



**sanofi aventis**

Because health matters

22-January-2007

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

**Re: Docket No. 2005N-0403/RIN 0910-AA49**

*Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs; Request for Comments*

Dear Sir/Madam:

Sanofi-aventis U.S. LLC appreciate the opportunity to comment on the above-referenced Federal Register notice; "*Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs.*"

We have the following comments on the proposed changes and recommendations:

**Proposal #1:** The proposed ruling would allow the Agency to assign the NDC number. The NDC number currently consists of the labeler code, product code, and package code; the product and package codes are currently assigned by the manufacturers. The FDA would now assign all three sections of the NDC number.

**Comment:** sanofi-aventis strongly disagrees with this proposed change to the current and long established practice of each firm assigning its own NDC product and packaging codes and believes that we can best manage the assignments of our product and packaging codes to meets our business needs. We believe that this proposed change to the current process would reduce our flexibility with respect to NDC assignments and increase the complexity and time of NDC management without providing benefit.

NDC assignment is an integral part of the sanofi-aventis drug product lifecycle starting from the research phase for promising new drugs. Our research group typically requires NDC code assignments well in advance of the New Drug Application submissions. These NDC assignments are maintained in our internal NDC database but may not be submitted to FDA before the respective NDAs are approved. Some assignments may never be submitted and some may change. In addition, we need to maintain the flexibility of choosing specific product and packaging codes for some products, which may exclude certain code numbers. For example, we may choose not to assign product codes with the digits 0, 6, 8, or 9 for certain tablet formulations. We may also choose to assign only product codes that contain leading zeros if the codes, without the zeros, were to be imprinted on small tablets.

NDC numbers may also be assigned to some products or packaging configurations for our internal tracking purpose that do not require drug listing submission to FDA. Sanofi-aventis needs the ability to continue to assign these NDC-like numbers for those items. If the Agency were to assign the complete NDC codes, would we still have the same amount of NDC flexibility for research drugs and marketed products as well as non-drug items?

**Comment:** An additional concern is the timeliness of NDC assignments by the Agency. Sanofi-aventis need the ability to fulfill NDC assignment requests quickly to meet our tight deadlines, which can be as short as one day. Would the Agency be able to provide NDC assignments to sanofi-aventis and thousands of other firms, domestic and foreign, under such timeframe? In our experience, drug listing submissions currently require five to ten business days to process by FDA.

**Proposal #2:** A new NDC number may be required if a change is made to an inactive ingredient.

**Comment:** Sanofi-aventis disagrees with this proposed change.

A minor change of inactive ingredient should not require assignment of a new NDC number. Such assignment may create confusion to distributors, pharmacies, doctors and patients. We believe that such minor changes in inactive ingredient are adequately communicated by the current industry practice of change notification on revised labeling or temporary sticker labeling.

**Proposal #3:** Based on the proposed ruling – Registration Establishments and Drug Listing information would be submitted electronically to the FDA.

**Comment:** Sanofi-aventis is strongly in favor of this proposal. The ability to submit drug listings and registrations electronically would greatly speed up the process.

**Proposal #4:** Based on the new proposed FDA ruling, registration information must be reviewed annually and if the information has not changed, the establishment must certify electronically that no changes have occurred.

**Comment:** Sanofi-aventis has no objection to this proposal.

**Proposal #5:** Names of the inactive ingredient(s) need to be supplied when obtaining a new NDC number.

**Comment:** Sanofi-aventis disagrees with this proposal. Requiring inactive ingredients to be provided would increase the drug listing burden on us and other pharmaceutical manufacturers. Furthermore, inactive ingredients are listed in product labeling which are included in each drug listing submission.

**Proposal #6:** New Drug Listing or revision of Drug Listings information will now be done electronically through the electronic drug registration and listing system by the FDA. Drug listing information must be reviewed in June and December of each year and if the information has not changed, the establishment must certify electronically that no changes have occurred.

**Comment:** Sanofi-aventis has no objection to this proposal.

**Proposal #7:** Based on the new proposed ruling, the FDA may require that the number of batches and batch size for each drug in the listing be provided.

**Comment:** Sanofi-aventis disagrees with this proposal. As the proposed ruling states, the batch size would be the number of unit dosage forms – or - if the unit dose form were not defined before primary packaging, it would be the total batch weight or volume before primary packaging. Providing the number of batches would be difficult as this is based on forecasts and demands, which may change.

**Proposal #8:** Private label distributors would be barred from directly drug listing their products with the Agency. Currently, private label distributors submit certain information to request a labeler code and may list drugs. If the private label distributor elects not to submit drug-listing information directly to the FDA and to obtain a labeler code, the registered establishment must submit the drug listing information. Manufacturers, repackers, relabelers, or drug product salvagers must submit drug-listing information for those drugs they manufacture, repack, relabel, or salvage for a private label distributor.

**Comment:** Sanofi-aventis disagrees with this proposal. Private label distributors should not be excluded from the drug-listing requirement. If the “registered establishment” were required to drug list for these distributors, it would greatly increase our reporting burden.

On behalf of sanofi-aventis U.S. LLC, we appreciate the opportunity to comment on the proposed Drug Listing Rule and hope that you will take our comments under consideration.

Sincerely,



Richard P. Gural, Ph.D.  
Vice President  
Regulatory Development