Providing Regulatory Submissions in Alternate Electronic Format

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Dat Doan, 240-402-8926, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2020
Electronic Submissions

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Guidance for Industry

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TABLE OF CONTENTS

Providing Regulatory Submissions in Alternate Electronic Format Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides recommendations on an alternate electronic format for submissions covered under an exemption from or a waiver of the requirements of section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). These recommendations pertain to the format of content contained in new drug applications (NDAs), abbreviated new drug applications (ANDAs), certain drug master files (DMFs), certain biologics license applications (BLAs), and certain investigational new drug applications (INDs) submitted to the Center for Drug Evaluation and Research (CDER) or to the Center for Biologics Evaluation and Research (CBER).

Sponsors and applicants who receive an exemption or waiver from filing in electronic common technical document (eCTD) format under section 745A(a) of the FD&C Act should still provide those exempted or waived submissions electronically. This recommendation is consistent with the efforts of Federal Agencies to transition their business processes and recordkeeping to a fully electronic environment.[2]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of Medical Policy in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research at the Food and Drug Administration.

[2] See https://www.archives.gov/records-mgmt/memos/ac22-2019.

II. BACKGROUND

In section 745A(a) of the FD&C Act, Congress granted FDA the authority to implement the Agency's statutory electronic submission requirements in guidance. In response to this authorization, FDA implemented binding guidance requiring submission of NDAs, BLAs, ANDAs, DMFs, and commercial INDs to the Agency in eCTD format. Recognizing that certain types of submissions are exempt from this requirement and that waivers of the requirement may be granted on a case-by-case basis, the Agency is issuing this draft guidance to describe the alternate electronic format companies should use for submissions covered under such exemptions and waivers.

III. HOW TO SUBMIT ELECTRONICALLY UNDER THIS GUIDANCE

A. How to Submit in Alternate Electronic Format (without xml backbone)

Although the alternate electronic format utilizes the same folder structure found in eCTD submissions, it does not include xml and other specific files needed for electronic display. The alternate electronic format does not require specialized software. Commercial off the shelf software or other methods may be used to either build or view the submission; but like eCTD, the alternate electronic format should follow the FDA technical specification *The Comprehensive Table of Contents Headings and Hierarchy*.[3] For information on file format and versions, see section III.E in this guidance.

Main Submission Folder

All documents and data files should be placed in a main folder (top-level) using *the same sequence number* (e.g., **0001***)* as the folder name. A table of contents with hyperlinks and bookmarks should be provided on the same level as the top-level folder for ease of navigation to all the files contained in the submission.

Folders

Inside the main folder (sequence folder), there should be five or fewer folders, depending on the documents being submitted: *m1, m2, m3, m4, and m5*. The documents should be organized and placed in their respective modules, folders, or subfolders as displayed in the FDA technical specification *The Comprehensive Table of Contents Headings and Hierarchy*.

Each item has an assigned module and subfolder where document and data files that belong to the item should be placed. Files pertaining to each module should be placed in the appropriate folder (e.g., m1 through m5). The terms *folder* and *subfolder*, as used in this guidance, are intended to be synonymous with *directory* and *subdirectory*. The main submission, regional administrative folders, and certain subfolders should have specific names. Table 1 shows the organization of modules and their descriptions.

[3] See https://www.fda.gov/media/76444/download.

Table 1. Module and Description Organization

Module	Description
1	Administrative Information
2	Summaries
3	Quality
4	Nonclinical Information
5	Clinical Information

Folder Organization

For recommendations on how to organize submission content, refer to the *eCTD Technical Conformance Guide.*[4] The majority of information in the *eCTD Technical Conformance Guide* is applicable to eCTD and non-eCTD submissions.

B. FDA Forms

Electronic submissions should include only FDA fillable forms (e.g., 1571, 356h, 2252) and electronic signatures to enable automated processing of the submission. FDA forms are available at https://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm. Scanned images of FDA forms should not be submitted.

C. Pre-Submission Considerations

Before making the first alternate electronic submission, a pre-assigned application number should be obtained by contacting CDER or CBER. For more information on obtaining a pre-assigned application number, see FDA's eCTD web page at https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/submit-using-ectd.

D. Submission Structure: Granularity, Files, and Folders

The level at which the submission content is broken out into separate files should be consistent with the International Council for Harmonisation (ICH) guidance for industry *M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use* (October 2017)[5] unless otherwise specified in the ICH guidance for industry *M2: eCTD Specification Questions & Answers and Change Requests* (March 2005).

The FDA technical specification *The Comprehensive Table of Contents Headings and Hierarchy* should be followed for the comprehensive listing of headings and hierarchy, and for section

[4] See https://www.fda.gov/media/93818/download.

[5] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

mapping the headings to their respective regulations. Given that this technical specification includes a comprehensive listing, not all headings are applicable to all submissions or submission types.

Letters, numbers, hyphens, and underscores may be used in the folder and file names, but you should not use blank spaces or special characters. When naming folders and files, the length of the path should not exceed 150 characters. Empty folders and files should not be included in the submission.

Sequence numbers are used to differentiate submissions within the same application and need not correspond to the order in which they are received by FDA. It is not necessary for sequence numbers and IND serial numbers to match for submissions to an IND.

Subfolders within each module are used to organize files in a submission. These subfolders should be placed in the sequence number folder.

E. File Formats and Versions

Files within an alternate electronic submission should adhere to the formats and versions specified in the associated FDA technical specification *Specifications for File Format Types Using eCTD Specifications*. PDF files should adhere to the FDA technical specification *Portable Document Format (PDF) Specifications*.

F. Datasets and Study Information

Datasets should only be provided in modules 3, 4, or 5, and not in modules 1 or 2.

For further information on the submission of study data, see the guidance for industry *Providing Regulatory Submissions in Electronic Format — Standardized Study Data* (December 2014).

G. Transmitting Electronic Submissions

The FDA Electronic Submissions Gateway (ESG)[6] enables the secure submission of regulatory information for review. For all submissions in alternate electronic format that are 10 gigabytes (GB) or smaller, the FDA ESG should be used.

For submissions that are greater than 10 GB, refer to the FDA technical specification *Transmitting Electronic Submissions using eCTD Specifications*.

H. Receipt Dates

The receipt date for an electronic submission is determined after the submission has passed a technical validation check, to ensure that it can be opened, processed, and archived. The

[6] Additional information concerning the FDA ESG is available at https://www.fda.gov/industry/electronic-submissions-gateway.

submitter is responsible for monitoring their receipt pathway to determine whether a submission has been rejected.

Additional information on receipt dates for electronic submissions is available in the guidance for industry *Providing Regulatory Submissions in Electronic Format — Receipt Dates* (February 2014).

Contact Information

For questions related to providing electronic submissions according to the recommendations in this guidance, contact the appropriate electronic submission coordinator:

CDER submissions: esub@fda.hhs.gov

CBER submissions: esubprep@fda.hhs.gov

Specific questions pertaining to the content of applications should be directed to the appropriate review division or office.

IV. FDA TECHNICAL SPECIFICATION DOCUMENTS REFERENCED IN THIS GUIDANCE

The following is a list of FDA technical specification documents referenced in this guidance:

1. *The Comprehensive Table of Contents Headings and Hierarchy*
2. *eCTD Technical Conformance Guide*
3. *Portable Document Format (PDF) Specifications*
4. *Transmitting Electronic Submissions Using eCTD Specifications*

For a complete listing of the current technical supportive files that you will need in order to submit in eCTD format, refer to the eCTD Submission Standards document located on the eCTD web page at https://www.fda.gov/ectd.

V. RELATED REFERENCES

The guidance documents referenced below can be accessed via FDA's guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.[7]

1. FDA guidance for industry, *Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act* (December 2014)

2. FDA guidance for industry, *Providing Regulatory Submissions in Electronic Format — Standardized Study Data* (December 2014)

3. FDA draft guidance for industry, *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (December 2017)

4. FDA draft guidance for industry, *Formal Meetings Between the FDA and Sponsors or Applicants of BSUFA Products* (June 2018)

5. FDA draft guidance for industry, *Providing Submissions in Electronic Format — Postmarketing Safety Reports* (June 2014)

6. FDA guidance for industry, *Providing Regulatory Submissions in Electronic Format — Receipt Dates* (February 2014)

7. ICH guidance for industry, *M2: eCTD Specification Questions & Answers and Change Requests* (March 2005)

8. ICH guidance for industry, *M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use* (October 2017)

9. FDA guidance for industry, *Integrated Summaries of Effectiveness and Safety: Location Within the Common Technical Document* (April 2009)

[7] *Note:* Draft guidances are not considered FDA's current thinking until finalized.