

EU eCTD Validation Criteria

v2.1 April 2009

NO.	CATEGORY	VALIDATION CRITERION	SOURCE	PRIORITY
1	DTD (ICH)	A valid ICH DTD exists	ICH Specification	A
2	DTD (EU)	A valid EU M1 DTD exists	ICH Specification	A
3	index.xml	The index.xml/eu-regional.xml is present and is placed in a correct position (i.e. ensure there is an EU Module 1 backbone file named eu-regional.xml in the folder xxxx/m1/eu)	ICH Q&A 36	A
4	DTD	The index.xml/eu-regional.xml are well-formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	ICH Q&A 36/EU Q&A 13	A
5	DTD	The checksum of the ICH and EU-M1 DTDs and .mod files found in the util/dtd folder is the same as that of the corresponding DTDs and .mod files located in the eCTD validator's installation folder (subfolder DTDs), or the same as the published reference DTDs if available.	ICH Q&A 36/EU Q&A 13	A
6	DTD (EU instance files)	If using EU instance files (e.g. eAF), the instance files are well formed and valid when compared to the corresponding DTD, schema, and related files in the 'm1/eu/util/dtd' folder.	EU Q&A 13	A
7	DTD (EU instance files)	If using EU instance files (e.g. eAF), the checksum of the DTD, schema and related files are the same as that of the corresponding DTD files located in the eCTD validator's installation folder (subfolder DTDs), or the same as the published reference DTDs if available. The comparison is performed byte for byte, ignoring white space.	EU Q&A 13	A
8	Util Folder	A .util folder exists and is in the correct location (xxxx/util)	ICH Specification	A
9	Checksum	The checksum-type attribute must have the value md5 or MD5.	ICH Specification	A
10	Checksum	The regenerated checksum for every referenced file is the same as each associated checksum provided in the backbone file (e.g. eu-regional.xml)	ICH Specification/EU Q&A 13	C
11	Checksum	The checksum of the index.xml, when calculated by the validation tool, should match the checksum provided in the index-md5.txt	EMEA	A
12	XML	XML: Every leaf or node extension 'title' attribute is not empty	ICH Specification	A
13	XML	XML: Mandatory leaf attributes are set according to the valid DTD (e.g. include a leaf ID, element name, checksum, operation etc.)	ICH Specification	A
14	XML	No invalid attribute values are used (country, language etc.)	ICH Specification	A
15	Modified File	No modified file references an invalid document: If operation is append, replace or delete, then the modified file attribute should point to a valid document (although if submissions are received non-sequentially then it is possible that a sequence refers to a file in a later sequence not yet received by the agency, so warning only should be given)	Extedo Internal	C
16	Modified File	Modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is <i>new</i> , the eCTD Validator verifies that: modified file must not exist / title is given / href must exist.	EU Q&A 13	A
17	Modified File	Modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is <i>append</i> , the eCTD Validator verifies that: modified file must exist / title is given / href must exist.	EU Q&A 13	A

18	Modified File	Modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is <i>replace</i> , the eCTD Validator verifies that: modified file must exist / title is given / href must exist.	EU Q&A 13	A
19	Modified File	Modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is <i>delete</i> , the eCTD Validator verifies that: modified file must exist / title is required* / href must not exist. (* not consistent with ICH criterion #20 - ICH change request raised).	EU Q&A 13	A
20	Modified File	Modified file entry is in accordance with ICH 3.0 or 3.2: If operation is append, replace or delete, then the modified file attribute must use the correct syntax (i.e. modified-file="..../0001/index.xml#a1234567")	EU Q&A 13	A
21	xlink:href	xlink:href conforms to the eCTD standard (using the relative path to the file and file name)	ICH Q&A 36	A
22	xlink:href	If operation is new, append or replace, then xlink:href should point to a document	ICH Q&A 36	A
23	xlink:href	If operation is delete, then xlink:href should be blank	EU Q&A 13	A
24	ID Attribute	The ID attribute value starts with a letter or underscore character	EU Q&A 13	B
25	Sequence Number	Sequence number is 4 digits (i.e. numbers between 0000 and 9999)	EMA	A
26	Sequence Number	Sequence number has not already been used	EMA	A
27	Sequence Number	The sequence folder name matches the sequence number in the eu-envelope in eu-regional.xml	EU Q&A 13	A
28	Sequence Number	The envelope-referenced sequence entry is valid (i.e. the related sequence referenced is loaded already in the tool)	EMA	C
29	Files/folders	All file formats used are valid (*MS Word files, if requested, should not be included in the eCTD backbone but provided separately in the same directory)	ICH Specification	A
30	Files/folders	Total folder/file path does not exceed 230 characters	ICH Specification/EU Q&A 13	A
31	Files/folders	File names do not exceed 64 characters	ICH Specification/EU Q&A 13	A
32	Files/folders	Individual files do not exceed 100 MB in size	ICH Specification/EU Q&A 13	B
33	Files/folders	All characters used in referenced file names are valid	EMA, ICH	A
34	Files/folders	The highly-recommended naming convention is observed for all folders and documents (including a check for unexpected filenames used)	EMA, ICH	C
35	Files/folders	EU M1.3 file name convention is followed (e.g. CC-FIXED-VAR.EXT) (*Less critical if the metadata is appropriate/correct)	EMA	B
36	Leaf	Checks for elements not having any leaf child nodes - all the lowest level heading elements included in the submission contain at least one leaf	ICH Q&A 36/EU Q&A 13	B
37	PDF	PDF Format is PDF 1.4	ICH Q&A 36	B
38	PDF	There are no broken links in a PDF document	ICH Specification	B
39	PDF	PDFs have 'Fast Web Access' active	ICH Q&A 36	B
40	PDF	PDFs open in "most recent view" (i.e. 'inherit zoom' for bookmarks and links, and 'default' in open dialogue box. (ICH eCTD spec p7-4)).	ICH Specification	C
41	PDF	All PDF links and Hyperlinks are relative (are not absolute/rooted)	ICH Q&A 36	B
42	Security	There is no security setting or password protection on any individual file	ICH Q&A 36	A

43	EU Envelope	There is a single eu-envelope with the country attribute value of emea if the procedure type = centralised	EU Q&A 13	C
44	EU Envelope	There is a eu-envelope element with a matching country attribute value for every country specific leaf included in Module 1	EU Q&A 13	B
45	File Reference	There are no unreferenced files in M1, M2, M3, M4 & M5 folders (including subfolders but excluding 'util' subfolders)	ICH Q&A 36	A

Prioritisation Key:	SUMMARY	
A: <u>SERIOUS</u>. Compliance is mandatory. Failure to comply results in an error message in the validation report, no load of eCTD into the review tool, and a replacement sequence should be requested.	A = reject sequence (applicant must submit a replacement)	
B = <u>MEDIUM</u> - Compliance is preferred. Failure to comply results in a warning being displayed. A degree of discretion should be applied by the agency to the feedback given to the applicant. It may be requested that the issue is resolved in a subsequent sequence.	B = accept but may request corrections (fix with a subsequent sequence)	Apply a degree of discretion. For example, if one study report is 105MB, it will not be in the interests of either the agency or the applicant to make changes. However, if the submission consists of 200 scanned reports, all over 500 MB, then the agency would have every reason to request changes.
C - <u>LOW</u> - Compliance is preferred. Failure to comply results in advice being displayed. Report to the applicant for future consideration. Resolution may result in the eCTD being easier to handle.	C = accept but will flag errors so that they are not repeated in subsequent sequences/submissions (no fix needed)	i.e advisory only

Changes v2.0:

1. Criterion #37 deleted
(see EU CR Q&A Tracking Table CR-20080610)

2. Reference of criterion #44 changed from EU Q&A 13 to ICH Q&A 36 (see EU CR Q&A Tracking Table CR-20080610-01)

3. Criterion #18 changed to indicate that a title must exist with a delete operation
- (see EU CR Q&A Tracking Table CR-20080610-02)