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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-D-0470]

**International Conference on Harmonisation; Draft Guidance on M3(R2)
Nonclinical Safety Studies for the Conduct of Human Clinical Trials and
Marketing Authorization for Pharmaceuticals; Availability**

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance entitled “M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals.” The draft guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The draft guidance, which is a revision of an existing guidance, discusses the types of nonclinical studies, their scope and duration, and their relation to the conduct of human clinical trials and marketing authorization for pharmaceuticals. The draft guidance is intended to facilitate the timely conduct of clinical trials and reduce the unnecessary use of animals and other drug development resources.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit written or electronic comments on the draft guidance by *[insert date 45 days after date of publication in the Federal Register]*.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993–0002. Send two self-addressed adhesive labels to assist the office in processing your requests. Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.regulations.gov>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance: Abigail Jacobs, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6484, Silver Spring, MD, 20993–0002, 301–796–0174, or Martin D. Green, Center for Biologics Evaluation and Research (HFM–475), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448, 301–827–3070.

Regarding the ICH: Michelle Limoli, Office of International Programs (HFG–1), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4480.

SUPPLEMENTARY INFORMATION:

I. Background

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

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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, Labour, 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, Health Canada, and the European Free Trade Area.

In June 2008, the ICH Steering Committee agreed that a draft guidance entitled “M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals” should be made available for public comment. The draft guidance is the product of the Multidisciplinary Safety and Efficacy (M3) Expert Working Group of the ICH.

Comments about this draft will be considered by FDA and the M3 Expert Working Group.

The purpose of the draft guidance is to recommend international standards for, and promote harmonization of, the nonclinical safety studies recommended to support human clinical trials of a given scope and duration. The revisions in this draft guidance further harmonize the recommendations in a number of areas and include a new section on exploratory clinical studies. The recommendations should promote safe and ethical development and availability of new pharmaceuticals.

The document provides guidance on nonclinical safety studies and their relation to the conduct of human clinical trials and marketing of a pharmaceutical, primarily addressing timing. The discussion includes safety pharmacology studies, repeated dose toxicity studies, toxicokinetic and nonclinical pharmacokinetic studies, reproduction toxicity studies, genotoxicity studies, and (for drugs that have special cause for concern or are intended for a long duration of use) an assessment of carcinogenic potential. The draft guidance discusses other nonclinical studies that should be conducted on a case-by-case basis as appropriate, including phototoxicity studies, immunotoxicity studies, juvenile animal toxicity studies, and abuse potential studies.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on this topic. 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.

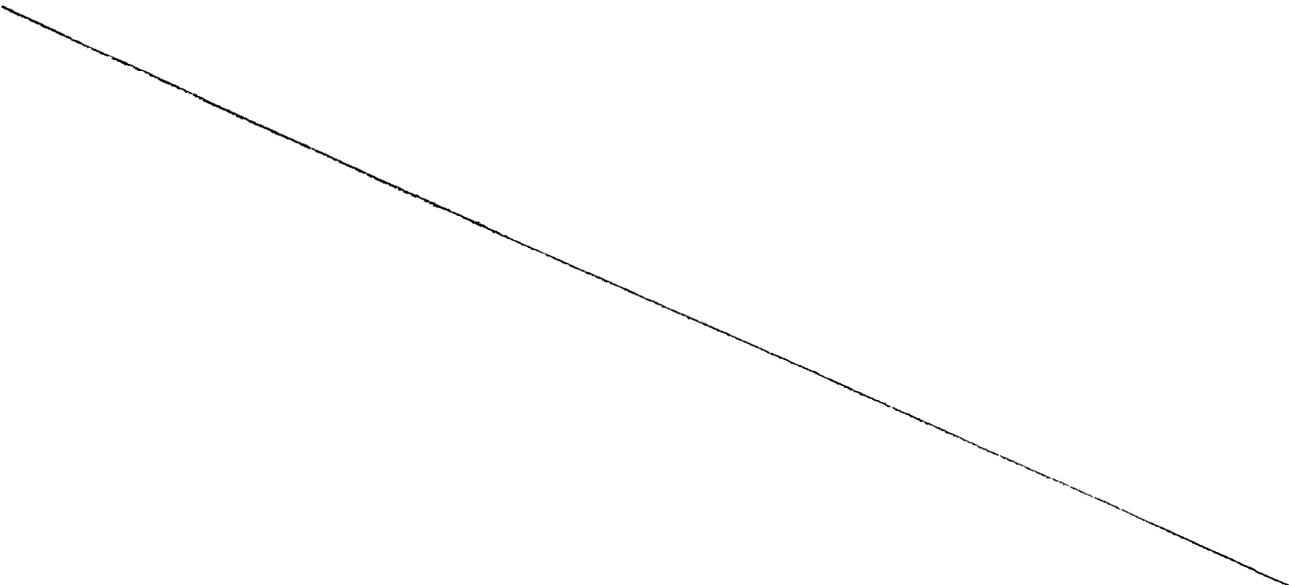
II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the draft guidance. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

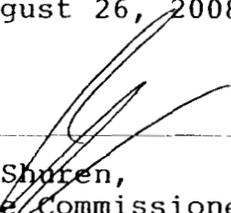
Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic comments or submissions will be accepted by FDA only through FDMS at <http://www.regulations.gov>.

III. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.regulations.gov>, <http://www.fda.gov/cder/guidance/index.htm>, or <http://www/fda.gov/cber/guidelines.htm>.



Dated: 8/26/08
August 26, 2008.



Jeffrey Shoren,
Associate Commissioner for Policy and Planning.

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Dawn P. Hankins