Specifications for eCTD v4.0 Validation Criteria

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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: http://estri.ich.org/
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: ***submissionUnit***, ***submission*** and ***application***
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	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). 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.
2022-10	1.2	Added Regional Validation Rule US-eCTD4-557.
2024-06	1.3	Added ICH Validation Rules eCTD4-080, eCTD4-081, eCTD4-082, eCTD4-083. Added Regional Validation Rules US-eCTD4-524, US-eCTD4-558, US-eCTD4-559. Removed Regional Validation Rule US-eCTD4-557 (replaced by eCTD4-082).
2024-09	1.3.1	Added Effective Date to Supported validations and TBD to validations added in version 1.3. Added Regional Validation Rule US-eCTD4-557 to show all supported validations.
2025-02	1.4	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. Removed Regional Validation Rule US-eCTD4-557 (replaced by eCTD4-082).
2025-10	1.5	Added Validations Rules US-eCTD4-560, US-eCTD4-561, US-eCTD4-562, US-eCTD4-563
2026-08	1.6	Added ICH and Regional Validation Rules eCTD4-084, eCTD4-085, and US-eCTD4-564. Updated Problem/Issue and Corrective Action in US-eCTD4-526.
2026-10	1.7	Added Effective Date to support validations eCTD4-084, eCTD4-085, US-eCTD4-560, US-eCTD4-561, US-eCTD4-562, US-eCTD4-563, and US-eCTD4-564.

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
High Error	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.
Warning	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
XML Message	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
General	US-eCTD4-501	Warning	Descriptions should adhere to character limits
	US-eCTD4-558	High Error	Message Header contains US Regional IG OID
Submission Unit	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
Sequence Number	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
Context of Use Priority Number	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
Context of Use	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
Related Context of Use	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
Document Reference	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
Keyword	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
Submission	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	High Error	All sequences within a regulatory activity should reference the same unique submission identifier
Application	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
Applicant	US-eCTD4-513	Warning	Company Name is missing
Application Reference	US-eCTD4-514	Warning	Application number referenced should include the application prefix and 6-digit value
Document	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
	eCTD4-085	High Error	When a Document element is submitted with updateMode="R", attribute-level updates to the document content cannot be performed concurrently.
Keyword Definition	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 ***value.item*** 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 valid OID

Type/Element	Number	Severity Description	Validation Criteria
	US-eCTD4-564	High Error	For all applications contained in a grouped submission, any referenced sender-defined keyword with the same code/codeSystem must have the same display name value when the group is established and throughout each individual application's lifecycle
Contact Party	US-eCTD4-515	Warning	Email address is greater than 64 characters
	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
Study Data	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

Type/Element	Number	Severity Description	Validation Criteria
	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
Promotional Material Submissions	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
Submission Package	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

Type/Element	Number	Severity Description	Validation Criteria
	eCTD4-074	High Error	The folder path value only contains the allowable special characters
	eCTD4-069	High Error	Unassociated file found
	eCTD4-084	High Error	Message Header requires both valid ICH and Regional IG OID values.
	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
	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
PDF	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

Type/Element	Number	Severity Description	Validation Criteria
	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
	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

Type/Element	Number	Severity Description	Validation Criteria
	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

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

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

4.2 Element Validations

4.2.1 General

Number:	US-eCTD4-501
Group:	General
Category:	Business Rule
Validation Criteria/Description:	Descriptions should adhere to character limits
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	Ensure future submissions do not have a description values that exceed the character limits
Guidance Source:	FDA eCTD v4.0 Technical Conformance Guide

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

4.2.2 Submission Unit

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

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

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

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

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

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

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

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

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

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

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

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

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

Number:	US-eCTD4-560
Group:	Submission Unit
Category:	Business Rule
Validation Criteria/Description:	Submission Unit Type is unique in the application for the regulatory activity
Severity Description:	Warning
Effective Date:	01/16/2027
Problem/Issue:	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.
Corrective Action:	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.
Guidance Source:	General good practice to ensure reviewability

4.2.3 Sequence Number

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

Number:	eCTD4-013
Group:	Sequence Number
Category:	Business Rule

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

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

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

Number:	eCTD4-016
Group:	Sequence Number
Category:	Business Rule

Validation Criteria/Description:	The Sequence Number must have one and only one value for the Submission element
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	The Sequence Number does not have one and only one value for each Submission in the submission unit
Corrective Action:	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
Guidance Source:	ICH eCTD v4.0 Implementation Guide

Number:	US-eCTD4-503
Group:	Sequence Number
Category:	Business Rule
Validation Criteria/Description:	Sequence number matches the sequence number folder name
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	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
Guidance Source:	FDA eCTD v4.0 Implementation Guide

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

4.2.4 Context of Use Priority Number

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

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

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

Guidance Source:	ICH eCTD v4.0 Implementation Guide

Number:	US-eCTD4-505
Group:	Priority Number
Category:	Schema
Validation Criteria/Description:	Context of Use Priority Number is a duplicate for the context group
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	Ensure the priority number assignment within a context group is not duplicated in future sequences
Guidance Source:	ICH eCTD v4.0 Implementation Guide

4.2.5 Context of Use

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

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

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

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

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

Number:	eCTD4-023
Group:	Context of Use
Category:	Schema

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

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

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

4.2.6 Related Context of Use

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

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

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

Problem/Issue:	The ***relatedContextOfUse.id@root*** 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
Corrective Action:	The submission unit needs to be resubmitted referencing a previous Context of Use or Leaf Reference
Guidance Source:	ICH eCTD v4.0 Implementation Guide

4.2.7 Document Reference

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

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

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

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

4.2.8 Keyword

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

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

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

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

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

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

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

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

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

4.2.9 Submission

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

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

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

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

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

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

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

Number:	US-eCTD4-506
Group:	Submission
Category:	Business Rule
Validation Criteria/Description:	The submission identifier referenced is valid
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	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
Guidance Source:	FDA eCTD v4.0 Implementation Guide

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

Problem/Issue:	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
Corrective Action:	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
Guidance Source:	FDA eCTD v4.0 Implementation Guide

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

Number:	US-eCTD4-561
Group:	Submission
Category:	Business Rule
Validation Criteria/Description:	All submission-type values are the same for all sequences within a regulatory activity
Severity Description:	High Error
Effective Date:	01/16/2027
Problem/Issue:	A submission-type value was submitted that is not the same as the submission-type value of the referenced regulatory activity
Corrective Action:	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
Guidance Source:	FDA eCTD v4.0 Implementation Guide

Number:	US-eCTD4-562

Group:	Submission
Category:	Business Rule
Validation Criteria/Description:	The submission identifier that starts a new regulatory activity must be unique in the application
Severity Description:	High Error
Effective Date:	01/16/2027
Problem/Issue:	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.
Corrective Action:	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
Guidance Source:	FDA eCTD v4.0 Implementation Guide

Number:	US-eCTD4-563
Group:	Submission
Category:	Business Rule
Validation Criteria/Description:	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.
Severity Description:	High Error
Effective Date:	01/16/2027
Problem/Issue:	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.
Corrective Action:	Ensure that the submission identifier that correctly references a regulatory activity is used in a subsequent submissions to that regulatory activity.
Guidance Source:	FDA eCTD v4.0 Implementation Guide

4.2.10 Application

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

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

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

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

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

Guidance Source:	ICH eCTD v4.0 Implementation Guide

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

Number:	US-eCTD4-509
Group:	Application
Category:	Business Rule
Validation Criteria/Description:	All grouped application type values must be the same
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	You have referenced more than one application and the application type values are not the same
Corrective Action:	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
Guidance Source:	FDA eCTD v4.0 Implementation Guide

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

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

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

Number:	US-eCTD4-512
Group:	Application
Category:	Business Rule
Validation Criteria/Description:	Correct application form is submitted
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	The wrong application FDA form based on form code was submitted based on your Application type in the ***application.code@code*** attribute value 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
Corrective Action:	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
Guidance Source:	FDA eCTD v4.0 Implementation Guide

4.2.11 Applicant

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

4.2.12 Application Reference

Number:	US-eCTD4-514
Group:	Application Reference
Category:	Business Rule
Validation Criteria/Description:	Application number referenced should include the application prefix and 6-digit value
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	The ***extension*** 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
Corrective Action:	Update the application reference in the next sequence of the regulatory activity
Guidance Source:	FDA eCTD v4.0 Implementation Guide

4.2.13 Document

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

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

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

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

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

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

Number:	eCTD4-048
Group:	Document
Category:	Business Rule
Validation Criteria/Description:	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)
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	The ***document.text.integrityCheck*** value is not provided for the document element
Corrective Action:	The submission unit needs to be resubmitted with a checksum value for all documents
Guidance Source:	ICH eCTD v4.0 Implementation Guide

Number:	eCTD4-049
Group:	Document
Category:	Business Rule
Validation Criteria/Description:	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)
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	The ***document.text.integrityCheck*** value is not a valid checksum
Corrective Action:	The submission unit needs to be resubmitted with a valid checksum value for all documents
Guidance Source:	ICH eCTD v4.0 Implementation Guide

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

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

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

Guidance Source:	ICH eCTD v4.0 Implementation Guide

Number:	eCTD4-085
Group:	Document
Category:	Business Rule
Validation Criteria/Description:	When a Document element is submitted with updateMode="R", attribute-level updates to the document content cannot be performed concurrently.
Severity Description:	High Error
Effective Date:	01/16/2027
Problem/Issue:	Document attribute (text@integrityCheckAlgorithm, text.integrityCheck, reference@value) updates are ignored when updateMode="R" is used, creating ambiguity between sender/receiver
Corrective Action:	Do not include document content attributes when using updateMode="R"; replace the Context of Use instead.
Guidance Source:	ICH eCTD v4.0 Implementation Guide

4.2.14 Keyword Definition

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

Number:	eCTD4-053
Group:	Keyword Definition
Category:	Business Rule
Validation Criteria/Description:	Keyword definition code must have a valid value
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	The ***keywordDefinition.code@code*** is not a valid value

Corrective Action:	The submission unit needs to be resubmitted with a valid keyword definition code
Guidance Source:	ICH eCTD v4.0 Implementation Guide

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

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

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

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

Number:	eCTD4-058
Group:	Keyword Definition
Category:	Business Rule
Validation Criteria/Description:	Keyword definition display name value is required
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	The ***keywordDefinition.value.item.displayName@value*** is not provided
Corrective Action:	The submission unit needs to be resubmitted providing a ***keywordDefinition.value.item.displayName@value***
Guidance Source:	ICH eCTD v4.0 Implementation Guide

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

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

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

Number:	eCTD4-083
Group:	Keyword Definition
Category:	Business Rule
Validation Criteria/Description:	Keyword Definition code system is a valid OID
Severity Description:	High Error
Effective Date:	02/18/2025
Problem/Issue:	The ***keywordDefinition.code@codeSystem*** is not a valid registered or known OID
Corrective Action:	The submission unit needs to be resubmitted with a valid keyword definition code code system

Guidance Source:	ICH eCTD v4.0 Implementation Guide

Number:	US-eCTD4-564
Group:	Keyword Definition
Category:	Business Rule
Validation Criteria/Description:	For all applications contained in a grouped submission, any referenced sender-defined keyword with the same code/codeSystem must have the same display name value when the group is established and throughout each individual application's lifecycle
Severity Description:	High Error
Effective Date:	01/16/2027
Problem/Issue:	A sender-defined keyword referenced in a group submission must have the same keywordDefinition.value.item.displayName@value across all member applications when the group is established and throughout each individual application's lifecycle
Corrective Action:	The submission unit needs to be resubmitted providing the matching sender-defined keywordDefinition.value.item.displayName@value for all applications in the group
Guidance Source:	Tech Conformance Guide US FDA eCTD v4.0 Implementation Guide

4.2.15 Contact Party

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

Number:	US-eCTD4-524
Group:	Contact Party
Category:	Business Rule

Validation Criteria/Description:	A regulatory contact should be provided for new regulatory activities
Severity Description:	Warning
Effective Date:	02/18/2025
Problem/Issue:	A regulatory contact is missing for the new regulatory activity
Corrective Action:	Ensure the submission/regulatory activity includes a contact (any type) for the initial submission unit
Guidance Source:	Tech Conformance Guide US FDA eCTD v4.0 Implementation Guide

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

4.3 Study Data Validation

Number:	US-eCTD4-516
Group:	Study Data
Category:	Business Rule
Validation Criteria/Description:	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
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	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

Corrective Action:	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
Guidance Source:	Providing Regulatory Submissions in Electronic Format—Standardized Study Data; Study Data Technical Conformance Guide

Number:	US-eCTD4-517
Group:	Study Data
Category:	Business Rule
Validation Criteria/Description:	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
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	You have submitted standardized XPT files or define.xml files without correct document type Valid document types for XPT files are: data-tabulation-dataset-sdtm data-tabulation-dataset-send analysis-dataset-adam Valid document types for corresponding define.xml files are: data-tabulation-data-definition analysis-data-definition
Corrective Action:	Resubmit using one of the valid document types for all submitted datasets
Guidance Source:	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

Number:	US-eCTD4-518
Group:	Study Data
Category:	Business Rule
Validation Criteria/Description:	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
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	You have not submitted SEND DM and corresponding define.xml for each study in Module 4, section 4.2 You have not submitted SDTM DM and corresponding define.xml for each study in Module 5, section 5.3 You have not submitted ADSL, and corresponding define.xml for each study in Module 5, section 5.3
Corrective Action:	Resubmit the submission with the SEND DM and corresponding define.xml for each study in Module 4, section 4.2 Resubmit including SDTM DM and corresponding define.xml for each study in Module 5, section 5.3 Resubmit including ADSL and corresponding define.xml for each study in Module 5, section 5.3
Guidance Source:	Providing Regulatory Submissions in Electronic Format—Standardized Study Data Study Data Technical Conformance Guide

Number:	US-eCTD4-519
Group:	Study Data
Category:	Business Rule
Validation Criteria/Description:	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”
Severity Description:	Warning
Effective Date:	09/16/2024

Problem/Issue:	You have submitted more than one dataset of the same type using the Context of Use status code value "active" for a study
Corrective Action:	In future submissions, ensure that only one dataset of each type is marked using the Context of Use status code value "active"
Guidance Source:	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

Number:	US-eCTD4-554
Group:	Study Data
Category:	Business Rule
Validation Criteria/Description:	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
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	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)
Corrective Action:	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
Guidance Source:	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

Number:	US-eCTD4-555
Group:	Study Data
Category:	Business Rule
Validation Criteria/Description:	Only one Study Id and Study Title code under the same eCTD heading should have the same Study Id
Severity Description:	Warning
Effective Date:	09/16/2024

Problem/Issue:	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
Corrective Action:	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
Guidance Source:	General Good Practice for Reviewability

4.4 Promotional Materials Submissions

Number:	US-eCTD4-520
Group:	Promotional Materials
Category:	Business Rules
Validation Criteria/Description:	A 2253 submission does not include the most current Product Labeling which must be submitted in section 1.14.6
Severity Description:	High Error - CDER
Effective Date:	09/16/2024
Problem/Issue:	Your 2253 submission did not include Product Labeling
Corrective Action:	Resubmit the 2253 submission with most current Product Labeling in section 1.14.6
Guidance Source:	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

Number:	US-eCTD4-521
Group:	Promotional Materials
Category:	Business Rules
Validation Criteria/Description:	The only valid FDA Form to include in a Promotional Labeling Submission is a 2253
Severity Description:	High Error - CDER
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	Resubmit without the non-2253 Form
Guidance Source:	Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising

	Materials for Human Prescription Drugs, Guidance for Industry

Number:	US-eCTD4-522
Group:	Promotional Materials
Category:	Business Rule
Validation Criteria/Description:	The Keyword code for issue-date is missing
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	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)
Corrective Action:	Ensure that an issue date keyword code value is provided for each promotional material in future 2253 submissions
Guidance Source:	Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs, Guidance for Industry

Number:	US-eCTD4-523
Group:	Promotional Materials
Category:	Business Rules
Validation Criteria/Description:	Promotional Material Issue Date Format is incorrect
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	The Promotional Material Issue Date Keyword Definition display name does not match the proper format of YYYYMMDD
Corrective Action:	Resubmit following the date format YYYYMMDD
Guidance Source:	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

Number:	eCTD4-059
Group:	Submission Package

Category:	Business Rule
Validation Criteria/Description:	Submission Unit file is named submissionunit.xml exists
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	The filename should be corrected to the specified naming convention required for eCTD v4.x
Guidance Source:	ICH eCTD v4.0 Implementation Guide

Number:	eCTD4-060
Group:	Submission Package
Category:	Business Rule
Validation Criteria/Description:	Checksum file named sha256.txt exists
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	The submission unit needs to be resubmitted with the sha256.txt file in the correct location and named sha256.txt
Guidance Source:	ICH eCTD v4.0 Implementation Guide

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

Number:	eCTD4-062
Group:	Submission Package

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

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

Number:	eCTD4-064
Group:	Submission Package
Category:	Business Rule
Validation Criteria/Description:	Document checksum value is valid
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	The submission unit needs to be resubmitted with the correct checksum for the submitted document
Guidance Source:	ICH eCTD v4.0 Implementation Guide

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

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

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

Number:	eCTD4-074

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

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

Number:	eCTD4-084
Group:	Submission Package
Category:	Business Rule
Validation Criteria/Description:	Message Header requires both valid ICH and Regional IG OID values.
Severity Description:	High Error
Effective Date:	01/16/2027
Problem/Issue:	Submission Unit does not include both valid ICH and Regional IG OID values
Corrective Action:	Resubmit to include valid ICH and Regional IG OID values
Guidance Source:	ICH eCTD v4.0 Implementation Guide

Number:	US-eCTD4-525

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

Number:	US-eCTD4-526
Group:	Submission Package
Category:	Business Rule
Validation Criteria/Description:	Fillable form not included
Severity Description:	High Error
Effective Date:	09/16/2024
Problem/Issue:	You have submitted without including the appropriate fillable form 356h, 2252, 1571, or 2253 (CBER only)
Corrective Action:	Resubmit with the appropriate fillable form 356h, 2252, 1571, or 2253
Guidance Source:	Providing Regulatory Submissions in Electronic Format—Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

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

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

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

4.6 PDF Validations

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

Number:	US-eCTD4-530
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Non-standard font (not embedded)
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	An updated PDF file with all non-standard fonts embedded should be submitted in the next sequence
Guidance Source:	FDA Portable Document Format Specifications

Number:	US-eCTD4-531
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	PDF security used
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	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)
Corrective Action:	An updated PDF file without restrictions should be submitted in the next sequence
Guidance Source:	Specification for Submission Format for eCTD

Number:	US-eCTD4-532
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	PDF version of document is incorrect
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document using a PDF version that is not consistent with ICH / regional guidance
Corrective Action:	No corrective action is necessary. Modify your SOPs to ensure that documents in future submissions conform to the

	published standards
Guidance Source:	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

Number:	US-eCTD4-533
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	PDF does not have 'Fast Web View' enabled
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a PDF without 'Fast Web View' enabled
Corrective Action:	Ensure that documents in future submissions have the 'Save As optimizes for Fast Web View' setting enabled
Guidance Source:	Specification for Submission Format for eCTD

Number:	US-eCTD4-534
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	PDF opening settings not optimal
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a PDF that does not open in the desired view
Corrective Action:	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)
Guidance Source:	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

Number:	US-eCTD4-535
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Document has password protection
Severity Description:	Warning

Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document that has password protection and cannot be opened. (Not applicable for FDA Forms)
Corrective Action:	The protected file should be resubmitted without password protection in the next sequence using a related Context of Use to indicate its replacement
Guidance Source:	Specification for Submission Format for eCTD

Number:	US-eCTD4-536
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Document has annotations
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	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
Corrective Action:	Ensure that documents in future submissions do not have annotations
Guidance Source:	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

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

Number:	US-eCTD4-538
Group:	PDF
Category:	Business Rule

Validation Criteria/Description:	Broken bookmark
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more bookmarks pointing to a file that does not exist
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-539
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Corrupt bookmark
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more bookmarks pointing to a file that cannot be opened
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-540
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Bookmark has non-existent named destination or page
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more bookmarks pointing to a named destination or page that does not exist
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-541

Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Multiple action bookmark
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more bookmarks containing multiple actions
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-542
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	External bookmark
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document that makes reference to one or more external bookmarks (e.g. web links, email links)
Corrective Action:	Ensure that documents in future submissions do not have bookmarks that are external to the application
Guidance Source:	ICH eCTD v3.2.2 Q&A 64

Number:	US-eCTD4-543
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Inactive bookmark
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document that has one or more inactive bookmarks
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-544

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

Number:	US-eCTD4-545
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Bookmark does not 'Inherit Zoom'
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more bookmarks that are not set to 'Inherit Zoom'
Corrective Action:	Ensure that all bookmarks are set to 'Inherit Zoom'
Guidance Source:	FDA Portable Document Format Specifications Specification for Submission Format for eCTD

Number:	US-eCTD4-546
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Broken hyperlink
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more hyperlinks pointing to a file that does not exist
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-547
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Corrupt link
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more links pointing to a file that cannot be opened
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-548
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Link has non-existent named destination or page
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more hyperlinks pointing to a named destination or page that does not exist
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-549
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Multiple action hyperlink
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document with one or more hyperlinks containing multiple actions
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

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

Number:	US-eCTD4-551
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Inactive hyperlink
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document that has one or more inactive hyperlinks
Corrective Action:	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
Guidance Source:	General good practice to ensure reviewability

Number:	US-eCTD4-552
Group:	PDF
Category:	Business Rule
Validation Criteria/Description:	Non-relative hyperlink
Severity Description:	Warning
Effective Date:	09/16/2024
Problem/Issue:	You have submitted a document that has one or more nonrelative (absolute) hyperlinks
Corrective Action:	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

Guidance Source:	Specification for Submission Format for eCTD FDA Portable Document Format Specifications

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