

Aventis Pharmaceuticals



August 1, 2002

Via fax and UPS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 01D-0435

Second Draft Guidance on Electronic Common Technical Document Specification
(version 2.0) and IV [67FR 40948, June 14, 2002]

Dear Sir/Madam:

Aventis Pharmaceuticals Inc. would like to thank you for the opportunity to comment on the above-referenced draft guidance entitled "Electronic Common Technical Document Specification".

This draft guidance defines the means for industry-to-agency transfer of regulatory information that will facilitate the creation, review, life cycle management, and archiving of the electronic submission.

Aventis submitted comments on 3/6/02 on the first draft guidance on eCTD Specification (version 1.0) released by the FDA for comments in November 2001. The 3/6/02 Aventis' comments regarding folder structure and indexing, file naming conventions and indexing, and cross-references remain valid for this second draft guidance (version 2.0). For your convenience, a copy of 3/6/02 Aventis' comments is provided in Appendix 1.

In addition, we offer the following comments/clarification for your consideration.

01D- 0435

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1. Issues related to the Clinical Summary

1.1 List of References in the Clinical Summary (section 2.7.5)

For the Clinical Overview (section 2.5) and for the Clinical Summary (section 2.7), the ICH M4 CTD Efficacy guideline describes a subsection (2.5.7 and 2.7.5) containing a list of references used in both documents.

However, the proposed structure of the Clinical Overview and the Clinical Summary in the second draft guidance on eCTD Specification (version 2.0) is different.

For the Clinical Overview, it is mentioned in that:

“Typically, this logical document should consist of a single file. The CTD defines further heading levels and navigation should be provided within the document to these sub-headings.” [Appendix 4; item 17; page 4-6]

It sounds therefore logical, from an authoring standpoint, to embed the list of references in subsection 2.5.7 as part of the Clinical Overview itself.

For the Clinical Summary, it is mentioned in that:

“Typically, this logical document should consist of a collection of four files, i.e. one single file for the following sections of the Clinical Summary:

- *Section 2.7.1 - Summary of Biopharmaceutic and Associated Analytical Methods*
- *Section 2.7.2 - Summary of Clinical Pharmacology Studies*
- *Section 2.7.3 - Summary of Clinical Efficacy (one file per indication)*
- *Section 2.7.4 - Summary of Clinical Safety*
- *Section 2.7.5 – List of references*

[Appendix 4; item 26 to 31; page 4-8/9]

Therefore, to follow the same structural architecture as for the Clinical Overview, we would like for the Clinical Summary to have the possibility to embed the list of references as a sub-heading of each of these individual documents instead of creating a separate and standalone document (section 2.7.5).

This should facilitate the authoring process (authors can generate their lists of references in each individual document independently) as well as the publishing process for the generation of pdf files.

Generating a single file for the references mentioned in each individual documents of the Clinical Summary will generate many issues at both the authoring and report publishing level as well as quality control issues and additional workload for the generation of cross-references between document.

We would like to have the flexibility to create one list of reference per individual file when creating the Clinical Summary. In this case, the DTD should be updated accordingly.

1.2 Synopses of Individual Studies (section 2.7.6)

For section 2.7.6 Synopses of Individual Studies, the ICH M4 CTD Efficacy guideline states that:

“The ICH E3 guideline (Structure and Content of Clinical Study Reports) suggests inclusion of a study synopsis with each clinical study report, and provides one example of a format for such synopses.

This section should include the table entitled Listing of Clinical Studies, described in guidance for Module 5, followed by all individual study synopses organised in the same sequence as the study reports in Module 5.”

It is mentioned in the second draft guidance on eCTD Specification, Appendix 4; item 32 (page 4-9) that:

“These synopses should already be located in the Clinical Study Reports in Module 5 and should not, therefore, be repeated in Module 2. It is considered sufficient to provide hyperlinks to the locations in Module 5.”

We fully agree with the principle. However, it seems difficult to provide hyperlinks from a non-existing document.

In addition, each summary document as described in the CTD contains a summary subsection for the results of individual studies.

Our understanding is that, in addition to the narrative descriptions included in these sections, a tabular listing of clinical studies should generally be provided in this document too.

It seems that similar components appear in different locations of the CTD/eCTD.

Please find below some suggestions related to the organization of these documents.

First option

- To append the Tabular Listings of clinical studies at the end of each individual summary document (sections 2.7.1, 2.7.2, 2.7.3, 2.7.4).

- To include cross-references from the Narrative Descriptions to the Tabular Listings and then insert cross-references from this Tabular Listings to the synopsis included in Module 5 and included at the beginning of each individual study report.

Second option

- To insert the Tabular Listings in Module 2.7.6 or Module 5.2 of the CTD.
- To include cross-references from the Narrative Descriptions to the Tabular Listings and insert cross-references from this Tabular Listings to the synopsis included in Module 5.

2. Issues related to Module 3 Quality

2.1 Folder and file structure

It is mentioned for the folder and file naming conventions in the second draft guidance on eCTD Specification, Appendix 3 that:

“...applicants may modify this specification where appropriate. For example, to include an additional folder for information where an appropriate folder name is not available in the eCTD specification.”

On the other hand, Appendix 4 does not seem to have the same flexibility in the file organization as does Appendix 3 to include additional files.

The flexibility granted to the applicant is essential since it will create more discrete units of information that will improve the clarity on what information has changed when filing amendments or post-approval changes.

The possibility to insert additional files in the folders listed in Appendix 4 should be more clearly stated.

An example from the file organization provided in Appendix 4 (page 4-12 and 4-13) is provided below (folder names in regular font, files in *italic*):

- 3.2.S.2 Manufacture (directory)
 - 3.2.S.2.1 Manufacturer (directory)
 - Manufacturer (pdf file)*
 - 3.2.S.2.2 Description of Manufacturing Process and Process Controls (directory)
 - Narrative description of the synthesis (pdf file)*
 - Flow chart (pdf file)*
 - 3.2.S.2.3 Control of Materials
 - List of materials (pdf file)*
 - Summary of procedures and specs for the raw materials (pdf file)*
 - Starting material 1 (pdf file)*
 - Starting material 2 (pdf file)*
 - 3.2.S.2.4 Control of Critical Steps and Intermediates
 - Critical step 1 (pdf file)*
 - Critical step 2 (pdf file)*
 - Critical step 3 (pdf file)*
 - Intermediate 1 (pdf file)*
 - Intermediate 2 (pdf file)*
 - Intermediate 3 (pdf file)*

Another example related to stability, sections 3.2.S.7 and 3.2.P.8 is also provided.

- 3.2.S.7 Stability (directory)
 - 3.2.S.7.1 Stability/Stability Development Batches (directory)
 - 3.2.7.1.1 *Stability Summary & Conclusion (pdf file)*
 - 3.2.7.1.2 *Stability data (pdf file)*
 - 3.2.S.7.2 Stability/Stability Production Batches (directory)
 - 3.2.S.7.2.1 *Stability Summary & Conclusion (pdf file)*
 - 3.2.S.7.2.2 Post-approval Stability Protocol and Stability Commitment (directory)
 - 3.2.S.7.2.2.1 *Post-approval Stability Protocol (pdf file)*
 - 3.2.S.7.2.2.2 *Stability Commitment (pdf file)*
 - 3.2.S.7.2.3 *Stability data (pdf file)*

The possibility to insert a file as a “reviewer guide” or other clarifying text in folders should be addressed, because it will help the review of the Module 3.

Some examples:

- 3.2.S.4 Control of Drug Substance
 - Reviewer Guide. pdf (new file)*
 - 3.2.S.4.1 *Specification 3.2.S.4.1 (pdf file)*
 - 3.2.S.4.2 Analytical Procedures (directory)
 - 3.2.S.4.3 Validation of Analytical Procedures (directory)
 - 3.2.S.4.4 *Batch Analysis (file)*
 - 3.2.S.4.5 Justification of Specification (directory)
- 3.2.S.2.5 Process Validation and/or Evaluation 3 (directory)
 - Additional clarifying text. pdf (new file)*
 - Process Validation (pdf file)*

2.2 Specific issue related to Drug Master File

The eCTD structure should cover the situation when information on drug substance, excipient or packaging material is submitted via a Drug Master File.

2.3 Excipients (section 3.2.P.4)

The numbering of the CTD section (item 81 of Appendix 4; page 4-20) should be clarified when several excipients are used.

For section 3.2.P.4.2 *Analytical Procedures and Section* and section 3.2.P.4.3 *Validation of Analytical Procedures*, we propose to follow the same rule: one separate file for each analytical procedure in order to be consistent with sections related to Drug Substance and Drug Product.

3. Issues related to the Document Life Cycle Management

3.1 Overall principles

The Document Life Cycle Management categorizes events related to variations in Europe and amendments or supplements in the United States.

In Appendix 6 of the second draft guidance on eCTD specification, it is stated that a specific folder indexed sequentially from 000 to nnn should be created for each subsequent submission after the first submission.

There is no clear recommendations in the second draft guidance on how to classify and manage submissions such as:

- Annual Reports
- Periodic Safety Update Reports
- Phase IV commitments
- Answers to questions

...

Does this mean that these above mentioned submissions and additional information to the original submission are outside the scope of the Document Life Cycle Management principle?

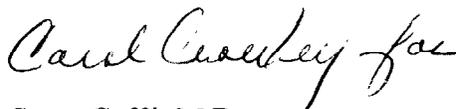
3.2 Initial document not formatted with a document approach

For marketed products, most submissions have not been prepared using the CTD backbone and more importantly do not follow a document approach, i.e. pagination, headings of the backbone and tables of contents of reports and cross-references are volume-based.

Does this mean that companies will have to reformat these submissions when applying for a variation/supplement once the eCTD becomes mandatory or is the scope of the eCTD and the Document Life Cycle Management concept only limited to new chemical entities? Any clarification regarding this important aspect would be much appreciated.

On behalf of Aventis Pharmaceuticals Inc. we appreciate the opportunity to comment on Electronic Common Document Specification and thank you for your consideration.

Sincerely,



Steve Caffé, M.D.

Vice President, Head US Regulatory Affairs

Appendix 1

**Aventis' comments
on the first draft guidance on eCTD Specification (Version 1.0)**

March 6, 2002

Aventis Pharmaceuticals

March 6, 2002



Via fax and UPS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 01D-0435

Draft Guidance on Electronic Common Technical Document Specification [66FR 59431, November 28, 2001]

Dear Sir/Madam:

Aventis Pharmaceuticals Inc. would like to thank you for the opportunity to comment on the above-referenced draft guidance entitled "Electronic Common Technical Document Specification". The document defines the means for industry-to-agency transfer of regulatory information that will facilitate the creation, review, life cycle management, and archiving of the electronic submission. We offer the following comments/clarification for your consideration.

Folder structure and indexing

With regard to folder structure and naming conventions detailed for each module, we suggest that all folders and subsequent folders be numbered with the corresponding CTD numbering section. This would enhance clarity and quality control, and be consistency with XML indexation scheme.

Some screenshots are provided below for illustration.

Figure 5-1 – Proposal for the folder structure of Module 2 (Appendix 5 Page 5-1)

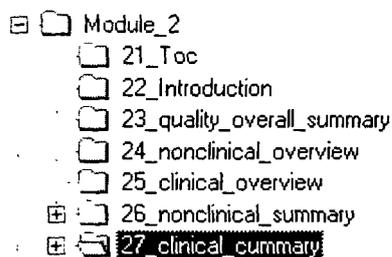
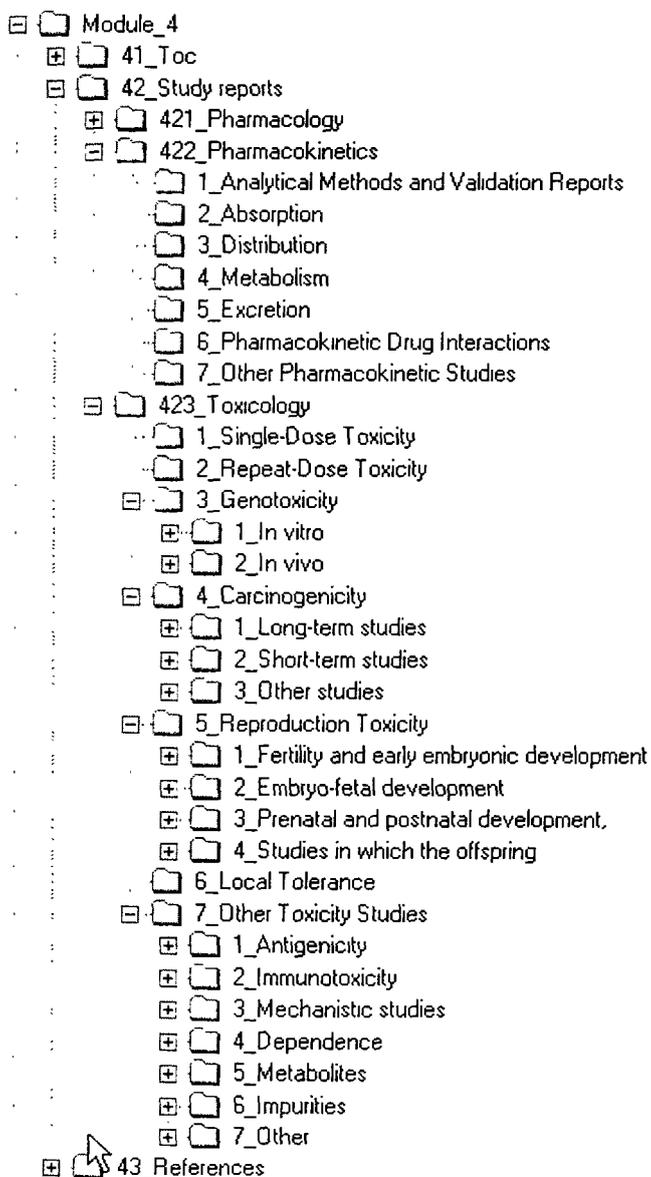


Figure 7-1 – Proposal for the folder structure of Module 4 (Appendix 7 Page 7-3)



Note 1: A folder has been systematically created for consistency in the structure presentation whether or not it contains only one file.

Note 2: Screenshots do not represent eCTD specification and conventions necessarily. They are provided only as a means to illustrate the use of folder numeric indexation.

File naming conventions and indexing

We would like to have a similar level of flexibility to index files included in a folder. Indexing would allow sorting, and therefore facilitate quality control. It would also standardize file names independently of the granularity adopted by the company.

A screenshot of the Clinical summary section is provided below for illustration.

Proposal for file naming conventions (including prefix number)

-  271_Clinical_WS-Biopharmaceutics.pdf
-  272_Clinical_WS-Pharmacology.pdf
-  273_Clinical_WS-Efficacy.pdf
-  274_Clinical_WS-Safety.pdf
-  275_Clinical_WS-Listing.pdf
-  276_Clinical_TS.pdf

Cross-references

The issue concerning cross-reference between documents is not addressed in the draft guidance.

Since we are moving from a volume to a document approach according to Appendix 12, page 12-4, and considering XML conventions for cross-referencing documents (XPath and Xlink), we strongly recommend basic recommendations to be included in the guidance.

In addition, the draft Guidance for Industry “Submitting Marketing Applications according to the ICH-CTD format – General Considerations” August 2001 recommends that the page numbering should be at the document level and not at the volume or module level. Use of tab identifiers is required to demarcate each document, attached as an appendix within a document, and therefore eliminate the volume approach (page 12, K. Pagination).

For cross-referencing between documents, will there be different requirements according to regional specification? Will there be different requirements for eCTD *versus* paper CTD?

On behalf of Aventis Pharmaceuticals Inc. we appreciate the opportunity to comment on the draft guidance for industry on Electronic Common Technical Document Specification, and thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read "Caffè", with a long horizontal flourish extending to the left.

Steve Caffè, MD
Vice President, Head GRAMS – North America
Global Regulatory Approvals and Marketing Support

process. The listing fee for a color additive petition ranges from \$1,600 to \$3,000, depending on the intended use of the color and the scope of the requested amendment. A complete schedule of fees is set forth in 21 CFR 70.19. An average of one category A and two category B color additive petitions are expected per year. The maximum color additive petition fee for a category A petition is \$2,600 and the maximum color additive petition fee for a category B petition is \$3,000. Since an average of three color additive petitions are expected per calendar year, the estimated total annual cost burden to petitioners for this start-up cost would be less than or equal to \$8,600.

Dated: May 23, 2002.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 02-15043 Filed 6-13-02; 8:45 am]

BILLING CODE 4160-01-S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 01D-0435]

International Conference on Harmonisation; Draft Guidance on Electronic Common Technical Document Specification; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a second draft guidance entitled "Electronic Common Technical Document Specification" (eCTD). 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 defines the means for industry-to-agency transfer of regulatory information that will facilitate the creation, review, life cycle management, and archiving of the electronic submission. The draft guidance is intended to assist industry in transferring electronically their marketing applications for human drug and biological products to a regulatory authority.

DATES: Submit written or electronic comments on the draft guidance by August 1, 2002. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the draft 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), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-3844, FAX 888-CBERFAX. Send two self-addressed adhesive labels to assist that office in processing your requests. 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. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT:

Regarding the draft guidance: Robert Yetter, Center for Biologics Evaluation and Research (HFM-25), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301-827-0373, or Gregory V. Brolund, Center for Drug Evaluation and Research (HFD-70), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-3517.

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 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's Health Products and Food Branch, and the European Free Trade Area.

In accordance with FDA's good guidance practices (GGPs) regulation (21 CFR 10.115), 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 will be placed in the docket and can be obtained through regular agency sources (see **ADDRESSES**). Draft guidances are left in the original ICH format. The final guidance is reformatted to conform to the GGP style before publication.

In June 2001, the ICH Steering Committee agreed that a draft guidance entitled "Electronic Common Technical Document Specification" would be made available for public comment and testing. The draft guidance, a product of the Multidisciplinary Group 2 (M2) Expert Working Group (EWG) of the ICH, was made available for comment in the **Federal Register** of November 28, 2001 (66 FR 59431). Comments about the draft guidance were considered by FDA and the M2 EWG, and in February 2002, the ICH Steering Committee agreed that a second draft guidance should be made available for public comment (step 2).

The draft guidance on the eCTD provides guidance on industry-to-agency electronic transfer of marketing applications for human drug and

biological products. The draft guidance defines the means for industry-to-agency transfer of regulatory information that will facilitate the creation, review, life cycle management, and archiving of the electronic submission. The draft guidance is intended to assist industry in transferring their marketing applications for human drug and biological products to a regulatory authority. The second draft guidance includes the following changes:

- The language in the guidance has been edited to improve clarity.
- The maximum length of a file name has been increased from 32 characters to 64 characters.
- Throughout the guidance, references to Common Technical Document (CTD) sections have been updated to reflect the current CTD.
- Appendix 4 has been reorganized.
- The examples in Appendix 6 have been updated.
- The Glossary of Terms has been completed.

This draft guidance, when finalized, will represent the agency's current thinking on "Electronic Common Technical Document Specification." 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 (see **ADDRESSES**) written or electronic comments on the draft guidance by August 1, 2002. 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 draft guidance and received comments may be seen in the Dockets Management Branch 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: June 6, 2002.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 02-15003 Filed 6-13-02; 8:45 am]

BILLING CODE 4160-01-S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 02D-0237]

International Conference on Harmonisation; Draft Guidance on Q1E Evaluation of Stability Data; 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 "Q1E Evaluation of Stability Data." 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). This draft guidance is an annex to an ICH guidance entitled "Q1A(R) Stability Testing of New Drug Substances and Products." The draft guidance is intended to provide guidance on how to use stability data, generated in accordance with the principles outlined in Q1A(R), to propose a retest period for the drug substance and a shelf life for the drug product.

DATES: Submit written or electronic comments on the draft guidance by August 1, 2002.

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. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. Submit written requests for single copies of the draft 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), Food and Drug Administration, 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. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance: Chi-wan Chen, Center for Drug Evaluation and Research (HFD-830), Food and Drug Administration, 5600 Fishers Lane,

Rockville, MD 20857, 301-827-2001; or Andrew Shrake, Center for Biologics Evaluation and Research (HFM-345), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1148, 301-402-4635.

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 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's Health Products and Food Branch, and the European Free Trade Area.

In accordance with FDA's good guidance practices (GGPs) regulation (21 CFR 10.115), this document is being

**INTERNATIONAL CONFERENCE ON HARMONISATION OF
TECHNICAL REQUIREMENTS FOR REGISTRATION OF
PHARMACEUTICALS FOR HUMAN USE**

ICH M2 EWG

Electronic Common Technical Document Specification

This specification has been developed by the ICH M2 Expert Working Group in accordance with the ICH Process as pertains to the M2 EWG.

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA'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.

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