DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2004D–0228]

Guidance for Industry on Fixed Dose Combination and Co-Packaged Drug Products for Treatment of HIV; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''Fixed Dose Combination and Co-Packaged Drug Products for Treatment of HIV.'' This guidance is intended to encourage sponsors to develop fixed dose combinations (FDC) and co-packaged products for the treatment of human immunodeficiency virus (HIV) infection. The availability of combination products may help to improve patient adherence to and facilitate distribution programs for treatment regimens for HIV.

DATES: Submit written or electronic comments on the draft guidance by [*insert date 60 days after date of publication in the* **Federal Register**]. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers

Lane, rm. 1061, Rockville, MD 20852. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Debra B. Birnkrant, Center for Drug Evaluation and Research (HFD–530), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301 827–2330.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Fixed Dose Combination and Co-Packaged Drug Products for Treatment of HIV.'' This guidance is intended to encourage the development of fixed dose combination (FDC) and co-packaged products for the treatment of human immunodeficiency virus (HIV). The guidance addresses the agency's current thinking regarding the types of information that should be provided in an application seeking approval for an FDC or co-packaged product for the treatment of HIV.

Combination therapy is essential for the treatment of HIV/AIDS. At least three active drugs, usually from two different classes, are required to suppress the virus, allow recovery of the immune system, and reduce the emergence of HIV resistance. In the United States and developing countries, simplified HIV regimens in the form of co-packaged drugs (such as blister packs) or FDCs may facilitate distribution of antiretroviral therapies and improve patient adherence to the regimens.

Although there are more than 20 unique antiretroviral drugs approved in the United States, only a few are approved for use as FDC products, and none are approved as co-packaged products. Some antiretrovirals should not be combined due to overlapping toxicities and potential viral antagonism. Other

antiretrovirals should not be used in pregnant women and other special populations. It is important, therefore, that possible combinations of these products be evaluated for safety and efficacy in the various populations that may have need of them.

Recently, newer FDCs that have not been approved by FDA have received attention, and some are being promoted for use in resource poor nations where HIV/AIDS has reached epidemic proportions. These FDCs may offer cost advantages and allow simplified dosing because all three drugs are in one pill. However, the safety, efficacy, and quality of these products have not been evaluated by FDA. Products whose safety, efficacy, and quality do not conform to expected standards may pose a threat to individual patients by increasing the chances of substandard performance, which may lead not only to treatment failure, but also to the development and spread of resistant virus.

FDA is prepared to move swiftly to evaluate such products when applications for them are submitted for approval. This guidance seeks to clarify what regulatory requirements would be applied to such applications, what issues might be of concern, and how these should be addressed. Different considerations apply depending on whether a sponsor owns or has a right of reference to all of the data required to support an application or a sponsor plans to rely on literature or the FDA's findings of safety and effectiveness for an approved drug. Where appropriate, this guidance addresses the issues associated with these different scenarios.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the agency's current thinking on FDC and co-packaged products for treating HIV infection. 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 requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit written comments on the guidance to the Division of Dockets Management (see **ADDRESSES**). Two copies of mailed 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 and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: May 14, 2004.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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