Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
A.1	ICH DTD	The specified filename is used	P/F		File is named ich-ectd-3-2.dtd
A.2	ICH DTD	The file is placed in the correct folder	P/F		In the folder /XXXX/util/dtd
A.3	ICH DTD	A currently acceptable version of the DTD is used (checksum matches the published value)	P/F		Currently acceptable versions are described in the current ICH eCTD Specification. (The checksum for the DTD in eCTD v3.2 (ich-ectd-3-2.dtd) is 1d6f631cc6b6357f0f4fe378e5f79a27)
B.1	ICH stylesheet	The specified filename is used	P/F		File is named ectd-2-0.xsl
B.2	ICH stylesheet	The file is placed in the correct folder	P/F		In the folder /XXXX/util/style
B.3	ICH stylesheet	The checksum for the stylesheet used must match the published checksum for the stylesheet associated with the DTD used for the sequence	P/F		For example, the checksum corresponding to the stylesheet from eCTD specification v3.2 (ectd-2-0.xsl) is 3a07a202455e954a2eb203c5bb443f77
C.1	TW M1 DTD	The specified filename is used	P/F		File is named tw-regional.dtd
C.2	TW M1 DTD	The file is placed in the correct folder	P/F		In the folder /XXXX/util/dtd
C.3	TW M1 DTD	A currently acceptable version of the DTD is used (checksum matches the published value)	P/F		Currently acceptable versions with reference to any transition guidance are described in current TW M1 Specification. The checksum for the DTD for TW m1 v1.0 shall match the published value (see webpage)
D.1	TW M1 leaf MOD file	The specified filename is used	P/F		File is named tw-leaf.mod
D.2	TW M1 leaf MOD file	The file is placed in the correct folder	P/F		In the folder /XXXX/util/dtd
D.3	TW M1 leaf MOD file	The checksum for the tw-leaf.mod file used must match the published checksum for the tw-leaf.mod file associated with the DTD used for the sequence	P/F		For example, the checksum for tw-leaf.mod from TW eCTD Module 1 v1.0 shall match the published value (see webpage)
E.1	TW M1 envelope MOD file	The specified filename is used	P/F		File is named tw-envelope.mod
E.2	TW M1 envelope MOD file	The file is placed in the correct folder	P/F		In the folder /XXXX/util/dtd
E.3	TW M1 envelope MOD file	The checksum for the tw-envelope.mod file used must match the published checksum for the tw-envelope.mod file associated with the DTD used for the sequence	P/F		For example, the checksum for t-envelope.mod from TW eCTD Module 1 v1.0 shall match the published value (see webpage) .
F.1	TW M1 stylesheet	The specified filename is used	P/F		File is named tw-regional.xsl

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
F.2	TW M1 stylesheet	The file is placed in the correct folder	P/F		In the folder /XXXX/util/style
F.3	TW M1 stylesheet	The checksum for the stylesheet used must match the published checksum for the stylesheet associated with the DTD used for the sequence	P/F		For example, the checksum for the stylesheet from TW eCTD Module 1 v1.0 shall match the published value (see webpage)
G.1	Index XML	The file is placed in the correct folder	P/F		The root folder /XXXX
G.2	Index XML	The file is named correctly	P/F		File is named index.xml
G.3	Index XML	The file is well formed	P/F		Well formed with respect to the rules of the XML specification
G.4	Index XML	The file is valid	P/F		Valid with respect to the ICH eCTD DTD file included in the util/dtd folder
G.5	Index XML	The reference to the DTD in index.xml is directed to the DTD provided in the util folder.	P/F		This is the ICH DTD in /XXXX/util/dtd, and tested for validity by rules A.1 - A.3. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3).
G.6	Index XML	The reference to the stylesheet in index.xml is directed to the stylesheet provided in the util folder.	P/F		This is the ICH stylesheet in /XXXX/util/style and tested for validity by rules B.1 - B.3. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3).
H.1	Index MD5 txt	The file is placed in the correct folder	P/F		The root folder /XXXX
H.2	Index MD5 txt	The file is named correctly	P/F		The file is named index-md5.txt
H.3	Index MD5 txt	The regenerated checksum for the index.xml matches the value in the file index-md5.txt.	P/F		
I.1	TW regional XML	The file is placed in the correct folder	P/F		The folder /XXXX/m1/tw
I.2	TW regional XML	The file is named correctly	P/F		File is named tw-regional.xml
I.3	TW regional XML	The file is well formed	P/F		Well formed with respect to the rules of the XML specification
I.4	TW regional XML	The file is valid	P/F		Valid with respect to the TW Module 1 DTD file included in the util/dtd folder.
I.5	TW regional XML	The reference to the DTD in tw-regional.xml is directed to the DTD provided in the util folder.	P/F		This is the TW Regional DTD in /XXXX/util/dtd, and tested for validity by rules C.1-C.3. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3)

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
I.6	TW regional XML	The reference to the stylesheet in tw-regional.xml is directed to the stylesheet provided in the util folder.	P/F		This is the stylesheet in /XXXX/util/style, and tested for validity by rules F.1-F.3. A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3).
I.7	TW regional XML	The UUID is well formed according to ISO/IEC 11578:1996 and ITU-T Rec X.667 | ISO/IEC 9834-8:2005	P/F		This criterion will test whether the UUID is well formed.
I.8	TW regional XML	The UUID in this incoming sequence must be identical to the one in the previous sequence.	P/F	Y	This rule checks that the UUID is correct and the sequence is being loaded into the correct eCTD Application.
J.1	Submission Structure	All the lowest level heading elements in the XML (including node-extensions) included in the submission contain at least one leaf	P/F		
K.1	leaf attributes	The leaf attribute 'checksum-type' has a value of md5 or MD5	P/F		Note that this value is not case sensitive.
K.2	leaf attributes	The regenerated checksum for each file matches the value in the leaf attribute 'checksum'	P/F	Y	Note that if the content file is in an earlier sequence within the same eCTD application then the checksum can only be regenerated if access to this file is available.
K.3	leaf attributes	For every leaf the 'title' attribute is not empty	P/F		
K.4	leaf attributes	All leaves with an operation attribute value of new, replace or append must have a value for the cross reference (xlink:href)	P/F		The value for the cross reference (xlink:href) should be valid, and not contain any illegal characters. (Legal characters are lower case characters a-z, digits 0-9 and hyphens, as documented in the ICH eCTD specification). A valid reference means a URI - see http://www.w3.org/TR/xml/ and http://www.ietf.org/rfc/rfc3986.txt (version 2005 page 22, section 3.3).
K.5	leaf attributes	All leaves with an operation attribute value of delete must have no value for the cross reference (xlink:href)	P/F		The attribute does not need to be included, or can be declared but with a null value.
K.6	leaf attributes	The file referenced by the cross reference (xlink:href) must exist in the same or a previously submitted sequence within the same eCTD application	P/F	Y	The link within the XML leaf element is valid, i.e. the target exists.
K.7	leaf attributes	All leaves with an operation attribute value of replace, delete or append must have a value for modified-file	P/F		
K.8	leaf attributes	All leaves with an operation attribute value of new must have no value for modified-file	P/F		The attribute does not need to be included, or can be declared but with a null value.

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
K.9	leaf attributes	The leaf referenced by the modified file must exist in a previously submitted sequence within the same eCTD application.	P/F	Y	
K.10	leaf attributes	For all leaves (except leaves within node extensions- and leaves in module 3.2.A) with an operation attribute value of replace, delete or append, the modified file must be present in the same CTD section of the dossier.	P/F	Y	'Same CTD section' refers to the position in the table of contents. Sections are defined by the CTD and also by attributes in the eCTD. For example, applicants cannot replace content in the application form section with revised content that is being provided in the cover letter section. eCTD attributes also create applicant defined sections. For example, each 'substance' or 'manufacturer' attribute in m3-2-s-drug-substance, or 'product-name' attribute in m3-2-p–drug-product will create a new CTD section, and lifecycle between these sections is also not allowed. Due to inconsistency between tools how attributes are handled in the past, attributes in module 3.2.A should be allowed to be edited or not automatically copied. To avoid unnecessary errors these modules are exempt as well.
K.11	leaf attributes	Two leaf elements should not have the same leaf ID.	P/F		ID must be unique within each sequence.
K.12	leaf attributes	For all leaves with an operation attribute value of replace, delete or append the modified file must not have been replaced or deleted by any other leaf element in any sequence including the current one.	P/F	Y	Documents can be replaced or deleted just once. The modified file must not have been subject to another replace or delete operation in any of the available sequences.
K.BP1	leaf attributes	For all leaves within node extensions or module 3.2.A with an operation attribute value of replace, delete or append, the modified file should be present in the same node extension or attribute-defined section.	BP	Y	The definition of ‘same CTD section’ is as in criterion K.10. If the node extension is not in the same section the criterion K.10 still applies.
K.BP2	ICH Attributes	ICH attributes must not contain leading or trailing spaces, nor start or end with hyphens.	BP	Y	The problem is with attributes in the XML that define re-useable sections. Hyphens or spaces at the beginning or end of a attribute name are not allowed.
L.1	Node extensions	For every node-extension the 'title' attribute is not empty	P/F		
M.1	Sequence number	The sequence folder name is a 4 digit number	P/F		i.e. numbers between 0000 and 9999
M.2	Sequence number	The sequence number (folder name) has not already been used	P/F	Y	
M.3	Sequence number	The sequence folder name matches the sequence number in each envelope in tw-regional.xml	P/F		
M 4	Sequence number	Sequence number follows correct order.	P/F	Y	

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
N.1	Envelope Attributes	If the submission unit type is 'initial' or 'reformat' then the related-sequence attribute must have a value equal to the current sequence.	P/F		Refer to TW m1 specification. When submitting a first submission initialising a regulatory activity or proving a reformatted application, the related sequence attribute should be populated with the same number of that current sequence.
N.2	Envelope Attributes	If the submission unit type is not equal to ‘initial’ or ‘reformat' then the entry for related sequence must not be equal to the value for the current sequence.	P/F		Refer to TW m1 specification. When submitting additional lifecycle sequences within an ongoing regulatory activity, the related sequence attribute should be populated with the number of the sequence that started this regulatory activity.
N3	Envelope Attributes	**T**he INN attribute **is** given **if submission unit is 'initial'.**	**P/F**		It is the intent to assure the INN data field is completed. It is strongly recommended to re-use the active ingredient name as of the application form. Separation of multiple names by colon.
N4	Envelope Attributes	Drug permit license need to be provided by applicants only when submission objective is ‘change’ or ‘extension’ or ‘expiration’.	P/F		
N.5	Envelope Attributes	The invented name code of the envelope should be filled in for the regulatory activity.	P/F		
O.1	Files/Folders	The files provided in the folders for Module 1 are in acceptable formats	P/F		Refer to table in TW Module 1 specification: this is XML (where a specification exists), PDF, JPEG/JPG, PNG, SVG and GIF.
O.2	Files/Folders	The files provided in the folders for Module 2-5 are in acceptable formats	P/F		Refer to table in TW Module 1 specification: this is XML (where a specification exists), PDF, JPEG/JPG, PNG, SVG and GIF.
O.3	Files/Folders	Total file folder path length must not exceed 230 characters	P/F		Counting starts from the first digit of the sequence number in the sequence number folder name, and includes the filename.
O.4	Files/Folders	File names, including the extension, must not exceed 64 characters	P/F		
O.5	Files/Folders	Folder names must not exceed 64 characters	P/F		

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
O.6	Files/Folders	Only valid characters are used in file names	P/F		Lower case characters a-z, digits 0-9 and hyphens are allowed (as documented in the ICH eCTD specification).
O.7	Files/Folders	Only valid characters are used in folder names	P/F		Lower case characters a-z, digits 0-9 and hyphens are allowed (as documented in the ICH eCTD specification).
O.8	Files/Folders	There are no unreferenced files in M1, M2, M3, M4 and M5 folders	P/F		Including all subfolders within the m1-m5 folders but excluding ‘util’ folder and subfolders
O.9	Files/Folders	The only files in the sequence folder (/XXXX/…) are the index.xml and index-md5.txt	P/F		
O.10	Files/Folders	There are no empty folders	P/F		
O.11	**Files/Folders**	**The sections 1.1.2, 1.1.3, 1.4.1, 1.4.2 contain valid documents**	**P/F**		
O.12	**Files/Folders**	**The section 1.1 contains at least one valid document**	**P/F**		
O.13	Files/Folders	The folder name of the topest folder should be the same as pre-assigned application number	P/F		
O.14	Files/Folders	Individual files do not exceed 500 MB in size	P/F		Any deviation should always be reported by the validating tool. Files larger than 500 MB should be avoided due to potential archiving issues and to make the assessment easier.
O.BP1	Files/Folders	The recommended folder structure and folder names in the ICH and TW specifications are used	BP		Any deviation, including additional subfolders, should always be reported by the validating tool. Although navigation of an eCTD is typically carried out via the XML backbone, it is also helpful if the underlying files and folders follow the ICH and TW naming guidance.

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
O.BP2	Files/Folders	The recommended file names from the ICH and TW specifications are used for all files	BP		Any deviation should always be reported by the validating tool. Note that the components of the file names in italics in Appendix 4 of the ICH eCTD specification are to be specified by the applicant (i.e. this is variable text).
P.1	PDF Files	No PDF has been created and saved as version 1.3 or earlier	P/F		PDF 1.3 or earlier is not acceptable for technical reasons. No exceptions will be made. For example, if a literature reference is received in PDF 1.3 or earlier, then the applicant must provide it in PDF 1.4, 1.5, 1.6 or 1.7, even if this means copying the full text into a new document or even getting a paper copy and scanning it.
P.2	PDF Files	The submission does not contain corrupted files	P/F		This can be achieved by opening a PDF file in software which is compliant to ISO 32000-1; if the file opens without error, the PDF file is considered to be conformant. Absence of detection of conformance means corrupted PDF.
P.BP1	PDF Files	Files have been created and saved as PDF 1.4, 1.5, 1.6, or PDF 1.7	BP		For PDF files with apparent versions of 1.3 or earlier, the version information should be taken from the first eight characters from the first line of the header in the file. For versions 1.4 and higher, the version should be taken from the document catalogue dictionary, if present. If both the header information and the catalogue information are present, then the document catalogue dictionary information takes precedent, see PDF 32000-1:2008 specification, chapter 7.5.2 for further details. Only the PDF versions specified are recommended by ICH. This test is important due to archiving and also that PDF files can be correctly open and read by assessors.
P.BP2	PDF Files	Hyperlinks and bookmarks within documents, or between documents within the same sequence, have a valid target.	BP		Only links that open in the same software application are tested. Other links (e.g. web links and e-mail addresses) are not considered to link to essential content and should not be tested. If this BP criterion is not met, the assessor might not be able to conveniently find the relevant documents and read the submission as intended by the applicant.

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
P.BP3	PDF Files	All hyperlinks and bookmarks are set to 'inherit zoom'	BP		Using 'inherit zoom' ensures that assessors do not need to spend time repeatedly setting the view when using the links for navigation to new documents.
P.BP4	PDF Files	PDFs must have 'Fast Web View' active	BP		The use of 'Fast Web View' helps ensure optimum performance of the review system.
P.BP5	PDF Files	PDF Document Properties for the Initial View are set for 'Page Layout = Default' and 'Magnification = Default'	BP		Setting page layout and magnification to default allows the assessor to set his/her own preferences to define how the PDF is displayed, rather than the settings being taken from each individual PDF file.
P.BP6	PDF Files	All PDF hyperlinks and bookmarks are relative	BP		Relative links and bookmarks will continue to work when the submission is copied and loaded into new a environment at the agency side. Absolute (rooted) links and bookmarks will not.
P.BP7	PDF Files	The bookmarks pane should be visible if bookmarks are included within a PDF document	BP		Fulfilling this BP criterion make it more convenient for the assessor in knowing there are bookmarks without opening the pane.
P.BP8	PDF Files	The bookmarks pane should not be visible if there are no bookmarks included within a PDF document	BP		Fulfilling this BP criterion makes it more convenient for the assessor in knowing there are no bookmarks without opening the pane to check.
P.BP9	PDF Files	All hyperlinks and bookmarks between two PDFs must be configured as specified in ISO 32000-1:2008	BP		Consult the PDF specifications as in ISO 32000-1:2008 for section 7.11.2.3 on how the paths need to be written in PDF. The paths cannot contain back slashes, only forward slashes. See also 12.6.4.3 for the remote goto action. The link to another PDF cannot be made with javascript code in the PDF. Please note, not all PDF tools display the path for the link with forward slashes. However, the presence of a backslash in a link as displayed in a PDF viewer or editor does not necessarily mean that the link is NOT according to the ISO specifications. Therefore, tests for backslashes must be performed in eCTD validation software. This BP criterion is important because links who are not according to section 7.11.2.3 may not work on certain devices, such as non-Windows operating systems or tablets.
P.BP10	PDF Files	All non standard fonts are embedded.	BP		A a non-standard font has beeen uesed and it was failed to fully embed the font. Standard fonts should be used. If non-standard fonts are used it should be fully embedded in the PDF file.

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES' (Y) *	Comments
P.BP11	**PDF Files**	**There is no security setting to open any individual file**	**P/F**		**This includes passwords, certificate security, or adobe policy server settings. This test should not be used to test for corrupted files.**
P.BP12	**PDF Files**	**There are no further security settings applied to any individual file**	**P/F**		**All 'restrictions' should be 'allowed' when viewing the Document Preferences > Security settings. This includes any of the following document restrictions: printing, changing the document, document assembly, content copying, content copying for accessibility, page extraction, filling of form fields, signing, creation of template pages.**

		Description of Type of check			
P/F	Pass/Fail	These are validation criteria that can either be passed or failed. eCTDs that fail to meet one or more of these criteria will be returned to the applicant for fixing and resubmission as the same sequence number.			
BP	Best Practice	Any deviation from the criterion should always be reported by the validating tool. These are validation criteria that it is considered good practice to ensure are correct in the submitted eCTD. The applicant should make every effort to address these areas before the eCTD is submitted to the agency.			
*	'Y'-criteria	Test marked with “Y” needs the relevant former sequences for the specific criterion to be present for the result to be fully reliable. If these sequences are not present when testing, any FAIL results for these criteria should be interpreted carefully. When reporting a 'Fail' for these 'Y' criteria, validation tools should also report the specific missing sequences that are related to the 'Fail'.			