

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00D-1407]

DMB

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Certifier	<u>[Signature]</u>

International Conference on Harmonisation; Guidance on S7A Safety Pharmacology Studies for Human Pharmaceuticals; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance entitled "S7A Safety Pharmacology Studies for Human Pharmaceuticals." The guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The guidance provides a definition, general principles, and recommendations for the nonclinical safety pharmacology studies. The guidance is intended to help protect clinical trial participants and patients receiving marketed products from potential adverse effects of pharmaceuticals, while avoiding unnecessary use of animals and other resources.

DATES: This guidance is effective [*insert date of publication in the Federal Register*]. Submit written comments at any time.

ADDRESSES: Submit written requests for single copies of the 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. Single copies of the recommendations may be obtained by mail from the Office of Communication, Training and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research (CBER), or by calling the CBER Voice Information System at 1-800-835-4709 or 301-827-1800. Copies may be obtained from CBER's FAX Information System at 1-888-CBER-FAX or 301-827-3844. Send two self-addressed adhesive

labels to assist the 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. Requests and comments should be identified with the docket number found in brackets in the heading of this document. See the **SUPPLEMENTARY INFORMATION** section of this document for electronic access to the guidance.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance:

Joseph J. DeGeorge, Center for Drug Evaluation and Research (HFD-024), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-5476, or

Martin D. Green, Division of Clinical Trials and Design, Center for Biologics Evaluation and Research (HFM-579), 1401 Rockville Pike, Rockville, MD 20852, 301-827-5349,

Regarding the ICH:

Janet J. Showalter, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-0864.

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 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.

In accordance with FDA's good guidance practices (GGPs) regulation (21 CFR 10.115; 65 FR 56468, September 19, 2000), this document is being called a guidance, rather than a guideline.

To facilitate the process of making ICH guidances available to the public, the agency has changed its procedure for publishing ICH guidances. As of April 2000, we no longer include the text of ICH guidances in the **Federal Register**. Instead, we publish a notice in the **Federal Register** announcing the availability of an ICH guidance. The ICH guidance is placed in the docket and can be obtained through regular agency sources (see the **ADDRESSES** section). Draft guidances are left in the original ICH format. The final guidance is reformatted to conform to the GGP style before issuance.

In the **Federal Register** of August 7, 2000 (65 FR 48246), FDA published a notice of availability for a draft tripartite guidance entitled "S7A Safety Pharmacology Studies for Human Pharmaceuticals." The notice gave interested persons an opportunity to submit comments by September 6, 2000.

After consideration of the comments received and revisions to the guidance, a final draft of the guidance was submitted to the ICH Steering Committee and endorsed by the three participating regulatory agencies in November 2000.

The guidance describes general principles and recommendations for safety pharmacology evaluations. The guidance is intended to help protect clinical trial participants and patients receiving marketed products from potential adverse reactions to pharmaceuticals and avoid unnecessary use of animals and other resources. The guidance generally applies to new chemical entities and biotechnology-derived products for human use. The guidance may be applied to marketed pharmaceuticals when appropriate. For example, adverse clinical events, a new patient population, or a new route of administration may raise concerns not previously addressed.

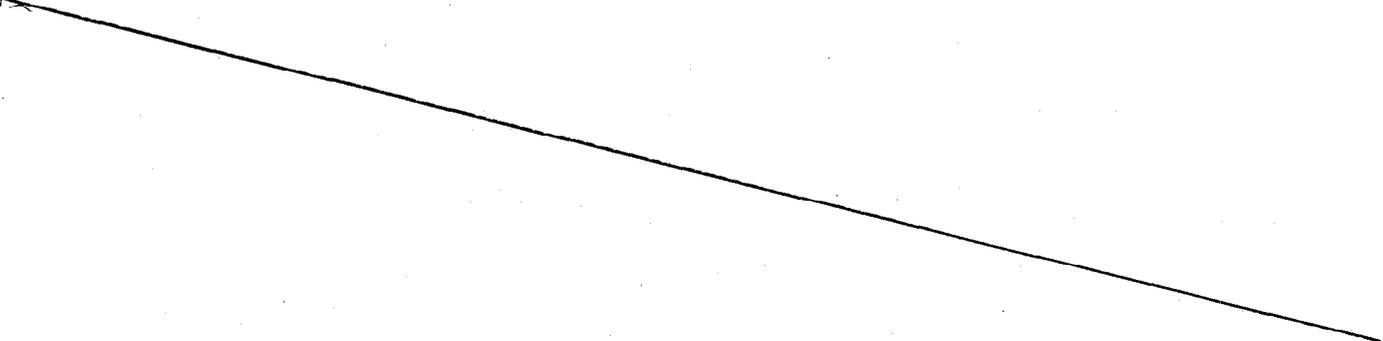
The guidance incorporates the following changes:

1. The guidance recommends that in the absence of a safety pharmacology response, the highest tested dose should be a dose associated with moderate toxicity. The draft guidance recommended that the highest dose tested should equal or exceed those doses producing some adverse effects.

2. The guidance recommends that, in addition to respiratory rate, other measures of respiratory function (e.g., tidal volume or hemoglobin oxygen saturation) should be evaluated in assessing effects of the test substance on the respiratory system.

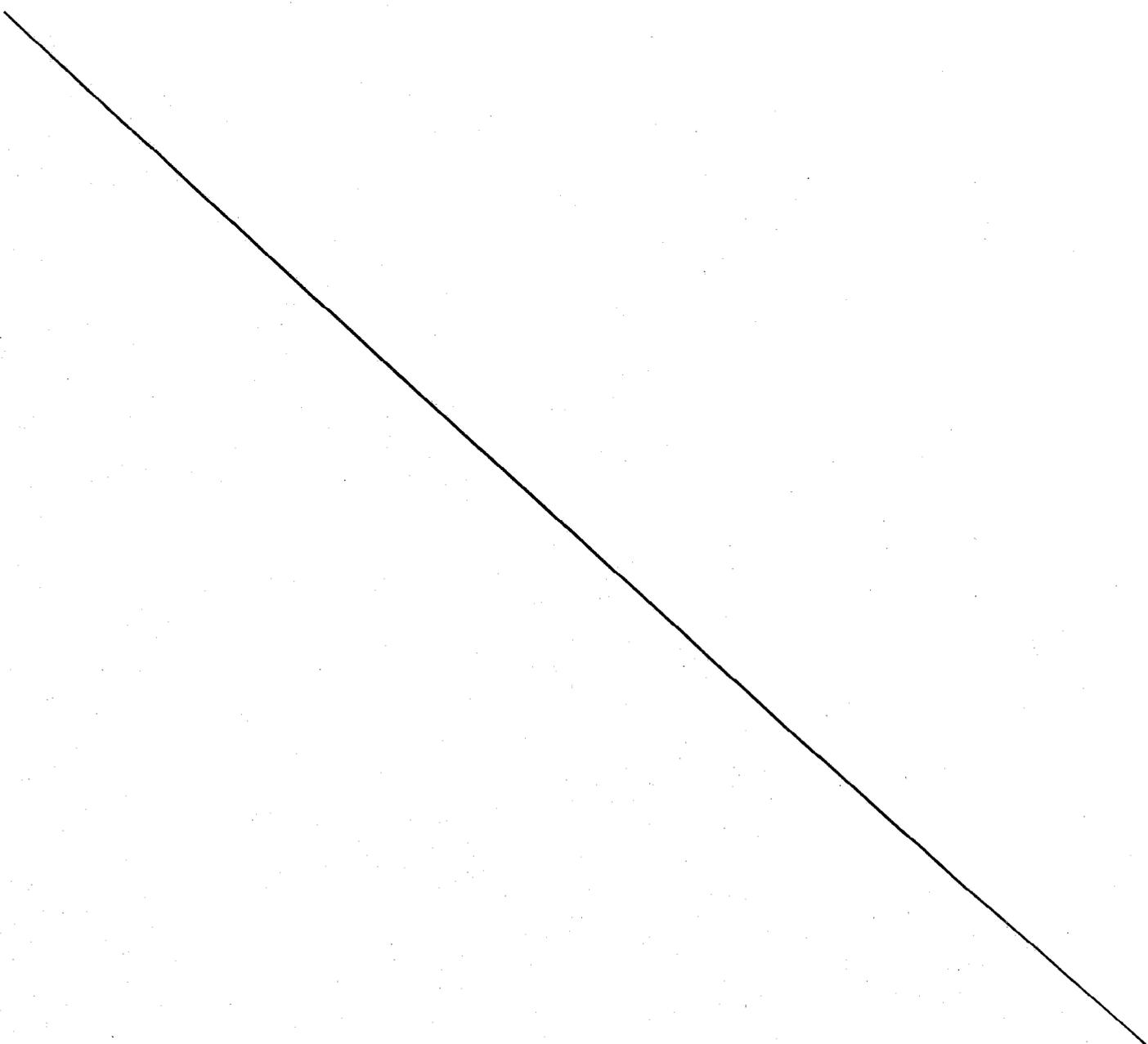
3. Concerning the application of good laboratory practice (GLP), the guidance clarifies that secondary pharmacodynamic studies that contribute to the safety evaluation should be conducted in compliance with GLP.

This guidance represents 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

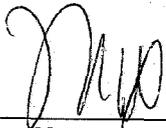
Interested persons may submit to the Dockets Management Branch (address above) written comments on the guidance at any time. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.



III. Electronic Access

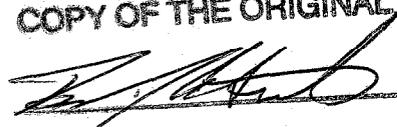
Persons with access to the Internet can obtain the guidance at <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/cber/publications.htm>.

Dated: 7-6-01
July 6, 2001.



Margaret M. Dotzel,
Associate Commissioner for Policy.

**CERTIFIED TO BE A TRUE
COPY OF THE ORIGINAL**



[FR Doc. 01-????? Filed ??-??-01; 8:45 am]

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