

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 02D-0427]

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Certifier G. Trumble

Guidance for Industry on Antiretroviral Drugs Using Plasma Human Immunodeficiency Virus Ribonucleic Acid Measurements—Clinical Considerations for Accelerated and Traditional Approval; 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 “Antiretroviral Drugs Using Plasma HIV RNA Measurements—Clinical Considerations for Accelerated and Traditional Approval.” This guidance is intended to assist sponsors in the clinical development of drugs for the treatment of human immunodeficiency virus (HIV) infection. Specifically, this guidance addresses the agency’s current thinking regarding designs of clinical trials that use HIV ribonucleic acid (RNA) measurements to support accelerated and traditional approvals of antiretroviral drug products.

DATES: Submit written or electronic comments on agency guidances 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. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Jeffrey S. Murray, 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 guidance for industry entitled "Antiretroviral Drugs Using Plasma HIV RNA Measurements—Clinical Considerations for Accelerated and Traditional Approval." This guidance is intended to assist sponsors in the clinical development of drugs for the treatment of HIV infection. Specifically, this guidance addresses the agency's current thinking regarding designs of clinical trials that use HIV RNA measurements to support accelerated and traditional approvals of antiretroviral drug products. It is also intended to serve as a focus for continued discussions among the Division of Antiviral Drug Products (DAVDP), pharmaceutical sponsors, the academic community, and the public.

The draft version of this document, first issued in August 1999, was based on a DAVDP advisory committee meeting, convened in July 1997, to discuss the use of HIV RNA endpoints for traditional approval of antiretroviral drugs. This document has been updated to address public comments to the draft version and to include pertinent information from a DAVDP advisory committee meeting held in January 2001 that addressed issues relating to trial

design in HIV-infected patients who have already been heavily treated for the disease. The guidance summarizes the rationale for using HIV RNA as a primary endpoint in clinical trials to support both accelerated and traditional approval. It describes the amount and type of safety and efficacy data recommended for new drug applications. The guidance also reviews pertinent clinical trial design issues including choice of control arms, study procedures, and statistical considerations. An appendix addresses the use of experimental HIV RNA assays in phase 3 studies.

This guidance does not address specific phase-1 and -2 development issues, development of alternate dosing regimens, or the use of HIV-1 resistance testing. These issues will be addressed in separate future guidance documents.

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 clinical considerations for accelerated and traditional approval of antiretroviral drugs using plasma HIV RNA measurements. 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, at any time, submit written or electronic comments on the guidance to the Dockets Management Branch (see **ADDRESSES**). 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 and received comments are available for public examination in the

Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

