NATIONAL ASSOCIATION OF PHARMACEUTICAL MANUFACTURERS
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December 2, 1998

Stephanie R. Gray
Director, Office of Compliance
Center for Drug Evaluation and Research HFD-300 Room 254
Metro Park North 1
7520 Standish Place
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Dear Ms. Gray:

This correspondence is provided to make you aware of recent interpretations of the regulations by the Drug Listing Branch that are creating problems for our member companies. We request your assistance in clarifying the issues for us.

The first matter deals with labeling and label changes allowed within 21 C.F.R. 207.35(b)(4)(i), which determines when a change in a product requires a change in NDC number. In the past, the industry had been informed that a change from a proprietary name to a generic name on a generic product would not be considered a "product name" change requiring a new NDC number. Recent submissions of this nature have been rejected by the Drug Listing personnel.

The second issue deals with potential narrow interpretations of 21C.F.R. 207.35(b)(4)(i) in the future which could raise numerous labeling problems for generic companies. It is our understanding that some or all of the staff in the Drug Listing Branch believe that any change to the formulation, even minor changes permitted under SUPAC, requires a firm to adopt a new NDC number. While we agree that certain qualitative changes that affect the product appearance or result in a product containing a substance known to cause allergy are covered, we do not believe that all qualitative changes should require an NDC number change. In addition, minor formulation changes permitted under SUPAC, whereby the resultant product is judged to be bioequivalent to the previous product, could, under current interpretation, qualify for a new NDC number. Yet the products are equivalent, with no change in color, size or dosage form. A mandatory NDC number change for SUPAC would be counterproductive. In the past, the Branch has accepted these changes without the NDC number change.

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According to the Drug Registration and Listing Instruction Booklet (May 1996), the product/package component of a drug's NDC number will change if the product name, dosage form, strength, concentration, or an active ingredient is changed. (See Drug Registration and Listing Instruction Booklet, p.16). The types of changes permitted under SUPAC do not involve changes to a drug's name, dosage form, strength, concentration, or active ingredients. Yet, nevertheless, the Drug Listing Branch, in contravention of the Branch's own guidance, is now demanding new product/package codes.

To require a new NDC number, for any reason, results in needless confusion in the marketplace and work counter to the goals of the Act. Wholesalers, retailers and consumers of the products in question all recognize the products under their current NDC numbers. Ordering, payment, and reimbursement processes are inextricably tied to the current NDC numbers. Federal programs, such as the Medicaid Drug Rebate Program and the Federal Supply Schedule use NDC numbers for reporting and pricing. Computer drug interaction systems and prescription insurance claim processing systems at retail pharmacies recognize products by the current NDC number. All of these parties would have to be notified of the NDC number change to update their records. The effect of this process has the potential to be enormous if the changes are frequent. At considerable cost, generic companies would be required to update all labeling, cartons, inserts, promotional materials and product price list.

The third issue deals with the use of Drug Listing information for the import of raw materials. On the Drug Product Listing Form 2657, column 94-99, there is a place for the FDA Application Number to be listed. In the Drug Registration and Listing Instruction Booklet, there are instructions to enter the NDA/ANDA number for prescription products or the final monograph number for OTC products. It has been common practice for drug substance manufacturers not to fill in this part of the form, as a drug substance manufacturer often does not know the identity of its customer at the time of import entry. Drug Listing personnel have approved forms submitted in this manner. Recently, imported bulk drug substance shipments have been held up at the port of entry due to lack of an FDA Application Number. This has resulted in unnecessary detentions and shipment delays.

The final issue deals with the requirements for registering distributors of drug products by our member companies. The FDA Form 2657 requires that such "distributed by" products have an NDC number, yet the number is not required on the label, and in some instances, distributors do not use the number. When this field is not filled in on the Form 2657, the form is immediately rejected.

We seek your assistance in obtaining clarification on these important issues. Our attempts to communicate with Drug Listing personnel have resulted in strict interpretations of the regulations, and no progress in resolving the matters. We are able to meet with you as soon as possible at your convenience.

Sincerely,

Robert S. Milanese
President

DEPARTMENT OF HEALTH & HUMAN SERVICES

and Drug Administration
Rockville MD 20857

JUN 9 1999

Robert S. Milanese
President
National Association of Pharmaceutical Manufacturers
320 Old County Road
Garden City, NY 11530-172

Dear Mr. Milanese:

Thank you for your letter of December 2, 1998, concerning recent problems experienced by some of your member companies with the drug listing process and the agency's interpretation of the drug registration and listing regulation 21 Code of Federal Regulations 207 (21 CFR 207). We appreciate getting views from trade organizations on our registration and listing system, as that helps accomplish our goal of an efficient and effective registration and listing system for the industry.

We apologize for the delay in responding to your concerns. FDA's Drug listing Branch has been reorganized and the registration of drug firms and the listing of drug products are performed by a private contractor. FDA's Information Management Team is responsible for overseeing this contract. When registration and listing questions arise they are referred to the Office of Compliance to resolve. The questions you raised were evaluated and this response is intended to address your concerns:

Your first question concerned the need for a new NDC number for a change from a proprietary name to an established (generic) name by the same manufacturer of a drug product. Upon consideration of this, we believe that this change would not necessarily require a new NDC. In reaching this opinion, we have taken into consideration the fact that a drug product's established name is a mandatory part of the proprietary product's labeling. Therefore, a new NDC will not ordinarily be required when a manufacturer changes a product from the proprietary name to the established name, provided there is no change in the product's characteristics that distinguish one drug product from another. It is noted, however, that circumstances may arise that warrant the assignment of a new NDC when changes like this occur, e.g., the company continues to market the product under both the proprietary and the established names, therefore each product would need to have its own NDC number.

In response to your second question, we do not believe that the minor changes permitted under SUPAC require a change in the NDC. This is because such a change under SUPAC would require firms to attest to the fact that the revised product is bioequivalent to and as safe as the original product. Again, this is contingent upon the provision that the product changes(s) do not change the product's characteristics by which one version of the product can be distinguished from another.

With respect to your question concerning filling in the approved application number on the drug listing form, we offer the following comment. The application number or OTC monograph number is needed to determine the legal marketing status of the drug product. If the product is not being marketed under the authorization of an application or an OTC monograph, the listing submission needs to reflect this fact by inserting the word 'none' in the appropriate place. The persons preparing these listing forms need to be made aware of the importance of the application number field. If it is not filled in, a deficiency letter will be sent and the product will not be listed until the information is provided.

Your last question asks about the requirements for registering distributors of drug products by your member companies and refers to the Form FDA-2657. I believe that your question is actually about listing, rather than registration. You specifically ask whether the NDC number of a distributor has to be filled in on Form FDA-2657 for the distributor's products to be listed? In reviewing the requirement of 21 CFR 207.25(b)(8), it is noted that it states that all drug products in commercial distribution must be listed and assigned an NDC number. This applies whether the product is marketed by a manufacturer, repacker, relabeler, or distributor. You correctly state that an NDC number is not required on a product label or labeling (21 CFR 207.25(b)(3)). This, however, does not mean that this number is not required on the listing form. Your members should be informed that whether a distributor uses the Form FDA-2657 to list its product or the manufacturer uses Form FDA-2658 to list the product for the distributor, the distributor's NDC number for the product must be provided.

I hope that this addresses your concerns. The drug listing contractor's staff will be advised of the contents of this letter and this should resolve the incidents that gave rise to your letter. If you need additional information or have other questions you would like to discuss, you may contact Herbert Gerstenzang (HFD-330) at (301) 827-7315.

Sincerely,

Stephanie R. Gray
Director, Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

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