and (b). FDA estimates that, for each of these devices, an establishment would expend approximately 80 hours per year/per device developing and revising the labeling. This would make the annual burden 816,000 hours.

From its registration and listing databases, FDA has determined that there are approximately 300 establishments engaged in the manufacture and distribution of approximately 600 general purpose laboratory reagents subject to the labeling requirements in § 809.10(d). FDA estimates that these establishments would expend about 40 hours per year/per device developing and maintaining the labeling required by this section. This would result in an annual burden of 24,000 hours.

FDA estimates for each ASR it would take approximately 1 hour to design a new label to conform with § 809.10(e) and approximately 3 hours to review the new label through to chain of review, including legal and marketing people. As shown above, FDA estimates that the total hours to design/review labels is approximately 100 hours per respondent (25 x 4). The total hours to design/review labels are estimated at 30,000 (100 x 300). These estimates do not take into account economies of scale in designing and revising the labeling on ASRs. FDA estimates that entities work approximately 25 percent of that time ascertaining that the labeling meets the new requirements. Consequently, FDA estimates that the total number of reporting hour burden for designing/review of labeling is approximately 25 hours per respondent (100 x .25). FDA also estimates that the total reporting hour burden for § 809.10(e) is approximately 7,500 hours.

Based upon discussions with manufacturers, FDA estimates that it will take manufacturers of over-the-counter drugs of abuse test kits approximately 40 hours to gather the information required by § 809.10(f), another 40 hours to design and prepare the labeling, and an additional 20 hours per year to review and revise the labeling, as necessary. Thus, the total burden hours for preparing and reviewing labeling will be 100 hours per manufacturer. FDA estimates that there are 20 manufacturers of these devices. This will result in a total burden of 2,000 hours.

FDA estimates for each ASR it would take approximately 1 hour to rewrite the professional materials to ascertain compliance with § 809.30(d). FDA also estimates it would take approximately 4 hours to review rewritten materials through the chain of review, including legal and marketing people. As shown above, FDA estimates that the total number of hours to rewrite/review promotional materials is approximately 125 hours per respondent (25 x 5). The total reporting hours for all ASRs is estimated at 37,500 (125 x 300). This estimate does not take into account economies of scale. Often the promotional materials are a catalogue of products. FDA estimates that entities work approximately 20 percent of that time ascertaining that the promotional materials meet the new requirements. Consequently, FDA estimates that the total number of reporting hour burden for rewriting/reviewing promotional materials is approximately 25 (125 x .20) hours per respondent. FDA estimates that the total reporting hour burden for promotional materials is approximately 7,500 (37,500 x .20).

**Recordkeeping**

The Vision Council of America provided sales figures that were used to estimate the burden for § 801.410(f). Beginning in 1998, the vision industry has experienced a steady but declining growth rate of 2.6 percent for the distribution of lenses. It is assumed that this growth rate continued in 1999 and 2000. This resulted in an increase in the number of eyeglasses shipped annually to 89 million lenses shipped by the year 2000. The following sales figures were based on the above assumptions.

TABLE 3.—ANNUAL PERCENTAGE SALES IN EYEGLASS SHIPMENTS

| Year | Sales (Millions) | Percent Change | Eyeglass Shipments |
|---|---|---|---|
| 1998 | 15.8 | +2.6 % | 84.51 |
| 1999 | 16.2 | +2.6 % | 86.7 |
| 2000 | 16.6 | +2.6 % | 89.0 |

By also assuming that the glass/plastic lenses-produced ratio remained as in previous years (22 percent glass and 78 percent plastic), that glass lenses must be tested individually, and only 5 percent of the plastic lenses must be tested, then 23,070,000 lenses should be tested. This figure was derived by taking 22 percent of 89 million glass lenses (19,600,000) and adding it to 5 percent of the remaining plastic lenses (5% x 69,400,000 = 3,470,000).

Next, divide the total tests (23,070,000) by 30 manufacturers to return the annual frequency of recordkeeping figure of 769,000. Previously, FDA and industry experts estimated that, on average, each test could be completed and recorded in 3 seconds. Industry, therefore, could complete and record 1,200 tests per hour. It is estimated that the total burden for this collection is 19,225 hours, which is calculated by dividing the total records figure (23,070,000) by tests per hour (1,200). The hours per recordkeeper is calculated by dividing the total number of hours (19,225) by the number of manufacturers (30).

Under provisions of § 801.421(d), FDA estimates that 10,000 hearing aid dispensers dispense 1,600,000 hearing aids per year. Each record required by § 801.421(d) documents the dispensing of a hearing aid to a hearing aid user. FDA estimates that each recordkeeping entry requires approximately 0.25 staff hours. The total burden, then, is 400,000 hours (1,600,000 x 0.25).

Dated: October 10, 2001.

**Margaret M. Dotzel,**

*Associate Commissioner for Policy.*

[FR Doc. 01–25943 Filed 10–15–01; 8:45 am]

**BILLING CODE 4160–01–S**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

**[Docket No. 00D–0186]**

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

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of guidance entitled ''M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use'' (M4 CTD). The guidance was developed under the auspices of the International Conference on Harmonisation of

Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The guidance, which is being made available simultaneously in four parts (general organization, quality, safety, and efficacy), describes a harmonized format for new product applications (including applications for biotechnology-derived products) for submission to the regulatory authorities in the three ICH regions. The M4 CTD 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 or electronic comments on agency guidances 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; 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. 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. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. 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: 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, or David Green, Center for Biologics Evaluation and Research (HFM–579), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301–827–5349.

*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, or Neil Goldman, Center for Biologics Evaluation and Research (HFM–20), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301–827–0372.

*For the efficacy (clinical) sections*: Robert Temple, Center for Drug Evaluation and Research (HFD–40), Food and Drug Administration, 9201 Corporate Blvd., Rockville, MD 20850, 301–594–6758, or Lou Marzella, Center for Biologics Evaluation and Research (HFM–582), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301–827–5080.

*Regarding the ICH*: Janet J. Showalter, Office of International Programs (HFG–1), 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, when possible, 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, Labor, 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 format of the technical documentation in an application to market a new medicinal product in the three ICH regions had not been considered in the ICH process although there are substantial differences in the organization of product applications in different parts of the world. ICH, therefore, convened three Expert Working Groups (with expertise in quality, safety, and efficacy of human drug and therapeutic biological products) to develop harmonized guidance for the format of sections of a marketing application for a new medicinal product. This effort is called the ''common technical document.'' The resulting ICH guidance M4 CTD describes an acceptable format for applications for new human pharmaceuticals that (supplemented with regional particulars) can be used for submission to the regulatory authorities in each of the three ICH regions. The organization and format guidance provided in the M4 CTD is intended to be used together with information about the content of an application, which is provided in other ICH and FDA guidances.

In the **Federal Register** of February 11, 2000 (65 FR 7024), the agency announced the availability of initial components of the draft CTD guidance and requested public comment. Comments from that announcement were considered in developing a draft tripartite guidance, which was made available in the **Federal Register** of August 24, 2000 (65 FR 51621). The notice for the draft guidance gave interested persons an opportunity to submit comments by September 30, 2000.

To facilitate the process of making ICH guidances available to the public, the agency has changed 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 of this document). Draft guidances are left in their original ICH format. Final guidances are reformatted and edited to

conform to the good guidance practices (GGP) style before publication.

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.

In accordance with FDA's GGP regulation (21 CFR 10.115), ICH guidance documents are now being called guidances, rather than guidelines.

## II. The Common Technical Document

The M4 CTD guidance describes a harmonized format 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 guidance addresses the organization of information presented in new product applications. With appropriate modifications, the guidance can also be applied to abbreviated or other applications. The guidance is not intended to indicate what studies should be included, but indicates 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.

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 1: Administrative Information and Prescribing Information
- 1.1 Table of Contents of the Submission Including Module 1
- 1.2 Documents Specific to Each Region (for example, application forms, prescribing information)

Module 2: Common Technical Document Summaries
- 2.1 CTD Table of Contents
- 2.2 CTD Introduction
- 2.3 Quality Overall Summary
- 2.4 Nonclinical Overview
- 2.5 Clinical Overview
- 2.6 Nonclinical Written and Tabulated Summaries
  - Pharmacology
  - Pharmacokinetics
  - Toxicology
- 2.7 Clinical Summary
  - Biopharmaceutics and Associated Analytical Methods
  - Clinical Pharmacology Studies
  - Clinical Efficacy
  - Clinical Safety
  - Synopses of Individual Studies

Module 3: Quality
- 3.1 Module 3 Table of Contents
- 3.2 Body of Data
- 3.3 Literature References

Module 4: Nonclinical Study Reports
- 4.1 Module 4 Table of Contents
- 4.2 Study Reports
- 4.3 Literature References

Module 5: Clinical Study Reports
- 5.1 Module 5 Table of Contents
- 5.2 Tabular Listing of All Clinical Studies
- 5.3 Clinical Study Reports
- 5.4 Literature References

The 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 CTD; (2) the Quality section; (3) the Safety, or nonclinical, section; and (4) the Efficacy, or clinical, section.

It should be noted that, as part of the ICH process, additional guidance is being developed to facilitate the submission of CTD applications using standardized electronic (computer) formats. This ''electronic CTD,'' or ''E–CTD,'' is an ultimate aim of current harmonization efforts in this area. There may be some modifications in the CTD format to facilitate the preparation and utility of the E–CTD, although substantive modifications are not anticipated.

This guidance represents the agency's current thinking on the organization and format of a common application for new products (i.e., the common technical document). 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.

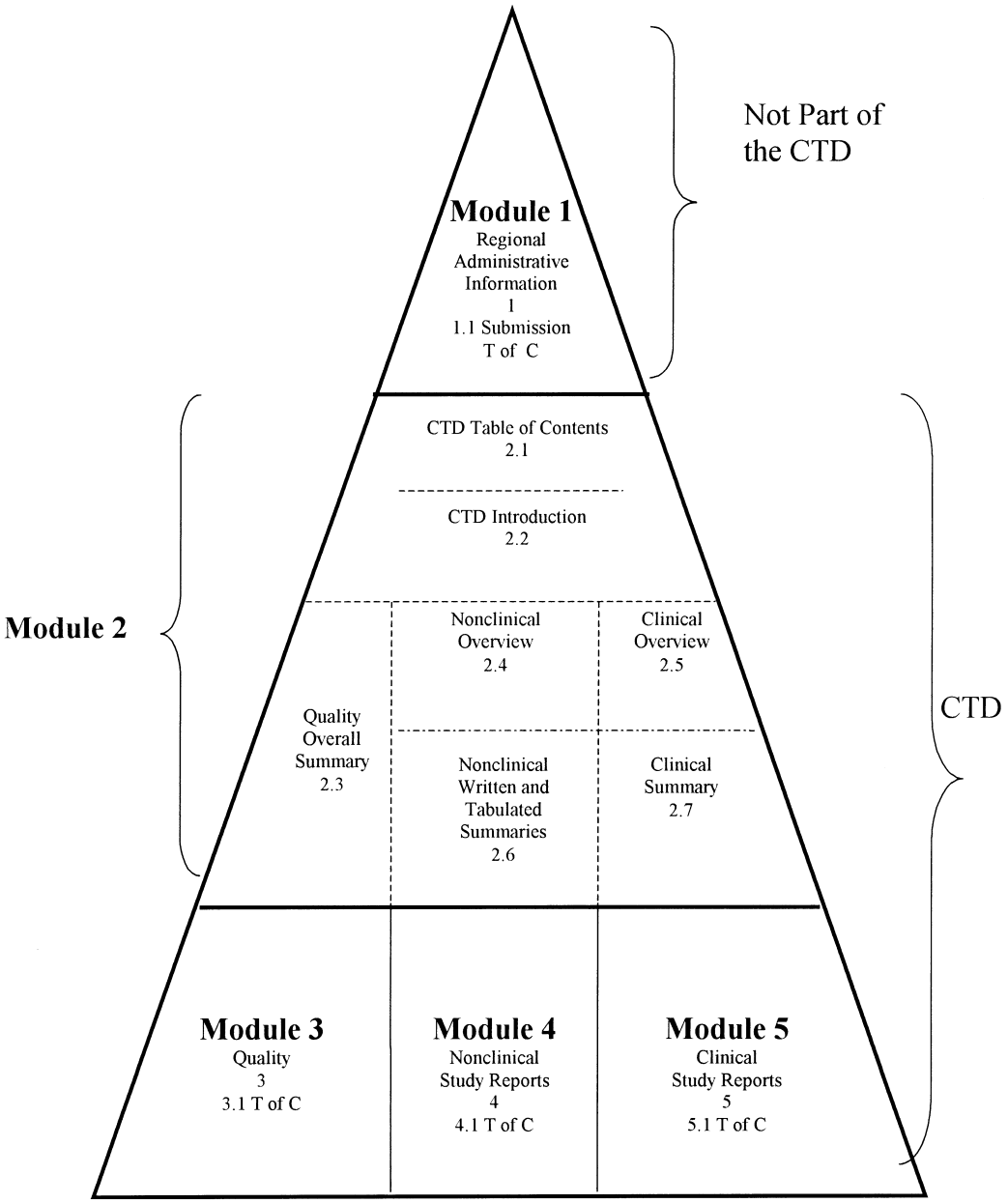
## III. Comments

Interested persons may, at any time, submit to the Dockets Management Branch (address above) written comments regarding the guidance. 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 Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

## IV. Electronic Access

Copies of the guidance are available on the Internet at *http://www.fda.gov/ohrms/dockets/default.htm, http://www.fda.gov/cder/guidance/index.htm, or http://www.fda.gov/cber/publications.htm.*

**Diagrammatic Representation of the ICH Common Technical Document**




Dated: October 9, 2001.

**Margaret M. Dotzel,**

*Associate Commissioner for Policy.*

[FR Doc. 01–25921 Filed 10–15–01; 8:45 am]

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