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 (HFM–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 (HFM–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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BILLING CODE 4160–01–S

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.

Section 333A(a)(1)(A) of the PHS Act requires that the Secretary give priority in assignment of NHSC personnel to entities serving HPSAs with the greatest health professional shortage. Section 333A(c) of the PHS Act requires that the Secretary establish criteria specifying the manner in which he determines HPSAs of greatest shortage and published in the **Federal Register**.

The Secretary is developing a new method for designating HPSAs and determining HPSAs of greatest shortage. A Notice of Proposed Rulemaking (NPRM), relating to primary care HPSAs, was initially published in 1998. Major revisions were made in response to the comments received, and the Secretary anticipates publishing a new NPRM this year. Subsequent to the adoption of a new rule relating to primary care HPSAs, the Secretary intends to propose new methods for designating dental care and mental health care HPSAs and to publish new criteria for determining HPSAs of greatest shortage for primary care, dental care and mental health care HPSAs. In the interim, to determine HPSAs of greatest shortage, the Secretary will continue to use the current criteria set forth in this notice.

Approach for Determining Greatest Shortages

1. Three factors (population-to-provider ratio, poverty rate, and travel distance/time to nearest accessible source of care) are applicable to all categories of HPSAs (primary care, dental and mental health).

2. Additional factors specifically related to each HPSA category are included (*e.g.*, infant mortality/low birth weight rates (IMR/LBW) for primary care; presence of fluoridated water for dental; ratios of the population under 18 and over 65 and the prevalence of alcohol or substance abuse for mental health).

3. A scale is developed for scoring each factor. The scale generally includes five scoring levels, and reflects different patient utilization patterns for primary care, dental and mental health services.

4. Relative weights for the various factors are established, based on the significance of the factors in determining a shortage.

5. Each HPSA is scored on each factor.

6. The factor scores are weighted and summed for each HPSA.

7. The total scores for each HPSA are ranked from highest to lowest for each HPSA category.

8. A level is selected annually to identify the boundary between the HPSAs of greatest shortage and all other HPSAs.

9. Those HPSAs with total scores equal to or greater than the selected boundary level within each category are identified as the HPSAs of greatest shortage.

Criteria for Determining Primary Care HPSAs of Greatest Shortage

Note: GE is defined as greater than or equal to.

1. Score for population-to-full-time-equivalent primary care physician (PCP) ratio:

Ratio > 10,000:1, or No PCPs and Population GE 2500 = 5 points
10,000:1 > Ratio GE 5,000:1, or No PCPs and Population GE 2000 = 4 points;
5,000:1 > Ratio GE 4,000:1, or No PCPs and Population GE 1500 = 3 points;
4,000:1 > Ratio GE 3,500:1, or No PCPs and Population GE 1000 = 2 points;
3,500:1 > Ratio > 3,000:1, or No PCPs and Population GE 500 = 1 point.

2. Score for percent of population with incomes below poverty level (P):

P GE 50% = 5 points;
50% > P GE 40% = 4 points;
40% > P GE 30% = 3 points;
30% > P GE 20% = 2 points;
20% > P GE 15% = 1 point;
P < 15% = 0 points.

3. Infant Health Index:

IMR GE 20 or LBW GE 13 = 5 points;
20>IMR>18 OR 13>LBW>11 = 4 points;
18>IMR>15 or 11>LBW>10 = 3 points;
15>IMR>12 or 10>LBW>9 = 2 points;
12>IMR>10 or 9>LBW>7 = 1 point;
IMR<10 or LBW<7 = 0 points.

4. Score for travel distance/time to nearest source of accessible care outside the HPSA:

Nearest Source of Care is defined as the closest location where the residents of the area or population that is designated have access to comprehensive primary care services.

Time GE 60 minutes or Distance GE 50 miles = 5 points;
60 min > Time GE 50 min or 50 mi > Dist GE 40 mi = 4 points;
50 min > Time GE 40 min or 40 mi > Dist GE 30 mi = 3 points;
40 min > Time GE 30 min or 30 mi > Dist GE 20 mi = 2 points;
30 min > Time GE 20 min or 20 mi > Dist GE 10 mi = 1 point;
Time < 20 min or Dist < 10 mi = 0 points.

Criteria for Determining Dental HPSAs of Greatest Shortage

1. Score for population-to-full-time-equivalent provider ratio:

Ratio GE 10,000:1, or no dentists and population GE 3,000 = 5 points;
10,000:1 > Ratio GE 8,000:1, or no dentists and population GE 2,500 = 4 points;
8,000:1 > Ratio GE 6,000:1, or no dentists and population GE 2,000 = 3 points;
6,000:1 > Ratio GE 5,000:1, or no dentists and population GE 1,500 = 2 points;
5,000:1 > Ratio GE 4,000:1, or no dentists and population GE 1,000 = 1 point.

2. Score for percent of population with incomes below poverty level (P):

P GE 50% = 5 points;
50% > P GE 40% = 4 points;
40% > P GE 30% = 3 points;
30% > P GE 20% = 2 points;
20% > P GE 15% = 1 point;
P < 15% = 0 points.

3. Score for travel distance/time to nearest source of accessible care outside the HPSA:

Nearest Source of Care is defined as the closest location where the residents of the area or population that is designated have access to dental care services.

Time GE 90 minutes or Distance GE 60 miles = 5 points;
90 min > Time GE 75 min or 60 mi > Dist GE 50 mi = 4 points;
75 min > Time GE 60 min or 50 mi > Dist GE 40 mi = 3 points;
60 min > Time GE 45 min or 40 mi > Dist GE 30 mi = 2 points;
45 min > Time GE 30 min or 30 mi > Dist GE 20 mi = 1 point;
Time < 30 min or Dist < 20 mi = 0 points.

4. Score for Fluoridation:

Fluoridated Water Available for ≥50% of Population = 0 points;
Fluoridated Water Available for <50% of Population = 1 point.

For primary care and dental care HPSAs, the population-to-practitioner ratio is double weighted, as it is a primary factor in the designation of HPSAs under section 332 of the PHS Act. The poverty rate is also doubled. The poverty rate is widely acknowledged in professional literature as a key measure of need for primary health services, and income levels have been shown to correlate directly with access to health care and with health status measures. This results in a maximum possible score of 26 points.

Criteria for Determining Mental Health HPSAs of Greatest Shortage

1. Score for population-to-full-time-equivalent provider ratio:

The reporting of the number of psychiatrists present is required in all mental health HPSA applications; the

reporting of other mental health professionals is optional. Other mental health professionals include: clinical psychologists, clinical social workers, marriage and family therapists, and psychiatric nurse specialists. Depending upon the data reported, the scales utilize a population-to-psychiatrist ratio and/or a population-to-core mental health provider ratio. (Core mental health providers include psychiatrists and other mental health professionals.) The table below defines the various provider to population ratios and related scores:

Psychiatrist ratio	Core mental health ratio	Score
GT 45,000:0 and	GT 4,500:0	8
	GT 4500:1 and LT 6000:1.	7
LT 20,000:1 and GT 15,000:1 and.	GT 6000:1 and LT <9,000:1.	6
LT 30,000:1 and GT 15,000:1 or.	GT 4,500:1 and LT 6,000:1.	5
LT 45,000:1 and GT 20,000:1 and.	GT 4,500:0 and LT 6,000:0.	4
GT 20,000:1 and	GT 6,000:1	3
GT 30,000:1	.....	2
	GT 9,000:1	1

2. Score for percent of population with incomes below poverty level (P)

P GE 50% = 5 points;
50% > P GE 40% = 4 points;
40% > P GE 30% = 3 points;
30% > P GE 20% = 2 points;
20% > P GE 15% = 1 point;
P < 15% = 0 points.

3. Score for travel distance/time to nearest source of accessible care outside the HPSA:

Nearest Source of Care is defined as the closest location where the residents of the area or population that is designated have access to mental health care services.

Time GE 60 minutes = 5 points;
<60 min and >50 minutes = 4 points;
<50 minutes and >40 minutes = 3 points;
<40 minutes and >30 minutes = 2 points;
<30 minutes and >20 minutes = 1 point.

4. Scores for Additional Factors

(a) Youth Ratio: Ratio of Children under 18 to Adults 18–64:

≥60% = 3 points;
<60 and >40 = 2 points;
<40 and >20 = 1 point.

(b) Elderly Ratio: Ratio of Adults over 65 to Adults 18–64

≥25% = 3 points;
<25 and >15 = 2 points;
<15 and >10 = 1 point.

(c) Substance Abuse prevalence: Area's rate is in worst quartile for nation/region/or state:

Yes = 1 point;
No = 0 points.

(d) Alcohol Abuse prevalence: Area's rate is in worst quartile for nation/region/or state:

Yes = 1 point;
No = 0 points.

Since a larger number of factors are considered in the mental health HPSA scoring methodology, there is no doubling of the weights. The possible points for the population to provider ratio, 8, is greater than for any of the other factors, in recognition of its primary importance as mentioned above. The maximum score is 26.

Facility HPSA Scores

All geographic and population group HPSAs are scored using the above methodologies. In general, public or nonprofit private facilities designated as HPSAs based on the provision of services to a geographic or population group HPSA receive the score of the HPSA they serve. The exception is for Federally Qualified Health Centers and Rural Health Centers which are automatically designated under the Health Care Safety Net Amendments of 2002. These facilities will be scored as an entity, using the same factors used for the designation of areas and populations described above, but applied to the entity itself. Designated facilities which serve interned populations (Federal and State correctional facilities and State/county mental hospitals) are designated based on internee/inpatient data that differs from the data used in geographic and population group HPSAs. Poverty rate and travel distance/time to nearest accessible source of care are not data reported or required under the facility HPSA designation criteria and, likewise, do not appear to be directly applicable in determining HPSA scores for these institutionalized populations.

Consequently, correctional facility/mental hospital HPSA scores are extrapolated from the degree-of-shortage (DOS) groups determined in the HPSA designation process. *See* 42 CFR part 5, Appendices A, B and C. The determination of DOS groups for these facilities is based primarily on internee/inpatient-to-provider ratios, which is similar to the first factor used for determining HPSAs of greatest shortage (population-to-provider ratio).

For all correctional facilities, the following scores apply: DOS group 1 = 21, DOS group 2 = 15, and DOS group 3 = 9. These were derived by dividing the HPSA score range (1–25) into quartiles, then setting the HPSA score at the midpoints, respectively. Correctional facilities only have DOS 1–3, so the midpoints for the top three quartiles were used. For State and county mental hospitals, this approach was adjusted due to the different distribution of mental health facilities among the DOS groups , with DOS group 1 = 20, DOS group 2 = 16, DOS group 3 = 12, and DOS group 4 = 8.

Paperwork Reduction Act: The criteria used to make determinations under section 333A(a)(1)(A) of the health professional shortage areas (HPSAs) with the greatest shortages described in this announcement will not involve data collection activities that fall under the purview of the Paperwork Reduction Act of 1995. If the methods for determining health professional shortage area with the greatest shortages fall under the purview of the Paper work Reduction Act, the Program will assist HRSA in seeking OMB clearance for proposed data collection activities.

Dated: May 22, 2003.

Elizabeth M. Duke,

Administrator.

[FR Doc. 03–13478 Filed 5–29–03; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Child Health and Human Development; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of a meeting of the National Advisory Child Health and Human Development Council.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which