

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00D-0186]

International Conference on Harmonisation; Draft Guidance on M4 Common Technical Document; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

DMB

Display Date	8-23-00
Publication Date	8-24-00
Certifier	S. R. Reese

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance entitled “M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use” (M4 Common Technical Document). The draft guidance was developed under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use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 The draft guidance, which is being made available simultaneously in four parts, describes a harmonized format and content for new product applications (including applications for biotechnology-derived products) for submission to the regulatory authorities in the three ICH regions. The M4 Common Technical Document is intended to reduce the time and resources used to compile applications, ease the preparation of electronic submissions, facilitate regulatory reviews and communication with the applicant, and simplify the exchange of regulatory information among regulatory authorities.

DATES: Submit written comments on the draft guidance by September 30, 2000.

ADDRESSES: Submit written comments on the draft guidance to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Copies of the draft guidance are available on the Internet at <http://www.fda.gov/cder/guidance/index.htm> or at <http://www.fda.gov/cber/publications.htm>. Submit written requests for single copies of the draft guidance to the Drug Information Branch (HFD-210), Center for Drug Evaluation

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and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; or the Office of Communication, Training and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research (CBER), 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-3844, FAX 888-CBERFAX. Send two self-addressed adhesive labels to assist the office in processing your requests.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance: For the safety (nonclinical) components: Joseph J. DeGeorge, Center for Drug Evaluation and Research (HFD-24), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-5476.

For the quality components: Charles P. Hoiberg, Center for Drug Evaluation and Research (HFD-810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2570; and Neil D. Goldman, Center for Biologics Evaluation and Research (HFM-20), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301-827-0377.

For the efficacy (clinical) sections: Robert J. DeLap, Center for Drug Evaluation and Research (HFD-105), Food and Drug Administration, 9201 Corporate Blvd., Rockville, MD 20850, 301-827-2250.

Regarding the ICH: Janet J. Showalter, Office of International Programs (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.

ICH was organized to provide an opportunity for harmonization initiatives to be developed with input from both regulatory and industry representatives. ICH is concerned with harmonization 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 Therapeutics Products Programme, and the European Free Trade Area.

The ICH process has achieved significant harmonization of the technical requirements for the approval of pharmaceuticals for human use in the three ICH regions. However, until recently, the application documents in the three ICH regions had not been examined, and there are different requirements in the regions for the composition and organization of product applications. As a result, three Expert Working Groups for Quality, Safety, and Efficacy have been developing harmonized guidance for the content and format of common sections of an application, called the “common technical document.” Once finalized, the guidance “M4 Common Technical Document” will describe an acceptable format and content for applications for human pharmaceuticals that, once supplemented with regional particulars, can be used with new products for submission to the regulatory authorities in the three ICH regions. In the **Federal Register** of February 11, 2000 (65 FR 7024), the agency announced the availability of initial components of the draft guidance and requested public comment. Comments from that announcement were considered in developing this draft guidance.

In July 2000, the ICH Steering Committee agreed that a draft guidance entitled “M4 Common Technical Document” should be made available for public comment. Comments about the draft guidance will be considered by FDA and the appropriate expert working group.

To facilitate the process of making ICH guidances available to the public, the agency is changing its procedures for publishing ICH guidances. Since 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). The draft guidance is left in the original ICH format. The final guidance will be reformatted to conform to the GGP style before publication.

In accordance with FDA’s good guidance practices (GGP) (62 FR 8961, February 27, 1997), ICH guidance documents are now being called guidances, rather than guidelines.

II. The Common Technical Document

The draft guidance describes a harmonized format and content for new product applications (including applications for biotechnology-derived products) for submission to the regulatory authorities in the three ICH regions. The common technical document is intended to reduce the time and resources used to compile applications, ease the preparation of electronic submissions, facilitate regulatory reviews and communication with the applicant, and simplify the exchange of regulatory information among regulatory authorities.

The draft guidance addresses the organization of information presented in new product applications. With appropriate modifications, the draft guidance may be applied to abbreviated or other applications. The draft guidance is not intended to indicate what studies should be included, but merely to indicate an appropriate format for data that are submitted.

The common technical document should be viewed as the common part of a submission for new products, presented in a modular fashion with summaries and tables. It is intended that one

of the modules (module I) in the common technical document be reserved as a region-specific module, and thus will not be harmonized.

When finalized, the common technical document modular structure is envisioned as shown in the graphic at the end of this notice and the following table of contents for the document:

Module I: Administrative Information and Prescribing Information Documents are region specific; for example, application forms, prescribing information.

Module II: Common Technical Document Summaries

A. Overall Common Technical Document Table of Contents

B. Overall Summaries

1. Introduction

2. Quality Overall Summary

3. Nonclinical Overall Summary

4. Clinical Overall Summary

C. Nonclinical Summaries

1. Pharmacology

a. Written summary

b. Tabulated summary

2. Pharmacokinetics

a. Written summary

b. Tabulated summary

3. Toxicology

a. Written summary

b. Tabulated summary

D. Clinical Written Summary

1. Biopharmaceutics and Associated Analytical Methods

2. Clinical Pharmacology

3. Clinical Efficacy
4. Clinical Safety
5. Synopses of Individual Studies

Module III: Quality

- A. Table of Contents
- B. Body of Data

Module IV: Nonclinical Study Reports

- A. Table of Contents
- B. Study Reports
- C. Key Literature References

Module V: Clinical Study Reports

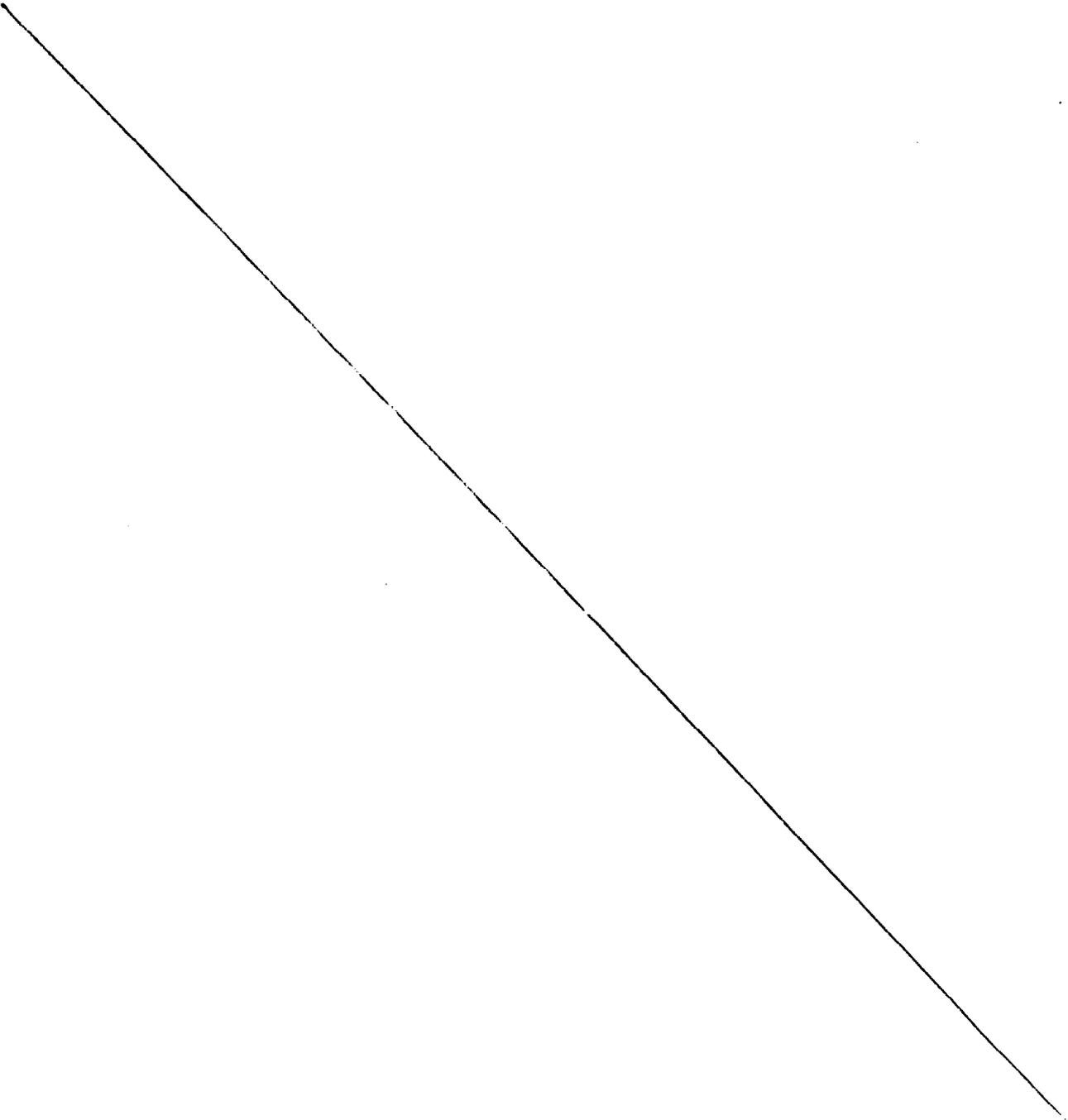
- A. Table of Contents
- B. Study Reports
- C. Key Literature References

The draft guidance being made available with this notice is the product of the ICH Common Technical Document Expert Working Groups for Quality, Safety, and Efficacy. To facilitate the handling of the guidance, it is being made available in four parts: (1) A description of the organization of the M4 Common Technical Document; (2) the Quality section; (3) the Safety, or nonclinical section; and (4) the Efficacy, or clinical section.

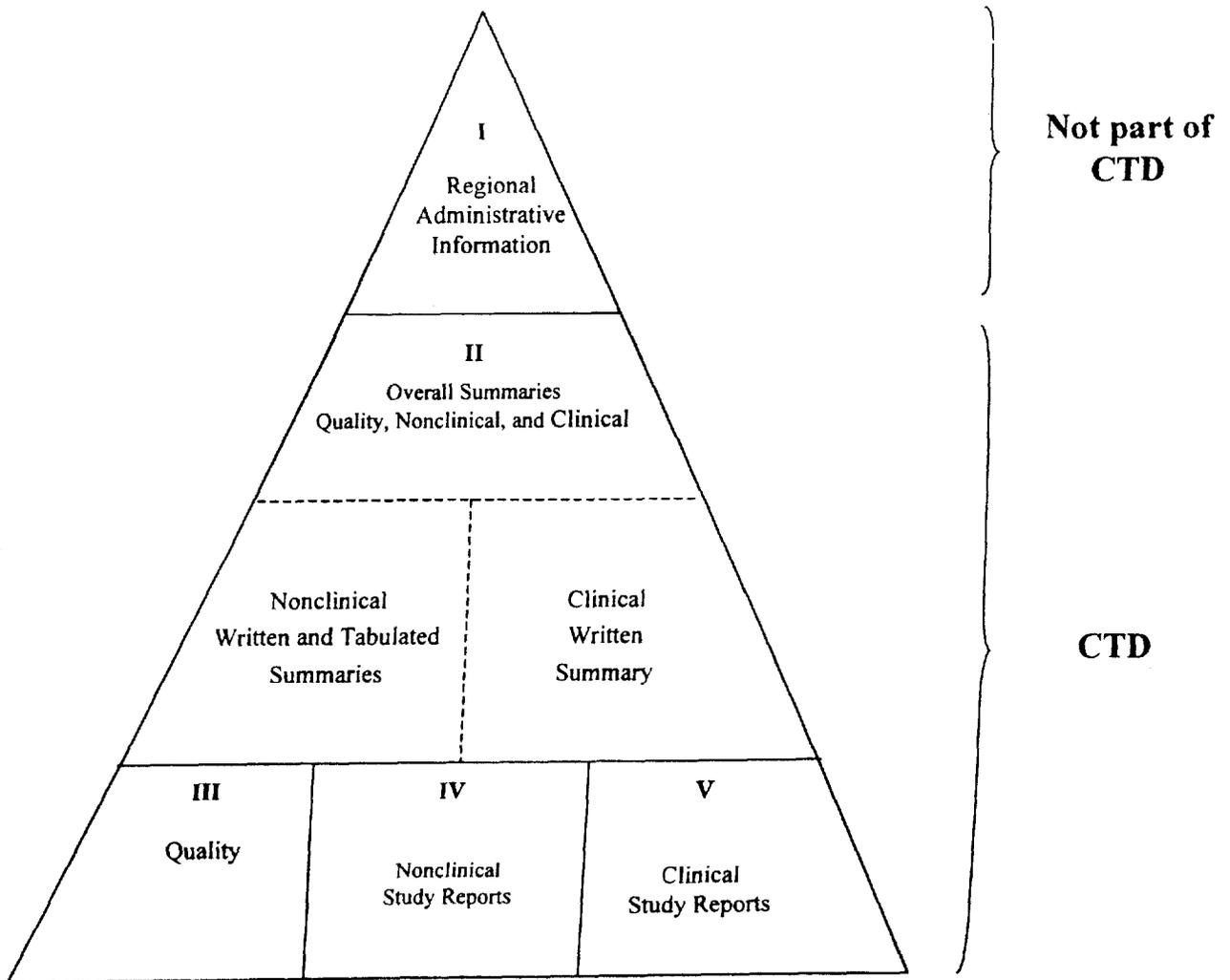
This draft guidance represent the agency's current thinking on the content and format of a common application for new products (i.e., the common technical document). The draft guidance does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

Interested persons may submit to the Dockets Management Branch (address above) written comments on the draft guidance by September 30, 2000. 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 components of the draft guidance and received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.



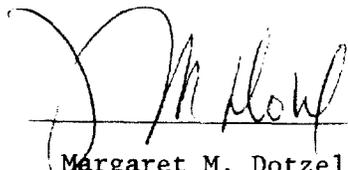
Diagrammatic Representation of the ICH Common Technical Document



Dated: 8/15/00

cd00118

August 15, 2000



Margaret M. Dotzel
Associate Commissioner for Policy

[FR Doc. 00-???? Filed ??-??-00; 8:45 am]

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COPY OF THE ORIGINAL**

