Electronic Common Technical Document (eCTD) v4.0
TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*

For questions regarding this technical specifications document, contact CDER at esub@fda.hhs.gov or CBER at esubprep@fda.hhs.gov

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)

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U.S. FOOD & DRUG
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eCTD v4
TECHNICAL CONFORMANCE GUIDE

September 2022

REVISION HISTORY

DATE	VERSION	SUMMARY OF REVISIONS
December 2019	1.0	Initial Revision
January 2021	1.1	Revisions based on comments received during a public comment period. Changes include removal the following: 1) Two-way communications and associated data elements; 2) Regulatory Review Time; 3) Document media type; and 4) Category Event.
September 2022	1.2	Revisions based on ICH eCTD v4.0 Implementation package including removal of Transition Mapping Message and addition of Forward Compatibility. ***Added section:*** Section 2.1 (Forward Compatibility from eCTD v3.2.2 to eCTD v4.0) ***Removed section:*** Section 1.8 (Transition Mapping Message)

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1. INTRODUCTION

1.1 Background

This Electronic Common Technical Document (eCTD) Technical Conformance Guide (Guide) provides specifications, recommendations, and general considerations on how to submit eCTD-based electronic submissions to the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER). The Guide supplements the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (eCTD Guidance).[1] The eCTD Guidance implements the electronic submission requirements of Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) with respect to electronic submissions for certain investigational new drug applications (INDs); new drug applications (NDAs); abbreviated new drug applications (ANDAs); certain biologics license applications (BLAs); and master files submitted to CDER or CBER. eCTD v4.0 submissions meet the eCTD requirements defined in the eCTD guidance. These submissions may apply to combination products with CDER or CBER as the lead center.[2]

1.2 Purpose

This Guide provides technical recommendations to sponsors and applicants for the standardized electronic submission format of INDs, NDAs, ANDAs, BLAs, and master files. The Guide is intended to complement and promote interactions between sponsors and applicants and FDA's electronic submission support staff. However, it is not intended to replace the need for sponsors and applicants to communicate directly with support staff regarding implementation approaches or issues relating to electronic submissions. Because of the inherent variability across studies and applications, it is difficult to identify all issues that may occur related to the preparation and transmission of electronic submissions. Therefore, prior to submission, sponsors and applicants should discuss questions with the appropriate center's electronic submission support staff within the appropriate center, CDER: esub@fda.hhs.gov or CBER: esubprep@fda.hhs.gov.

1.3 Document Revision and Control

FDA issued an initial *Federal Register* notice announcing availability of this Guide for public comment on its contents. Future revisions will be posted directly on the eCTD Web page[3] and the

[1] Found on the FDA eCTD website: https://www.fda.gov/ectd

[2] See 21 CFR Part 3. Combination products are comprised of any combination of a drug and a medical device; a medical device and a biological product; a biological product and a drug; or a drug, a medical device, and a biological product. Combination products are assigned to a lead center for review; see 21 CFR 3.4.

[3] See above for the eCTD Web page link

revision history page of this document will contain sufficient information to indicate which sections of this Guide have been revised.

1.4 Relationship to Other Documents

This Guide integrates and updates information discussed previously in the eCTD Guidance and other specifications documents (including Agency presentations).

This Guide should be considered a companion document to the following:

- *Guidance to Industry Providing Regulatory Submissions in Electronic Format —Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*[4]
- The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) eCTD v4.0 Implementation Package
- ICH Specification for Submission Format for eCTD
- FDA eCTD v4.0 Module 1 Implementation Package
- FDA Study Data Technical Conformance Guide
- FDA Data Standards Catalog
- Specifications for eCTD v4 Validation Criteria
- eCTD v4.0 Comprehensive Table of Contents Headings and Hierarchy
- Portable Document Format (PDF) Specifications
- Example Submissions using eCTD v4 specifications

1.5 What's New in eCTD v4.0

1.5.1 Single Submission Unit message

The eCTD v4.0 message, submissionunit.xml and submission content, contains all information necessary to submit a complete sequence to the FDA. The submissionunit.xml is used to organize both the ICH and Regional sequence content, including the study data that was previously submitted in a separate Study Tagging xml file.

In addition, there was a change to the overall message structure, the previous eCTD backbone is replaced by a more dynamic message structure. The eCTD v4.0 message relies heavily on code lists to manage additional metadata for the submission contents. The eCTD structure is not hard coded into the message, and only the headings relevant to the sequence need to be submitted with submission contents.

Refer to the FDA Module 1 eCTD v4.0 Implementation Guide for additional information about the submission unit message, folder structure and its contents.

1.5.2 Context of Use

The Context of Use is used to place documents under a CTD heading and associated keywords. The combination of the context of use and keywords create a context group under which one or

[4] This document does not currently reflect the eCTD v4.0 requirements.

more documents may be placed per the instructions in the M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use guidance for industry document.

1.5.3 Keywords

Keywords are used to further define the submission content under an eCTD section. Keywords replace the eCTD 3.2.2 attributes and valid values. This information is more dynamic in the v4.0 message and rules will need to be followed to ensure the required keywords are provided in the message. Only one keyword of each keyword type should be provided on a heading (i.e., context of use).

The message contains new keyword code concepts – specifically document type keywords (see Section 1.5.3.1 in this document) that replace file-tags and sender-defined keywords (see Section 1.5.3.2 in this document) to enable additional organization of content.

1.5.3.1 *Document Type Keywords*

The document type keywords are a replacement for file-tags to organize study data into additional headings. Document types will continue to follow the same rules as previous file-tags; however, they are now provided as keywords. This document will note specific uses of document type keywords when submitting content to the FDA.

1.5.3.2 *Sender-defined Keywords*

In the eCTD v4.0 message, keywords may be defined by the submitter using the keyword definitions. Sender-defined keywords are sent for each application, but it is recommended that the submitter manages the keyword definitions across applications to enable the use of grouped submissions. The display name for the keywords greater than 512 characters will be truncated when displayed to reviewers.

1.5.3.2.1 *Creating Sender-defined Keywords*

Sender-defined keywords should only be sent once for any application. The status of keywords will always be “active”. Once the keyword definition is established, the value will be displayed for each Context of Use that references the sender-defined keyword.

Specific to grouped submissions (see Section 2.2.4 in this document) the sender-defined keywords should be managed across applications. If the codes assigned to the sender-defined keywords are not shared across applications, the submitter will not be able to effectively use the grouped submission option.

1.5.3.2.2 *Updating Sender-defined Keywords*

Updates to sender-defined keywords should be made only when there is a typo or error in the value. A new keyword definition should be submitted if there is a new sender-defined keyword that needs to be used.

Updating the value of a sender-defined keyword will change its value for all uses of that keyword definition – i.e., the change will take effect across submission units in that application. The change should also be applied to all applications using the keyword definition.

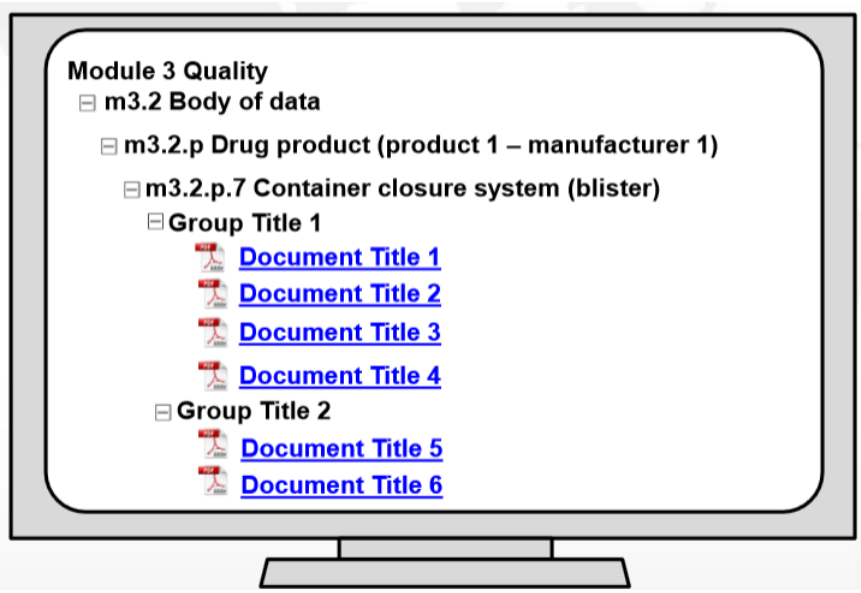
1.5.3.2.3 *Group Title Keywords*

Group title keywords are new in eCTD v4.0 and are a type of sender-defined keywords. The group title keyword allows the submitter to create further organization of documents under specified headings that allow for more than one document (as specified in the M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use guidance in industry[5]).

Documents associated with a group title will be displayed separately under the eCTD heading and other associated keywords. The group title keyword will be applied to the lowest heading level.

The figure below depicts the use of two group titles and is achieved by sending two different context of uses with the same heading value, but different group title keywords.

Figure 1: Group Title Display



The group title keyword is not intended to replace other specified keywords – it is only intended to allow for the further organization of content where multiple documents are combined to provide information for a specific topic area. This keyword should be used sparingly for this specific purpose.

1.5.4 Context Groups and Life Cycle

In the eCTD v4.0 message, a context group is the combination of the context of use and keywords used to place a document under an eCTD section. Context groups require that the context of use

[5] Also represented in the ICH eCTD v4.0 code lists.

and keyword combinations stay the same when submission content is replaced. The replace function will track the changes made to the submission contents when one document (referenced by a context of use) is replaced by one, many, or many to one. The figures below depict the document life cycle in a context group.

Figure 2: Replacing Many Documents with one in the same Context Group

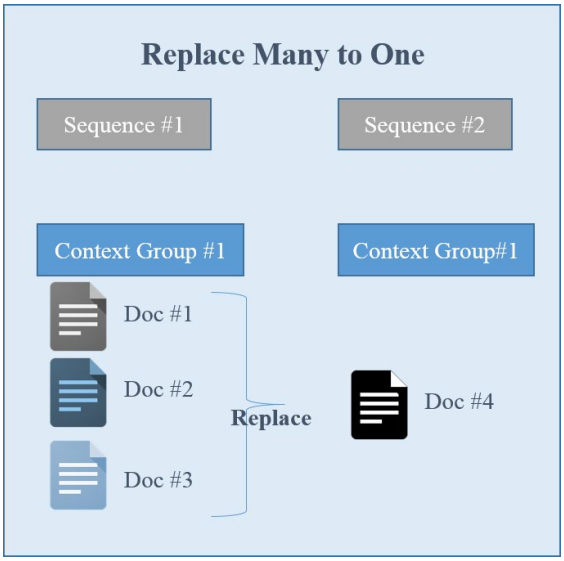
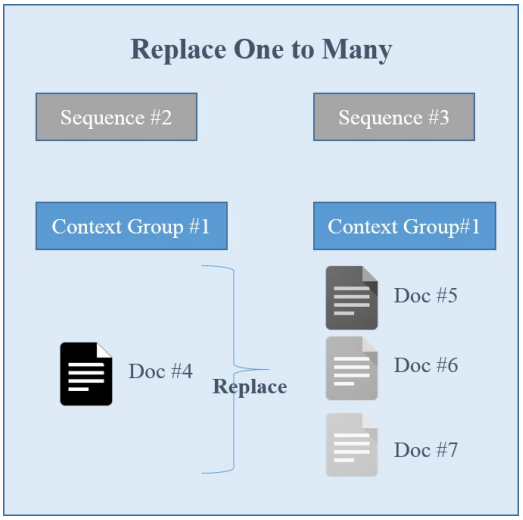
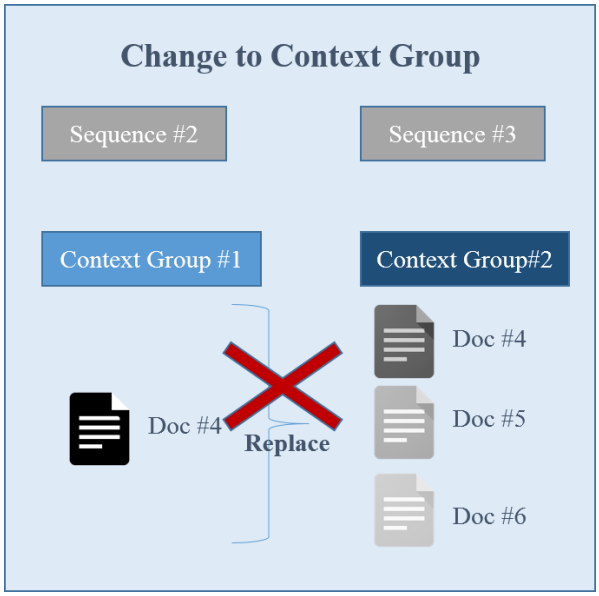


Figure 3: Replacing One Document with many in the same Context Group



If the context group is not the same, the replacement is not allowed. The figure below depicts many documents replacing one document from a prior sequence in a different context group.

Figure 4: Replacement that is not allowed

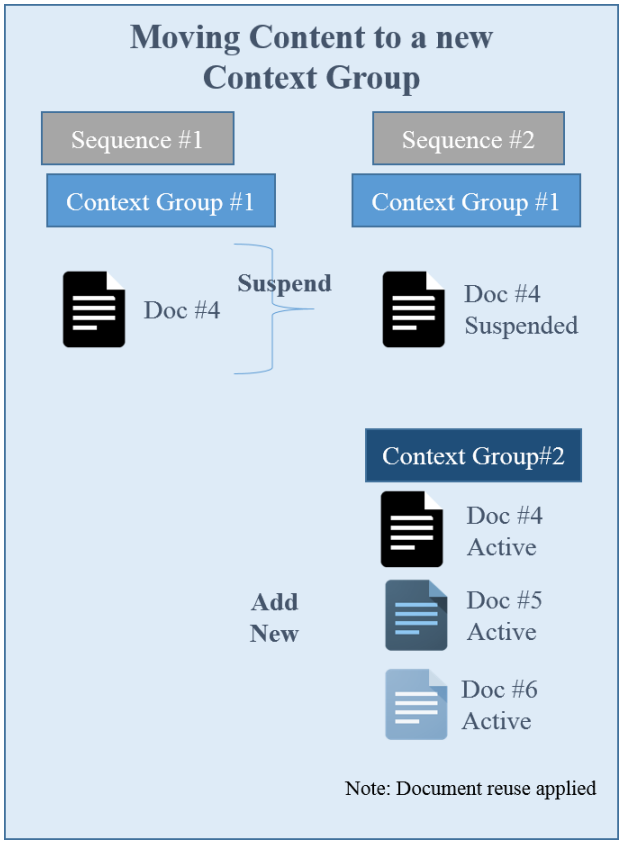


The context groups are intended to keep content organized and life cycle maintained in an application. Providing the content to the incorrect section in the eCTD will result in the content not being displayed in the expected location for the reviewers. Therefore, if the heading placement or keywords need to change for the referenced submission contents – a new context group shall be created and the old context group should be suspended as follows:

- Create a new submission unit message.
- Use the status of "suspend" to inactivate all the content that was incorrectly referenced in the section.
- Reference the documents using a new context of use, ensuring that the keywords (e.g., 'name', 'manufacturer', 'dosage form', 'study id study title') are an exact match to the section the documents should be placed.
- Resubmission of the files and document elements is not necessary as it is referenced by the document's unique identifier.

The figure below depicts the submission contents that are suspended and those submitted under a new context group (i.e., the new CTD heading and/or keywords). Note that the content under the new context group will not be related to the previous content, however document reuse may be applied (See Section 1.5.5 in this document for Document Reuse).

Figure 5: Moving Content to a New Context Group



1.5.5 Document Reuse

The eCTD v4.0 message may contain references to documents previously submitted in separate applications by referencing the document's unique identifier. Therefore, a document can be referenced without including the physical file in the new message. The content will be displayed from the document repository[6] instead of relying on the sequence physical folder structure to contain all the files referenced in the message. When submitting a reference to an existing document, it is important to ensure that all document hyperlinks are relevant to the new context of use.

[6] Documents cannot be reused across the CDER and CBER document repositories.

2. GENERAL GUIDELINES AND CONSIDERATIONS

The following subsections provide general guidelines and considerations for additional information in the eCTD v4.0 message.

2.1 Forward Compatibility from eCTD v3.2.2 to eCTD v4.0

Forward Compatibility is used for any dossier that has v3.2.2 content and the application is being converted to a v4.0 message.

Please note that forward compatibility will not be implemented in the first phase of eCTD v4.0 implementation. Consult the FDA eCTD v4.0 website for updates to the eCTD v4.0 implementation timelines.

The submitter should take into consideration the following submission requirements and recommendations when converting to eCTD v4.0:

- When submitting the first eCTD v4.0 sequence to an eCTD v3.2.2 dossier the next available sequence number is submitted as a whole number. For example, if the last eCTD v3.2.2 message has a sequence number "0003", the first eCTD v4.0 submission unit will be sequence number "4".
- Submissions should be coded according to the current regulatory activity. If the submission is a continuation of an open regulatory activity, the initial sequence number is needed to link the submission to the v3.2.2 regulatory activity. The v3.2.2 sequence number should only be submitted to the first eCTD v4.0 submission for the open regulatory activity.
- Once a v4.0 submission unit has been received for an application, all future sequences must be sent in v4.0 – i.e., a v3.2.2 message received after the initial v4.0 message is received will be rejected.
- All v3.2.2 applications included in an eCTD v4.0 Grouped Submission will be converted to v4.0 messages.
- When submitting v4.0 content that should be grouped with v3.2.2 content the keyword codes and values must match.
- Consider a strategy across applications for sender-defined keywords, especially in the case of grouped submissions. Keyword Definitions need to be established prior to or during the submission of a Grouped Submission in eCTD v4.0.
- Understand specific requirements that require changes to the current eCTD v3.2.2 attributes provided – e.g., study id and study title.

Forward Compatibility enables life cycle and document reuse of v3.2.2 content, the submitter should take into consideration the following requirements:

- The "Leaf Reference" is used to life cycle and reuse v3.2.2 content.
- Document reuse includes content previously submitted in eCTD v3.2.2 within or across applications, including applications that have not been converted to v4.0.
- Life Cycle

- Life cycle of submission content is only allowed for active (e.g., new, replace) leaf elements (i.e., content that is in the current view).
- Suspend eCTD v3.2.2 content (i.e., to inactivate content) within an application.
- When v3.2.2 content is replaced, it must follow v4.0 context group life cycle rules; the headings and attributes remain the same when replacing content by sending the same values in the new eCTD v4.0 keyword and context of use.

Refer to the ICH eCTD v4.0 Implementation Guide and FDA Module 1 eCTD v4.0 Implementation Guide for additional information about the Forward Compatibility.

2.2 eCTD Submission Tracking Information

The rules for submission tracking information (i.e., the allowable application types for the submission) are presented in Section 5 of this document and specific guidance is provided in the subsections below.

2.2.1 Presubmissions

Any information submitted in eCTD format before the original application or supplement submission (specifically for NDA, ANDA and BLAs), should be coded with a submission unit type value of "presubmission" and the first submission unit to an application should start with a sequence number of 1. Any presubmissions to a subsequent supplement application should start with the next available sequence number in the application.

Note: *Refer to Section 2.1 for additional guidance for open regulatory activities.*

2.2.2 Rolling Submissions

Rolling submissions are allowed for an NDA or BLA. The submission type for the set of submission units transmitted before the application is complete are managed the same as presubmissions to the original application until it is ready for review. The rolling submission should be coded with a submission type value for "original application" and submission unit type value for "presubmission". The cover letter and form should state "presubmission to rolling submission – part 1 of XXX" (depending on how many parts before the final submission).

The final submission unit completing the application should be coded with a submission type value for "original application" and submission unit type value for "application" to start the respective review clock. The cover letter and form of the final submission should state "original application – part XXX of XXX of rolling submission".

2.2.3 Master Files

For information on Drug Master File submissions, including Letters of Authorization, please refer to the Drug Master File website (https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs).

2.2.4 Grouped Submissions

A grouped submission is also known as a global supplement, global submission, bundled supplement, bundled submission, multiple product submission or trans-BLA. This type of submission eliminates the need to submit multiple, identical submissions to different applications. The documents referenced in the grouped submission are applied to all applications identified. The grouped submission concept does not replace or affect previously existing cross-referencing functionality (use of m1.4.4 or cross application reference links).

A grouped submission contains a single *submissionunit.xml* that contains all application numbers and their respective sequence numbers in the group. For each unique application number in the group, only one sequence number should be provided for each regulatory activity.

Refer to the FDA Module 1 eCTD v4.0 Implementation Guide for additional information about Grouped Submissions.

The following items listed below provide general information and use limitations for submitting a grouped submission to multiple applications[7]:

General Information:

- Initial grouped submissions should only include new context of uses.
- When using life cycle operations of suspend or replace in a subsequent grouped submission, the life cycle operation will apply to all context of use in all submissions referenced in the grouped set of applications.
- The grouped submission's content must reside in the same exact location within the eCTD structure for all applications included in the group.

Consider Forward Compatibility when establishing Grouped Submission in eCTD v4.0. Refer to Section 2.1.

Use Limitations[8]:

- Only one application type can be used for all applications in a grouped submission.
- Only one submission type can be used for all regulatory activities in a grouped submission.

[7] Electronic consideration(s) for grouped submissions will not supersede the policy and practice of bundled submissions as it may or may not affect user fees per the *Guidance for Industry: Guidance for Industry Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees.*

[8] See Table 1 "Grouped Submission Limitations and Use" for further restrictions.

Table 1: Grouped Submission Limitations and Use

Application Types Allowed	Submission Types Allowed	Center Acceptance of Grouped Submission	
		CDER	CBER
ANDA	Labeling Supplement, Chemistry Manufacturing Controls Supplement, Product Correspondence, Promotional Labeling Advertising, REMS Supplement	YES	NO
BLA	Efficacy Supplement, Labeling Supplement, Chemistry Manufacturing Controls Supplement, Product Correspondence, Promotional Labeling Advertising, REMS Supplement	YES	YES
MF	Product Correspondence	YES	NO
IND	Annual Report, Product Correspondence	YES	NO
NDA	Efficacy Supplement, Labeling Supplement, Chemistry Manufacturing Controls Supplement, Product Correspondence, Promotional Labeling Advertising, REMS Supplement	YES	NO

2.3 eCTD v4.0 Message-specific Information

2.3.1 Submission Unit Title

The title[9] of the submission unit is optional and does not restrict the number of characters allowed, but only the first 128 characters will be displayed to reviewers. Therefore, the value provided for the submission unit title should be a high-level description of the submission's purpose and should also help differentiate between similar types of submission units or sequences.

Some examples of helpful submission descriptions are listed below:

- Supplement provides for new manufacturing site
- New site for Active Pharmaceutical Ingredient (API) manufacture, DSM Ltd, Groningen, NL
- Proposed indication of an efficacy supplement
- Pharmtox Information Amendment – Final Study Report A1001
- Clinical Information Amendment – New Protocol A001100
- Response to an Information Request (IR) letter and date.

[9] In eCTD v3.2.2 this was included as the "submission-description".

- Type of amendment (clinical – new protocol, clinical – protocol amendment, pharmacology, toxicology, etc.)

The title should not:

- contain a response to FDA inquiries
- replace the cover letter
- pose questions to the FDA
- contain information that is in support of an application or is needed in the approvability or acceptability of an application, or
- contain information that is critical or needs to be reviewed.

2.3.2 Application References

Application references[10] should be provided when an application references other applications (e.g., Drug Master File). A cross-reference only needs to be identified in one submission unit file.

2.3.3 Contacts

The eCTD v4.0 message may contain multiple contacts for a regulatory activity/submission. The contacts that can be submitted to the FDA include the following:

- **Regulatory Contact[11]** – this is an individual that the FDA Regulatory Project Manager will contact regarding submission/regulatory activity status.
- **Technical Contact** – this is an individual that the FDA technical staff will contact when there is an issue with the technical aspects of the eCTD v4.0 message (e.g., structure and content of the XML message and/or submission files).
- **United States Agent** – this is an individual acting on behalf of the submitter to submit information to the FDA.

Contacts should be sent once for each regulatory activity and updated as necessary.

2.3.4 Document Titles

Document titles[12] are displayed to the reviewer when viewing an eCTD application. Although some eCTD viewing tools list file names, the two are not related. All modules of the eCTD should contain descriptive eCTD document titles that are short, meaningful, and indicative of each document's content. The eCTD section number should not be included in the document title.

For documents of the same type (e.g., cover letter, Form FDA 356h, and annual report documents), additional information should be provided in the document title so reviewers can distinguish documents submitted in different sequences. For example, the document title for a cover letter should also include the date (e.g., 2016-12-31). Additionally, if documents of the same type are being provided in different file formats, a file format (e.g., "MS Word") should be

[10] In eCTD v3.2.2 this was included as the "cross-reference-application-number"

[11] The Regulatory Contact may be specific to the submission type – e.g., Promotional Labeling and Advertising Regulatory Contact. Refer to the controlled vocabulary files for the possible regulatory contact types.

[12] In eCTD v3.2.2 this was termed "leaf title"

included at the end of the document title. This helps reviewers quickly identify which software applications are necessary to open the files.

Per eCTD Guidance (*Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*[13]), when naming folders and files, the length of the entire path must not exceed 180 characters. The character limit on the document title field is 512 characters.

2.3.5 Study Data Document Types

In eCTD v4.0 the file-tags have been changed to keywords. Specifically, document type keywords are used to further describe submission content. Document type keywords are required for all files in Section 4.2.x and 5.3.1.x – 5.3.5.x. Document Types are not required for 4.3 Literature references, 5.2 Tabular listings, 5.4 Literature references and 5.3.6 Postmarketing reports. These documents may be submitted as single separate files without a document type keyword.

2.4 Resubmission of non-eCTD documents

In general, resubmission of previously submitted content is neither necessary nor encouraged. However, there are occasional circumstances in which a "baseline" submission is helpful to the reviewer. One example is CMC information contained in module 3. In a circumstance such as this, the FDA will accept the resubmission of non-eCTD content (e.g., paper, eNDA) but the previously submitted content should be submitted as a separate submission, as opposed to being included in a supplement or an amendment to a regulatory activity. The cover letter should state that the submission contains only previously submitted content and certify that the sequence does not include any changes or updates to the application. For marketing applications, the certification should include a table with a listing of approvals that relate to the content being resubmitted. For INDs and master files, the list should include amendments that relate to the content being resubmitted.

In most cases, the submission of a "baseline" or other previously submitted content will require that the previous content be reorganized to meet the eCTD format requirements. You should not resubmit the previous content "as-is" unless the content was in the CTD format and the eCTD backbone was not used when content was originally submitted.

The submission type should be coded as "Product Correspondence". On the 356h form, you should select "Product Correspondence" for the Submission type and enter "Submission of previous non-eCTD content in the eCTD format".

Prior to resubmitting content, you should contact the responsible review division to determine if resubmission is acceptable.

[13] This document does not currently reflect the eCTD v4.0 requirements.

3. SUBMISSION CONTENTS

The following section will provide specific guidance on the submission contents of a submission unit and any instructions for the submission unit message.

3.1 Module 1 - Administrative Information and Prescribing Information

Module 1 includes, but is not limited to: administrative, labeling, REMS, and promotional material documents. The subject matter for each document should be assigned to the lowest level of the hierarchy outlined in the associated FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy*[14]. (Note that some headings apply only to specific applications or specific submission types.)

3.1.1 Cover Letter and Reviewer's Guide

Cover letters contain pertinent information which aid communication within the review process. It is recommended that the cover letter include the following information:

- Regulatory description of the submission, including appropriate regulatory information, and any desired hyperlinks to submitted information
- Technical description of the submission, including the approximate size of the submission (e.g., 2 gigabytes)
- Statement that the submission is virus free, with a description of the software (name, version, and company) that was used to check the files for viruses
- A regulatory and technical point of contact for the submission, including email address.

A reviewer's guide[15] is beneficial when accompanying an original NDA, BLA, or combination product[16] application. The reviewer's guide should include a high-level overview of the submission with hyperlinks to submitted information. The reviewer's guide should not contain a copy of the eCTD table of contents. Rather, an outline format describing the submission's content is preferred, including tables or lists, and avoiding a continuous narrative description of the application's content.

The reviewer's guide should be provided as a document separate from the cover letter and placed in Section 1.2 of the eCTD with a descriptive document title.

3.1.2 Patient Experience Data

If submitting patient experience data as part of an application for marketing approval, the following table should be populated and included in the Reviewer's Guide (section 1.2). Patient experience data (e.g., clinical outcome assessments) collected as part of a clinical trial should be submitted as part of the relevant clinical trial data. Other patient

[14] https://www.fda.gov/media/150309/download

[15] This is different than a Study Data Reviewer's Guide (SDRG). Additional information on the SDRG can be found in the Study Data Technical Conformance Guide located on at: https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources

[16] See additional recommendation for combination products in Section 4 of this document

experience data that is separate from clinical trials should be submitted to section 5.3.5.4

o	The patient experience data that was submitted as part of the application, include:				The patient experience data that was submitted as part of the application, include:
	o	Clinical outcome assessment (COA) data, such as			
			o	Patient reported outcome (PRO)	
			o	Observer reported outcome (ObsRO)	
			o	Clinician reported outcome (ClinRO)	
			o	Performance outcome (PerfO)	
	o	Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)			
	o	Patient-focused drug development or other stakeholder meeting summary reports			
	o	Observational surveys studies designed to capture patient experience data			
	o	Natural history studies			
	o	Patient preference studies (e.g., submitted studies or scientific publications)			
	o	Other: (Please specify)			

3.1.3 Cross Referencing Previously Submitted Information that is not in eCTD Format

If reference to a non-eCTD submission is needed, place a cross-reference document (e.g., table showing where to find non-eCTD documents) in Section 1.4.4 of the eCTD. The information in the document should include:

- the application number
- the date of submission (e.g., letter date)
- the file name (if applicable)
- the page number (if necessary)
- the submission identification (e.g., submission number, volume number if paper, electronic folder if applicable) of the referenced document.

3.1.4 Labeling

This section describes how to provide specific labeling documents:

Labeling History

A history that summarizes labeling changes should be provided as a single PDF file. The history summary should include the following information:

- Complete list of the labeling changes being proposed in the current submission and the explanation for the changes
- Date of the last approved labeling

- History of all changes since the last approved labeling (with each change, note the submission that originally described the change and the explanation for the change)
- List of supplements pending approval that may affect the review of the labeling in the current submission.

Content of Labeling

The FDA guidance for industry *Providing Regulatory Submissions in Electronic Format — Content of Labeling*[17] gives details on providing the content of labeling files.

Labeling Samples

Each labeling sample (e.g., carton labels, container labels, package inserts) should be provided as an individual PDF file. The samples should:

- Include all panels, if applicable
- Be provided in their actual size, and
- Reflect the actual color proposed for use.

3.1.5 Advertisements and Promotional Labeling Material

As described in the guidance for industry "Providing Regulatory Submissions in Electronic and Non-Electronic Format--Promotional Labeling and Advertising Materials for Human Prescription Drugs", certain types of promotional-material-related submissions, including postmarketing submissions of promotional materials are required to be submitted in eCTD format.

While HTML (a commonly used file type for websites) is an acceptable file format type to use for eCTD Module 1 promotional submissions, submission of HTML files that depend on JavaScript, PHP or server-side scripts that generate dynamic content should not be submitted because these dependent files are not on the list of acceptable file format types. An acceptable alternative for these types of HTML files is to utilize PDF. Please refer to the PDF Specifications for details.[18]

3.1.6 Marketing Annual Reports

A bookmark should be included for each study or trial described in the postmarketing requirement/commitments files. The reporting period covered by the annual report should be included in the eCTD document title (e.g. Status of Postmarketing Study Commitments - MMDDYY-MMDDYY).

3.1.7 Information Amendments

Documents for information amendments should be included in the applicable eCTD module using the appropriate eCTD heading to describe the document's subject matter.

[17] This document does not currently reflect the eCTD v4.0 requirements.

[18] See "Special Considerations for Promotional, Labeling, and Advertising Material" in the Portable Document Format (PDF) Specifications located in the eCTD Submission Standards catalog. The catalog is located on the FDA eCTD website (https://www.fda.gov/ectd)

Section 1.11 may be used for submission of responses to Information Requests (IR), where the information being submitted does not fit under any heading in Module 2, 3, 4 or 5. The IR response should be submitted under the appropriate subheading 1.11.1 – 1.11.3 within Section 1.11, for quality, nonclinical, or clinical information, respectively. The subheading 1.11.4 for multiple module information should be used if the IR response covers multiple subject areas. If the IR response impacts documents submitted in Modules 2 – 5, the new or replacement documents should be submitted to the appropriate location in Module 2 – 5 and referenced in the document from Section 1.11.

3.1.8 Field Copy Certification

For marketing applications, the Field Copy Certification (i.e., a copy of the letter described below) should be included with the electronic application in Section 1.3.2 of the eCTD. The District office should be notified by letter that the eCTD submission will be submitted to FDA, and because the field offices have access to the complete submission on the FDA network, an individual field copy is no longer required. The letter should include:

- Drug and application number
- FDA center and division
- Application is in eCTD format.

3.1.9 Risk Evaluation and Mitigation Strategy (REMS)

A REMS supplement is a supplemental application proposing a new REMS or modifications (major and/or minor) to an approved REMS.

Use the submission type of REMS Supplement in the submissionunit.xml and select REMS supplement on the 356h form.

If the REMS supplement is part of another supplement, the submission type should be coded with the appropriate supplement type (e.g., efficacy, CMC). On the 356h form, you should select both supplements for the submission type.

REMS assessments, REMS revisions, and REMS correspondences are not supplements, and the submission type should be coded as "product correspondence". On the 356h form, you should select "other" for the submission type.

The following table is provided to assist applicants on where to place documents under the eCTD Module 1 REMS 1.16 sub-headings.

eCTD Section: 1.16 Risk Management	
eCTD Section Heading	**Description**
1.16.1 Risk Management (Non-REMS)	Applicants should place risk management plans (RMP), risk minimization action plans (RiskMAPs), and RiskMAP reports under this heading. Submission of a Risk Evaluation and Mitigation Strategy (REMS) should ***not*** be placed under this heading as REMS are to be included under heading 1.16.2. However, if the applicant is

eCTD Section: 1.16 Risk Management	
eCTD Section Heading	**Description**
	submitting a rationale for not submitting a proposed REMS, it should be placed here
1.16.2 Risk Evaluation and Mitigation Strategy (REMS)	Do not include any files under this heading. The files should be specific for the lowest level of the hierarchy outlined in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy* available on our eCTD Website [19]and provided below for sub-heading 1.16.2.
1.16.2.1 Final REMS	The final REMS document, all REMS materials in their final format, and the REMS supporting document (for original REMS, REMS modifications, and REMS revisions)[20] should be submitted in Microsoft Word and PDF format. FDA can also accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the approval, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST). For more information on submitting REMS in SPL format, please email, REMS_Website@fda.hhs.gov.
1.16.2.2 Draft REMS	The proposed REMS document, all REMS materials, and the REMS supporting document in clean and track changes (for original REMS, REMS modifications, and REMS revisions) should be submitted in Microsoft Word format as individual files. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format. Applicants can also submit the proposed REMS document in SPL format. If you intend to submit the proposed REMS document in SPL format, include the SPL file with your proposed REMS submission. The REMS SPL file should be referenced in the eCTD xml backbone under Section 1.16.2.2. The REMS SPL file should be placed in a folder named "spl", along with copies of any REMS materials referenced in the REMS SPL file.
1.16.2.3 REMS Assessment	Applicant's REMS assessment report, abbreviated REMS assessment for an efficacy supplement, and responses to FDA

[19] https://www.fda.gov/media/150309/download

[20] See draft Guidance for Industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions,* available at*:* https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

eCTD Section: 1.16 Risk Management	
eCTD Section Heading	**Description**
	"Requests for Information or Comments," that are associated with an assessment should be placed here.
1.16.2.4 REMS Assessment Methodology	Any survey or other methodology used to assess the REMS should be placed here.
1.16.2.5 REMS Correspondence	Official REMS related correspondence to the FDA that is not associated with a submission under review should be placed here. Applicants' responses to FDA "Requests for Information or Comments," that are associated with a REMS supplement or an assessment that is under review should be included under applicable sub-headings.
1.16.2.6 REMS Modification History	It is recommended that applicants submit a REMS history that summarizes all type of changes (revisions, minor modifications, and major modifications) made to the REMS since its approval.[21] The REMS history should be in tabular format similar to the history of labeling changes and submitted as a single PDF file.

3.2 Module 2 – Summaries

3.2.1 Bioequivalence Summary Tables

For ANDAs, Bioequivalence Summary Tables should be provided in Section 2.7.1 of the eCTD. Additional information about ANDA submissions is available on the ANDA Forms and Submission Requirements Web page located at: https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/abbreviated-new-drug-application-anda-forms-and-submission-requirements.

3.3 Module 3 – Quality

3.3.1 Lot Distribution Data

Lot distribution data should be submitted for BLAs according to the guidance for industry *Electronic Submission of Lot Distribution Reports* available at: https://www.fda.gov/media/89610/download

3.3.2 Literature References

The files pertaining to key literature references should be provided as individual PDF files in Section 3.3 of the eCTD. The document titles should be short and meaningful (e.g., eCTD document title: SmithJA 2002 Impurities).

[21] See draft Guidance for Industry *Risk Evaluation and Mitigation Strategies: Modifications and Revisions,* available at*:* https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs for a more detailed description of the REMS history

3.4 Module 4 – Nonclinical

The organization of Module 4 is the same for all applications and related submissions. The guidance provided below addresses general considerations for the submission contents (i.e., the physical files and folders) and the contents of the message (i.e., the additional metadata for the submission contents – e.g., headings and keywords). In addition, specific topics have additional guidance to ensure complete submission of contents.

The documents for Module 4 should be placed in the m4 folder. The subject matter for each document should be specific for the lowest level of the hierarchy outlined in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy*[22]. The headings for study reports should also be specific for the lowest level of the hierarchy. Each document should be provided as an individual PDF file (or appropriate file format for study data). Module 4 includes specific keywords (e.g., document type keywords) that are included in the eCTD v4.0 code lists and are required by the eCTD guidance.

3.4.1 Study Reports

Typically, a single document should be provided for each study report included in this module. However, if the study reports are provided as multiple documents, the subject matter of each document should be confined to a single item from the list provided in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy*[23].

In the following examples, study reports should be provided as separate (granular) documents:

- **Documents previously submitted within an application**: If a document has been provided in a previous submission (e.g., referencing a previously provided protocol), the applicant should provide only an eCTD document reference to the protocol and not resubmit the protocol document.
- **Inclusion of additional information**: Study reports should be provided as separate documents. Additional information (e.g., audit information or a publication based on the study) should be provided as a separate file, rather than replacing the entire study report.

3.4.2 Literature References

Each literature reference should be provided as an individual PDF file in Section 4.3 of the eCTD. The file names and eCTD document titles should be short and meaningful (e.g., eCTD document title: SmithJA 2002 Impurities).

3.4.3 Datasets

The FDA technical specifications document *Study Data Technical Conformance Guide* provides details on the submission of datasets and related files (e.g., data definition file,

[22] https://www.fda.gov/media/150309/download
[23] Ibid.

program files).[24] Datasets should be provided only in modules 3-5 of the eCTD. Updated datasets should "replace" the old dataset.

3.5 Module 5 – Clinical

The organization of Module 5 is the same for all applications and related submissions. The guidance provided below addresses general considerations for the submission contents (i.e., the physical files and folders) and the contents of the message (i.e., the additional metadata for the submission contents – e.g., headings and keywords). In addition, specific topics have additional guidance to ensure complete submission of contents.

The documents for Module 5 should be placed in the m5 folder. The subject matter for each document should be specific for the lowest level of the hierarchy outlined in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy*[25]. The headings for study reports should also be specific for the lowest level of the hierarchy. Each document should be provided as an individual PDF file (or appropriate file format for study data). Module 5 includes specific keywords (e.g., document type keywords) that are included in the eCTD v4.0 code lists, and are required by the eCTD guidance.

Refer to the ICH eCTD v4.0 Implementation Package for additional information on the eCTD v4.0 controlled vocabulary.

3.5.1 Tabular Listing of All Clinical Studies

The tabular listing of all clinical studies should be provided as a single PDF file in Section 5.2 of the eCTD. For ease of review, hyperlinks to the referenced studies in m5 should be provided. Document type keywords do not apply to the tabular listing of clinical studies.

3.5.2 Study Reports

Typically, a single document should be provided for each study report included in this section. However, if the study reports are provided as multiple documents, the subject matter of each document should be confined to a single item from the list provided in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy*[26].

In the following scenarios, study reports should be provided in the following manner:

- **Documents previously submitted within an application**: If a document has been provided in a previous submission (e.g., referencing a previously provided protocol), the applicant should provide only an eCTD document reference to the protocol and not resubmit the protocol document.
- **Inclusion of additional information**: Study reports should be provided as separate documents and any additional information (e.g., audit information or a publication based on the study) should be provided as a separate file, rather than replacing the entire study

[24] https://www.fda.gov/media/150309/download
[25] Ibid.
[26] Ibid

report.

Typically, study reports should be provided according to the FDA guidance for industry *ICH E3 Structure and Content of Clinical Study Reports*. The individual documents that should be included in a study report are listed in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy*[27]. In the case where no other document type is appropriate, the "study report body" document type may be used.

In cases when a legacy report has already been prepared as a single electronic document, the entire study report should be provided as a single document, not including the case report forms (CRFs) (see Section 3.5.3 in this document) and individual data listings. The document type of "legacy clinical study report" should be used for this type of study report.

Human Factors Study reports should be placed in Module 5.3.5.4 Other Study Reports and Related Information and should include the appropriate human factors document type keywords (e.g., hf validation protocol, hf validation report, hf validation other) to describe the document's contents.

3.5.3 Case Report Forms (CRFs)

An individual subject's complete CRF should be provided as a single PDF file. If a paper CRF was used in the clinical trial, the electronic CRF should be a scanned image of the paper CRF including all original entries with all modifications, addenda, corrections, comments, annotations, and any extemporaneous additions. If electronic data capture was used in the clinical trial, a PDF-generated form or other PDF representation of the information (e.g., subject profile) should be submitted.

The subject's unique identifier should be used as the title of the document and the file name. These names are used to assist reviewers in finding the CRF for an individual subject. Each CRF must have bookmarks as part of the comprehensive table of contents required under 21 CFR 314.50(b). Each CRF domain and study visit should be bookmarked to assist reviewers in their review of CRFs. For addenda and corrections, avoid confusion by making a hypertext link from the amended item to the corrected page or addendum. Bookmarks for these items should be displayed at the bottom of the hierarchy.

Each CRF should be included with its corresponding clinical study report and should include a document type of 'case report forms'. FDA does not use the eCTD heading 5.3.7 for CRFs, therefore documents should not be placed under this heading.

3.5.4 Periodic Safety Reports

Periodic safety reports[28] consist of two parts: a descriptive portion and the individual case safety reports (ICSRs). Only the descriptive portion of the periodic report may be submitted to the eCTD.

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[27] https://www.fda.gov/media/150309/download

[28] Periodic adverse drug experience reports or periodic adverse experience reports, as described in 21 CFR 314.80 and 600.80, respectively.

The descriptive portion of the report may be sent as either the periodic adverse (drug) experience report (PADER) or the ICH-E2C periodic safety update report (PSUR) (allowed with approved waiver). Either format may be submitted to the eCTD in Section 5.3.6 as an individual PDF file without any document type keywords. Include the reporting period in the document title.

Do not submit ICSR E2B formatted XML files in eCTD.

3.5.5 IND Safety Reports

Each individual IND safety report with its associated study should be provided in Section 5.3 of the eCTD. Document titles that clearly relate to the individual cases should use "Safety Report" along with "initial" or "follow-up", depending on the content of the individual safety report.

Each IND safety report should be described by using the document type keyword of 'safety report' and should be submitted as "new" without replacing any previously submitted information.

For additional details on providing IND safety reports, refer to the FDA guidance for industry *Safety Reporting Requirements for INDs and BA/BE Studies*.

3.5.6 Literature References

Provide each literature reference as an individual PDF file in Section 5.4 of the eCTD, as appropriate. The document titles should be short and meaningful (e.g., eCTD document title: SmithJA 2002 Impurities).

3.5.7 Datasets

The FDA technical specifications document *Study Data Technical Conformance Guide* provides details on the submission of datasets and related files (e.g., data definition file, program files).[29] Datasets should be provided only in modules 3-5 of the eCTD. Updated datasets should "replace" the old dataset.

4. COMBINATION PRODUCTS[30]

Generally, drug or biological product information for combination drug and device product information and related engineering and manufacturing information should be located in the same eCTD sections that would provide similar information for the drug or biological product alone. This particularly applies to device constituent parts that also serve as the drug container closure system. For example, the M3 quality module should contain information on such device constituents in Section 3.2.P.7 and the message may include a keyword for the "container" type. Supportive documents for container closure device constituents should be

[29] Available at https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources.

[30] As set forth in 21 CFR part 3, a combination product is a product composed of any combination of a drug, device, or biological product.

placed in Section 3.2.R. For other types of device constituent parts that do not have a logical location within 3.2.P, the information should be placed in 3.2.R. For example, quality data for a free standing laser would be in 3.2.R. Quality information on the combination product as a whole (not the separate constituent parts) should be located in 3.2.P with appropriate hyperlinks to 3.2.R. The following recommendations should be followed by sponsors/applicants for combination products:[31]

1. General format comments
   a. Use of eCTD headings: Adhere to eCTD headings as defined in the FDA technical specification *Comprehensive Table of Contents Headings and Hierarchy*[32].
   b. Group titles may be used in this section to provide additional organization to the submission contents
   c. Document titles: As there are no-subheadings permitted under 3.2.R, when placing combination product files in this section, prefix the document title with "DEVICE" as this will help the reviewer differentiate between combination and other categories of files.

2. Module 1, Section 1.2
   To facilitate the review, a reviewer's guide should be provided in Section 1.2 cover letters. The reviewer's guide is separate and referenced from the cover letter. It should provide a high-level overview (with reference links) of the submission's content and should list the location of information in the eCTD. [33] For example, it should identify where drug, device, and combination product information is located. Additionally, the reviewer's guide should identify the location of information that cannot be further identified within the electronic format. This particularly applies to the following:

   - Documents that are not currently listed as numerical items in ICH and FDA specifications and guidance documents (e.g., *Comprehensive Table of Contents Headings and Hierarchy*[34]). For example, the reviewer's guide should provide reference links to each document in Section 3.2.R.
   - Sections which are repeated through the use of different keywords (e.g. = product name "Albuterol; product name = "Dry Powder Inhaler").

3. Module 1.1. Forms
   Form 356h should identify all facilities involved in the manufacture and testing of the combination product (drug, device, drug-device combination). Also, see item 4.a below for additional information in Section 3.2.P.3 Manufacture

[31] FDA recognizes the breadth of combination product designs. The information in this guide is to promote consistency and facilitate timely review. The agency recommends that applicants, who wish to provide data in a different location, should contact the review division for discussion. Applicants that wish to continue to use a location based on legacy submissions for the same application may continue to use that location.
[32] https://www.fda.gov/media/150309/download
[33] If referencing previously submitted information not in the eCTD format, see Section 3.1.3 of this guide- "Cross Referencing Previously Submitted Information that is not in eCTD Format"
[34] https://www.fda.gov/media/150309/download

4. Module 3

a. Section 3.2.P.3 Manufacture

Combination product manufacturing applies to the entire combination product (e.g., drug –device combination) in accordance with 21 CFR Part 4. [35] In Section 3.2.P.3 include applicable device information pertaining to manufacturing or assembly of the finished combination product as a whole. As applicable, this section may hyperlink to unique device constituent manufacturing information in 3.2.R.

i. Section 3.2.P.3.1 Manufacturer(s)

- For each facility identify the type of manufacturing and testing activities that occur
- For each facility that is subject to 21 CFR part 4, identity whether it follows the combination product streamlined manufacturing approach and identify the base set of regulations (i.e., 21 CFR 211 or 820).
- Provide a detailed list of all manufacturing facilities; what activities occur at the site (e.g., assembly, filling, sterilization, testing, other); what constituents are at the site (e.g., drug only, device only, both drug and device). For the facilities that have both the drug and device, identify which combination product operating system is used at the site.

ii. Section 3.2.P.3.2 Batch Formula (nm, df)

Use this section to describe only the drug components and composition.

iii. Section 3.2.P.3.3 Description of Manufacturing Process and Process Controls (nm, df)

This section would contain any submitted general descriptions/summaries. It may cross-reference to Section 3.2.R to support the manufacturing process.

- Management Controls
- Design Control, General
- Purchasing Controls
- Corrective Action

b. Section 3.2.P.5 Drug Product

Section 3.2.P.5, should usually be an element of a repeated section, as appropriate. The first 3.2.P Drug Product section would be for the drug product (e.g., "midazolam injection"). The second 3.2.P Drug Product section might be for the final combination product lot release specifications that include the specification requirements for the device constituent (e.g. "midazolam pre-filled syringe"). These specifications should rely on the

[35] 21 CFR Part 4 "Current Good Manufacturing Practice Requirements for Combination Products" is accessible at https://www.federalregister.gov/documents/2013/01/22/2013-01068/current-good-manufacturing-practice-requirements-for-combination-products

device design transfer data (see design control information) and should link to the supporting eCTD data section, e.g., in Section 3.2.R.

c. Section 3.2.P.7 Container Closure System

Continue to use this section for devices that serve as primary or secondary container closure. Please refer to FDA guidance on Container Closure for additional information.[36] This section may link to Section 3.2.R as appropriate for device constituent testing.

d. Section 3.2.R Regional Information

This section may be used for device engineering design documentation and narrative explanations that are not otherwise provided in Section 3.2.P.7. Examples of the information include the following:

A. Design Input Requirements
B. Design Output Specifications (e.g., device description, drawings, specifications, bill of materials, etc.)
C. Design Verification Plan/Summary Report and supporting data (e.g., software, electromechanical conformance, bench testing, biocompatibility)
D. Design Validation Plan/Summary Report and supporting data (e.g., performance testing, narrative discussion of the applicability of data provided in Module 5).
E. Risk Management File
F. Traceability Matrix

Note: Section 3.2 R does not provide for subordinate sections. Every file is listed under a common heading. Document titles should be clear, concise and indicative of the document's content. See Section 2.3.4 of this guide for additional information on document titles. In this section, for device related files, each document title should be prefixed with "DEVICE:"

5. Module 5

Human Factors Validation Study results for the combination product should be placed in eCTD Section 5.3.5.4 Other Study Reports with links from appropriate Module 3 files, and include the code for the appropriate human factors document type keywords (e.g., hf validation protocol, hf validation report, hf validation other). The code values for these document type keywords should be provided when the relevant content is submitted.

Additionally, a cross-reference (e.g., hyperlink) of the submission contents from Module 5 to Module 3 may be made, as applicable.

[36] Guidance to Industry: Container Closure Systems for Packaging Human Drugs and Biologics; https://www.fda.gov/regulatory-information/search-fda-guidance-documents/container-closure-systems-packaging-human-drugs-and-biologics

5. APPENDIX A: RULES FOR SUBMISSION TRACKING INFORMATION

The following tables outline the allowable submission tracking information for the submission unit, submission, and application.

Table 2: Submission Type and Descriptions of Use

Submission Type	Submission Unit Types	Valid For Application Types
Original Application	Presubmission Application Amendment Resubmission	IND, NDA, ANDA, BLA, MF, EUA
Efficacy Supplement	Presubmission Application Amendment Resubmission	NDA, BLA
Chemistry Manufacturing Controls Supplement	Presubmission Application Amendment Resubmission	NDA, ANDA, BLA
Labeling Supplement	Presubmission Application Amendment Resubmission	NDA, ANDA, BLA
Annual Report	Report Amendment	IND, NDA, ANDA, BLA, MF
Product Correspondence	Correspondence Amendment	IND, NDA, ANDA, BLA, MF
Postmarketing Requirements or Postmarketing Commitments	Original Amendment	NDA, BLA
Promotional Labeling Advertising	Original Resubmission Amendment	NDA, ANDA, BLA
IND Safety Reports	Report Amendment	IND

Submission Type	Submission Unit Types	Valid For Application Types
Periodic Safety Reports (Periodic Adverse Drug Experience Report (PADER) or Periodic Safety Update Report (PSUR))	Report Amendment	NDA, ANDA, BLA
REMS Supplement	Application Amendment Resubmission	NDA, ANDA, BLA

Table 3: Submission Unit Type and Descriptions of Use

Submission Unit Type	Description	Valid For the Listed Submission Types
Presubmission	A submission to the Agency that occurs prior to the actual submission of a full application (e.g., rolling review, reviewable unit, clinical information that the applicant requests comment on prior to submitting their application). Not all applications will have presubmissions.	Original Application, Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement
Application	The submission that represents the application's primary supportive material. There should only be one submission with a sub-type of application within a given submission group.	Original Application, Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement, REMS Supplement
Amendment	A submission that contains additional supportive material to augment information previously submitted. Examples include responses to information requests, additional draft labeling during negotiations, etc.	Original Application, Efficacy Supplement, Chemistry Manufacturing Controls Supplement, REMS Supplement, Annual Report, Product Correspondence, Postmarketing Requirements or Postmarketing Commitments, Promotional Labeling

Submission Unit Type	Description	Valid For the Listed Submission Types
		Advertising, IND Safety Reports, Periodic Safety Reports (Periodic Adverse Drug Experience Report (PADER) or Periodic Safety Update Report (PSUR)
Resubmission	A submission that contains additional information for the Agency to consider following the issuance of an action communication to the applicant (e.g., complete response or inactivation). For promotional labeling and advertising, the submission of revised promotional materials that were previously submitted as an original submission sub-type. Includes requests for advisory on launch materials, requests for advisory on nonlaunch materials, pre-submission of promotional materials for accelerated approval products, and materials submitted under the Pre-Dissemination Review of Television Ads Program.	Original Application, Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement, REMS Supplement, Promotional Labeling Advertising
Report	A submission that contains a new annual report, IND Safety Report, or Periodic Safety Report (Periodic Adverse Drug Experience Report (PADER) or Periodic Safety Update Report (PSUR)).	Annual Report, IND Safety Reports, Periodic Safety Reports (Periodic Adverse Drug Experience Report (PADER) or Periodic Safety Update Report (PSUR))
Original	Submission of original promotional materials including all promotional labeling and advertising submissions, or Postmarketing Requirements or Postmarketing Commitments	Promotional Labeling Advertising, Postmarketing Requirements or Postmarketing Commitments

Submission Unit Type	Description	Valid For the Listed Submission Types
Correspondence	**Routine:** administrative changes, e.g., change of address, authorized official, or meeting requests. **Donor re-entry request:** An applicant's request to re-enter a deferred donor when regulations and/or guidance do not provide a qualification method or process for their specific situation. (21 CFR 610.41(b)) **License re-issuance:** request from applicant to change legal name. **Lot distribution report:** Postmarketing report required by 21 CFR 600.81 to be submitted every six (6) months upon approval/licensing of vaccine or biologic product. **Final labeling**	Product Correspondence

6. REFERENCES

The following are technical specifications documents incorporated by reference into the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. These documents are located on the FDA eCTD Web page at: https://www.fda.gov/ectd.

1. ICH eCTD v4.0 *Implementation Package* (also accessible at https://www.ich.org/page/ich-electronic-common-technical-document-ectd-v40)

2. FDA technical specification, *FDA eCTD v4.0 Module 1 Implementation Package*

3. FDA guidance for industry, *M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use*

4. ICH M8 technical specification, *eCTD v4.0 IWG Question and Answer and Specification Change Request Document*

5. FDA technical specification, FDA eCTD *v4.0 Table of Contents Headings and Hierarchy*

6. FDA technical specification, *Specifications for File Format Types Using eCTD Specifications*

7. FDA technical specification, *FDA Portable Document Format (PDF) Specifications*

8. FDA guidance for industry, *Integrated Summaries of Effectiveness and Safety: Location Within the Common Technical Document*

9. FDA technical specification, Transmission Specifications, *Specification for Transmitting Electronic Submissions Using eCTD Specifications*

10. FDA technical specification, eCTD Validation Specifications, *Specifications for eCTD v4.0 Validation Criteria*

7. RELATED REFERENCES

The following references are relevant to the content in this document, but are not explicitly referenced.

1. FDA guidance for industry, *Providing Regulatory Submissions in Electronic Format - Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act* (accessible at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs under Electronic Submissions)

2. FDA guidance for industry, *Providing Regulatory Submissions in Electronic Format - Standardized Study Data* (accessible at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs under Electronic Submissions)

3. FDA guidance for industry, *Providing Regulatory Submissions in Electronic Format - Receipt Dates* (accessible at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs under Electronic Submissions)

4. FDA guidance for industry, M4: The CTD - Quality, Questions and Answers/Location Issues *(accessible at* https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs under ICH-Multidisciplinary)

5. FDA guidance for industry, Sponsor Responsibilities—Safety Reporting Requirements and Safety Assessment for IND and Bioavailability/Bioequivalence Studies (accessible at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs under Safety - Issues, Errors, and Problems)