

# Specifications for eCTD v4.0 Validation Criteria

## Table of Contents

<b>1.</b>	<b><i>Common Abbreviations and Terms</i></b> .....	<b>2</b>
<b>2.</b>	<b><i>Specifications for eCTD v4.0 Validation Criteria</i></b> .....	<b>5</b>
<b>3.</b>	<b><i>Summary of eCTD v4.0 Validation Errors</i></b> .....	<b>6</b>
<b>4.</b>	<b><i>eCTD Validation Errors</i></b> .....	<b>15</b>
<b>4.1</b>	<b>eCTD v4.0 XML Message</b> .....	<b>15</b>
<b>4.2</b>	<b>Element Validations</b> .....	<b>16</b>
4.2.1	General.....	16
4.2.2	Submission Unit.....	16
4.2.3	Sequence Number .....	20
4.2.4	Context of Use Priority Number .....	23
4.2.5	Context of Use .....	24
4.2.6	Related Context of Use .....	27
4.2.7	Document Reference.....	28
4.2.8	Keyword.....	29
4.2.9	Submission.....	31
4.2.10	Application.....	35
4.2.11	Applicant.....	39
4.2.12	Application Reference .....	39
4.2.13	Document.....	39
4.2.14	Keyword Definition .....	43
4.2.15	Contact Party.....	46
<b>4.3</b>	<b>Study Data Validation</b> .....	<b>47</b>
<b>4.4</b>	<b>Promotional Materials Submissions</b> .....	<b>51</b>
<b>4.5</b>	<b>Submission Package Validation Rules</b> .....	<b>52</b>
<b>4.6</b>	<b>PDF Validations</b> .....	<b>58</b>

## 1. COMMON ABBREVIATIONS AND TERMS

The following table defines some common terms in this document and specific to eCTD v4.0.

Abbreviation/Term	Definition
CEN	European Committee for Standardization
Class	Class is used in this document to qualify a base level element from the HL7 standard
Context Group	Defines the context of a group of documents with the same Context of Use code and Keyword code combination  Previously known as "Document Group" in eCTD v4.0 Implementation Guide version 1.1
Context of Use code and Keyword code combination	The combination includes both the code and code system for the Context of Use and Keyword in order to define the specific context group under which the documents are grouped
Controlled vocabulary	The collection of terminologies that includes lists of terms that are used to codify terms and/or values to be used in the exchange of information between parties
Datatype	Datatype is used in this document to qualify elements and attributes that come from a datatype in the HL7 standard
Document	Document is used in this document to identify a content file representing a document required or provided to be submitted. In the eCTD v4.0 message a document will be represented by a document element referencing the file location and providing a title. The document element will be presented in its context of use. Since a document can be used multiple times, a Document Reference element allows a document to be specified for the Context of Use. Each time the document is used in the same submission unit, that document may have a different Context of Use. The relationship is provided via the Document Reference element. Accordingly, each Context of Use must reference a document
eCTD	Electronic Common Technical Document
ESTRI	Electronic Standards for the Transfer of Regulatory Information  Content may be found at: <a href="http://estri.ich.org/">http://estri.ich.org/</a>
EWG	Expert Working Group
Forward Compatibility	Refers to converting v3.2.2 content into v4.0 references to achieve life cycle and document reuse

Abbreviation/Term	Definition
HL7	Health Level 7 – International Health Data Standards Development Organisation
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ISO	International Organization for Standardization
IWG	Implementation Working Group
OID	Object Identifiers
Payload	The payload schema is the eCTD v4.0 base and it contains all of the elements in eCTD v4.0, including items from the Common Product Model and Common Message Element schema. It is organised with the following three elements in the structure: <b><i>submissionUnit, submission and application</i></b>
RPS	Regulated Product Submission – HL7 standard
SDO	Standards Development Organisation
URI	Uniform Resource Identifier
UUID	Universally Unique Identifiers
XML	Extensible Markup Language

## Revision History

Date	Version	Summary of Changes
2021-06	1.0	Initial version for eCTD v4.0 and eCTD v3.2.2 Transition Mapping Message.
2022-09	1.1	<p>Revisions to update ICH eCTD v4.0 validation rules to include the following change requests: Unique identifiers (00660), CoU Priority Numbers (00670), Document Reference (00690), Context of Use Code (00700), and Transition Mapping Message (00710).</p> <p>The Transition Mapping Message validations have been removed. In addition, Forward Compatibility validations, and Regional updates to align with eCTD v3.2.2 validations (e.g., 1738) have been added.</p>
2022-10	1.2	Added Regional Validation Rule US-eCTD4-557.
2024-06	1.3	<p>Added ICH Validation Rules eCTD4-080, eCTD4-081, eCTD4-082, eCTD4-083.</p> <p>Added Regional Validation Rules US-eCTD4-524, US-eCTD4-558, US-eCTD4-559.</p> <p>Removed Regional Validation Rule US-eCTD4-557 (replaced by eCTD4-082).</p>
2024-09	1.3.1	<p>Added Effective Date to Supported validations and TBD to validations added in version 1.3.</p> <p>Added Regional Validation Rule US-eCTD4-557 to show all supported validations.</p>
2025-02	1.4	<p>Added Effective Date to Supported ICH and Regional Validations Rules added in version 1.3 eCTD4-080, eCTD4-081, eCTD4-082, eCTD4-083, US-eCTD4-524, US-eCTD4-558, US-eCTD4-559.</p> <p>Removed Regional Validation Rule US-eCTD4-557 (replaced by eCTD4-082).</p>
2025-10	1.5	Added Validations Rules US-eCTD4-560, US-eCTD4-561, US-eCTD4-562, US-eCTD4-563

## 2. SPECIFICATIONS FOR eCTD v4.0 VALIDATION CRITERIA

These specifications detail the validation criteria applied when FDA processes eCTD v4.0 submissions. They provide a description of the error, an explanation of the error, the corrective steps necessary to correct the error and the severity level that has been assigned to the error.

### Severity Levels

The severity levels outline the impact on the official receipt of your submissions.

Severity	Description
<b>High Error</b>	The error is a serious technical error which prevents the processing of the submission and will require resubmission. The submission is considered not received by FDA.
<b>Warning</b>	The error may impact the reviewability of the submission but cannot be determined without further inspection by the review staff. The submission will likely be considered received by FDA.

### Validation Rule Categories

Category	Description
Schema	The validation is based on rules that are found in the schema.
Business Rule	The validation is based on business rules for the data element.

### 3. SUMMARY OF ECTD v4.0 VALIDATION ERRORS

Type/Element	Number	Severity Description	Validation Criteria
<a href="#"><u>XML Message</u></a>	eCTD4-001	High Error	Message must be Well Formed XML based on XML 1.0
	eCTD4-002	High Error	Message must be valid against the ICH specified version of the RPS schema
<a href="#"><u>General</u></a>	US-eCTD4-501	Warning	Descriptions should adhere to character limits
	US-eCTD4-558	High Error	Message Header contains US Regional IG OID
<a href="#"><u>Submission Unit</u></a>	eCTD4-003	High Error	Submission Unit identifier is required (1..1)
	eCTD4-004	High Error	Submission Unit id root must be a UUID
	eCTD4-005	High Error	Only one Submission Unit element can exist for a message
	eCTD4-006	High Error	Submission Unit code value is required (1..1)
	eCTD4-007	High Error	Submission Unit must have a valid code value
	eCTD4-008	High Error	Submission Unit Code System value is required (1..1)
	eCTD4-009	High Error	Submission Unit code must have a valid OID for the Code System value
	eCTD4-010	High Error	The Submission Unit status code requires the code attribute value "active"
	eCTD4-011	High Error	The Submission Unit must have at least one Context of Use element in the message
	US-eCTD4-502	High Error	Submission Unit Type is valid for the submission/regulatory activity
	US-eCTD4-560	Warning	Submission Unit Type is unique in the application for the regulatory activity
<a href="#"><u>Sequence Number</u></a>	eCTD4-012	High Error	Sequence Number is required (1..1)
	eCTD4-013	High Error	Sequence Number must be a whole number between 1 and 999999
	eCTD4-014	High Error	Sequence Number for initial submission unit in the application starts with the value of "1"

Type/Element	Number	Severity Description	Validation Criteria
	eCTD4-015	High Error	Sequence Number is unique in the application for the applicant
	eCTD4-016	High Error	The Sequence Number must have one and only one value for the Submission element
	US-eCTD4-503	High Error	Sequence number matches the sequence number folder name
	US-eCTD4-504	High Error	More than one sequence number value is referenced for the same application number
<a href="#"><u>Context of Use Priority Number</u></a>	eCTD4-017	High Error	Context of Use Priority Number is required
	eCTD4-018	High Error	Context of Use Priority Number must be a whole number between 1 and 999999
	eCTD4-019	High Error	Context of Use Priority Number shall have one and only one value
	US-eCTD4-505	Warning	Context of Use Priority Number is a duplicate for the context group
<a href="#"><u>Context of Use</u></a>	eCTD4-020	High Error	Context of Use identifier is required
	eCTD4-021	High Error	Context of Use id root must be a unique identifier
	eCTD4-075	High Error	Context of Use code must be valid for the referenced code system
	eCTD4-022	High Error	Context of Use status code element is required
	eCTD4-023	High Error	Context of Use status code value can only be "active" or "suspended"
	eCTD4-080	High Error	A Context of Use identifier or v3.2.2 Leaf Reference must already exist when using the status code of "suspended"
	eCTD4-081	High Error	Context of Use code system is a valid OID
<a href="#"><u>Related Context of Use</u></a>	eCTD4-024	High Error	Related Context Of Use identifier is required when Related Context Of Use is provided
	eCTD4-025	High Error	Context of Use and Related Context of Use referenced must have the same Context of Use code and Keyword code combination (or matching v3.2.2 equivalents)
	eCTD4-026	High Error	Related Context of Use id root can only reference previously submitted active Context of Use identifiers or v3.2.2 Leaf Reference

Type/Element	Number	Severity Description	Validation Criteria
<a href="#"><u>Document Reference</u></a>	eCTD4-027	High Error	Document Reference identifier is required for all active new Context of Use elements
	eCTD4-028	High Error	Document Reference element not allowed for suspended Context of Use elements
	eCTD4-076	High Error	Document referenced in the CoU must exist
<a href="#"><u>Keyword</u></a>	eCTD4-029	High Error	Keyword code is required for each keyword element on a Context of Use
	eCTD4-030	High Error	Keyword code system attribute is required for each keyword element
	eCTD4-031	High Error	Keyword code system must be a valid OID
	eCTD4-032	High Error	Keyword code system must have a valid value
	eCTD4-070	High Error	Required keywords for a Context of Use code attribute must be included
	eCTD4-071	High Error	The Keyword Type must be valid for the Context of Use heading
	eCTD4-072	High Error	On each Context of Use element, a valid Keyword Type shall only be used once
<a href="#"><u>Submission</u></a>	eCTD4-033	High Error	Submission identifier is required (1..1)
	eCTD4-077	High Error	Submission identifier is a UUID
	eCTD4-034	High Error	Submission code is required (1..1)
	eCTD4-035	High Error	Submission code must have a valid value for the region
	eCTD4-036	High Error	Submission code system attribute is required (1..1)
	eCTD4-037	High Error	Submission code system must have a valid regional code system OID
	US-eCTD4-506	High Error	The submission identifier referenced is valid
	US-eCTD4-507	High Error	All grouped submission submission-type values are the same
	US-eCTD4-508	High Error	Submission-type is valid for application-type
	US-eCTD4-561	High Error	All submission-type values are the same for all sequences within a regulatory activity



Type/Element	Number	Severity Description	Validation Criteria
	US-eCTD4-562	High Error	The submission identifier that starts a new regulatory activity must be unique in the application
	US-eCTD4-563	Warning	All sequences within a regulatory activity should reference the same unique submission identifier
<a href="#"><u>Application</u></a>	eCTD4-038	High Error	Application identifier is required (1..1)
	eCTD4-039	High Error	Application code is required
	eCTD4-040	High Error	Application code must have a valid value
	eCTD4-041	High Error	Application code system is required
	eCTD4-042	High Error	Application code system is a valid OID
	US-eCTD4-509	High Error	All grouped application type values must be the same
	US-eCTD4-510	High Error	Application number must contain 6 digits only
	US-eCTD4-511	High Error	Application number in the FDA form matches the application number in submissionunit.xml
	US-eCTD4-512	High Error	Correct application form is submitted
<a href="#"><u>Applicant</u></a>	US-eCTD4-513	Warning	Company Name is missing
<a href="#"><u>Application Reference</u></a>	US-eCTD4-514	Warning	Application number referenced should include the application prefix and 6-digit value
<a href="#"><u>Document</u></a>	eCTD4-043	High Error	Document identifier is required (1..1)
	eCTD4-044	High Error	Document identifier must have a valid value
	eCTD4-045	High Error	Document id root must be a UUID
	eCTD4-046	High Error	Document identifier is unique (i.e., it is not a duplicate identifier and not an update to a document title)

Type/Element	Number	Severity Description	Validation Criteria
	eCTD4-047	High Error	Document title is required
	eCTD4-048	High Error	Document text element requires a checksum value unless a document title update is submitted (i.e., this is the only scenario making this element optional)
	eCTD4-049	High Error	Document text element requires a valid checksum value unless a document title update is submitted (i.e., this is the only scenario making this element optional)
	eCTD4-050	High Error	Document path is required
	eCTD4-051	High Error	Document path must exist
	eCTD4-082	High Error	Document identifier must be referenced by a CoU
<u>Keyword Definition</u>	eCTD4-052	High Error	Keyword definition code is required (1..1)
	eCTD4-053	High Error	Keyword definition code must have a valid value
	eCTD4-054	High Error	Keyword definition value code is required (1..1)
	eCTD4-055	High Error	Keyword definition value code must have a valid value
	eCTD4-056	High Error	Keyword definition value is required (1..1)
	eCTD4-057	High Error	Keyword definition value has one and only one <i>value.item</i> element
	eCTD4-058	High Error	Keyword definition display name value is required
	eCTD4-068	High Error	Keyword definition display name value is as previously submitted
	eCTD4-073	High Error	The Keyword Definition for a Study Id and Study Title (ich_keyword_type_8) must follow the correct format
	eCTD4-078	High Error	Keyword definition must exist and match v3.2.2 value
	eCTD4-083	High Error	Keyword Definition code system is a <u>valid OID</u>
<u>Contact Party</u>	US-eCTD4-515	Warning	Email address is greater than 64 characters

Type/Element	Number	Severity Description	Validation Criteria
	US-eCTD4-524	Warning	A regulatory contact should be provided for new regulatory activities
	US-eCTD4-559	Warning	Contact Party type is unique for each Contact Person
<a href="#">Study Data</a>	US-eCTD4-516	High Error	A dataset named ts.xpt with information on study start date must be present for each study in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4, and in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
	US-eCTD4-517	High Error	The correct document type must be used for all standardized datasets and corresponding define.xml files in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4, and in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
	US-eCTD4-518	High Error	For Standard for Exchange of Nonclinical Data (SEND) data, a Demographic (DM) dataset and define.xml must be submitted in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4  For Study Data Tabulation Model (SDTM) data, a DM dataset and define.xml must be submitted Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2  For Analysis Data Model (ADaM) data, an ADaM Subject level analysis dataset (ADSL) dataset and define.xml must be submitted in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
	US-eCTD4-519	Warning	For each study referenced in Module 4 and Module 5, no more than one dataset of the same file name and document title should be submitted using the Context of Use status code value “active”
	US-eCTD4-554	Warning	Study Id in the Study Id and Study Title Keyword Definition should match STUDYID or SPREFID listed in the referenced Trial Summary (ts.xpt) file
	US-eCTD4-555	Warning	Only one Study Id and Study Title Keyword code under the same eCTD heading should have the same Study Id

Type/Element	Number	Severity Description	Validation Criteria
<a href="#"><u>Promotional Material Submissions</u></a>	US-eCTD4-520	High Error CDER	A 2253 submission does not include the most current Product Labeling which must be submitted in section 1.14.6
	US-eCTD4-521	High Error CDER	The only valid FDA Form to include in a Promotional Labeling Submission is a 2253
	US-eCTD4-522	Warning	The Keyword code for issue-date is missing
	US-eCTD4-523	Warning	Promotional Material Issue Date Format is incorrect
<a href="#"><u>Submission Package</u></a>	eCTD4-059	High Error	Submission Unit file is named submissionunit.xml exists
	eCTD4-060	High Error	Checksum file named sha256.txt exists
	eCTD4-061	High Error	Only one Submission Unit file is allowed
	eCTD4-062	High Error	Submission Unit checksum file value is valid
	eCTD4-063	High Error	Submission Unit File is found in sequence number folder
	eCTD4-064	High Error	Document checksum value is valid
	eCTD4-065	High Error	File name length is met
	eCTD4-066	High Error	Folder name length is met
	eCTD4-067	High Error	Folder path length is met
	eCTD4-074	High Error	The folder path value only contains the allowable special characters
	eCTD4-069	High Error	Unassociated file found
	US-eCTD4-525	High Error	Submission is not an eCTD
	US-eCTD4-526	High Error	Fillable form not included
	US-eCTD4-527	Warning	File does not contain a valid file extension

Type/Element	Number	Severity Description	Validation Criteria
	US-eCTD4-528	Warning	Folder contains no files or sub folders
	US-eCTD4-556	High Error	Grouped submission contains at least one file to identify the primary application
<a href="#">PDF</a>	US-eCTD4-529	Warning	Failed to process PDF contents
	US-eCTD4-530	Warning	Non-standard font (not embedded)
	US-eCTD4-531	Warning	PDF security used
	US-eCTD4-532	Warning	PDF version of document is incorrect
	US-eCTD4-533	Warning	PDF does not have 'Fast Web View' enabled
	US-eCTD4-534	Warning	PDF opening settings not optimal
	US-eCTD4-535	Warning	Document has password protection
	US-eCTD4-536	Warning	Document has annotations
	US-eCTD4-537	Warning	Document is an image and contains no text
	US-eCTD4-538	Warning	Broken bookmark
	US-eCTD4-539	Warning	Corrupt bookmark
	US-eCTD4-540	Warning	Bookmark has non-existent named destination or page

Type/Element	Number	Severity Description	Validation Criteria
	US-eCTD4-541	Warning	Multiple action bookmark
	US-eCTD4-542	Warning	External bookmark
	US-eCTD4-543	Warning	Inactive bookmark
	US-eCTD4-544	Warning	Non-relative bookmark
	US-eCTD4-545	Warning	Bookmark does not 'Inherit Zoom'
	US-eCTD4-546	Warning	Broken hyperlink
	US-eCTD4-547	Warning	Corrupt link
	US-eCTD4-548	Warning	Link has non-existent named destination or page
	US-eCTD4-549	Warning	Multiple action hyperlink
	US-eCTD4-550	Warning	External hyperlink
	US-eCTD4-551	Warning	Inactive hyperlink
	US-eCTD4-552	Warning	Non-relative hyperlink
	US-eCTD4-553	Warning	Link does not 'Inherit Zoom'

#### 4. ECTD VALIDATION ERRORS

The validation rules are organized by the type of validation or data elements.

##### 4.1 eCTD v4.0 XML Message

<b>Number:</b>	eCTD4-001
<b>Group:</b>	XML Message
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Message must be Well Formed XML based on XML 1.0
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The XML is not well-formed according to the version of the XML standard
<b>Corrective Action:</b>	The XML must be corrected to become well-formed
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-002
<b>Group:</b>	XML Message
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Message must be valid against the ICH specified version of the RPS schema
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The message is not valid against the current ICH specified version of the RPS schema
<b>Corrective Action:</b>	The XML should be corrected to meet the schema validations
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

## 4.2 Element Validations

### 4.2.1 General

<b>Number:</b>	US-eCTD4-501
<b>Group:</b>	General
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Descriptions should adhere to character limits
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Submission unit title (128 character limit), document title (512 character limit) or keyword definition display name (512 character limit) exceeds character limits and was truncated
<b>Corrective Action:</b>	Ensure future submissions do not have a description values that exceed the character limits
<b>Guidance Source:</b>	FDA eCTD v4.0 Technical Conformance Guide

<b>Number:</b>	US-eCTD4-558
<b>Group:</b>	General
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Message Header contains US Regional IG OID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	02/18/2025
<b>Problem/Issue:</b>	Submission Unit does not include a US Regional IG OID
<b>Corrective Action:</b>	Resubmit to include US Regional IG OID
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

### 4.2.2 Submission Unit

<b>Number:</b>	eCTD4-003
<b>Group:</b>	Submission Unit
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Submission Unit identifier is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submissionUnit.id@root</i> is not provided



<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the element and a value for <i>id@root</i> for the submission unit
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-004
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit id root must be a UUID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submissionUnit.id@root</i> is not a UUID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the Submission Unit UUID
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-005
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Only one Submission Unit element can exist for a message
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The message has more than one submission unit element in the message payload
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with only one submission unit element included
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-006
<b>Group:</b>	Submission Unit
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Submission Unit code value is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submissionUnit.code@code</i> value is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a code value
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-007
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit must have a valid code value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submissionUnit.code@code</i> is not a valid value (for the region)
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid code value <b>Regional Note:</b> Refer to the US Submission Unit code value set
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-008
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit Code System value is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submissionUnit.code@codeSystem</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid code value <b>Regional Note:</b> Refer to the US Submission unit code system OID
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-009
<b>Group:</b>	Submission Unit
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Submission Unit code must have a valid OID for the Code System value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submissionUnit.code@codeSystem</i> is not a valid registered or known OID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid code system OID

	<b>Regional Note:</b> Refer to the US Submission unit code value set for the code system OID
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-010
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The Submission Unit status code requires the code attribute value "active"
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The submission unit does not have a status code value of active
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with an active status code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-011
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The Submission Unit must have at least one Context of Use element in the message
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The submission unit does not have any Context of Use elements
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with at least one Context of Use element
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-502
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit Type is valid for the submission/regulatory activity
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	A Submission Unit Type code was submitted that is not allowed for the submission/regulatory activity and/or application

<b>Corrective Action:</b>	Resubmit the Submission Unit using a valid code for the submission unit type. You may resubmit using the same sequence number of the submission
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide FDA eCTD v4.0 Technical Conformance Guide

<b>Number:</b>	US-eCTD4-560
<b>Group:</b>	Submission Unit
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit Type is unique in the application for the regulatory activity
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	TBD
<b>Problem/Issue:</b>	The submission unit type was provided in a previous submission to the same regulatory activity. Certain submission unit types (application, original, report, correspondence) can only be submitted once for each regulatory activity.
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that the submission unit types which should only be used once for each regulatory activity, are not used again for subsequent submissions to the same regulatory activity.
<b>Guidance Source:</b>	General good practice to ensure reviewability

#### 4.2.3 Sequence Number

<b>Number:</b>	eCTD4-012
<b>Group:</b>	Sequence Number
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Sequence Number is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The sequence number value is not provided
<b>Corrective Action:</b>	The submission unit may need to be resubmitted with a sequence number
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-013
<b>Group:</b>	Sequence Number
<b>Category:</b>	Business Rule

<b>Validation Criteria/Description:</b>	Sequence Number must be a whole number between 1 and 999999
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The sequence number value is not a whole number between 1 and 999999
<b>Regional Note:</b>	The sequence number must be a whole number with no leading zeros
<b>Corrective Action:</b>	The submission unit may need to be resubmitted with a sequence number value between 1 and 999999
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-014
<b>Group:</b>	Sequence Number
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Sequence Number for initial submission unit in the application starts with the value of "1"
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The sequence number for the initial submission unit in an application is not the value "1"
<b>Corrective Action:</b>	The initial submission unit needs to be resubmitted with the sequence number value of 1
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-015
<b>Group:</b>	Sequence Number
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Sequence Number is unique in the application for the applicant
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The sequence number is not unique in a submission/application
<b>Corrective Action:</b>	The submission unit needs to be resubmitted to make the sequence number unique for the application
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-016
<b>Group:</b>	Sequence Number
<b>Category:</b>	Business Rule

<b>Validation Criteria/Description:</b>	The Sequence Number must have one and only one value for the Submission element
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The Sequence Number does not have one and only one value for each Submission in the submission unit
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a value. The submission unit needs to be resubmitted to be different than the values that exist for the submission/application
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-503
<b>Group:</b>	Sequence Number
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Sequence number matches the sequence number folder name
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The sequence number used in your submissionunit.xml file does not match the sequence number folder name in the physical folder directory sent in the submission package
<b>Corrective Action:</b>	Resubmit your submission unit ensuring that the sequence number used in your submissionunit.xml file matches the sequence number folder name in the physical folder directory sent in the submission package
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-504
<b>Group:</b>	Sequence Number
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	More than one sequence number value is referenced for the same application number
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	A different sequence number was referenced in the same application of a grouped submission
<b>Corrective Action:</b>	Resubmit and use the same sequence number for each submission within each of the applications in the group
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

#### 4.2.4 Context of Use Priority Number

<b>Number:</b>	eCTD4-017
<b>Group:</b>	Priority Number
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Context of Use Priority Number is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The priority number value is not provided
<b>Corrective Action:</b>	The submission unit would need to be resubmitted providing priority numbers
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-018
<b>Group:</b>	Priority Number
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Context of Use Priority Number must be a whole number between 1 and 999999
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The priority number value is not a whole number between 1 and 999999
<b>Corrective Action:</b>	The submission unit would need to be resubmitted with for the priority number value between 1 and 999999
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-019
<b>Group:</b>	Priority Number
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Context of Use Priority Number shall have one and only one value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	There is more than one Context of Use priority number provided for each Context of Use
<b>Corrective Action:</b>	The submission unit would need to be resubmitted providing priority numbers one priority number for each Context of Use element

<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide
-------------------------	------------------------------------

<b>Number:</b>	US-eCTD4-505
<b>Group:</b>	Priority Number
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Context of Use Priority Number is a duplicate for the context group
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The Context of Use priority number matches an existing value for the context group and defaults to the most recent sequence values first and then alphabetically by document title
<b>Corrective Action:</b>	Ensure the priority number assignment within a context group is not duplicated in future sequences
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

#### 4.2.5 Context of Use

<b>Number:</b>	eCTD4-020
<b>Group:</b>	Context of Use
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Context of Use identifier is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>contextOfUse.id@root</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a value for the Context of Use identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-021
<b>Group:</b>	Context of Use
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Context of Use id root must be a unique identifier
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024



<b>Problem/Issue:</b>	The <i>contextOfUse.id@root</i> value is not a UUID or combination of namespace OID and local value for the namespace
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a Context of Use unique identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-075
<b>Group:</b>	Context of Use
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Context of Use code must be valid for the referenced code system
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Context of Use code is not a valid value for the referenced code system
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a value for the Context of Use code for the referenced code system
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-022
<b>Group:</b>	Context of Use
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Context of Use status code element is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>contextofUse.statusCode</i> element is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a status code for each Context of Use
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-023
<b>Group:</b>	Context of Use
<b>Category:</b>	Schema

<b>Validation Criteria/Description:</b>	Context of Use status code value can only be "active" or "suspended"
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>contextOfUse.statusCode@code</i> value is not "active" or "suspended"
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid status code value for the Context of Use
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-080
<b>Group:</b>	Context of Use
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	A Context of Use identifier or v3.2.2 Leaf Reference must already exist when using the status code of “suspended”
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	02/18/2025
<b>Problem/Issue:</b>	The Context of Use identifier or v3.2.2 Leaf Reference is not found in a previous submission unit
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing an existing value for the Context of Use identifier or v3.2.2 Leaf Reference
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-081
<b>Group:</b>	Context of Use
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Context of Use code system is a valid OID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	02/18/2025
<b>Problem/Issue:</b>	The <i>contextOfUse.code@codeSystem</i> is not a valid registered or known OID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid context of use code system
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

#### 4.2.6 Related Context of Use

<b>Number:</b>	eCTD4-024
<b>Group:</b>	Related Context of Use
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Related Context Of Use identifier is required when Related Context of Use is provided
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>relatedContextOfUse.id@root</i> attribute is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a Related Context of Use identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-025
<b>Group:</b>	Related Context of Use
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Context of Use and Related Context of Use referenced must have the same Context of Use code and Keyword code combination (or matching v3.2.2 equivalents)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>contextOfUse.code@code</i> and <i>keyword.code@code</i> combination (or matching v3.2.2 equivalents) does not match the previous Context of Use referenced in the related Context of Use
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with corrections to resolve the inaccurate use of related Context of Use
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-026
<b>Group:</b>	Related Context of Use
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Related Context of Use id root can only reference previously submitted active Context of Use identifiers or v3.2.2 Leaf Reference
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024

<b>Problem/Issue:</b>	The <i>relatedContextOfUse.id@root</i> does not reference a previously submitted active Context of Use identifier or Leaf Reference, or identifier or Leaf Reference does not exist or is not allowed by the Region
<b>Corrective Action:</b>	The submission unit needs to be resubmitted referencing a previous Context of Use or Leaf Reference
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

#### 4.2.7 Document Reference

<b>Number:</b>	eCTD4-027
<b>Group:</b>	Document Reference
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document Reference identifier is required for all active new Context of Use elements
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>documentReference.id@root</i> attribute is not provided when the new Context of Use is active
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a Document Reference identifier when the new Context of Use is active
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-028
<b>Group:</b>	Document Reference
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Document Reference element not allowed for suspended Context of Use elements
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>documentReference</i> element is provided when the Context of Use is suspended
<b>Corrective Action:</b>	The submission unit needs to be resubmitted without a Document Reference when the Context of Use is suspended
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-076
<b>Group:</b>	Document Reference
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document referenced in the CoU must exist

<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The document referenced in the CoU cannot be found
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with an existing v4.0 document identifier or v3.2.2 Leaf Reference
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

#### 4.2.8 Keyword

<b>Number:</b>	eCTD4-029
<b>Group:</b>	Keyword
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Keyword code is required for each keyword element on a Context of Use
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keyword.code@code</i> attribute is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a Keyword code for each <i>keyword</i> element on a Context of Use
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-030
<b>Group:</b>	Keyword
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Keyword code system attribute is required for each keyword element
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keyword.code@codeSystem</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a Keyword code system for each Keyword code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-031
<b>Group:</b>	Keyword
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword code system must be a valid OID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024

<b>Problem/Issue:</b>	The <i>keyword.code@codeSystem</i> is not a valid registered or known OID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid keyword code system
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-032
<b>Group:</b>	Keyword
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword code system must have a valid value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keyword.code@code</i> is not part of the external controlled vocabulary or defined in the application's keyword definitions
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid code system for the keyword code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-070
<b>Group:</b>	Keyword
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Required keywords for a Context of Use code attribute must be included
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	A required <i>keyword.code@code</i> is not submitted for the Context of Use heading
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with all required keywords for the Context of Use
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-071
<b>Group:</b>	Keyword
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The Keyword Type must be valid for the Context of Use heading
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024

<b>Problem/Issue:</b>	The Keyword code value(s) <i>contextOfUse.code</i> submitted for the Context of Use heading is (are) invalid for the eCTD heading
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with valid keyword types for the Context of Use
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-072
<b>Group:</b>	Keyword
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	On each Context of Use element, a valid Keyword Type shall only be used once
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The same Keyword type has been used more than once for the Context of Use element
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with only one Keyword of the same Keyword type for each Context of Use
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

#### 4.2.9 Submission

<b>Number:</b>	eCTD4-033
<b>Group:</b>	Submission
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Submission identifier is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submission.id.item@root</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a submission identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-077
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission identifier is a UUID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024

<b>Problem/Issue:</b>	The <i>submission.id.item@root</i> is not a UUID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a Submission UUID
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-034
<b>Group:</b>	Submission
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Submission code is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submission.code@code</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a Submission code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-035
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission code must have a valid value for the region
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submission.code@code</i> is not a valid value
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with valid Submission code
	<b>Regional Note:</b> Refer to the US Submission code value set
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-036
<b>Group:</b>	Submission
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Submission code system attribute is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submission.code@codeSystem</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a Submission code system
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide



<b>Number:</b>	eCTD4-037
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission code system must have a valid regional code system OID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>submission.code@codeSystem</i> is not a valid, registered or known OID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid Submission code system <b>Regional Note:</b> Refer to the US Submission code system OID
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-506
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The submission identifier referenced is valid
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The submission identifier must be received or processed before any subsequent submission units (e.g., amendments, resubmissions) may be received or processed for the regulatory activity
<b>Corrective Action:</b>	Submit the referenced submission first before using it as a submission identifier in future submissions or follow the instructions for the submission identifier for open regulatory activities
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-507
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	All grouped submission submission-type values are the same
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024

<b>Problem/Issue:</b>	More than one submission element is submitted in the submission unit and the submission-type code values are not the same for all submissions in the group
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the same submission-type code value for all submission elements in the submissionunit.xml. You may resubmit using the original sequence number of the submission
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-508
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission-type is valid for application-type
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	A submission-type value was submitted that is not allowed for the application type
<b>Corrective Action:</b>	Resubmit the submission unit using a valid submission-type value for that application. You may resubmit using the same sequence number for the submission
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide FDA eCTD v4.0 Technical Conformance Guide

<b>Number:</b>	US-eCTD4-561
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	All submission-type values are the same for all sequences within a regulatory activity
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	TBD
<b>Problem/Issue:</b>	A submission-type value was submitted that is not the same as the submission-type value of the referenced regulatory activity
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the same submission-type code value for the regulatory activity. You may resubmit using the original sequence number of the submission
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-562
----------------	--------------

<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The submission identifier that starts a new regulatory activity must be unique in the application
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	TBD
<b>Problem/Issue:</b>	The submission identifier value referenced has already been submitted for an existing regulatory activity in the application and the submission unit type indicates the start of a new regulatory activity.
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a unique submission identifier value for the regulatory activity. You may resubmit using the original sequence number of the submission
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-563
<b>Group:</b>	Submission
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	All sequences within a regulatory activity must reference the same unique submission identifier. The v3.2.2 sequence number should only be submitted to the first eCTD v4.0 submission for the open regulatory activity.
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	TBD
<b>Problem/Issue:</b>	The submission unit type indicates the continuation of a regulatory activity and needs to reference the submission identifier already used to start this regulatory activity.
<b>Corrective Action:</b>	Ensure that the submission identifier that correctly references a regulatory activity is used in a subsequent submissions to that regulatory activity.
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

#### 4.2.10 Application

<b>Number:</b>	eCTD4-038
<b>Group:</b>	Application
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Application identifier is required (1..1)
<b>Severity Description:</b>	High Error

<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>application.id.item@root</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with an application identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-039
<b>Group:</b>	Application
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Application code is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>application.code@code</i> attribute is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing an Application code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-040
<b>Group:</b>	Application
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Application code must have a valid value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>application.code@code</i> is not a valid value
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid Application code value
	<b>Regional Note:</b> Refer to the US Application code value set
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-041
<b>Group:</b>	Application
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Application code system is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>application.code@codeSystem</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing an Application code system

<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide
-------------------------	------------------------------------

<b>Number:</b>	eCTD4-042
<b>Group:</b>	Application
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Application code system is a valid OID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>application.code@codeSystem</i> is not a valid OID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid Application code system  <b>Regional Note:</b> Refer to the US Application code value system OID
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-509
<b>Group:</b>	Application
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	All grouped application type values must be the same
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have referenced more than one application and the application type values are not the same
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the same application-type for all applications referenced in the submissionunit.xml. You may resubmit using the same sequence number for the submission unit
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-510
<b>Group:</b>	Application
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Application number must contain 6 digits only
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>application.id.item@extension</i> attribute value must be 6 digits only

<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a properly formatted application number. You may resubmit using the same sequence number for the application
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-511
<b>Group:</b>	Application
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Application number in the FDA form matches the application number in submissionunit.xml
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Application number in the FDA form does not match <i>application.id.item@extension</i> attribute value in submissionunit.xml
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the corrected application number in the FDA form and submissionunit.xml file
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-512
<b>Group:</b>	Application
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Correct application form is submitted
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	<p>The wrong application FDA form based on form code was submitted based on your Application type in the <i>application.code@code</i> attribute value</p> <p>For example, a context of use with the form-type keyword for a 1571 was submitted for an application type NDA, or a context of use with form type 356h was submitted for an IND</p>
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the correct application form keyword. Please modify your SOPs to ensure that your submission has the correct type of form correctly named, and it is referenced in the correct eCTD location
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

#### 4.2.11 Applicant

<b>Number:</b>	US-eCTD4-513
<b>Group:</b>	Applicant
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Company Name is missing
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have omitted the company name in the <i>applicant.sponsoringOrganization.name.part@value</i> attribute in the submissionunit.xml file
<b>Corrective Action:</b>	No corrective action is necessary unless FDA notifies you that it is unable to process your submission
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

#### 4.2.12 Application Reference

<b>Number:</b>	US-eCTD4-514
<b>Group:</b>	Application Reference
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Application number referenced should include the application prefix and 6-digit value
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>extension</i> value does not include a case-sensitive (specifically uppercase) application type prefix (e.g., IND, MF, etc.) and the assigned value (e.g., 6 digits) for the application number being referenced
<b>Corrective Action:</b>	Update the application reference in the next sequence of the regulatory activity
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

#### 4.2.13 Document

<b>Number:</b>	eCTD4-043
<b>Group:</b>	Document
<b>Category:</b>	Schema
<b>Validation Criteria/Description:</b>	Document identifier is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024

<b>Problem/Issue:</b>	The <i>document.id@root</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a Document identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-044
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document identifier must have a valid value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The Document identifier is not a valid value
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a corrected valid Document identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-045
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document id root must be a UUID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>document.id@root</i> value is not a UUID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a Document UUID
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-046
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document identifier is unique (i.e., it is not a duplicate identifier and not an update to a document title)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The Document identifier value is not unique
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a correction to the unique identifier
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide



<b>Number:</b>	eCTD4-047
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document title is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>document.title@value</i> does not have a value or does not exist
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a corrected document title value for all documents
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-048
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document text element requires a checksum value unless a document title update is submitted (i.e., this is the only scenario making this element optional)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>document.text.integrityCheck</i> value is not provided for the document element
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a checksum value for all documents
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-049
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document text element requires a valid checksum value unless a document title update is submitted (i.e., this is the only scenario making this element optional)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>document.text.integrityCheck</i> value is not a valid checksum
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid checksum value for all documents
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-050
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document path is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>document.text.reference@value</i> value is not provided, and the <i>updateMode</i> value is not present indicating a document title change
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a document path for all documents
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-051
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document path must exist
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The document path provided in the eCTD XML (i.e., <i>reference</i> element is present) does not physically exist
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a correct document path
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide eCTD v4.0 Comprehensive Table of Contents Headings and Hierarchy

<b>Number:</b>	eCTD4-082
<b>Group:</b>	Document
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document identifier must be referenced by a CoU
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	02/18/2025
<b>Problem/Issue:</b>	A new Document in the submissionUnit.xml is not referenced by a CoU within that submissionUnit.xml
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with all new document objects referenced by a CoU

<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide
-------------------------	------------------------------------

#### 4.2.14 Keyword Definition

<b>Number:</b>	eCTD4-052
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition code is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keywordDefinition.code@code</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a keyword definition code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-053
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition code must have a valid value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keywordDefinition.code@code</i> is not a valid value
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid keyword definition code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-054
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition value code is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keywordDefinition.value.item@code</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a keyword definition value code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-055
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition value code must have a valid value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keywordDefinition.value.item@code</i> is not a valid value
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid keyword definition value code
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-056
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition value is required (1..1)
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keywordDefinition.value</i> element is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid keyword definition value
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-057
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition value has one and only one <i>value.item</i> element
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	More than one <i>keywordDefinition.value.item</i> element is provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a one <i>value.item</i> element per keyword definition value
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-058
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule

<b>Validation Criteria/Description:</b>	Keyword definition display name value is required
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keywordDefinition.value.item.displayName@value</i> is not provided
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing a <i>keywordDefinition.value.item.displayName@value</i>
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-068
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition display name value is as previously submitted
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>keywordDefinition.value.item.displayName@value</i> provided does not match the value previously submitted value and the <i>updateMode</i> is not present
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing the <i>keywordDefinition.value.item.displayName@value</i> with update mode to make a change to the keyword definition's display name value
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-073
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The Keyword Definition for a Study Id and Study Title (ich_keyword_type_8) must follow the correct format
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	A Keyword Definition with <i>keywordDefinition.code@code</i> value of ich_keyword_type_8 does not have the <i>keywordDefinition.value.item.displayName@value</i> formatted as studyID_\$studyTitle
<b>Corrective Action:</b>	The Submission unit needs to be resubmitted providing the correct format for all Keyword Definition for the Study Id and Study Title
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-078
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword definition must exist and match v3.2.2 value
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The <i>displayName</i> value of the Keyword Definition element does not exist or match the v3.2.2 value
<b>Corrective Action:</b>	The submission unit needs to be resubmitted providing the exact v3.2.2 values for the eCTD v4.0 keyword definition display name
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-083
<b>Group:</b>	Keyword Definition
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Keyword Definition code system is a valid OID
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	02/18/2025
<b>Problem/Issue:</b>	The <i>keywordDefinition.code@codeSystem</i> is not a valid registered or known OID
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid keyword definition code code system
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

#### 4.2.15 Contact Party

<b>Number:</b>	US-eCTD4-515
<b>Group:</b>	Contact Party
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Email address is greater than 64 characters
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The email address exceeds the character limit
<b>Corrective Action:</b>	Resend the email address within the character limit
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-524
<b>Group:</b>	Contact Party
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	A regulatory contact should be provided for new regulatory activities
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	02/18/2025
<b>Problem/Issue:</b>	A regulatory contact is missing for the new regulatory activity
<b>Corrective Action:</b>	Ensure the submission/regulatory activity includes a contact (any type) for the initial submission unit
<b>Guidance Source:</b>	Tech Conformance Guide US FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-559
<b>Group:</b>	Contact Party
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Contact Party type is unique for each Contact Person
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	02/18/2025
<b>Problem/Issue:</b>	The <i>contactParty.code</i> has changed but the item was not updated with other changes
<b>Corrective Action:</b>	Resubmit the <i>contactParty</i> with the original code and resend the other updates to the <i>contactPerson</i> element
<b>Guidance Source:</b>	Tech Conformance Guide US FDA eCTD v4.0 Implementation Guide

### 4.3 Study Data Validation

<b>Number:</b>	US-eCTD4-516
<b>Group:</b>	Study Data
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	A dataset named ts.xpt with information on study start date must be present for each study in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4, and in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
<b>Severity Description:</b>	High Error

<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have not submitted a dataset named ts.xpt with information on study start date for each study in Module 4, section 4.2, or in Module 5, section 5.3
<b>Corrective Action:</b>	Resubmit, including a dataset named ts.xpt with information on study start date for each study in Module 4, section 4.2, and Module 5, section 5.3
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic Format—Standardized Study Data; Study Data Technical Conformance Guide

<b>Number:</b>	US-eCTD4-517
<b>Group:</b>	Study Data
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The correct document type must be used for all standardized datasets and corresponding define.xml files in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4, and in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	<p>You have submitted standardized XPT files or define.xml files without correct document type</p> <p>Valid document types for XPT files are:  data-tabulation-dataset-sdtm  data-tabulation-dataset-send  analysis-dataset-adam</p> <p>Valid document types for corresponding define.xml files are:  data-tabulation-data-definition  analysis-data-definition</p>
<b>Corrective Action:</b>	Resubmit using one of the valid document types for all submitted datasets
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic Format—Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specification Providing Regulatory Submissions in Electronic Format—Standardized Study Data Study Data Technical Conformance Guide

<b>Number:</b>	US-eCTD4-518
<b>Group:</b>	Study Data



<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	<p>For Standard for Exchange of Nonclinical Data (SEND) data, a Demographic (DM) dataset and define.xml must be submitted in Module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4</p> <p>For Study Data Tabulation Model (SDTM) data, a DM dataset and define.xml must be submitted Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2</p> <p>For Analysis Data Model (ADaM) data, an ADaM Subject level analysis dataset (ADSL) dataset and define.xml must be submitted in Module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2</p>
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	<p>You have not submitted SEND DM and corresponding define.xml for each study in Module 4, section 4.2</p> <p>You have not submitted SDTM DM and corresponding define.xml for each study in Module 5, section 5.3</p> <p>You have not submitted ADSL, and corresponding define.xml for each study in Module 5, section 5.3</p>
<b>Corrective Action:</b>	<p>Resubmit the submission with the SEND DM and corresponding define.xml for each study in Module 4, section 4.2</p> <p>Resubmit including SDTM DM and corresponding define.xml for each study in Module 5, section 5.3</p> <p>Resubmit including ADSL and corresponding define.xml for each study in Module 5, section 5.3</p>
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic Format—Standardized Study Data Study Data Technical Conformance Guide

<b>Number:</b>	US-eCTD4-519
<b>Group:</b>	Study Data
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	For each study referenced in Module 4 and Module 5, no more than one dataset of the same file name and document title should be submitted using the Context of Use status code value “active”

<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted more than one dataset of the same type using the Context of Use status code value “active” for a study
<b>Corrective Action:</b>	In future submissions, ensure that only one dataset of each type is marked using the Context of Use status code value “active”
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic Format— Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specification FDA eCTD v4.0 Technical Conformance Guide Study Data Technical Conformance Guide

<b>Number:</b>	US-eCTD4-554
<b>Group:</b>	Study Data
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Study Id in the Study Id and Study Title Keyword Definition should match STUDYID or SPREFID listed in the referenced Trial Summary (ts.xpt) file
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Study Id in the Study Id and Study Title Keyword Definition does not match the STUDYID or SPREFID listed in the referenced ts.xpt file (not an exact match)
<b>Corrective Action:</b>	Ensure ts.xpt is referenced under the correct Keyword Definition. If ts.xpt is under the correct Keyword Definition, update the STUDYID or SPREFID in the ts.xpt and other referenced study data files. Modify your SOPs to ensure that a consistent Study Id (exact match) is used
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide Providing Regulatory Submissions in Electronic Format— Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specification Study Data Technical Conformance Guide General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-555
<b>Group:</b>	Study Data
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Only one Study Id and Study Title code under the same eCTD heading should have the same Study Id
<b>Severity Description:</b>	Warning

<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	More than one Study Id and Study Title Keyword code under the same eCTD heading used the same Study Id in the display name value of their referenced Keyword Definition
<b>Corrective Action:</b>	If this was not intended, resubmit the Context of Use with the reference to the correct Keyword Definition for the Study Id and Study Title
<b>Guidance Source:</b>	General Good Practice for Reviewability

#### 4.4 Promotional Materials Submissions

<b>Number:</b>	US-eCTD4-520
<b>Group:</b>	Promotional Materials
<b>Category:</b>	Business Rules
<b>Validation Criteria/Description:</b>	A 2253 submission does not include the most current Product Labeling which must be submitted in section 1.14.6
<b>Severity Description:</b>	High Error - CDER
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Your 2253 submission did not include Product Labeling
<b>Corrective Action:</b>	Resubmit the 2253 submission with most current Product Labeling in section 1.14.6
<b>Guidance Source:</b>	FDA Form 2253 instructions 21 CFR 314.81(b)(3)(i) Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs, Guidance for Industry

<b>Number:</b>	US-eCTD4-521
<b>Group:</b>	Promotional Materials
<b>Category:</b>	Business Rules
<b>Validation Criteria/Description:</b>	The only valid FDA Form to include in a Promotional Labeling Submission is a 2253
<b>Severity Description:</b>	High Error - CDER
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted an eCTD submission with an eCTD Submission Type of Promotional Labeling and included a Form which is not a 2253. Only 2253 Forms are allowed with a submission of this type
<b>Corrective Action:</b>	Resubmit without the non-2253 Form

<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs, Guidance for Industry
-------------------------	---

<b>Number:</b>	US-eCTD4-522
<b>Group:</b>	Promotional Materials
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The Keyword code for issue-date is missing
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The Keyword code for issue-date was not provided for one or more promotional materials Context of Use elements in a 2253 submission (promotional-material-doc-type=promotional 2253)
<b>Corrective Action:</b>	Ensure that an issue date keyword code value is provided for each promotional material in future 2253 submissions
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs, Guidance for Industry

<b>Number:</b>	US-eCTD4-523
<b>Group:</b>	Promotional Materials
<b>Category:</b>	Business Rules
<b>Validation Criteria/Description:</b>	Promotional Material Issue Date Format is incorrect
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The Promotional Material Issue Date Keyword Definition display name does not match the proper format of YYYYMMDD
<b>Corrective Action:</b>	Resubmit following the date format YYYYMMDD
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs, Guidance for Industry

## 4.5 Submission Package Validation Rules

<b>Number:</b>	eCTD4-059
----------------	-----------

<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit file is named submissionunit.xml exists
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The submission unit file is not found. It may be in another location or may not be named submissionunit.xml or is in mixed case format
<b>Corrective Action:</b>	The filename should be corrected to the specified naming convention required for eCTD v4.x
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-060
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Checksum file named sha256.txt exists
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The checksum file is not found. It may be in another location or may not be named sha256.txt or is in mixed case format
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the sha256.txt file in the correct location and named sha256.txt
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-061
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Only one Submission Unit file is allowed
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	There is more than one submissionunit.xml file included in the submission package that is intended for the one validation check
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with just one submissionunit.xml file
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-062
----------------	-----------

<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit checksum file value is valid
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The submission unit checksum in the sha256.txt file does not match the calculated checksum for the submissionunit.xml file
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with a valid checksum sha256.txt file
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-063
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission Unit File is found in the sequence number folder
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The submissionunit.xml file is not placed at the correct location in the folder structure to be detected by receiving systems
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the submissionunit.xml placed in the top-level of the directory of the submission contents package
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-064
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document checksum value is valid
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The Document checksum(s) of eCTD XML (see validation rules for message – specifically the text element) is not the same as checksum of the file in the folder
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the correct checksum for the submitted document
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-065
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	File name length is met
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The file name length exceeds the allowable number of characters. Note: 64 characters allowed
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with file names that meet the 64-character limit
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-066
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Folder name length is met
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The folder name length exceeds the allowable number of characters. Note: 64 characters allowed
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with folder names that meet the 64 characters allowed
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-067
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Folder path length is met
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The folder path length exceeds the allowable number of characters. Note: 180 characters allowed
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with the folder path within the 180 characters allowed
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-074
----------------	-----------

<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	The folder path value only contains the allowable special characters
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The folder path value in the <i>text.reference@value</i> attribute includes invalid special characters
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with only allowable special characters in the folder path
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide

<b>Number:</b>	eCTD4-069
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Unassociated file found
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	There is a file found in the submission folder structure that is not referenced as a document or Context of Use
<b>Corrective Action:</b>	The submission unit needs to be resubmitted with all files associated with a document and Context of Use element
<b>Guidance Source:</b>	ICH eCTD v4.0 Implementation Guide eCTD v4.0 Comprehensive Table of Contents Headings and Hierarchy

<b>Number:</b>	US-eCTD4-525
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Submission is not an eCTD
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Submission must be in eCTD format to be accepted
<b>Corrective Action:</b>	Resubmit using eCTD format
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic Format— Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications



<b>Number:</b>	US-eCTD4-526
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Fillable form not included
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted without including the appropriate fillable form 356h, 2252, or 1571
<b>Corrective Action:</b>	Resubmit with the appropriate fillable form 356h, 2252, or 1571
<b>Guidance Source:</b>	Providing Regulatory Submissions in Electronic Format—Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

<b>Number:</b>	US-eCTD4-527
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	File does not contain a valid file extension
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	The file does not have a file extension such as .pdf, xpt, etc. or it is not valid
<b>Corrective Action:</b>	Resubmit the file with a valid file extension
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide; FDA Specification for File Format Types

<b>Number:</b>	US-eCTD4-528
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Folder contains no files or sub folders
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Your submission includes a file folder that contains no files or sub folders
<b>Corrective Action:</b>	Consider removing any miscellaneous folders from the folder structure in future submissions
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

<b>Number:</b>	US-eCTD4-556
<b>Group:</b>	Submission Package
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Grouped submission contains at least one file to identify the primary application
<b>Severity Description:</b>	High Error
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	Your grouped submission does not contain at least one file to indicate the primary application for the group
<b>Corrective Action:</b>	Resubmit your grouped application with at least one file to indicate the primary application (e.g., form or cover letter)
<b>Guidance Source:</b>	FDA eCTD v4.0 Implementation Guide

#### 4.6 PDF Validations

<b>Number:</b>	US-eCTD4-529
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Failed to process PDF contents
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with contents that cannot be processed, e.g. a corrupted or invalid PDF document
<b>Corrective Action:</b>	An updated valid PDF file should be submitted in the next sequence
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-530
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Non-standard font (not embedded)
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have used a non-standard font and failed to fully embed the font. You should limit fonts to standard fonts. If you use non-standard fonts you should fully embed them in the PDF file
<b>Corrective Action:</b>	An updated PDF file with all non-standard fonts embedded should be submitted in the next sequence

<b>Guidance Source:</b>	FDA Portable Document Format Specifications
-------------------------	---

<b>Number:</b>	US-eCTD4-531
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	PDF security used
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a PDF file with security settings that limit the ability to select text or graphics, or make other changes. This prevents agencies from copying text and taking other actions with submitted documents. (Not applicable for FDA Forms)
<b>Corrective Action:</b>	An updated PDF file without restrictions should be submitted in the next sequence
<b>Guidance Source:</b>	Specification for Submission Format for eCTD

<b>Number:</b>	US-eCTD4-532
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	PDF version of document is incorrect
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document using a PDF version that is not consistent with ICH / regional guidance
<b>Corrective Action:</b>	No corrective action is necessary. Modify your SOPs to ensure that documents in future submissions conform to the published standards
<b>Guidance Source:</b>	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

<b>Number:</b>	US-eCTD4-533
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	PDF does not have 'Fast Web View' enabled
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a PDF without 'Fast Web View' enabled

<b>Corrective Action:</b>	Ensure that documents in future submissions have the 'Save As optimizes for Fast Web View' setting enabled
<b>Guidance Source:</b>	Specification for Submission Format for eCTD

<b>Number:</b>	US-eCTD4-534
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	PDF opening settings not optimal
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a PDF that does not open in the desired view
<b>Corrective Action:</b>	Ensure that PDF Opening settings are correct for all future submissions. The initial view of the PDF files should be set as Bookmarks and Pages in the Navigation Panel. If there are no bookmarks, the initial view should be set to Pages only. PDFs should open in 'most recent view' (i.e. 'inherit zoom' for bookmarks and links, and 'default' in open dialogue box)
<b>Guidance Source:</b>	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

<b>Number:</b>	US-eCTD4-535
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document has password protection
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that has password protection and cannot be opened. (Not applicable for FDA Forms)
<b>Corrective Action:</b>	The protected file should be resubmitted without password protection in the next sequence using a related Context of Use to indicate its replacement
<b>Guidance Source:</b>	Specification for Submission Format for eCTD

<b>Number:</b>	US-eCTD4-536
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document has annotations
<b>Severity Description:</b>	Warning

<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that has PDF annotations. Only PDFs in module 1, sections 1.14, 1.15 and Annotated Case Report Forms are permitted to have annotations
<b>Corrective Action:</b>	Ensure that documents in future submissions do not have annotations
<b>Guidance Source:</b>	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

<b>Number:</b>	US-eCTD4-537
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Document is an image and contains no text
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that is a scanned image only and is not text searchable
<b>Corrective Action:</b>	Ensure that documents in future submissions are text searchable whenever possible (minimize the use of scanned documents)
<b>Guidance Source:</b>	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

<b>Number:</b>	US-eCTD4-538
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Broken bookmark
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more bookmarks pointing to a file that does not exist
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have broken bookmarks
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-539
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule

<b>Validation Criteria/Description:</b>	Corrupt bookmark
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more bookmarks pointing to a file that cannot be opened
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have corrupt bookmarks
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-540
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Bookmark has non-existent named destination or page
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more bookmarks pointing to a named destination or page that does not exist
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have bookmarks linking to non-existent pages or named destinations
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-541
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Multiple action bookmark
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more bookmarks containing multiple actions
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have bookmarks triggering multiple actions
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-542
<b>Group:</b>	PDF

<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	External bookmark
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that makes reference to one or more external bookmarks (e.g. web links, email links)
<b>Corrective Action:</b>	Ensure that documents in future submissions do not have bookmarks that are external to the application
<b>Guidance Source:</b>	ICH eCTD v3.2.2 Q&A 64

<b>Number:</b>	US-eCTD4-543
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Inactive bookmark
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that has one or more inactive bookmarks
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have inactive bookmarks
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-544
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Non-relative bookmark
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that has one or more nonrelative (absolute) bookmarks
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions have only relative bookmarks
<b>Guidance Source:</b>	Specification for Submission Format for eCTD FDA PDF Specifications

<b>Number:</b>	US-eCTD4-545
----------------	--------------

<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Bookmark does not 'Inherit Zoom'
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more bookmarks that are not set to 'Inherit Zoom'
<b>Corrective Action:</b>	Ensure that all bookmarks are set to 'Inherit Zoom'
<b>Guidance Source:</b>	FDA Portable Document Format Specifications Specification for Submission Format for eCTD

<b>Number:</b>	US-eCTD4-546
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Broken hyperlink
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more hyperlinks pointing to a file that does not exist
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have broken hyperlinks
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-547
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Corrupt link
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more links pointing to a file that cannot be opened
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have corrupt links
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-548
----------------	--------------



<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Link has non-existent named destination or page
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more hyperlinks pointing to a named destination or page that does not exist
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have links pointing to non-existent pages or named destinations
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-549
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Multiple action hyperlink
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more hyperlinks containing multiple actions
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have links triggering multiple actions
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-550
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	External hyperlink
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that makes reference to one or more web references in a hyperlink (e.g. web links, email links)
<b>Corrective Action:</b>	Ensure that documents in future submissions do not have hyperlinks that are external to the application
<b>Guidance Source:</b>	ICH eCTD v3.2.2 Q&A 64

<b>Number:</b>	US-eCTD4-551
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Inactive hyperlink
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that has one or more inactive hyperlinks
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have inactive hyperlinks
<b>Guidance Source:</b>	General good practice to ensure reviewability

<b>Number:</b>	US-eCTD4-552
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Non-relative hyperlink
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document that has one or more nonrelative (absolute) hyperlinks
<b>Corrective Action:</b>	Corrective action may be necessary and you will be contacted if it is necessary. Ensure that documents in future submissions do not have non-relative hyperlinks
<b>Guidance Source:</b>	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

<b>Number:</b>	US-eCTD4-553
<b>Group:</b>	PDF
<b>Category:</b>	Business Rule
<b>Validation Criteria/Description:</b>	Link does not 'Inherit Zoom'
<b>Severity Description:</b>	Warning
<b>Effective Date:</b>	09/16/2024
<b>Problem/Issue:</b>	You have submitted a document with one or more links that are not set to 'Inherit Zoom'
<b>Corrective Action:</b>	Ensure that all links in future submissions are set to 'Inherit Zoom'

**Guidance Source:**

FDA Portable Document Format Specifications  
Specification for Submission Format for eCTD