

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. 99D-5047]

**Guidance for Industry on Pharmacokinetics in Patients With Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling; 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 "Pharmacokinetics in Patients With Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling." This guidance provides recommendations to sponsors planning to conduct studies to assess the influence of hepatic impairment on the pharmacokinetics and, where appropriate, the pharmacodynamics of drugs or therapeutic biologics.

**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, or to the Office of Communication, Training, and Manufacturers Assistance (HFMA-40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. 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:**

Mehul U. Mehta, Center for Drug Evaluation and Research (HFD-860), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2567; or

David Green, Center for Biologics Evaluation and Research (HFMA-579), Food and Drug Administration, 1401 Rockville

Pike, Rockville, MD 20852, 301-827-5349.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the availability of a guidance for industry entitled "Pharmacokinetics in Patients With Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling." This document provides guidance on: (1) When pharmacokinetic studies in patients with hepatic impairments should be conducted; (2) the recommended design and conduct of studies to characterize the effects of impaired hepatic function on the pharmacokinetics of a drug; (3) inclusion criteria for patient populations to be studied; (4) analysis, interpretation, and reporting of the results of the studies; and (5) the description of study results in drug labeling.

In the **Federal Register** of December 7, 1999 (64 FR 68357), FDA published a notice announcing the availability of a draft version of this guidance. A number of comments were received in the docket for the 1999 draft guidance. After careful consideration of the comments, the draft guidance was revised. Although we made a number of clarifying edits and tried to make the guidance more user friendly, the only substantive change to the draft guidance was to correct the implication that certain drugs should be studied in patients with concurrent hepatic and renal impairment.

This level 1 final 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 pharmacokinetic studies in patients with impaired hepatic function. 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 to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments on the guidance at any time. 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 Dockets Management Branch 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 <http://www.fda.gov/cder/guidance/index.htm>, <http://www.fda.gov/cber/guidelines.htm>, or <http://www.fda.gov/ohrms/dockets/default.htm>.

Dated: May 22, 2003.

**Jeffrey Shuren,**

*Assistant Commissioner for Policy.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Health Resources and Services Administration**

**Criteria for Determining Priorities Among Health Professional Shortage Areas**

**AGENCY:** Health Resources and Services Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** In accordance with the requirements of section 333A(b)(1) of the Public Health Service (PHS) Act, as amended by the Health Care Safety Net Amendments of 2002, 42 U.S.C. 254f-1(b)(1), the Secretary of HHS shall establish the criteria which he will use to make determinations under section 333A(a)(1)(A) of the health professional shortage areas (HPSAs) with the greatest shortages. This notice sets forth the current greatest shortage criteria for primary care, dental and mental health HPSAs, which will be used pending the adoption of new criteria through rulemaking.

**EFFECTIVE DATE:** May 30, 2003.

**FOR FURTHER INFORMATION CONTACT:**

Andy Jordan, Acting Chief, Shortage Designation Branch, National Center for Health Workforce Analysis, Bureau of Health Professions, Health Resources and Services Administration, 5600 Fishers Lane, Parklawn Building, Room 8C-26, Rockville, Maryland 20857, (301-594-0816).

**SUPPLEMENTARY INFORMATION:** Section 332 of the PHS Act, 42 U.S.C. 254e, provides that the Secretary shall designate HPSAs based on criteria established by regulation. HPSAs are defined in section 332 to include (1) urban and rural geographic areas with shortages of health professionals, (2) population groups with such shortages, and (3) facilities with such shortages. The required regulations setting forth the criteria for designating HPSAs are codified at 42 CFR Part 5.