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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00D-1601]

Guidance for Industry and for FDA Employees on Import Alert #66-66; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the guidance entitled "Import Alert #66-66, Detention Without Physical Examination of API's That Appear To Be Misbranded Under 502(f)(1) Because They Do Not Meet the Requirements for the Labeling Exemptions in 21 CFR 201.122." This document provides guidance for industry and FDA employees on FDA's interpretation of the Federal Food, Drug, and Cosmetic Act (the act) and the labeling exemptions in title 21 of the Code of Federal Regulations regarding bulk chemicals that can be used as active pharmaceutical ingredients (API's) and may be destined for pharmaceutical processors formulating finished drug products. The document includes FDA's guidance to industry and FDA district offices for detention without physical examination of API's from certain manufacturers.

DATES: Submit written comments on the guidance to the Dockets Management Branch (address below) by [*insert date 60 days after date of publication in the Federal Register*]. After [*insert date 60 days after date of publication in the Federal Register*], submit written comments to the contact person listed below.

ADDRESSES: Submit written requests for single copies of the guidance document entitled “Import Alert #66–66, Detention Without Physical Examination of API’s That Appear To Be Misbranded Under 502(f)(1) Because They Do Not Meet the Requirements for the Labeling Exemptions in 21 CFR 201.122” to the Division of Import Operations and Policy (HFC–170), Office of Regulatory Affairs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send two self-addressed adhesive labels to assist that office in processing your requests. You may fax your request to 301–594–0413. Submit written comments on this guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments should be identified with the docket number found in brackets in the heading of this document. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance.

FOR FURTHER INFORMATION CONTACT: Thaddeus J. Poplawski, Division of Import Operations and Policy (HFC–170), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–6553.

SUPPLEMENTARY INFORMATION:

I. Background

A large volume of bulk chemicals that can be used as API’s in human medicines are being offered for entry into the United States. In order to be used as a pharmaceutical, an API is required to be included in an FDA approved new drug application (NDA), abbreviated new drug application (ANDA), or investigational new drug application (IND).

Imported API’s labeled for further manufacturing and processing or labeled as chemical substances are frequently destined for pharmaceutical processors that formulate finished drug products under approved NDA’s. These drug substances, consigned to individuals or processors who formulate and distribute human drugs, may be misbranded under section 502(f)(1) of the act (21 U.S.C. 352(f)(1)).

Sponsors of IND's frequently import from foreign countries either the dosage form or the API for use in laboratory research or clinical trials.

Some persons importing API's have found that they could obtain entry of these articles if they simply supply an NDA or IND number at the point of entry. FDA is advising its district offices that they should be alert to the possibility that: (1) The NDA or IND number provided does not cover the source of the particular API or (2) the persons importing the API have no authorization to refer to the particular NDA or IND number.

Section 502(f)(1) of the act provides that API or bulk chemical that can be used as an API must have labeling that lists adequate directions for its use, unless the API is subject to exemptions from labeling found in § 201.122 (21 CFR 201.122). If the API appears not to meet the requirements for the exemptions in § 201.122, and also lacks labeling listing adequate directions for its use, the article may be subject to refusal of admission under section 801(a)(3) of the act (21 U.S.C. 381(a)(3)) because it appears to be misbranded under section 502(f)(1) of the act.

A. Exemption Under § 201.122

API labeling invariably lacks adequate directions for use as required by section 502(f)(1) of the act. However, such drugs may be subject to an exemption under § 201.122. This regulation requires specific labeling on the package when adequate directions for use are missing, such as "Caution: For manufacturing, processing, or repacking."

However, the exemption under § 201.122 will not apply to a substance intended for a use in the manufacture, processing, or repacking of the API that causes the finished article to be a new drug, unless:

1. An approved NDA covers the production and delivery of the API to the application holder by persons named in the application; or
2. If no application is approved with respect to the API, the label statement "Caution: For manufacturing, processing, or repacking" is immediately supplemented by the words "in the preparation of a new drug or new animal drug limited by Federal law to investigational use,"

and the delivery is made for use only in the manufacture of such new drug or new animal drug limited to investigational use as provided in 21 CFR part 312 or 21 CFR 511.1.

The API/manufacture combinations listed in Attachment A to Import Alert #66-66 appear to represent importations of API's to be used for the manufacture, processing, or repacking of drugs that the act and regulations require to be the subject of an approved NDA or a valid IND. However, either the person receiving the API or the person importing the API appears not to meet the statutory and/or regulatory labeling requirements. Further, it appears that the agency has never inspected the declared manufacturer's current good manufacturing practice for that imported API.

B. Guidance

FDA's district offices are provided guidance to detain, without physical examination, the API's from the manufacturers named in the attachment to this Import Alert.

Districts may detain without physical examination API's from the persons listed in Attachment A to Import Alert #66-66 because it appears that the API is misbranded based on its lack of adequate directions for use as required by section 502(f)(1) of the act and its failure to meet the requirements of the exemption found in § 201.122. Persons importing these API's may obtain release of the detained articles if these persons can supply evidence establishing that the article is:

1. Intended for pharmacy compounding that meets the requirements of section 503A of the act (21 U.S.C. 353a), including that the API: (a) Is accompanied by a valid certificate of analysis; (b) is manufactured by an establishment registered under section 510 of the act (21 U.S.C. 360); and (c) does not appear on a list of drugs identified in 21 CFR 216.24, that have been withdrawn or removed from the market for reasons of safety or effectiveness.

2. Intended for use in the manufacture, processing, or repacking of an over-the-counter (OTC) product or prescription product that does not require an NDA; or

3. A new animal drug, or intended for use in the manufacture, processing, or repackaging of a new animal drug, subject to an NADA; and, therefore, the API is not subject to this import alert.

Persons importing API's may obtain release of the detained articles by supplying evidence establishing that the article is:

1. Intended for use in the manufacture, processing, or repackaging of a human drug that is itself the subject of an approved NDA, and that the API is from the appropriate source; or
2. It is covered by IND requirements at § 312.110(a).

This guidance is not intended to address new animal drugs or investigational new animal drugs addressed by Import Alert number 68-09. If the imported API's are intended for use in an NADA or INAD (investigational new animal drug notice), refer to Import Alert number 68-09.

If the API's are intended for the compounding of finished drugs by pharmacies, persons importing the API's must comply with the requirements in section 503A of the act.

This guidance does not apply to excipients or API's intended for use in OTC drugs or prescription drugs that do not require a new drug application.

II. Significance of Guidance

This Level 1 guidance is being issued consistent with FDA's good guidance regulation (21 CFR 10.115; 65 FR 56468, September 19, 2000). The guidance represents the agency's current thinking on the detention without physical examination of API's that appear to be misbranded under 502(f)(1) of the act because they do not meet the requirements for the labeling exemptions in § 201.122. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the applicable statutes and regulations.

This guidance document is effective immediately because prior public participation to its implementation is not feasible or appropriate due to the risk to the public health.

III. Electronic Access

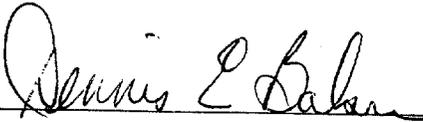
Persons with access to the Internet may obtain the guidance at http://www.fda.gov/ora/fiars/ora__import__ia6666.html

IV. Comments

Interested persons may submit to the Dockets Management Branch (address above) written comments regarding this immediately-in-effect guidance by [*insert date 60 days after date of publication in the Federal Register*]. After [*insert date 60 days after date of publication in the Federal Register*], submit written comments regarding this guidance to the contact person (address above). Such comments will be considered when determining whether to amend the current guidance. Two copies of any comments are to be submitted, except that individuals may submit

one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance document and received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: 11/27/00
November 27, 2000.



Dennis E. Baker,
Associate Commissioner for Regulatory Affairs.

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COPY OF THE ORIGINAL


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