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AIRBORNE:

June 9, 2003

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

Dear Sir/Madam:

We commend the U.S. Food and Drug Administration (FDA) for proposing regulations relating to bar code label requirements for human drug products and blood. As the Agency appropriately articulates, the need for such requirements is necessary to help ensure against errors associated with incorrectly administered or dispensed medications and blood products. Overall, establishing requirements and standards of this type will help to address existing problems while advancing healthcare for all patients and healthcare practitioners. Given Cardinal Health's role as a leading provider of products supporting the healthcare industry, we support the FDA's goals in establishing this regulation. However, in reviewing the proposed rules we found that some provisions in these rules were either unclear or unworkable in practical application. As such, we would respectfully submit our comments below in an attempt to assist the Agency with the important task it has begun.

Part 201 – Labeling

§201.25 Bar code labeling requirements.

1. §201.25(b) provides that:

> *(b) What drugs are subject to these bar code requirements? The following drug products are subject to the bar code label requirements: Prescription drug products (excluding samples), biological products, and over-the-counter drug products that are dispensed under an order and are commonly used in hospitals. For purposes of this section, an over-the-counter drug product is "commonly used in hospitals" if it is packaged for institutional use, labeled for institutional use, or marketed, promoted, or sold to hospitals.*

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OTC Products:

While we support the overall premise of this provision, we believe that it too broadly defines which over-the-counter ("OTC') drug products should be subject to the bar code requirements. Specifically, the proposed regulation requires that the bar code requirements should apply to ". . . an over-the-counter drug product [that] is 'commonly used in hospitals' if it is packaged for institutional use, labeled for institutional use, or marketed, promoted, or sold to hospitals." We believe that the proposed rule should be narrowed such that bar coding is only required for OTC products which are actually designated to be used in institutional settings by the manufacturer, repacker, relabeler or private label distributor of that product (collectively the "Manufacturer"). The mere fact that such OTC products can be "marketed, promoted or sold" to hospitals or other institutions should not trigger this requirement.

As the Agency is probably aware, there is an ongoing consolidation and diversification in the healthcare sector (private, public and not-for-profit). Hospitals, outpatient clinics and pharmacies, physicians' offices, hospice centers, long-term care providers and/or insurers are fast becoming part of integrated delivery networks (IDN's). As such, today's institutions may have facets associated with them that are more akin to non-traditional institutional settings. For example, a number of hospitals have outpatient clinics and pharmacies associated with them. In those cases, OTC products would be sold to the hospital, but not used for institutional purposes. Rather, those OTC products will be provided to employees or outpatients of that pharmacy (similar to retail pharmacies or typical physician's offices). As such, it would be unnecessary for bar coding requirements to be imposed on these OTC products as is currently required pursuant to the language in the proposed rule. This premise is supported by the FDA's comments that the Agency ". . .decided against requiring all OTC drugs to carry a bar code because it is unlikely that putting bar codes on all OTC drugs would have a significant impact on reducing medication errors and offset the large costs associated with requiring bar codes on all OTC drugs." (68 Fed. Reg. 12505). That being the case, we would urge the Agency to limit the bar code label requirements to only those products which the Manufacturer has *specifically* packaged or labeled and which carry the designation "institutional use" or "hospital use" (or some similar language). In those cases, it is quite clear that the Manufacturer intends that such products be used in traditional institutional settings where the bar coding requirement would provide its intended benefit. The mere act of marketing, promoting or selling to an institution alone where those OTC products will not be used for institutional purposes should not trigger the bar code requirement. Of course, this approach would not preclude any Manufacturer from bar coding products regardless of their intended use. Thus, Manufacturers would be free to follow the bar code requirements if they believed that this was commercially advantageous based upon their customers' needs and in the event these

OTC products were to be used in both institutional and non-institutional settings by that customer.

Bar Code Requirements in Light of Product Size:

The proposed rule provides that all drug products, regardless of container size, have a bar code placed on the container. While we understand the Agency's reluctance to provide exemptions to this requirement, we believe that there still should be some accommodation given the practical hardships and issues this requirement may cause given the current state of the technology and the products at issue. Specifically, the Agency has invited comments as to whether "any specific product or class of products should be exempt from a bar code requirement" and the reasons why. To that effect we would propose that drug products contained in blow-fill-seal containers be exempted from this bar code labeling requirement at an individual dose level. Specifically, blow-fill-seal is a process employed for producing one-piece, plastic, ampule-like containers commonly used for respiratory agents. In this case, the unit-dose plastic ampules are provided to institutions within a multi-dose carton. These cartons contain the proper labeling for the product and would also contain the required bar-code designations. However, given the nature of these plastic ampules, labeling these individual ampules with adhesive labels or directly with ink cannot be effectively done. Furthermore, imprinting directly into the unit-of-use container will be costly and provide various technical hardships thus making the process costly and difficult. As such, we would urge the Agency to limit the bar code requirement for blow-fill-seal products to the unit-of-sale container for that product as opposed to the actual unit-of-use or unit-dose ampule.

Bar Code Requirements for Radiopharmaceuticals:

The proposed rule provides that all drug products have a bar code placed on the container, down to the unit dose level. For radiopharmaceuticals, the requirement that a bar code be used by a health care worker would be contrary to other safety concerns, since exposure to radiation is a significant concern for workplace safety. This is based upon the fact that the Nuclear Regulatory Commission and similar state agencies require that medical licensees who possess radioactive materials limit workers' radiation exposure to levels As Low As Reasonable Achievable (ALARA). Patients, who have limited exposure and receive the benefit of this medical treatment and/or diagnosis, are not held to this requirement for radiation exposure. If the unit dose container of the radiopharmaceutical were bar coded, healthcare workers administering the radiopharmaceutical would be required to take the radiopharmaceutical from its outer container in order to read the bar code. This would increase that worker's cumulative radiation exposure. The outer container, typically made of lead, is designed to provide radiation shielding for the worker and members of the general public, thus minimizing radiation exposure to workers and the environment. By taking the radiopharmaceutical's

immediate container out of this shielding in order to read the bar code label, the health care worker would greatly increase his/her radiation exposure. This process would generally occur several times a day. This is contrary to safe work practices in this area of medicine. Historically, the medication error rate for this class of drugs is extremely low, as evidenced by data collected by the Nuclear Regulatory Commission. Thus, the potential benefit of using bar coded products would be greatly outweighed by the increased risk of radiation exposure to health care workers in this medical specialty. Thus, we request that the FDA consider exempting radiopharmaceutical drugs from the bar coding requirement.

Bar Code Requirements for Medical Devices:

The proposed rule intentionally omits medical devices from the bar coding requirement. We agree with the Agency that medical devices ". . . present different issues compared to drugs, biological products, and blood" and that different classes of medical devices offer different degrees of risks (e.g., a bandage versus a cardiac stent). As such, we agree with the Agency that while bar coding requirements should be addressed as far as medical devices are concerned, that process should be addressed in a separate rule which allows for the Agency, healthcare practitioners and the affected medical device industry the opportunity to more fully address the parameters associated with such a requirement.

To that effect, we would recommend that the Agency focus upon the development of a subsequent proposed rule limited to medical devices. That proposed rule should attempt to standardize a common primary identifier (i.e., UPN number) while working to address a bar code methodology which will clearly identify reprocessed, repackaged or refurbished medical devices.

2. §201.25(c) provides that:

> *(c) What does the bar code look like, and where does the bar code go? (1) Each drug product described in paragraph (b) in this section must have a bar code that contains, at a minimum, the appropriate National Drug Code (NDC) number in a linear bar code that meets Uniform Code Council (UCC/EAN) standards. Additionally, the bar code must: (i) Be surrounded by sufficient blank space so that the bar code can be scanned correctly; and (ii) Remain intact under normal conditions of use. (2) The bar code must appear on the drug's label as defined by section 201(k) of the act.*

Linear Bar Code and Standard Employed:

Overall we support the Agency's proposed stance that the bar code requirement be limited to the NDC number in a linear bar code format. As the Agency's comments set

forth, the primary purpose of having mandatory bar codes on drug products is to reduce the potential occurrences of medication errors. As the Agency is aware, the NDC number functions as a unique identifier for specific drug products used in healthcare settings. By requiring that the NDC number be included in the bar code, this should unquestionably result in a reduction in medication errors for those institutions utilizing bar code scanning technology. Conversely, it is highly questionable that the addition of the lot number or expiration dating will provide similar tangible benefits. As the Agency indicates, there are no data which shows that adding the lot number and expiration date information would make it easier to identify drugs that were recalled or expired. Nor is there support for the position that the benefits of having such a requirement exceed the costs associated with requiring that information be included in the bar code (and the expenses to institutions in purchasing bar code scanning devices and/or software capable of reading this additional information). As such, the linear bar code requirement limited to the NDC number provides the best overall result at a reasonable and affordable expense.

Similarly, we support the Agency's position that the linear bar code format for drugs and biological products (other than blood and blood products) be any linear bar code employing the UCC/EAN standard. We support the FDA's position that adopting a linear bar code in the UCC/EAN standard (which includes the NDC number), as opposed to a specific bar code symbology, will give firms some flexibility and allow for potential changes as linear bar code symbologies develop and evolve. By taking this approach, the Agency is requiring the adoption of an established standard currently available and widely used in the marketplace while permitting for some flexibility and room for improvement.

3. Related Comments concerning the proposed Rule.

Practical Considerations Prompted by Bar Coding Requirements:

While we strongly support the FDA's position in creating the proposed rules, we question whether the effectiveness of these rules may not be undermined by another position the Agency has historically taken regarding the repackaging of unit-dose medications by FDA-registered repackaging facilities. Specifically, the Agency's stance under its October 1992 Draft Guidance document entitled *Draft Guideline on Repackaging of Solid Oral Dosage Form Drug Products (Docket 92D-0345)* provides that those repackagers required to comply with FDA regulations (e.g., complying with cGMP requirements, obtaining a drug establishment registration for the facility, etc.), are limited to six (6) month dating for product repackaged into unit-dose containers where no stability studies are conducted. However, where a licensed *pharmacy* provides essentially the same services (for its own use) as a repackager but does so under the guise of pharmacy practice, this limitation of six (6) month expiration dating does not apply. Generally, pharmacy practice adopts the USP standards either through state pharmacy regulations or established pharmacy practice standards. USP standards provide that in

the absence of stability data for repackaged unit-dose drug product, the "beyond-use dating period is one year or the time remaining of the expiration date, whichever is shorter." *USP 26-NF 21 (2003 Ed.), Packaging Practice - Repackaging a Single Solid Oral Drug Product into a Unit-Dose Container <1146> at page 2395.* This distinction is an important one in terms of obtaining the ultimate goal of the proposed rule – to have bar coded drug product widely available in institutional settings so as to prevent medication errors.

Various commentators as well as the FDA itself have acknowledged that the impetus for these proposed rules is to have bar code labeling in place on all prescription drug products. However, the ongoing availability of unit-dose drug product in institutions such as hospitals and nursing homes has and will continue to be an issue. This view is echoed in the July 26, 2002, comments provided by the American Society of Health-System Pharmacists (ASHP) to the Agency:

> Bar codes should be required on all pharmaceutical product packages ***down to the unit-dose – single unit level.*** This should include prescription and over-the-counter medications, as well as vaccines and blood products. For bar coding to be effective in hospitals and health systems, products in unit-dose packages ***must*** be made available by pharmaceutical manufacturers. While we have received reports that some major pharmaceutical manufacturers are about to make a public commitment to add bar coding to all packaging, including unit-dose, some of our members report a disturbing trend whereby fewer and fewer pharmaceutical manufacturers are producing products in unit-dose, leaving repackaging up to individual hospitals. This is a major concern of ASHP. Not only does repacking introduce new opportunities for mistakes to be made, it adds an additional cost, which most average- to small-size hospitals cannot afford. Repacking also takes pharmacists away from their most important duty in hospitals—*managing patients' drug therapy.*

That being the case, it is abundantly clear that the lack of unit-dose product availability is trending in a negative fashion as far as drug manufacturers are concerned.[1] Furthermore, the requirement that bar coding be placed on product at unit-dose level may very well further exacerbate this problem as even more drug manufacturers chose not to produce product in unit-dose packaging so as to avoid the additional expense associated with bar coding drug product at this level.

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[1] Bar code experts have noted this deficiency on a number of occasions. "At present, only about 35% of medications in a typical hospital have labels containing a bar code at the unit-dose level. Automating the point of care would require hospital pharmacies to apply bar-coded labels (or to arrange for them to be applied by a repackager) to roughly two thirds of their inventory." *Neuenschwander M, Cohen M, Vaida A, et. al. Practical Guide to Bar Coding for Patient Medication Safety. Am J Health-System Pharmacists; 2003; 60· 774.*

One very viable solution to this problem would be to permit FDA-regulated repackagers to provide unit-dose packaging services to hospitals and other institutions where bar coding would be placed on these repackaged items. However, to make this a viable option, the historic limitation on the dating of such product to six (6) months (in the absence of stability data) must be increased to at least twelve (12) months (in the absence of stability data). The reasons for this approach are as follows. First, performing stability data for such unit-dose product by repackagers is cost-prohibited. Second, six (6) month dating is insufficient given the time required to repackage the product into unit-dose containers coupled with the time needed to deliver that unit-dosed product to the end user. This is supported by the fact that most pharmacies tend to remove drug product having six (6) month expiration dating (or less) from their inventory as opposed to stocking such product. As a result, the potential waste in terms of product and associated expenses with the six (6) month dating scenario simply make the current repackaging scenario for FDA-regulated repackagers unworkable.

The tangible benefits to the public health in allowing FDA-regulated repackagers to repackage drug product into unit-dose bar coded containers having at least twelve (12) months (in the absence of stability data) are as follows: (1) provides a for a far wider range of available drug products in bar coded unit-dose format; (2) provides for entities utilizing FDA mandated parameters such as cGMP's to be conducting manufacturing-type activities as opposed to pharmacies performing similar tasks without such safeguards and controls; (3) will lessen the number of pharmacies choosing to undertake such internal repackaging activities given that such services would be available from authorized third-party vendors (i.e., FDA-regulated repackagers); and, (4) provides for greater overall utilization and benefits envisioned from the proposed bar code rule in terms of preventing medication errors.

In conclusion, we support the Agency's activities in creating this much needed and beneficial bar coding rule. However, to accomplish what is needed so as to effectuate the end result of reducing medication errors, practical considerations must be addressed and changes made to certain provisions of this rule (and related FDA positions). As such, we hope that our comments have provided the Agency with some assistance in this regard. If you have any additional questions or need anything further, please fee free to contact me at (614) 757-7721 or e-mail at robert.giacalone@cardinal.com. On behalf of Cardinal Health, we thank you for considering our comments and the efforts the Agency has made in crafting this rule.

Yours very truly,

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