Roche

December 22, 2003

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

RE: Written Comments on Interim Rules

(1) Registration of Food Facilities Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Interim Rule (Docket No. 02N-0276, Federal Register Vol. 68 No. 197, October 10, 2003)

(2) Prior Notice of Imported Food Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Interim Rule (Docket No. 02N-0278, Federal Register Vol. 68 No. 197, October 10, 2003)

Dear Sir/Madam:

We welcome the opportunity to comment on the above interim rules for the registration of food facilities and prior notice of imported food. We believe the following general observations emphasize points where the interim rule may be enhanced. We trust that you will give careful consideration to our attached comments as you finalize the rule.

Relative to food products, one very important aspect of the Bioterrorism Act is the registration requirement of domestic and foreign facilities, which would include factory, warehouse, manufacturer, processor, or packer (registration is one time only). Failure to register is a prohibited act. Food offered by an unregistered foreign facility will be held at the port of entry until the facility is registered.

We are apprehensive about registering our pharmaceutical sites as food facilities. The final rule should be expanded to recognize materials that may be used for pharmaceutical use versus food use. At first glance, it would appear that the new regulations would not affect the pharmaceutical industry; however, several items discussed in the attached comments, do raise concern.

Please contact me if you need further assistance or have any questions regarding these comments.

Sincerely,

HOFFMANN-LA ROCHE INC.

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Attachment
HLR No. 2003-3736

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1. Pharmaceutical Ingredients

Pharmaceutical ingredients which are also items used in foods (i.e., sugar, starches, preservatives, cellulose, salts, colors, gelatin/capsules, flavors, etc.) are affected. If the registration process is not completed by the manufacturer, shipments of pharmaceutical excipients will be refused and detained.

The potential exists for a negative impact on the manufacture of finished pharmaceutical products and may also impact finished products being imported from other sites.

2. Active Pharmaceutical Ingredients

The potential impact on the manufacture of drug products could be significant if pharmaceutical ingredients are refused and detained based on the Harmonized Tariff Schedule Codes flagged with Prior Notice Indicators.

The CBP requires any product, including food, offered for entry to the U.S. to be identified according to Harmonized Tariff Schedule (HTS) codes. CBP uses these tariff codes, in part, to determine which imports should be reviewed by other government agencies for admissibility. In FDA's case, CBP has, for many years, also used HTS codes to program the Automated Commercial System (ACS) to send entry information about FDA-regulated products to FDA electronically for review. Building on previous lists, FDA has compiled a list of the HTS codes that apply to foods for which FDA believes prior notice is or may be required under the prior notice regulations. FDA provided this list to CBP so that CBP can modify or "flag" the HTS codes in its entry systems to screen for foods for which prior notice to FDA is required to ensure that, as appropriate, prior notice has been provided. FDA issued a guidance to inform the food industry which HTS codes have been "flagged" in CBP entry systems with prior notice indicators. FD3 indicates that FDA believes the article may be subject to prior notice, and FD4 indicates that FDA believes the article is food that is subject to prior notice.

With an FD3 indicator, the prior notice requirement can be "overridden" when proof is provided (such as the appropriate FDA product code and drug listing number) at the time of entry submission. This assures that the importation will not be sent to "General Order" and detained or denied.

Our company has already requested that the FD prior notice indicator be changed from FD4 to FD3 for two HTS Codes described below. Based on the information provided and, in consultation with internal offices, CFSAN recommended reclassifying or amending the FD flags from FD 4 to FD 3 for these products:

The two HTS codes encompass three of our active pharmaceutical ingredients which are vitamin derivatives that are not used in food but are active pharmaceutical ingredients. The two HTS codes and associated active pharmaceutical ingredients are:

HTS Code: 2936295020
Article Description: Vitamins D and Their Derivatives
API: Calcitriol (a vitamin D analog). This is the active ingredient for Rocaltrol Capsules.

HTS Code: 2936210000
Article Description: Vitamins A and Their Derivatives
API: Tretinoin (all-trans retinoic acid and is related to retinol (vitamin A)). This is the active ingredient for Vesanoid Capsules.

HTS Code: 2936210000
Article Description: Vitamins A and Their Derivatives
API: Isotretinoin (13-cis-retinoic acid and is related to both retinoic acid and retinol (vitamin A)). This is the active ingredient for Accutane Capsules.

3. Placebos

Placebos are part of clinical trials, the performance of which are an important step in the process to obtain market approval of a medicine. The potential impact on clinical studies could be significant if placebos are refused and detained.

Placebos (i.e. tablets/capsules) for clinical trial purposes or machine testing may be affected. Based on the composition (most contain primarily sugar and/or starches), the U.S. Bureau of Customs and Border Protection (CBP) has ruled that placebos are classifiable under 2106.90 as "Food preparations not elsewhere specified or included".

At this point in time, the fact that this "food item" is only used in clinical trials does not exclude these facilities from the registration requirement. It appears that a foreign supplier needs to be registered before we can proceed with future importations and that our U.S. site would require registration as well. These would also be subject to the Prior Notice Rule. The registration number of the facility is necessary in order to provide FDA with a completed prior notice submission on all of the imports of placebos.

We request that at a minimum the FDA prior notice indicator be changed to FD3 for Code 2106.90, where the importer can prove the sole pharmaceutical use of placebos. We urge that further consideration be given to exempt placebos (in bulk form as well as in form as finished packs) from registration of the facilities and prior notice regulations.