN, RSS, Data Matrix), and will allow for modification and improvement as new symbologies are developed in the future.

4. Assuming that we require bar codes on all human drug products, where on the package should the bar codes be placed? Are there benefits to placing bar codes on immediate containers, such as the bottles, tubes, foiled-wrapped tablets, and capsules, found inside prescription or OTC product cartons? Is there a way to distinguish whether certain containers with a barcode will have a more significant effect on preventing errors than others?

For prescription drug products, it is advantageous to barcode all levels of product packaging, down to the unit-of-use. This includes immediate containers such as bottles, vials, tubes, ampoules, and blister packages. Note that product bar-coding is only useful when the dispensing institutions have barcode scanning equipment available to make proper use of the codes,

including at the point of use or distribution. We recommend leaving it up to individual manufacturers where specifically to place the barcode on a given package, as the variety in package sizes, types, and styles would make standardization extremely difficult. In general, bar codes should be presented in locations that are easily visible and accessible to the individual doing the dosing and/or dispensing of the product.

For some very small packaging components, the addition of bar codes may require that existing text elements be re-evaluated. It is therefore recommended that any barcode requirements be made in conjunction with a review and possible revision of the “Small Label” text requirements, as defined in 21 CFR 201.10(i).

5. What products already contain bar codes? Who (i.e. hospitals, nursing homes, outpatient clinics, retail pharmacies, etc.) uses these bar codes and how? As with all comments, if data exists, please provide it for the record.

Currently, Aventis prints UPC codes containing the product NDC number on all sales units of prescription drug products for retail sale. Examples of sales units include: 1 bottle of 60 tablets, 1 carton of 100 tablets in blister packages, 1 carton of 10 ampoules. Additionally, Aventis has special Unit Dose Identification Packs (UDIP) for some products, which are designed specifically for hospital/institutional use, which are tablets or capsules in blister packages. Each individual blister cavity (containing 1 tablet or capsule) is printed with a barcode encoding the product NDC number. The intent is that each individual blister cavity is a fully labeled and identifiable package, with the barcode available to enable automated verification at the point of use.

B. Medical Device Questions

No response.

C. General Questions and Economic Impact Questions

1. Will barcode printing costs cause you to modify your packaging choices, such as reconsidering the use of blister packages or influencing future package choices? If so, how.

Requirements for an NDC barcode should not have a substantial impact on selection of packaging styles or materials. Because the NDC barcode can be pre-printed, the cost for including this code on most packaging materials is negligible. The major potential issue with adding an NDC barcode is that many unit-dose packages are very small, and thus offer only a limited amount of printing space. For these components, the addition of bar codes may require that existing text elements be re-evaluated. It is therefore recommended that any barcode requirements be made in conjunction with a review and possible revision of the “Small Label” text requirements, as defined in 21 CFR 201.10(i).

If requirements include the encoding of Lot Number and/or Expiry Date into a barcode, there is likely to be a significant impact on the types of styles and materials chosen for product packaging. These codes would have to be printed “on-line” for each individual batch packaged, and the development and procurement of adequate on-line printing systems will be both costly

and time-consuming. In addition, some packaging materials (most notably aluminum foil) do not provide surfaces suitable for the high quality printing necessary for small bar codes, and may require changing to other more expensive materials.

The incremental space required for Lot/Exp bar codes could also result in increased size of packaging components. This would lead to increased cost (materials, handling, storage, shipping, etc) as well as an increase in the waste stream.

2. Have you implemented barcode technology in your product line? If so, what elements and symbology are included in the barcode?

Aventis currently prints UPC codes containing the product NDC number on all sales units of prescription drug products for retail sale. This code includes the product NDC number, along with a Healthcare Item identifier prefix, and a Modulus-10 Check Digit. Additionally, Aventis prints Primary and Secondary identification bar codes on all shipping case labels for retail products. The shipping case label bar codes include NDC Number, Quantity, Lot Number, and Expiry Date, and utilize UCC/EAN-128 symbology.

3. If you manufacture and barcode products, how do verification requirements for bar codes affect your ability to add bar codes? How much barcode verification is appropriate as part of the quality system?

Currently, all product identification bar codes on Aventis products are pre-printed. These codes are verified multiple times (artwork approval, proof approval, incoming QC inspection), but they are not 100% verified on the packaging line. If new regulations require addition of bar-coding of Lot Number and/or Expiry date, these codes would be printed on-line directly during the packaging process. The codes would therefore require full 100% electronic verification, to ensure that they print correctly. The cost for verification equipment is estimated at \$15,000 per packaging line. Aventis operates approximately 80 packaging lines, so the total capital cost for verification equipment is estimated at \$1.2 million.

4. Can bar codes be produced with a dose-specific unique identifying number, lot number, and expiration date at your highest production line speeds?

A barcode containing only a dose-specific identifying number can be pre-printed and would not affect packaging line speeds. At this time, we are not aware of any on-line printing systems capable of printing bar codes for Lot/Exp on our fastest lines (up to 400 units/minute). Requirements for Lot/Exp bar-coding would likely require slowing down packaging lines up to 40%, which would have a severe negative impact on cost of goods.

5. What equipment solutions are vendors offering to manufacturers for bar-coding or scanning? How quickly can such systems run? What type of packaging line is equipment used for?

Vendors currently offer ink-jet and laser printing equipment that is potentially capable of on-line printing of Lot/Exp bar codes. This technology is fairly new, however, and the actual performance and quality has not yet been fully determined.

6. What is the expected rate of technology acceptance in all health care sectors of machine-readable technologies? What are the major inhibiting factors to the current use of machine-readable technologies? What would be the expected benefit of using machine-readable technology in the delivery of health care services (including drug products)? What would be the expected benefit of machine-readable technology for other potential uses (e.g., reports, record keeping, inventory control, formulary setting, etc.)?

It is expected that the use of product identification bar-coding at all levels of drug product packaging could help reduce the potential for medication errors. This expectation, however, is only realistic if appropriate standards are set and maintained, and that the dispensing institutions have barcode scanning systems in place to make use of the bar codes.

7. Assuming a final rule is issued requiring bar-coding, when should it become effective? For example, would some industries or products require more time than others to comply with a bar-coding requirement? Would a certain compliance time sharply reduce costs of relabeling?

Assuming that the issuance of a final rule is made, there should be a 2-tiered implementation schedule. Manufacturers should be given a minimum of 2 years to comply with a requirement for bar-coding of primary product identification (i.e. NDC). If rule is issued requiring bar-coding of Lot and/or Expiry information, manufacturers should be given a minimum of 4 years from issuance to comply with this portion of the requirement.

Associated Costs:

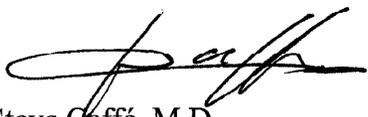
For printing of primary product identification bar codes, there is no substantial equipment or capital requirements. These bar codes would likely require only the purchase of software for creating codes and setting them in artwork- the associated costs here are negligible.

If requirements call for printing of variable data, such as Lot/Exp bar codes, this will require development and purchase of on-line printing equipment for each packaging line. Aventis estimates that we operate approximately 80 lines producing packaged products for the US market. The capital expenditure for printing and verification systems is estimated at \$50,000 (\$35,000 for printing / \$15,000 for verification) for each packaging line. The expenses associated with sourcing, procuring, installing and validating these systems are estimated at \$10,000 per line. Based on these estimations, the total cost associated with printing Lot and Expiry bar codes on all Aventis prescription drug products is approximately \$4.8 million.

In conclusions, Aventis believes that adding an NDC barcode to products will not be a major issue, however, the main issue is space on smaller labels. If FDA requires the addition of Lot # and/or Expiry Date barcodes, the impact would be very significant. In this scenario, we would have to develop and acquire on-line printing technology to print this batch-specific information. This would obviously require significant capital money, and development time and effort

On behalf of Aventis Pharmaceuticals Inc., we appreciate the opportunity to comment on the "Bar Code Label Requirements for Human Drug Products" and thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read "Steve Caffé". The signature is fluid and cursive, with a large initial "S" and a long horizontal stroke at the end.

Steve Caffé, M.D.
Vice President, Head US Regulatory Affairs

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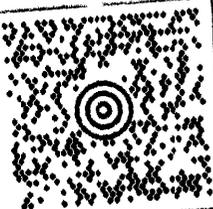
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