DuPont Pharmaceuticals Company

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February 2,200 1

Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20857

Re: DuPont Pharmaceuticals Company Comments to Docket No. OOD-1601
"Guidance for Industry and for FDA Employees on Import Alert #66-66"
(Published December 4, 2000, 65 Fed. Reg. 75718)

Background

The FDA issued Import Alert #66-66 on 10/3/00 entitled, "Detention without physical examination of APIs 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". The FDA also issued on 12/4/00 in 65 Federal Register 75718 a document entitled "Guidance for industry and for FDA employees on Import Alert #66-66".

The stated objective of the FDA in issuing this alert was straight forward, the FDA did not want to allow the importation of APIs that were not approved to make pharmaceuticals. The alert instructed all FDA field personnel at ports of entry to start checking all imported APIs to verify the APIs were approved for the use listed in the importation paperwork. The alert instructed all FDA field personnel to do this check using the FDA's new computer system and database called the Establishment Evaluation System (EES).

The alert derived its enforcement power by referencing CFR Section 502(f)(l), Misbranding. With few exceptions, most API labeling lacks complete "adequate directions for use" as required by Section 502(f)(l). This CFR section contains two exemptions where a label does not have to list complete adequate directions for use that are applied to APIs.[1]

1. The label on APIs used in approved NDAs contain the statement "Caution: For manufacturing, processing, or repacking."

[1] Note: ingredients that are intended for experimental work **(pre IND, reference standard, etc.) do not fall under IA #66-66. These ingredients must comply with all the labeling requirements for chemicals.**

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2. The label on APIs used in pending NDAs or filed INDs contain the statement "Caution: For manufacturing processing, or repackaging and the delivery is made for use only in the manufacturer of such new drug or animal drug limited to investigational use as providedin CFR part 312 or part 511.1."

Because the EES has not yet been rolled out to FDA field personnel at all points of entry, the alert established a procedure to have field personnel at those entry points call Joseph E. Tracey at the Division of Import Operations (DIOP) to access the EES system for them so they could complete their check. In addition, to assist the field personnel at these non-operational EES ports of entry, DIOP cross-referenced historical import records with the EES database. DIOP looked for past instances where an import record indicated an API was going to be used to manufacturer a pharmaceutical and that API manufacturer was not approved in the pharmaceutical's NDA.' DIOP attached a 27-page list of over 500 APIs to the import alert it issued in October and instructed field personnel they could detain these APIs without inspection or calling DIOP. DIOPs position is, these APIs were misbranded since the labeling on the API only contained the statement appropriate for an API that would be used in an already approved NDA and it instructed the FDA field personnel it was the importers responsibility to provide proof that the API is appropriately labeled.

Issue

Import Alert #66-66 as issued does not establish any procedures to ensure field offices, without access to EES, have the most current inforrnation and can act accordingly. Without the most current information, APIs may be detained inappropriately at ports of entry.

Recommendations

The alert should be updated to instruct field offices to utilize real time access to the EES database and not rely on the list generated from historical data as soon as EES is rolled out to them.

As long as there are field offices that do not have access to the EES, DIOP should publish or post on their web page an updated list at least every three months removing from the list any company and API that has demonstrated they now meet the labeling requirements.

DIOP has set a goal of having public read only access of the EES via the Internet for 2002. Since the list in the alert can only be as accurate as the information contained in EES, DIOP should establish an interim procedure where manufacturers can review the information currently contained in the EES to ensure that it is complete and up to date.

Additional comments

At times a new manufacturer of API under an approved NDA will be pursued outside the USA. In order to develop data for submission of a Supplement to the approved NDA, importation of API is necessary to manufacture finished drug product. Batches of material may be full manufacturing scale lots which are purchased from the new supplier. Some of the material will be used for investigational use,. but there may be API not utilized until SNDA approval that will be left over from this batch to be used for sale. Therefore, an allowance for this situation should be included in this Import Alert to permit shipments for investigational use and probable market use in the future when approval is obtained from the agency.

Sincerely,

D. DeGraft-Johnson

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SPH42

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