Hollister-Stier
Laboratories LLC

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June 11, 2003

Dockets Management Branch (HFA-305)
[Docket No. 02n-0204]
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: 21 CFR Parts 201, 606, and 610, [Docket No. 02n-0204] Proposed Rule
Bar Code Label Requirements for Human Drug Products and Blood
Comments on Proposed Rule

Dear Sir or Madam:

Hollister-Stier Laboratories LLC (Hollister-Stier), a small business entity, is submitting written comments regarding the proposed rule "Bar Code Label Requirements for Human Drug Products and Blood" listed in the March 14, 2003, Federal Register. 68 Fed. Reg. 12,500.

Hollister-Stier is a licensed biologics manufacturer of allergenic extracts. Allergenic extracts are indicated for use by experienced physicians (allergists) in diagnosis and treatment of patients presenting symptoms of allergy after exposure to certain allergens. Following diagnosis by skin testing, a patient-specific formulation is compounded to include various allergens. The dose administered is a highly individualized matter that varies according to the degree of sensitivity of the patient and various other factors.

The FDA is proposing a new rule that would require certain human drug product labels and biological product labels to include bar codes. The proposed rule calls for the use of a linear bar code that would contain the drug or biological product's National Drug Code (NDC) number. The proposed rule is designed to reduce the number of medication errors in hospitals and other health care settings, by allowing 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.

02N-0204 C78

Hollister-Stier recognizes the value of applying bar coded labels to help reduce medication errors in hospital settings. Allergenic extracts are unique products, however, and applying the proposed rule to manufacturers of allergenic extracts will not have the intended effect on medication errors, and will only serve to place onerous and unnecessary burdens on the manufacturers and on FDA. Therefore, manufacturers of allergenic extracts should be **exempt** from this requirement.[1] Allergenic extracts are a clearly-defined and well-recognized subset of biological products, and FDA therefore need not be concerned that a final rule that expressly exempted allergenic extract manufacturers from the bar coding provision would be misused by manufacturers of other products.

The proposed rule is intended to prevent the administration of the wrong dose, administration to patients who may be allergic to the drug, administration of the wrong drug product, incorrect administration of the drug or missed doses. Hollister-Stier acknowledges that a barcode system would have value in reducing administration errors in hospitals and other institution healthcare settings where drugs are well-defined (i.e. specific drug name, specific dose, specific route of administration, specific administration interval). Bar coding of allergenic extracts, however, will not achieve FDA's objectives because of the unique nature of the products and the manner in which they are used.

Allergenic extracts and the patients receiving these products do not fit the conditions set forth in the proposed rule.

The proposed bar code rule does not account for allergenic extracts, and the ways in which they are used, radically differ from other products that FDA proposes to subject to the bar coding requirement. Specifically:

- Allergy diagnosis and treatment is performed in outpatient allergy clinics, not in controlled in-patient hospital/institution settings.
- Allergists use allergenic extracts to diagnose and desensitize patients by formulating custom mixtures from therapeutic or stock concentrates that are specific to a patient. These allergenic extract prescription mixtures may consist of one to 20 or more extracts, with variable concentrations, dosages, and schedules.
- Allergenic extracts, are not "specific well-defined drugs." Extracts are "compounded" or formulated from various source materials and individualized for each patient based upon a specific diagnosis and environmental symptom history.

[1]The exemption proposed by Hollister-Stier should properly cover manufacturers of all types of allergenic extracts, including those products defined as adjunct allergenic products (i.e. diluents labeled for use in allergy, and diagnostic controls, including Positive Skin Test Control Histamine).

- Each dose is individualized, based on a number of factors.
- The route of administration is constant, i.e. subcutaneous injection. Nurses administering these products in physician/allergist offices are specifically trained to administer them in this manner. Nurse responsibilities extend beyond the injection, as they must question the patient as to the reaction to prior injections, and observe the patient for a period of time after the injection for any injection reactions.
- The proposed rule indicates that dosage will be part of the bar code. However, a manufacturer would not be able to apply individualized and variable patient dosage information to a bar code. Interval of dosage is variable for allergenic treatments administered to patients. Initial introduction of treatment formulation for desensitization is established and closely monitored by the physician/allergist. Doses may be given once or twice weekly in increasing volume increments, and increasing product strengths. Once a maintenance dose is attained, doses may extend from weekly to monthly depending on patient sensitivity and environmental factors as determined by the physician/allergist.
- There are many variables involved in formulating allergenic extracts to meet each specific patient's needs. This limits the meaningful value of the intended regulation, and brings into question how unique formulations, variable strengths, doses and administration interval could ever be successfully controlled by the use of bar codes.

Bar coding allergenic extract products will not reduce medication error rates because the products are not commonly used in hospitals.

First, the proposed rule would require bar coding for human prescription drugs and OTC drugs dispensed under an order **and commonly used in hospitals**. Allergenic extracts, however, are not commonly dispensed or administered in a hospital setting. Allergenic extracts are sold directly to physicians who specialize in the diagnosis and treatment of allergies, in private office or clinic settings.

FDA itself has observed that bar coding drug products distributed directly to physicians' offices will serve no meaningful purpose. The agency stated in the proposed rule that it "decided to omit prescription drug samples from a proposed bar code requirement because most samples are given to patients at physicians' offices." FDA reasoned that "[b]ecause [it has] no evidence to suggest that physicians' offices are likely to be equipped with bar code scanners in the immediate future, the benefits associated with preventing medication errors through bar codes on prescription drug samples are unlikely to be realized in this health care setting." 68 Fed. Reg. at 12,505.

Requiring the assignment of an NDC number to each unique allergenic extract product is unduly burdensome and could increase the chance of labeling error.

The proposed rule would also require that the bar codes contain the products' NDC Numbers to identify at a minimum, each drug product, dosage, strength, nature and form. This NDC number must be applied to both the product label and, to be visible, would be

included on the box containing the product.

Hollister-Stier currently does not have NDC Numbers for each of its allergenic extracts. FDA has allowed generic groupings for allergens under one NDC code for the allergenic extract industry. Hollister-Stier, for example, has more than 75 Pollen Glycerin Extracts listed in its product catalog. The NDC number assigned to this group of allergenic extracts is 65044 (labeler code)-9950 (Product Code)-0 (Packaging Code). All of Hollister-Stier's products fall into one of 11 generic NDC Categories.

Hollister-Stier actively markets approximately 200 allergens with at least 4 package configurations for each. Under the proposed rule, we would be required to assign an individual NDC number to each unique allergenic extract, which would require the generation and use of more than 800 new NDC numbers. The large number of Hollister-Stier extracts and new NDC numbers required under this proposed rule are sharply at odds with the agency's assumptions and expectation, and would have enormous information generating and collection implications for both Hollister-Stier and FDA.

The proposed rule also states that both the vial and outer package must contain bar codes specific to the drug. We believe the proposed rule will generate more potential for labeling errors than currently exists in the allergenic product industry because:

1. we will have to generate more than 800 new NDC Numbers,
2. allergenic extract vials are small and require the use of very small labels,
3. manufacturers frequently produce small product lots which are typically hand labeled, and
4. we would discontinue using "window" outer packaging, which means that bar coding with the 800 new NDC numbers would have to be applied both to vials and the new outer packaging, increasing the chance that labeling errors could occur.

FDA has underestimated the economic impact of complying with the bar code rule on small businesses that manufacture allergenic extracts.

FDA estimates that the cost of compliance will be $600 for small businesses that manufacture biological products. 68 Fed. Reg. at 12,528. This estimate is not accurate in the case of small businesses that manufacture allergenic extracts. Hollister-Stier has fewer than 500 employees and qualifies as a small business. As noted above, we would need to add more than 800 new NDC Code numbers to our product labels and packaging.

We have discussed this issue with our current vendor and have determined that because of the small size of many of our labels, the addition of a bar code would require a flag label attachment. Our current vendor cannot provide this type of label, and therefore, Hollister-Stier would incur additional costs to locate and set up a new vendor. In addition, we understand that only a very small number of vendors are able to produce these flag attached labels.

We have attempted to estimate some of the start up costs that Hollister-Stier would incur if required to comply with the proposed bar code rule. We believe these costs would include:

$37,000 for the required equipment and artwork to add bar codes to labels and boxes, e.g. artwork plates, label dies, bar code readers, and new inkjet printers for box printing. This equipment would need to be purchased for both Hollister-Stier for labels produced internally, and for our various outside vendors who produce labels and boxes.

$39,000 for approximately 640 hours of computer programming time for testing and validation of the new label format.

$17,000 for Inventory Control, Purchasing, and Regulatory personnel time for internal control of each label/package change which is required per procedure. This cost includes an estimate of more than 530 hours at $31 per hour.

$18,000 for Standard Operating Procedure changes, which includes personnel time for changing, routing, review and approval of more than 12 procedures.

Unknown but substantial for costs of special flag labels with bar codes. Hollister-Stier's current annual costs for traditional labels are approximately $4,000. Our current vendor is unable to supply a cost estimate, but we anticipate the costs for the flag labels with bar codes could exceed the current expenditure by three or four times.

The above cost estimates are conservative because they do not include an estimate of additional labor costs for box set up, additional Quality Assurance and Regulatory Release labor costs, or additional production costs on an annualized on-going basis. Other costs not included in these estimates include those associated with enlisting consultants in bar coding, necessary to offer guidance and understanding with regard to the bar code process. Accordingly, we anticipate the initial phases of bringing Hollister-Stier into compliance with the proposed bar code requirement could cost Hollister-Stier more than $120,000, well in excess of the agency's estimated cost of $600.

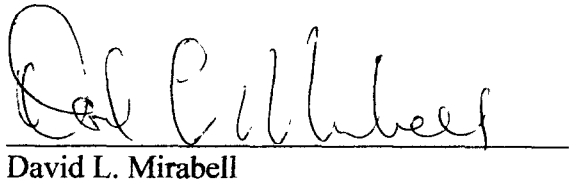
The proposed rule also would require manufacturers to report label changes to FDA on an annual basis, which for Hollister-Stier would initially entail the submission of sample labels and boxes for each of its 800 labels and 800 boxes. FDA's estimate indicated that each report for one label takes 1 minute. The Hollister-Stier estimate for this process is 15 minutes per individual label report, or approximately 400 hours. We also point out that Hollister-Stier, over the last three years of Annual Reporting, has submitted some 30 product labels per report, a number that greatly exceeds the agency's estimate of one product per establishment for biological product manufactures, as noted in Table 1 of the proposed rule. 68 Fed. Reg. At 12,516. Clearly the label change reporting requirement alone will place an onerous and unnecessary burden on Hollister-Stier and the agency.

In closing, we have summarized in general terms the additional burdens that imposing the proposed bar coding rule on allergenic extract manufacturers would have on Hollister-Stier and on FDA. We estimated that complying with the proposed rule will impose an initial, additional financial burden in excess of $120,000, and will consume over 1500 hours of personnel time. A small business like Hollister-Stier cannot bear such a burden. In addition, we note that the benefits associated with preventing medication errors through the use of bar codes are unlikely to be realized if the rule is imposed on allergenic extract manufacturers. Hollister-Stier's products are not commonly dispensed to hospitals, but rather are distributed to physician's offices. As FDA noted in the proposed rule, physicians are not likely to be equipped with bar code scanners in the immediate future. Accordingly, the intended objective of the proposed bar coding rule will not be attained in the allergenic extract industry.

Hollister-Stier, therefore respectively requests that the allergenic extract industry be fully and expressly exempted from the bar coding requirement in the agency's final rule. The agency need not be concerned that manufacturers of other products would seek to misuse the exemption because allergenic extracts are a clearly-defined and well-recognized subset of biological products.

Please contact me by phone at 1-509-482-1721 or email at david_mirabell@hollister-stier.com should you have any questions.

Sincerely,



David L. Mirabell
Director, Regulatory Affairs and Professional Services

DLM/GKB