

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

Phase 1 US Test Case Decode Report

## Sample Submission Methodology

To aid review we have organised the submissions by US Validation Priority, Non-validation issues and then ICH eCTD Q&A Questions 36 Validation Criteria.

## US eCTD Severity High Validation Violation Submissions

**HIGH:** 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.

Table 1: US eCTD Severity High Validation Violation Submissions

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2802	3043		M1	Application Number	High	Application Number can only contain numeric characters as integer datatype.	<application-number> in us-regional.xml has an invalid value. <application-number> should contain only numeric characters.
US-2803	1519		M1	Application Number	High	Application Number does not match the folder name.	<application-number> in us-regional.xml has an invalid value. <application-number> should match the value of application folder.
US-2804	3036		M1	Application Number	High	Application Number must contain 6 characters. Violates pattern constraint of '[0-9][0-9][0-9] [0-9] [0-9] [0-9]'.	<application-number> in us-regional.xml has an invalid value. <application-number> should be exactly 6 digits.
US-2805	1527		M1	Application Number	High	Application Number must remain constant.	Value of <application-number> is inconsistent across sequences. <application-number> must remain constant.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2812	1731		STF	STF Cumulative Approach	High	Cumulative STF files are not allowed.	STF references ID of leaf with operation=delete. This should not be included the in STF xml.
US-2831	1493	1	General	XML Validation	High	Invalid XML file	Index.xml not found.
US-2866	3064		M1	Related Sequence	High	Related Sequence Number must contain 4 characters. Violates pattern constraint of '[0-9][0-9][0-9][0-9]'.	Related sequence in us-regional.xml has invalid value. Related sequence must be a 4-digit number.
US-2867	3071		M1	Related Sequence	High	Related submission Number (ed. Sequence number) can only contain numeric characters. Must be an integer datatype.	Related sequence in us-regional.xml has invalid value. Related sequence must be a 4-digit number.
US-2868	1714	19	M1	Submission Number	High	Sequence Number does not match the folder name.	Sequence folder does not match value in the regional XML.
US-2869	1697		M1	Submission Number	High	Sequence Number is not unique.	Related sequence number is the same value as the sequence number in the regional XML.
US-2872	1799		STF	STF File References	High	STF cannot reference another STF.	STF doc-content xlink:href links to a leaf ID of STF leaf. The STF doc-content xlink:href should link to study content.
US-2879	3057		M1	Submission Number	High	Submission Number (ed. Sequence number) can only contain numeric characters. Must be an integer datatype.	Sequence folder value is incorrect. The value must matches the value in the us-regional.xml.
US-2880	3050		M1	Submission Number	High	Submission Number (ed. Sequence number) must contain 4 characters. Violates pattern constraint of '[0-9][0-9][0-9][0-9]'.	Sequence folder value is incorrect. The value must be a 4-digit number.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

---

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2889	1459		General	DTD Version	High	Unsupported DTD version in backbone XML file.	index.xml is invalid. The value of the dtd-version is incorrect.
US-2890	1463		General	DTD Version	High	Unsupported DTD version in regional XML file.	us-regional.xml is invalid. The value of the dtd-version is incorrect.
US-2891	1782		STF	STF DTD Version	High	Unsupported STF DTD version in leaf element.	DTD version attribute of STF leaf in index.xml does not match value declared in the STF XML.
US-2892	1786		STF	STF DTD Version	High	Unsupported STF DTD version in STF XML file.	STF XML version is invalid. The required DTD version does not match the expected value.
US-2899	1510	1	General	XML Validation	High	XML file error.	Index.xml not found.
US-2906	1493	1	General	XML Validation	High	Invalid XML file.	Index.xml not found.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

Phase 1 US Test Case Decode Report

## US eCTD Severity Medium Validation Violation Submissions

**MEDIUM:** The error may impact the reviewability of the submission but cannot be determined without further inspection by the review staff. The submission might be considered received by FDA.

Table 2: US eCTD Severity Medium Validation Violation Submissions

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2809	1561		M1	Related Sequence	Medium	Circular relationship found in related sequences.	The value of the related sequence number points to a sequence with a submission type amendment.
US-2813	1850		STF	STF File Rules	Medium	Document ID for STF must remain constant.	Value of <study-id> changed between sequence 0000 and 0001. This value must remain consistent for an STF.
US-2815	1051		File Checks	File References	Medium	Extraneous leaf element path.	Leaf with "operation=delete" has a value for the xlink:href.
US-2816	1068	4	File Checks	File References	Medium	Extraneous modified leaf element path.	Leaf has a modified-file value. This value should not be provided for a new leaf.
US-2817	1102		File Checks	File References	Medium	Leaf element path contains invalid characters: backslash(\), colon(:), asterisk(*), question mark(?), less than(<), greater than(>), pipe( )	xlink:href for 2.2 Introduction includes an invalid character (:).
US-2822	1102		File Checks	File References	Medium	Leaf element path contains invalid characters: backslash(\), colon(:), asterisk(*), question mark(?), less than(<), greater than(>), pipe( )	File referenced by leaf under 2.2 Introduction cannot be found.
US-2827	1255		File Checks	File Rules	Medium	Invalid file extension.	Leaf under 2.2 Introduction has an invalid file extension (.pdfxx).

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2828	1034		File Checks	File Operation	Medium	Invalid leaf element operation.	Operation attribute for 2.2 Introduction has no value. A value is required.
US-2829	1867		STF	STF File Rules	Medium	Invalid STF file extension	xlink:href for STF leaf has an incorrect file extension (stf-etics-1.xmll).
US-2830	1884		STF	STF File Rules	Medium	Invalid STF file name	File name for STF xml file is incorrect.
US-2832	1102		File Checks	File References	Medium	Leaf element path contains invalid characters: backslash(\), colon(:), asterisk(*), question mark(?), less than(<), greater than(>), pipe( )	xlink:href to 2.2 Introduction includes an invalid character ( ).
US-2833	1102		File Checks	File References	Medium	Leaf element path contains invalid characters: backslash(\), colon(:), asterisk(*), question mark(?), less than(<), greater than(>), pipe( )	xlink:href to 2.2 Introduction includes an invalid character (?).
US-2834	1017		File Checks	File Operation	Medium	Leaf element already replaced or deleted.	Leaf element with "operation=delete" under 2.7.3 is operating on a leaf ID that was already deleted in sequence 0001.
US-2835	1102		File Checks	File References	Medium	Leaf element path contains invalid characters: backslash(\), colon(:), asterisk(*), question mark(?), less than(<), greater than(>), pipe( )	xlink:href to 2.2 Introduction includes an invalid character (*).
US-2847	1935		STF	STF File Rules	Medium	Multiple STF doc-content file tags.	stf-etics-1.xml has a doc-content element with multiple file-tags. Only one file-tag should be used per doc-content element.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2848	1306	13	File Checks	Orphaned File	Medium	No leaf element for file.	The file m2/22-intro/md5.txt is orphaned and cannot be found in the index.xml or regional XML.
US-2849	1478		General	Node Extension	Medium	Node-extension does not have a title.	Node-extensions should not be used in US submissions. Node extension title does not have a value.
US-2850	1476		General	Node Extension	Medium	Node-extension exists.	Node-extensions should not be used in US submissions. Node-extension included in section 2.2.
US-2853	1314		File Checks	Orphaned File	Medium	Non-Required File Exists.	Util/dtd folder includes the ca-regional.dtd file.
US-2854	1357		General	Attribute Values (Repeat Groups)	Medium	Omitted attribute value.	3.2.P manufacturer information not provided in 0000 and was included in 0001.
US-2857	1442		General	DTD Version	Medium	Omitted DTD version in backbone XML file.	Required attribute value for dtd-version is not found. index.xml is invalid.
US-2858	1445		General	DTD Version	Medium	Omitted DTD version in regional XML file.	Required attribute value for dtd-version is not found. us-regional.xml is invalid.
US-2859	1170	4	File Checks	File References	Medium	Omitted leaf element modified file path.	Leaf with "operation=replace" does not have a modified file.
US-2860	1136	13	File Checks	File References	Medium	Omitted leaf element path.	File m2/22-intro/introduction.pdf cannot be found in the index.xml or regional XML.
US-2861	1289	20	File Checks	File Rules	Medium	Omitted leaf element title.	Leaf title of leaf under 3.2.P.1 does not contain a value.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2862	1918		STF	STF File Rules	Medium	Omitted STF doc-content file tag.	stf-etics-1.xml file has a doc-content element with no file-tag value.
US-2863	1748		STF	STF DTD Version	Medium	Omitted STF DTD version in leaf element.	Leaf pointing to STF XML file does not have a value for the version attribute.
US-2864	1752		STF	STF DTD Version	Medium	Omitted STF DTD version in STF XML file.	Required DTD version attribute does not have a value. STF XML is invalid.
US-2865	3015		STF	STF XML Validation	Medium	Preceding the element "file-tag" with the element property is recommended. Element "file-tag" is unexpected according to content model of parent element "doc-content". Expecting: property.	stf-etics-1.xml element "doc-content" with element "file-tag" includes element "property".
US-2874	1816		STF	STF File References	Medium	STF does not relate to any leaf elements.	STF XML does not have a value for doc-content xlink:href.
US-2875	1765		STF	STF DTD Version	Medium	STF DTD version must match the XML file.	The version attribute of STF leaf in index.xml does not match the value in the STF XML.
US-2876	1833		STF	STF File References	Medium	STF relates to a non-existent leaf element.	stf-etics-1.xml has an xlink:href that references an element that cannot be found in the index.xml.
US-2881	1362		General	Attribute Values (Repeat Groups)	Medium	The attribute appears multiple times.	The manufacturer attribute is repeated in the <m3-2-drug-product> element. Index.xml is invalid.
US-2882	1153		File Checks	File References	Medium	The leaf referenced in the modify-file element cannot be found.	Leaf has modified file pointing to leaf ID in sequence 0000 that cannot be found.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2883	3022		STF	STF XML Validation	Medium	The maximum occurrence of the category element is three. Element 'category' is unexpected according to content model of parent element 'document identifier'.	stf-etics-3.xml has an unexpected category value.
US-2885	1595		M1	Related Sequence	Medium	This submission type cannot have a child submission.	The submission type is “original-application” but has a related sequence number.
US-2886	1612		M1	Related Sequence	Medium	This submission type cannot have a related sequence.	The submission type is “original-application” but has related sequence number value.
US-2887	1629		M1	Related Sequence	Medium	This submission type requires a related sequence.	The submission type is “amendment” but no related sequence value is present.
US-2893	3029		STF	STF XML Validation	Medium	Use of content-block is not recommended. Element 'content-block' is unexpected according to content model of parent element 'document'.	The STF includes a content-block element.
US-2894	3001		STF	STF XML Validation	Medium	Use of the element “title” is not recommended. Element “title” is unexpected according to content model of parent element “doc-content”.	The STF “doc-content” title and leaf element title do not match.



# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2895	3008		STF	STF XML Validation	Medium	Use of the “property” element is required. The xlink:href attribute of the “doc-content” element is not used. The attribute '{http://www.w3c.org/1999/xlink}href' on the element “doc-content” is not defined in the DTD/Schema.	Missing STF DTD version in STF XML file.
US-2897	1102		File Checks	File References	Medium	Leaf element path contains invalid characters: backslash(\), colon(:), asterisk(*), question mark(?), less than(<), greater than(>), pipe( )	xlink:href for leaf under 2.2 Introduction has invalid characters (introduction>.pdf).
US-2898	1102		File Checks	File References	Medium	Leaf element path contains invalid characters: backslash(\), colon(:), asterisk(*), question mark(?), less than(<), greater than(>), pipe( )	xlink:href for leaf under 2.2 Introduction has an invalid character (introduction<.pdf).
US-2900	1119	2,6,8	File Checks	File References	Medium	You have referenced a file in the hlink:xref attribute of a leaf and the system is unable to locate the file.	File referenced by leaf under 2.2 Introduction cannot be found. The leaf is orphaned.
US-2901	1323	12	File Checks	Orphaned Leaf	Medium	You have referenced the file(s) listed in the validation report from the us-regional.xml or index.xml files without providing the actual file(s).	File referenced by leaf under 2.2 Introduction cannot be found. The leaf is orphaned.
US-2902	1969		STF	STF XML Validation	Medium	You have submitted an stf-xxxxxxx.xml file. When the STF XML file fails to load, having no XML elements in it, or no document-identifier (or study-identifier) XML element error 1969 will be present.	stf-etics-1.xml file is invalid.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

---

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2904	1901		STF	STF File Rules	Medium	Your leaf that points to the STF is under an invalid heading area or invalid module. For example, STF can only be associated with certain headings under Modules 4 or 5.	STF for incorrectly referenced under section 2.2.
US-2908	1969		STF	STF XML Validation	Medium	You have submitted an stf-xxxxxxx.xml file. When the STF XML file fails to load, having no XML elements in it, or no document-identifier (or study-identifier) XML element error 1969 will be present.	stf-etics-1.xml file is invalid.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

Phase 1 US Test Case Decode Report

## US eCTD Severity Low Validation Violation Submissions

**LOW:** The error is a technical error which may or may not impact the reviewability or the integrity of the submission. The submission will likely be considered received by FDA.

Table 3: US eCTD Severity Low Validation Violation Submissions

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2801	1272		File Checks	File Rules	Low	Leaf element title contains an invalid character per eCTD Specification.	index.xml file is invalid.
US-2806	1340		General	Attribute Values (Repeat Groups)	Low	Attribute value contains an invalid character per eCTD Specification.	index.xml file is invalid.
US-2807	1344		General	Attribute Values (Repeat Groups)	Low	Attribute value leads or ends with a space per eCTD Specification.	The value of the 3.2.P manufacturer attribute begins with a space.
US-2808	1374	11	General	Checksum	Low	Checksum value must match the actual checksum.	The checksum for 2.2 Introduction is invalid.
US-2810	1544		M1	Company Name	Low	Company name must remain constant.	The value of the "company-name" element in the us-regional.XML changed after the initial sequence.
US-2814	1368		General	Attribute Values (Repeat Groups)	Low	Extraneous attribute.	Index.xml file is invalid.
US-2819	1204		File Checks	File Rules	Low	File name contains invalid characters per eCTD Specification.	The file name in the leaf for 2.2 Introduction has invalid characters.
US-2820	1221		File Checks	File Rules	Low	File name exceeds maximum length (64 characters) per eCTD Specification.	The file name in the leaf for 2.2 Introduction has a length of 76 characters.

## Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

### Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2821	1238	17	File Checks	File Rules	Low	File size exceeds maximum (100 MB) per eCTD Specification.	File report-ref.pdf is 129MB.
US-2824	1391	11	General	Checksum	Low	Invalid checksum format.	The checksum for the 2.2 Introduction leaf is invalid.
US-2825	1408	11	General	Checksum	Low	Invalid checksum type.	The “checksum-type” attribute of the leaf under 2.7.3 has an invalid value.
US-2826	1663		M1	Submission Date	Low	Invalid date format per eCTD Specification.	The us-regional.xml is invalid. The format of the value “date-of-submission” does not match the required value in the DTD.
US-2836	1085		File Checks	File References	Low	Leaf element path length exceeds maximum (230 characters).	Path to files in 5.3.5.1 is 235 characters
US-2837	1272		File Checks	File Rules	Low	Leaf element title contains an invalid character per eCTD Specification.	index.xml is invalid.
US-2838	1276		File Checks	File Rules	Low	Leaf element title leads or ends with a space per eCTD Specification.	index.xml is invalid.
US-2845	1128		File Checks	File References	Low	More than one version of the required file exists.	More than one version of a required file exists.
US-2846	1578		M1	Related Sequence	Low	Multiple related sequences are not allowed.	The us-regional.xml includes 2 related-sequence elements 0000 and 0002.
US-2851	1480		General	Node Extension	Low	Node-extension title contains an invalid character.	Node-extensions should not be used in US submissions. index.xml is invalid.
US-2852	1482		General	Node Extension	Low	Node-extension title leads or ends with a space.	Node extensions should not be used for US submissions. Node-extension included in section 2.2;
US-2855	1425	11	General	Checksum	Low	Omitted checksum value.	A leaf with “operation=new” has no value for checksum.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

---

## Phase 1 US Test Case Decode Report

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2856	1680		M1	Submission Date	Low	Omitted date per eCTD Specification	The submission date in us-regional.xml does not have a value.
US-2873	1952		STF	STF File Rules	Low	STF doc-content title and leaf element title do not match.	The title of the leaf pointing to the STF XML does not match study document title.
US-2888	1344		General	Attribute Values (Repeat Groups)	Low	Attribute value leads or ends with a space per eCTD Specification	Attribute value leads or ends with a space per eCTD Specification.
US-2896	1340		General	Attribute Values (Repeat Groups)	Low	Attribute value contains an invalid character per eCTD Specification.	index.xml is invalid.
US-2903	1646		M1	Submission Date	Low	Your date or date format is invalid.	The value of the date in us-regional.xml is not formatted correctly.
US-2905	1480		General	Node Extension	Low	Node-extension title contains an invalid character.	Node extensions should not be used for US submissions. index.xml is invalid.
US-2907	1952		STF	STF File Rules	Low	Your STF doc-content title and leaf element title do not match; viewer will show the title of the leaf only.	The value of the title of the leaf pointing to the STF XML does not match study document title.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

Phase 1 US Test Case Decode Report

## Non-validation Error Submissions

These submissions are technically valid but contain know issues which can lead tools to:

- EITHER behave inconsistently,
- AND/OR report errors where there should not be errors,
- AND/OR display the content of the eCTD incorrectly,
- AND/OR report errors which the ETICS group think are not errors.

**Error! Reference source not found.** discusses these issues and lists what the ETICS group expected outcome is.

Table 4: Non-validation Error Submissions

Submission	Validation Violation	Expected Outcome
US-2811	Correct a study report location.	Incorrect leaf element "Title" value. Leaf included to delete STF from previous sequence and should be included on the study components.
US-2818	FDA Smart Forms.	PDF file is not validated for fast web delivery, version and Open magnification.
US-2823	Invalid characters.	Sample contains !@##\$%^&*() in element "title" in m2-2-introduction of sequence 0000.
US-2839	M4-5 – Datasets - Datasets are not always submitted in a datasets folder as defined by guidance (m4/datasets, m5/datasets). This causes issues when migrating sequences between tools.	In sequence 0000, one XPT file is in the m5/datasets folder.
US-2841	Module 4 – All study reports in Module 4 have attributes for "species, route of administration, duration" Alternately, no attributes are provided where they are required for Module 4 toxicology reports.	Unexpected attributes are included and are not required.

## Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

### Phase 1 US Test Case Decode Report

Submission	Validation Violation	Expected Outcome
US-2842	Module 4 – Multiple values for STF attribute “species”.	STF for study under 5.3.5.1 has multiple values for attribute “species.”
US-2843	Module 4-5 - stf.xml appends <i>first</i> submitted stf.xml, not the <i>most recently submitted</i> stf.xml. This results in different displays in different viewing tools.	The leaf pointing to the STF has operation “append”, but the file is points to the original STF, not the most recent.
US-2844	Module 5 – Case report forms located either in m537-crf-ipl or in the study folder. For sponsors submitting globally, it is more efficient to remove CRFs from one single folder than from each individual study folder, so we do not want viewing/validation errors for either option.	Sequence includes CRFs for study leaf elements and the files are located in other locations.
US-2870	Special Characters: e.g. copyright ©	Copyright symbol © inserted in leaf title of m2-2-introduction of sequence 0000.
US-2871	SPL: check xml file / images files / proper naming. Tested with a zip file in the SPL folder.	File phrmate.zip has invalid extension.
US-2877	STF Scenarios (e.g. same study in 2 different sections).	Two STF files with the same value for study-id are included.
US-2878	STF title changes with lifecycle.	Study title changes across sequences.
US-2884	The title of the leaf which points to the STF should match the study title.	Title of leaf pointing to STF XML does not match study document title in STF XML.
US-2909	M4-5 – Datasets - Datasets are not always submitted in a datasets folder as defined by guidance (m4/datasets, m5/datasets). This causes issues when migrating sequences between tools.	In Sequence 0000, the datasets folder was moved to m5\53-clin-stud-rep\535-rep-effic-safety-stud\confusion\5351-stud-rep-contr
US-2910	Cross-application linking (leaf cross-reference or hyperlinks).	The file referred in the backbone does not exist in the submission folder.
US-2911	Related sequence is expected but not present. Business example is an IND where an amendment does not have related sequence referencing back to the original-application.	Related sequence number element is empty.

# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

## Phase 1 US Test Case Decode Report

Submission	Validation Violation	Expected Outcome
US-2912	M1 – Folder structure is variable (sometimes a flat hierarchy, sometimes many subfolders). This causes issues when migrating sequences between tools.	PDF files were placed in extra folders in m1 (e.g., 1571 form in folder for 1-1-forms\1-1-1-form-1571, cover letter in folder 1-2-cover-letter, field copy in 1-3-admin-info\1-3-2-field-copy, etc.)
US-2913	M1 - Related sequence – Sequence related to 2 or more sequences.	US-regional.xml has 2 related sequences.
US-2914	Module 3 – Document granularity - Single document in 3.2.S, single document in 3.2.P, single document for 3.2.P.4 Excipients.	3.2.P leaf provided directly under m3-2-p-drug-product. This is not expected per the granularity document.
US-2915	Related sequence: related sequence should be to an amendment. This should produce an error.	Related sequence points to a second-level submission.
US-2916	SPL: check xml file / images files / proper naming. FDA request: Test with zip file in SPL folder.	JPG file provided with SPL does not have filename that matches SPL XML.
US-2917	SPL: check xml file / images files / proper naming. FDA request: Test with zip file in SPL folder.	Folder containing SPL content is named “etics-spl”. The correct folder name is “spl”.
US-2918	Module 4 – All study reports in Module 4 have attributes for “species, route of administration, duration.” Alternatively, no attributes provided where they are required for Module 4 toxicology reports.	Unexpected attributes are not included and are required.



# Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

Phase 1 US Test Case Decode Report

## ICH Q36 Validation Violation Submissions

Adherence to the items listed in the ICH eCTD Q&A Q36 is technically necessary to exchange eCTD messages. This list is a summary of what already exists in the ICH eCTD Specification 3.2 and are directly referenced in the US eCTD Validation Criteria (December, 2010/version 2.0).

Table 5: ICH Q36 Validation Violation Submissions

Submission	US	ICH	Group	Section	Severity	Validation Violation	Expected Outcome
US-2808	1374	11	General	Checksum	Low	Checksum value must match the actual checksum.	The checksum for 2.2 Introduction is invalid.
US-2816	1068	4	File Checks	File References	Medium	Extraneous modified leaf element path.	Leaf has a modified-file value. This value should not be provided for a new leaf.
US-2821	1238	17	File Checks	File Rules	Low	File size exceeds maximum (100 MB) per eCTD Specification.	File report-ref.pdf is 129MB.
US-2824	1391	11	General	Checksum	Low	Invalid checksum format.	The checksum for the 2.2 Introduction leaf is invalid.
US-2825	1408	11	General	Checksum	Low	Invalid checksum type.	The "checksum-type" attribute of the leaf under 2.7.3 has an invalid value.
US-2831	1493	1	General	XML Validation	High	Invalid XML file.	Index.xml not found.
US-2848	1306	13	File Checks	Orphaned File	Medium	No leaf element for file.	The file m2/22-intro/md5.txt is orphaned and cannot be found in the index.xml or regional XML.
US-2855	1425	11	General	Checksum	Low	Omitted checksum value.	A leaf with "operation=new" has no value for checksum.
US-2859	1170	4	File Checks	File References	Medium	Omitted leaf element modified file path.	Leaf with "operation=replace" does not have a modified file.

## Implementation of Regulatory Information Submission Standards (IRISS) eCTD Tool Interoperability Group (ETIG) eCTD Tool Interoperability and Compliance Study 3 (ETICS 3)

---

### Phase 1 US Test Case Decode Report

US-2860	1136	13	File Checks	File References	Medium	Omitted leaf element path.	File m2/22-intro/introduction.pdf cannot be found in the index.xml or regional XML.
US-2861	1289	20	File Checks	File Rules	Medium	Omitted leaf element title.	Leaf title of leaf under 3.2.P.1 does not contain a value.
US-2868	1714	19	M1	Submission Number	High	Sequence Number does not match the folder name.	Sequence folder does not match value in the regional XML.
US-2899	1510	1	General	XML Validation	High	XML file error.	Index.xml not found.
US-2900	1119	2,6,8	File Checks	File References	Medium	You have referenced a file in the xlink:xref attribute of a leaf and the system is unable to locate the file.	File referenced by leaf under 2.2 Introduction cannot be found. The leaf is orphaned.
US-2901	1323	12	File Checks	Orphaned Leaf	Medium	You have referenced the file(s) listed in the validation report from the us-regional.xml or index.xml files without providing the actual file(s).	File referenced by leaf under 2.2 Introduction cannot be found. The leaf is orphaned.
US-2906	1493	1	General	XML Validation	High	Invalid XML file.	Index.xml not found.