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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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[Docket No. 2002D-0492] (formerly Docket No. 02D-0492)

Guidance for Industry on Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers; 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 "Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers." This guidance provides a description and basis for a process by which to select a maximum recommended starting dose (MRSD) for a first-in-human clinical trial of a therapeutic in adult healthy volunteers.

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 Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://cd0527>

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/www.fda.gov/dockets/ecomments. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Lois M. Freed, Center for Drug Evaluation and Research (HFD-120), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2647.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers.” This guidance provides a description and basis for a process by which to select an MRSD for a first-in-human clinical trial of a new molecular entity in adult healthy volunteers. In the **Federal Register** of January 16, 2003 (68 FR 2340), FDA published a notice making available a draft guidance entitled “Estimating the Safe Starting Dose in Clinical Trials for Therapeutics in Adult Healthy Volunteers.” The notice gave interested persons an opportunity to submit comments. As a result of the comments, certain sections of this guidance were reworded to improve clarity. The guidance outlines a recommended standardized approach (including common conversion factors for calculating human equivalent doses) and vocabulary for selecting an MRSD based on animal data, and discusses factors to be considered in determining reasonable safety margins. This approach is applicable to a first-in-human trial of a new drug or biological therapeutic, regardless of intended clinical use. The guidance also discusses alternative approaches and provides some examples of circumstances under which alternative approaches for selection of an MRSD should be considered. Dose escalation is not addressed.

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 estimating the maximum safe starting dose in initial clinical trials for therapeutics in adult healthy volunteers. 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 guidance at any time. 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. The guidance and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

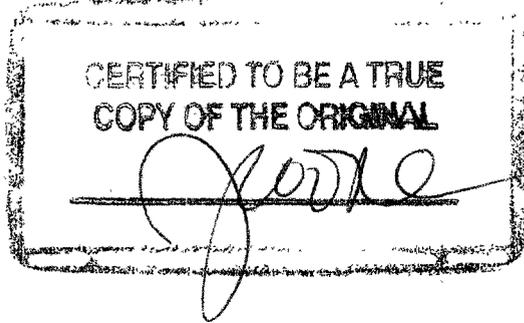
III. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.

Dated: 7/14/05
July 14, 2005.



Jeffrey Shuren,
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