person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under 21 CFR part 12 of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 21 CFR 10.33(b). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the **Federal Register**. If FDA grants the petition, the notice will state the issue to be reviewed, the form of review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before May 2, 1997 file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h) (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: March 4, 1997.

Joseph A. Levitt,

Deputy Director for Regulations Policy, Center for Devices and Radiological Health.

[FR Doc. 97–8273 Filed 4–1–97; 8:45 am]

BILLING CODE 4160–01–F

[Docket No. 94D–0017]

International Conference on Harmonisation; Draft Guideline on Dose Selection for Carcinogenicity Studies of Pharmaceuticals: Addendum on the Limit Dose; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is publishing a draft guideline entitled ''Dose Selection for Carcinogenicity Studies of Pharmaceuticals: Addendum on the Limit Dose.'' The draft guideline was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The draft guideline is intended to define the conditions under which it would be considered acceptable to use a ''limit dose'' for the high dose selection of nongenotoxic pharmaceuticals in long-term carcinogenicity studies. The draft guideline is an addendum to an earlier ICH guideline on criteria for establishing uniformity among international regulatory agencies for dose selection for carcinogenicity studies of human pharmaceuticals.

DATES: Written comments by June 2, 1997.

ADDRESSES: Submit written comments on the draft guideline to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857. Copies of the draft guideline are available from the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–5473.

FOR FURTHER INFORMATION CONTACT:

Regarding the guideline: Joseph J. DeGeorge, Center for Drug Evaluation and Research (HFD–24), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–6758.

Regarding the ICH: Janet J. Showalter, Office of Health Affairs FY–20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–0864.

SUPPLEMENTARY INFORMATION: In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission, the European Federation of Pharmaceutical Industries Associations, the Japanese Ministry of Health and Welfare, the Japanese Pharmaceutical Manufacturers Association, the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA, and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, the Canadian Health Protection Branch, and the European Free Trade Area.

At a meeting held on November 6, 1996, the ICH Steering Committee agreed that a draft guideline entitled ''Dose Selection for Carcinogenicity Studies of Pharmaceuticals: Addendum on the Limit Dose'' should be made available for public comment. The draft guideline is the product of the Safety Expert Working Group of the ICH. Comments about this draft will be considered by FDA and the Safety Expert Working Group.

The draft guideline is an addendum to an ICH final guideline published in the **Federal Register** of March 1, 1995 (60 FR 11278), entitled ''Guideline on Dose Selection for Carcinogenicity Studies of Pharmaceuticals.'' The draft guideline is intended to define the conditions under which it would be considered acceptable to use a ''limit dose'' for the high dose selection of nongenotoxic pharmaceuticals in long-term carcinogenicity studies.

Although not required, FDA has in the past provided a 75- or 90-day comment period for draft ICH guidelines. However, the comment period for this draft guideline has been shortened to 60 days so that comments may be received by FDA in time to be reviewed and then discussed at a July 1997 ICH meeting involving this guideline.

This draft guideline represents the agency's current thinking on dose selection for carcinogenicity studies of

pharmaceuticals. 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 statute, regulations, or both.

Interested persons may, on or before June 2, 1997, submit written comments on the draft guideline to the Dockets Management Branch (address above). 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 draft guideline and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. An electronic version of this draft guideline is available via the Internet using the World Wide Web (WWW). To connect to the CDER home page, type http://www.fda.gov/cder and go to the ''Regulatory Guidance'' section.

The text of the draft guideline follows:

Addendum to "Dose Selection for Carcinogenicity Studies of Pharmaceuticals"

Limit Dose

Under a defined set of conditions, it would be considered acceptable to limit the high dose administered for nongenotoxic pharmaceuticals in long-term carcinogenicity testing to a maximum, e.g., 1000 mg/kg/day in rats. This approach is only considered appropriate where the other accepted methods of dose selection have been evaluated and each has been considered not applicable based on scientific justification. Use of this alternative is considered appropriate when:

1. Neither a toxicity-based endpoint (MTD) nor a pharmacodynamic-based dose selection endpoint can be achieved; and

2. Determination of pharmacokinetic parameters needed to apply pharmacokinetic endpoints (the 25-fold ratio of rodent to human AUC or saturation of absorption) is not feasible or is inappropriate due to scientific or technical limitations.

Under such circumstances, it would be considered acceptable to use the maximum feasible dose (e.g., 5 percent of diet) for selection of the high dose. However, if in addition to meeting the criteria 1. and 2. above, the dose of the pharmaceutical for use in humans is 50 mg/day, a ''limit dose'' of 1000 mg/kg/day is considered acceptable for high dose selection (see NOTE). This endpoint is consistent with the principles set forth in the paragraphs on pharmacokinetic endpoints, achieving approximately the same margin of safety as specified there based on a mg/m^2 basis. For those pharmaceuticals used at maximum daily human doses higher or lower than 50 mg/day it is considered acceptable to limit the top dose in a rat carcinogenicity study proportionally.

NOTE

The dose of 50 mg/day in humans (leading to 1 mg/kg on an assumed human weight of 50 kg) is an approximate calculation based upon the following: A conversion from mg/kg to mg/m^2, the AUC ratio of 25, and a multiplication factor of 6 to account for the variance (approximately 95 percent confidence interval) for estimation of the AUC ratio from mg/m^2 ratio (rodent to human) (see, for the data, Contrera, et al., *Journal of the American College of Toxicology*, 14:1–10, 1995). A similar rationale and calculation can be applied for other rodent species.

Dated: March 25, 1997.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 97–8353 Filed 4–1–97; 8:45 am]

BILLING CODE 4160–01–F

National Institutes of Health

National Center for Research Resources; Closed Meetings

Pursuant to Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following National Center for Research Resources Special Emphasis Panel (SEP) meetings:

Name of SEP: General Clinical Research Centers.

Date: May 13–14, 1997.

Time: 8 a.m.

Place: Holiday Inn Iowa City, Johnson 1 & 2 Conference Room, 210 South Dubuque Street, Iowa City, IA 52240, (319) 337–4058.

Contact Person: Dr. Bela Gulyas, Scientific Review Administrator, 6705 Rockledge Drive, MSC 7965, Room 6018, Bethesda, MD 20892–7965, (301) 435–0811.

Name of SEP: Biomedical Research Technology.

Date: May 27–29, 1997.

Time: 8 a.m.

Place: Doubletree Hotel, Conference Rooms—Twinbrook, Montrose, and Parklawn, 1750 Rockville Pike, Rockville, MD 20852, (301) 468–1100.

Contact Person: Dr. Sharon Moss, Scientific Review Administrator, 6705 Rockledge Drive, MSC 7965, Room 6018, Bethesda, MD 20892–7965, (301) 435–0811.

Purpose/Agenda: To evaluate and review grant applications.

The meetings will be closed in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. Applications and/or proposals and the discussions could reveal confidential trade secrets or commercial property such as patentable material and personal information concerning individuals associated with the applications and/or proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

(Catalog of Federal Domestic Assistance Program No. 93.371, Biomedical Research Technology; 93.333, Clinical Research, National Institutes of Health, HHS)

Dated: March 27, 1997.

LaVerne Y. Stringfield,

Committee Management Officer, National Institutes of Health.

[FR Doc. 97–8294 Filed 4–1–97; 8:45 am]

BILLING CODE 4140–01–M

National Center for Research Resources; Closed 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 the following meeting:

Name of Committee: Scientific and Technical Review Board on Biomedical and Behavioral Research Facilities.

Dates of Meeting: May 28–30, 1997.

Time: 8 a.m.–until adjournment.

Place of Meeting: Doubletree Hotel, Halpine Room, 1750 Rockville Pike, Rockville, MD 20892, Tel: (301) 468–1100.

Scientific Review Administrator: Dr. D. G. Patel, National Institutes of Health, 1 Rockledge Center, Room 6018, 6705 Rockledge Drive, MSC 7965, Bethesda, MD 20892–7965, Telephone: (301) 435–0822.

Purpose/Agenda: To review and evaluate grant applications. The meeting will be closed in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. Applications and/or proposals and the discussions could reveal confidential trade secrets or commercial property such as patentable material and personal information concerning individuals associated with the applications and/or proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

(Catalog of Federal Domestic Assistance Program No. 93.167 Research Facilities Improvement Program, National Institutes of Health, HHS)

Dated: March 27, 1997.

LaVerne Y. Stringfield,

Committee Management Officer, National Institutes of Health.

[FR Doc. 97–8297 Filed 4–1–97; 8:45 am]

BILLING CODE 4140–01–M

National Institute of Mental Health; Closed Meetings

Pursuant to Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings of the National Institute of Mental Health Special Emphasis Panel:

Agenda/Purpose: To review and evaluate grant applications.

Committee Name: National Institute of Mental Health Special Emphasis Panel.

Date: April 3, 1997.

Time: 3 p.m.

Place: Parklawn, Room 9C–26, 5600 Fishers Lane, Rockville, MD 20857.

Contact Person: Phyllis D. Artis, Parklawn, Room 9C–26, 5600 Fishers Lane, Rockville, MD 20857, Telephone: 301, 443–6470.