

MEDICINES CONTROL COUNCIL



DEPARTMENT OF HEALTH
Republic of South Africa



SOUTH AFRICAN eCTD VALIDATION CRITERIA

This document is intended to provide requirements to applicants wishing to submit applications for the registration of medicines in eCTD format. It reflects the current situation and will be regularly updated with changes in legislation and experience gained. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

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ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
1. ICH DTD				
1.1	ICH DTD	The ICH DTD is named correctly.	P/F	
1.2	ICH DTD	The ICH DTD is placed in the correct folder.	P/F	
1.3	ICH DTD	A currently acceptable version of the ICH DTD is used (checksum matches the published value).	P/F	
1.4	ICH DTD	The version number of the ICH DTD/specification used in the sequence being tested is higher than or equal to the version of the DTD used in the sequence numerically preceding the incoming sequence in the eCTD lifecycle.	P/F	
1.5	ICH DTD	The version number of the ICH DTD/specification used in the sequence being tested is lower than or equal to the version of the DTD used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle.	P/F	
2. ICH Stylesheet				
2.1	ICH Stylesheet	The specified filename is used.	P/F	
2.2	ICH Stylesheet	The file is placed in the correct folder.	P/F	
2.3	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	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
3. Index XML				
3.1	Index XML	The index.xml is placed in the folder xxxx.	P/F	
3.2	Index XML	There is a backbone file named index.xml.	P/F	
3.3	Index XML	The index.xml file is well formed.	P/F	
3.4	Index XML	The index.xml file is valid.	P/F	
3.5	Index XML	The reference to the DTD in index.xml is directed to the DTD provided in the util folder.	P/F	
3.6	Index XML	The reference to the stylesheet in index.xml is directed to the stylesheet provided in the util folder.	P/F	
4. Index MD5				
4.1	Index MD5 txt	The file is placed in the correct folder.	P/F	
4.2	Index MD5 txt	The file is named correctly.	P/F	
4.3	Index MD5 txt	The checksum of the index.xml, when calculated by the validation tool, should match the checksum provided in the index-md5.txt	P/F	
5. Checksum				
5.1	Checksum	The checksum-type attribute must have the value md5 or MD5.	P/F	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
6. Sequence Number				
6.1	Sequence number	The sequence number is 4 digits (i.e. numbers between 0000 and 9999)	P/F	
6.2	Sequence number	The sequence number has not already been used*	P/F	
6.3	Sequence number	The sequence folder name matches the sequence number in the za- envelope in za-regional.xml	P/F	
7. ZA M1 DTD				
7.1	ZA M1 DTD	The ZA M1 DTD is named correctly.	P/F	
7.2	ZA M1 DTD	The ZA M1 DTD is placed in the correct folder.	P/F	
7.3	ZA M1 DTD	A currently acceptable version of the ZA M1 DTD is used (checksum matches the published value).	P/F	
7.4	ZA M1 DTD	The version number of the ZA M1 DTD/specification used in the sequence being tested is higher than or equal to the version of the ZA M1 DTD used in the sequence numerically preceding the incoming sequence in the eCTD lifecycle.	P/F	
7.5	ZA M1 DTD	The version number of the ZA M1 DTD/specification used in the sequence being tested is lower than or equal to the version of the ZA M1 DTD used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle.	P/F	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
8. ZA regional XML				
8.1	ZA regional XML	The za-regional.xml is placed in the folder xxxx/m1/za.	P/F	
8.2	ZA regional XML	There is a ZA M1 backbone file named za-regional.xml.	P/F	
8.3	ZA regional XML	The za-regional.xml is well formed.	P/F	
8.4	ZA regional XML	The za-regional.xml is valid.	P/F	
8.5	ZA regional XML	The reference to the DTD in za-regional.xml is directed to the DTD provided in the util folder.	P/F	
8.6	ZA regional XML	The reference to the stylesheet in za-regional.xml is directed to the stylesheet provided in the util folder.	P/F	
9. ZA Module 1				
9.1	ZA Module 1	A Letter of application must exist in section 1.0.	P/F	
9.2	ZA Module 1	The operation attribute of the Letter of application must be new.	P/F	
9.3	ZA Module 1	An Application Form must exist in section 1.2.1.	P/F	One or several application forms can be added to this section. Not for submission types Withdrawal and Cancellation, as here an application form is not required. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
9.4	ZA Module 1	An Electronic copy declaration must exist in section 1.2.2.4.	P/F	Not for submission types Withdrawal and Cancellation, as here the electronic copy declaration is not required. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
9.5	ZA Module 1	A Validation Template has to exist in section 1.8.	P/F	Not for submission types Withdrawal and Cancellation, as here a validation template is not required. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
9.BP1	ZA Module 1	The operation attribute of the Application form should be new.	BP	For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
9.BP2	ZA Module 1	The operation attribute of the Proof of payment should be new.	BP	For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
9.BP3	ZA Module 1	The operation attribute of the Electronic copy declaration should be new.	BP	For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
9.BP4	ZA Module 1	The operation attribute of the Tabulated Schedule of Amendments should be new.	BP	For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
9.BP5	ZA Module 1	The cross-references in the Patient Information Leaflet in section 1.3.2 should be hyperlinked to the package insert in section 1.3.1.1.	BP	Only for submission type "New application". For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
9.BP6	ZA Module 1	The cross-references in the package insert in section 1.3.1.1 should be hyperlinked to the actual references.	BP	Only for submission type "New application". For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.

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9.BP7	ZA Module 1	The references in Sections B to D of the Validation template in section 1.8 should be hyperlinked to the respective documents in the eCTD.	BP	Only for submission type "New application".
9.BP8	ZA Module 1	The references in the "Tabulated Schedule of Amendments" should be hyperlinked to the relevant documents dealing with the recommendations and responses.	BP	see "Amendments" guideline
9.BP9	ZA Module 1	A Tabulated Schedule of Amendments must exist in section 1.5.2.1.	BP	Only for submission types of pharmaceutical responses and amendments. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
10. ZA M1 envelope MOD file				
10.1	ZA M1 envelope MOD file	The ZA M1 envelope MOD file is named correctly.	P/F	
10.2	ZA M1 envelope MOD file	The ZA M1 envelope MOD file is placed in the correct folder.	P/F	
10.3	ZA M1 envelope MOD file	The checksum for the za-envelope.mod file used must match the published checksum for the za-envelope.mod file associated with the DTD used for the sequence.	P/F	

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11. ZA M1 leaf MOD file				
11.1	ZA M1 leaf MOD file	The ZA M1 leaf MOD file is named correctly.	P/F	
11.2	ZA M1 leaf MOD file	The ZA M1 leaf MOD file is placed in the correct folder.	P/F	
11.3	ZA M1 leaf MOD file	The checksum for the za-leaf.mod file used must match the published checksum for the za-leaf.mod file associated with the DTD used for the sequence.	P/F	
12. ZA M1 stylesheet				
12.1	ZA M1 stylesheet	The ZA M1 stylesheet is named correctly.	P/F	
12.2	ZA M1 stylesheet	The ZA M1 stylesheet is placed in the correct folder.	P/F	
12.3	ZA 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	
13. Node Extension				
13.1	Node extension	For every node-extension the "title" attribute is not empty.	P/F	
14. Files/Folders				
14.1	Files/Folders	The files provided in the folders for Module 1 are in acceptable formats.	P/F	Only PDF is allowed to be used as file format. Please refer to the ZA M1 specification, chapter 3.1.
14.2	Files/Folders	The files provided in the folders for Module 2-5 are in acceptable formats.	P/F	Please refer to the ICH specification for further information about file formats.
14.3	Files/folders	Total folder/file path does not exceed 180 characters.	P/F	

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14.4	Files/folders	File names do not exceed 64 characters.	P/F	
14.5	Files/Folders	Folder names must not exceed 64 characters.	P/F	
14.6	Files/folders	All characters used in referenced file names are valid (according to the name requirements of the ICH eCTD Specification).	P/F	
14.7	Files/Folders	All characters used in folder names are valid (according to the name requirements of the ICH eCTD Specification).	P/F	
14.8	Files/Folders	There are no empty folders	P/F	
14.9	Files/folders	There are no unreferenced files in M1, M2, M3, M4 and M5 folders (including sub-folders but excluding 'util' subfolders).	P/F	
14.10	Files/folders	The only files in the root folder are the index.xml and index-md5.txt.	P/F	
14.BP1	Files/Folders	Individual files do not exceed 200 MB in size.	BP	
14.BP2	Files/Folders	The recommended folder structure and folder names from the ICH and ZA specifications are used.	BP	
14.BP3	Files/Folders	The recommended file names from the ICH and ZA specifications are used for all files.	BP	
14.BP4	Files/folders	All files should have one and only one file extension. The file extension should be used to indicate the format of the file.	BP	

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14.BP5	Files/folders	If documents are placed in section 3.2.R (including subfolders), the structure must follow the structure given in the ZA M1 specification.	BP	A detailed description of the required folder and file names is given in the validation criteria for South Africa in the information about Files and Folder names.
15. ID Attributes				
15.BP1	ID Attribute	The ID attribute value starts with a letter or underscore character.	BP	
16. Leaf				
16.BP1	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.	BP	
17. Leaf Attributes				
17.1	Leaf Attributes	The regenerated checksum for every referenced file is the same as each associated checksum provided in the backbone file (e.g. za- regional.xml).	P/F	
17.2	Leaf Attributes	For every leaf the "title" attribute is not empty.	P/F	
17.3	Leaf Attributes	All leaves with an operation attribute value of replace, delete or append must have a value for modified-file.	P/F	
17.4	Leaf Attributes	All leaves with an operation attribute value of new must have no value for modified-file.	P/F	

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17.5	Leaf Attributes	The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2: If the operation is append, replace or delete, then the modified file attribute must use the correct syntax (i.e. modified-file="../0001/index.xml#a1234567")	P/F	
17.BP1	Leaf Attributes	No modified file references an invalid document: If the operation is append, replace or delete, then the modified file attribute should point to a valid document.	BP	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. This criterion can only be validated in the lifecycle (not part of a stand-alone validation).
18. xlink:href				
18.1	xlink:href	xlink:href conforms to the eCTD standard (using the relative path to the file and file name)	P/F	
18.2	xlink:href	If the operation is new, append or replace, then xlink:href should point to a document	P/F	
18.3	xlink:href	If the operation is delete, then xlink:href should not exist.	P/F	
18.4	xlink:href	No references in index files (xlink:href) should target files outside the eCTD life cycle.	P/F	

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19. Modified File				
19.1	Modified File	For all leaves except leaves within node extensions within the same CTD section 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	Using the operation attribute 'delete' to remove content in sections in ZA m1 which are no longer used, due to updates of the CTD, are exempt from this rule.
19.BP1	Modified File	For all leaves within node extensions within the same CTD section with an operation attribute value of replace, delete or append, the modified file should be present in the same node extension.	BP	Sections are defined by the CTD and also by attributes in the eCTD. 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.
20. PDF Files				
20.1	PDF Files	No PDF has been created and saved as version 1.3 or earlier	P/F	
20.2	PDF Files	There is no security setting or password protection to open any individual file.	P/F	
20.3	PDF Files	There are no further security settings applied to any individual file.	P/F	Files in the sections 33-lit-ref, 43-lit-ref, 54-lit-ref are excluded from this check.
20.4	PDF Files	The submission does not contain corrupted files.	P/F	
20.BP1	PDF Files	PDF Format is PDF 1.4, 1.5 , 1.6, or 1.7	BP	
20.BP2	PDF Files	Hyperlinks and bookmarks within documents, or between documents within the same sequence, have a valid target.	BP	

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20.BP3	PDF Files	Hyperlinks and bookmarks to destinations in a different sequence in the same eCTD have a valid target.	BP	
20.BP4	PDF Files	All hyperlinks and bookmarks are set to 'inherit zoom'.	BP	
20.BP5	PDF Files	PDFs must have "Fast Web View" active.	BP	
20.BP6	PDF Files	PDF Document Properties for the Initial View are set for 'Page Layout = Default' and 'Magnification = Default'	BP	
20.BP7	PDF Files	All PDF links and Hyperlinks are relative (are not absolute or rooted).	BP	
20.BP8	PDF Files	Bookmarks pane should be visible if bookmarks are included with a PDF document.	BP	
20.BP9	PDF Files	The bookmarks panel should not be visible if there are no bookmarks included within a PDF document.	BP	
20.BP10	PDF Files	All hyperlinks and bookmarks between two PDFs must be configured as specified in ISO 32000-1:2008	BP	
21. Envelope Attributes				
21.BP1	Envelope Attributes	If the submission type is a Response to a pre-registration recommendation or post-registration, then the related sequence attribute is a four digit number.	BP	
21.BP2	Envelope Attributes	If the submission type is not a Response to a pre-registration recommendation or post-registration, then the related sequence attribute must be "none".	BP	

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1. ICH DTD								
1.1	ICH DTD	The ICH DTD is named correctly.	P/F		6	DTD (ICH)	A valid ICH DTD exists	P/F
1.2	ICH DTD	The ICH DTD is placed in the correct folder.	P/F		6	DTD (ICH)	A valid ICH DTD exists	P/F
1.3	ICH DTD	A currently acceptable version of the ICH DTD is used (checksum matches the published value).	P/F		4	DTD	The checksum of the ICH and ZA-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. Please refer to document 2.27 eCTD Checksums for the checksum of the ZA DTD.	P/F
1.4	ICH DTD	The version number of the ICH DTD/specification used in the sequence being tested is higher than or equal to the version of the DTD used in the sequence numerically preceding the incoming sequence in the eCTD lifecycle.	P/F					
1.5	ICH DTD	The version number of the ICH DTD/specification used in the sequence being tested is lower than or equal to the version of the DTD used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle.	P/F					
2. ICH Stylesheet								
2.1	ICH Stylesheet	The specified filename is used.	P/F					
2.2	ICH Stylesheet	The file is placed in the correct folder.	P/F					
2.3	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					
3. Index XML								
3.1	Index XML	The index.xml is placed in the folder xxxx.	P/F		12	index.xml	The index.xml/za-regional.xml is present and is placed in a correct position (i.e. ensure there is an ZA Module 1 backbone file named za-regional.xml in the folder xxxx/m1/za)	P/F
3.2	Index XML	There is a backbone file named index.xml.	P/F		12	index.xml	The index.xml/za-regional.xml is present and is placed in a correct position (i.e. ensure there is an ZA Module 1 backbone file named za-regional.xml in the folder xxxx/m1/za)	P/F
3.3	Index XML	The index.xml file is well formed.	P/F		3	DTD	The index.xml/za-regional.xml are well-formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	P/F

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3.4	Index XML	The index.xml file is valid.	P/F		3	DTD	The index.xml/za-regional.xml are well-formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	P/F
3.5	Index XML	The reference to the DTD in index.xml is directed to the DTD provided in the util folder.	P/F		3	DTD	The index.xml/za-regional.xml are well-formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	P/F
3.6	Index XML	The reference to the stylesheet in index.xml is directed to the stylesheet provided in the util folder.	P/F					
4. Index MD5								
4.1	Index MD5 txt	The file is placed in the correct folder.	P/F					
4.2	Index MD5 txt	The file is named correctly.	P/F					
4.3	Index MD5 txt	The checksum of the index.xml, when calculated by the validation tool, should match the checksum provided in the index-md5.txt	P/F		2	Checksum	The checksum of the index.xml, when calculated by the validation tool, should match the checksum provided in the index-md5.txt	P/F
5. Checksum								
5.1	Checksum	The checksum-type attribute must have the value md5 or MD5.	P/F		1	Checksum	The checksum-type attribute must have the value md5 or MD5.	P/F
6. Sequence Number								
6.1	Sequence number	The sequence number is 4 digits (i.e. numbers between 0000 and 9999).	P/F		19	Sequence Number	The sequence number is 4 digits (i.e. numbers between 0000 and 9999)	P/F
6.2	Sequence number	The sequence number has not already been used.	P/F	This criterion can only be validated in the lifecycle (not part of a stand-alone validation).	20	Sequence Number	The sequence number has not already been used*	P/F
6.3	Sequence number	The sequence folder name matches the sequence number in the za- envelope in za-regional.xml	P/F		21	Sequence Number	The sequence folder name matches the sequence number in the za-envelope in za-regional.xml	P/F
7. ZA M1 DTD								
7.1	ZA M1 DTD	The ZA M1 DTD is named correctly.	P/F		5	DTD (ZA)	A valid ZA M1 DTD exists	P/F
7.2	ZA M1 DTD	The ZA M1 DTD is placed in the correct folder.	P/F		5	DTD (ZA)	A valid ZA M1 DTD exists	P/F
7.3	ZA M1 DTD	A currently acceptable version of the ZA M1 DTD is used (checksum matches the published value).	P/F		4	DTD	The checksum of the ICH and ZA-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. Please refer to document 2.27 eCTD Checksums for the checksum of the ZA DTD.	P/F

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7.4	ZA M1 DTD	The version number of the ZA M1 DTD/specification used in the sequence being tested is higher than or equal to the version of the ZA M1 DTD used in the sequence numerically preceding the incoming sequence in the eCTD lifecycle.	P/F					
7.5	ZA M1 DTD	The version number of the ZA M1 DTD/specification used in the sequence being tested is lower than or equal to the version of the ZA M1 DTD used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle.	P/F					
8. ZA regional XML								
8.1	ZA regional XML	The za-regional.xml is placed in the folder xxxx/m1/za.	P/F		12	index.xml	The index.xml/za-regional.xml is present and is placed in a correct position (i.e. ensure there is an ZA Module 1 backbone file named za-regional.xml in the folder xxxx/m1/za)	P/F
8.2	ZA regional XML	There is a ZA M1 backbone file named za-regional.xml.	P/F		12	index.xml	The index.xml/za-regional.xml is present and is placed in a correct	P/F
8.3	ZA regional XML	The za-regional.xml is well formed.	P/F		3	DTD	The index.xml/za-regional.xml are well-formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	P/F
8.4	ZA regional XML	The za-regional.xml is valid.	P/F		3	DTD	The index.xml/za-regional.xml are well-formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	P/F
8.5	ZA regional XML	The reference to the DTD in za-regional.xml is directed to the DTD provided in the util folder.	P/F		3	DTD	The index.xml/za-regional.xml are well-formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	P/F
8.6	ZA regional XML	The reference to the stylesheet in za-regional.xml is directed to the stylesheet provided in the util folder.	P/F					
9. ZA Module 1								
9.1	ZA Module 1	A Letter of Application must exist in section 1.0.	P/F					
9.2	ZA Module 1	The operation attribute of the Letter of Application must be new.	P/F					
9.3	ZA Module 1	An Application Form must exist in section 1.2.1.	P/F	One or several application forms can be added to this section. Not for submission types Withdrawal and Cancellation, as here an application form is not required. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				

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9.4	ZA Module 1	An Electronic copy declaration must exist in section 1.2.2.4.	P/F	Not for submission types Withdrawal and Cancellation, as here the electronic copy declaration is not required. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.5	ZA Module 1	A Validation Template has to exist in section 1.8.	P/F	Not for submission types Withdrawal and Cancellation, as here a validation template is not required. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.BP1	ZA Module 1	The operation attribute of the Application Form should be new.	BP	Not for submission types Withdrawal and Cancellation, as here a validation template is not required. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.BP2	ZA Module 1	The operation attribute of the Proof of Payment should be new.	BP	For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.BP3	ZA Module 1	The operation attribute of the Electronic copy declaration should be new.	BP	For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.BP4	ZA Module 1	The operation attribute of the Tabulated Schedule of Amendments should be new.	BP	For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.BP5	ZA Module 1	The cross-references in the Patient Information Leaflet in section 1.3.2 should be hyperlinked to the package insert in section 1.3.1.1.	BP	Only for submission type "New application". For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.BP6	ZA Module 1	The cross-references in the package insert in section 1.3.1.1 should be hyperlinked to the actual references.	BP	Only for submission type "New application". For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
9.BP7	ZA Module 1	The references in Sections B to D of the Validation template in section 1.8 should be hyperlinked to the respective documents in the eCTD.	BP	Only for submission type "New application".				
9.BP8	ZA Module 1	The references in the "Tabulated Schedule of Amendments" should be hyperlinked to the relevant documents dealing with the recommendations and responses.	BP	see "Amendments" guideline				

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)	ZA rule no. (V1.0)	Category (V1.0)	VALIDATION CRITERIA ZA (V1.0)	Severity (V1.0)
9.BP9	ZA Module 1	A Tabulated Schedule of Amendments should exist in section 1.5.2.1.	BP	Only for submission types of pharmaceutical responses and amendments. For more information please refer to the Guidance for the Submission of Regulatory Information in eCTD format.				
				Rule 22 is replaced by rule 1.2 and 2.2	22	Util Folder	A 'util' folder exists and is in the correct location (xxx/util).	P/F
10. ZA M1 envelope MOD file								
10.1	ZA M1 envelope MOD file	The ZA M1 envelope MOD file is named correctly.	P/F					
10.2	ZA M1 envelope MOD file	The ZA M1 envelope MOD file is placed in the correct folder.	P/F					
10.3	ZA M1 envelope MOD file	The checksum for the za-envelope.mod file used must match the published checksum for the za-envelope.mod file associated with the DTD used for the sequence.	P/F		4	DTD	The checksum of the ICH and ZA-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. Please refer to document 2.27 eCTD Checksums for the checksum of the ZA DTD.	P/F
11. ZA M1 leaf MOD file								
11.1	ZA M1 leaf MOD file	The ZA M1 leaf MOD file is named correctly.	P/F					
11.2	ZA M1 leaf MOD file	The ZA M1 leaf MOD file is placed in the correct folder.	P/F					
11.3	ZA M1 leaf MOD file	The checksum for the za-leaf.mod file used must match the published checksum for the za-leaf.mod file associated with the DTD used for the sequence.	P/F		4	DTD	The checksum of the ICH and ZA-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. Please refer to document 2.27 eCTD Checksums for the checksum of the ZA DTD.	P/F
12. ZA M1 stylesheet								
12.1	ZA M1 stylesheet	The ZA M1 stylesheet is named correctly.	P/F					
12.2	ZA M1 stylesheet	The ZA M1 stylesheet is placed in the correct folder.	P/F					
12.3	ZA 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					

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)	ZA rule no. (V1.0)	Category (V1.0)	VALIDATION CRITERIA ZA (V1.0)	Severity (V1.0)
13. Node Extension								
13.1	Node extension	For every node-extension the "title" attribute is not empty.	P/F		26	XML	XML:Every leaf or node extension 'title' attribute is not empty	P/F
14. Files/Folders								
14.1	Files/Folders	The files provided in the folders for Module 1 are in acceptable formats.	P/F	Only PDF is allowed to be used as file format. Please refer to the ZA M1 specification, chapter 3.1.	8	Files/folders	All file formats used are valid (MS Word files, if requested, should not be included in the eCTD backbone but provided separately - see Chapter 4.7 in the Guidance for Submission of Regulatory Information in eCTD Format)	P/F
14.2	Files/Folders	The files provided in the folders for Module 2-5 are in acceptable formats.	P/F	Please refer to the ICH specification for further information about file formats.	8	Files/folders	All file formats used are valid (MS Word files, if requested, should not be included in the eCTD backbone but provided separately - see Chapter 4.7 in the Guidance for Submission of Regulatory Information in eCTD Format)	P/F
14.3	Files/folders	Total folder/file path does not exceed 180 characters	P/F		9	Files/folders	Total folder/file path does not exceed 180 characters	P/F
14.4	Files/folders	File names do not exceed 64 characters	P/F		10	Files/folders	File names do not exceed 64 characters	P/F
14.5	Files/Folders	Folder names must not exceed 64 characters	P/F					
14.6	Files/folders	All characters used in referenced file names are valid (according to the name requirements of the ICH eCTD Specification).	P/F		11	Files/folders	All characters used in referenced file names are valid (according to the name requirements of the ICH eCTD Specification)	P/F
14.7	Files/Folders	All characters used in folder names are valid (according to the name requirements of the ICH eCTD Specification).	P/F					
14.8	Files/Folders	There are no empty folders.	P/F					
14.9	Files/folders	There are no unreferenced files in M1, M2, M3, M4 and M5 folders (including sub-folders but excluding 'util' subfolders).	P/F		7	File Reference	There are no unreferenced files in the root folder, M1, M2, M3, M4 & M5 folders (including sub-folders but excluding 'util' subfolders, the index-md5.txt and index.xml).	P/F
14.10	Files/folders	The only files in the root folder are the index.xml and index-md5.txt.	P/F					
14.BP1	Files/Folders	Individual files do not exceed 200 MB in size.	BP		28	Files/folders	Individual files do not exceed 100 MB in size	BP
14.BP2	Files/Folders	The recommended folder structure and folder names from the ICH and ZA specifications are used.	BP					
14.BP3	Files/Folders	The recommended file names from the ICH and ZA specifications are used for all files.	BP					

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)	ZA rule no. (V1.0)	Category (V1.0)	VALIDATION CRITERIA ZA (V1.0)	Severity (V1.0)
14.BP4	Files/folders	All files should have one and only one file extension. The file extension should be used to indicate the format of the file.	BP		39	PDF	All files should have one and only one file extension. The file extension should be used to indicate the format of the file.	BP
14.BP5	Files/folders	If documents are placed in section 3.2.R (including subfolders), the structure must follow the structure given in the ZA M1 specification.	BP	A detailed description of the required folder and file names is given in the validation criteria for South Africa in the information about Files and Folder names.				
15. ID Attributes								
15.BP1	ID Attribute	The ID attribute value starts with a letter or underscore character	BP		29	ID Attribute	The ID attribute value starts with a letter or underscore character	BP
16. Leaf								
16.BP1	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.	BP		30	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	BP
17. Leaf Attributes								
17.1	Leaf Attributes	The regenerated checksum for every referenced file is the same as each associated checksum provided in the backbone file (e.g. za- regional.xml).	P/F		37	Checksum	The regenerated checksum for every referenced file is the same as each associated checksum provided in the backbone file (e.g. za- regional.xml)	BP
17.2	Leaf Attributes	For every leaf the "title" attribute is not empty.	P/F		26	XML	XML:Every leaf or node extension 'title' attribute is not empty	P/F
17.3	Leaf Attributes	All leaves with an operation attribute value of replace, delete or append must have a value for modified-file.	P/F		14, 15, 16	Modified File	The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is append, the eCTD Validator verifies that: the modified file must exist / the title is given / href must exist. The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is replace, the eCTD Validator verifies that: the modified file must exist / the title is given. The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is delete, the eCTD Validator verifies that: the modified file must exist / the title is required / href must not exist.	P/F

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)	ZA rule no. (V1.0)	Category (V1.0)	VALIDATION CRITERIA ZA (V1.0)	Severity (V1.0)
17.4	Leaf Attributes	All leaves with an operation attribute value of new must have no value for modified-file.	P/F		13	Modified File	The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2: If the value of the operation attribute is new, the eCTD Validator verifies that: the modified file must not exist / the title is given / href must exist.	P/F
17.5	Leaf Attributes	The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2: If the operation is append, replace or delete, then the modified file attribute must use the correct syntax (i.e. modified-file="../0001/index.xml#a1234567")	P/F		17	Modified File	The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2: If the operation is append, replace or delete, then the modified file attribute must use the correct syntax (i.e. modified-file="../0001/index.xml#a1234567")	P/F
17.BP1	Leaf Attributes	No modified file references an invalid document: If the operation is append, replace or delete, then the modified file attribute should point to a valid document.	BP	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. This criterion can only be validated in the lifecycle (not part of a stand-alone validation).	35	Modified File	No modified file references an invalid document: If the 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)*	BP
18. xlink:href								
18.1	xlink:href	xlink:href conforms to the eCTD standard (using the relative path to the file and file name)	P/F		23	xlink:href	xlink:href conforms to the eCTD standard (using the relative path to the file and file name)	P/F
18.2	xlink:href	If the operation is new, append or replace, then xlink:href should point to a document	P/F		24	xlink:href	If the operation is new, append or replace, then xlink:href should point to a document	P/F
18.3	xlink:href	If the operation is delete, then xlink:href should not exist.	P/F		25	xlink:href	If the operation is delete, then xlink:href should be blank	P/F
18.4	xlink:href	No references in index files (xlink:href) should target files outside the eCTD life cycle.	P/F		27	xlink:href	No references in index files (xlink:href) should target files outside the eCTD life cycle.	P/F
19. Modified File								
19.1	Modified File	For all leaves except leaves within node extensions within the same CTD section 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	Using the operation attribute 'delete' to remove content in sections in ZA m1 which are no longer used, due to updates of the CTD, are exempt from this rule.				

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)	ZA rule no. (V1.0)	Category (V1.0)	VALIDATION CRITERIA ZA (V1.0)	Severity (V1.0)
19.BP1	Modified File	For all leaves within node extensions within the same CTD section with an operation attribute value of replace, delete or append, the modified file should be present in the same node extension.	BP	Sections are defined by the CTD and also by attributes in the eCTD. 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.				
				New rule 17.3	46	Modified File	The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2. If the value of the operation attribute is delete, the eCTD Validator verifies that the modified file must exist / the title is required / href must not exist.	P/F
				New rule 17.3	44	Modified File	The syntax of the modified file entry is in accordance with ICH 3.0 or 3.2. If the value of the operation attribute is append, the eCTD Validator verifies that the modified file must exist / the title is given / href must exist.	P/F
20. PDF Files								
20.1	PDF Files	No PDF has been created and saved as version 1.3 or earlier	P/F					
20.2	PDF Files	There is no security setting or password protection to open any individual file.	P/F		18	Security	There is no security setting or password protection on any individual file	P/F
20.3	PDF Files	There are no further security settings applied to any individual file.	P/F	Files in the sections 33-lit-ref, 43-lit-ref, 54-lit-ref are excluded from this check.	18	Security	There is no security setting or password protection on any individual file	P/F
20.4	PDF Files	The submission does not contain corrupted files.	P/F					
20.BP1	PDF Files	PDF Format is PDF 1.4, 1.5, 1.6, or 1.7	BP		31	PDF	PDF Format is PDF 1.4, 1.5, 1.6, or 1.7	BP
20.BP2	PDF Files	Hyperlinks and bookmarks within documents, or between documents within the same sequence, have a valid target.	BP		32	PDF	There are no broken links in a PDF document	BP
20.BP3	PDF Files	Hyperlinks and bookmarks to destinations in a different sequence in the same eCTD have a valid target.	BP		32	PDF	There are no broken links in a PDF document	BP
20.BP4	PDF Files	All hyperlinks and bookmarks are set to 'inherit zoom'.	BP		38	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)).	BP
20.BP5	PDF Files	PDFs must have "Fast Web View" active.	BP		33	PDF	PDFs have the 'Fast Web Access' option active	BP
20.BP6	PDF Files	PDF Document Properties for the Initial View are set for 'Page Layout = Default' and 'Magnification = Default'.	BP		38	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)).	BP

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)	ZA rule no. (V1.0)	Category (V1.0)	VALIDATION CRITERIA ZA (V1.0)	Severity (V1.0)
20.BP7	PDF Files	All PDF links and Hyperlinks are relative (are not absolute or rooted).	BP		34	PDF	All PDF links and Hyperlinks are relative (are not absolute or rooted)	BP
20.BP8	PDF Files	Bookmarks panel should be visible if bookmarks are included with a PDF document.	BP		36	PDF initial view	Bookmarks pane should be visible if bookmarks are included with a PDF document	BP
20.BP9	PDF Files	The bookmarks panel should not be visible if there are no bookmarks included within a PDF document.	BP					
20.BP10	PDF Files	All hyperlinks and bookmarks between two PDFs must be configured as specified in ISO 32000-1:2008	BP					
21. Envelope Attributes								
21.BP1	Envelope Attributes	If the submission type is a Response to a pre-registration recommendation or post-registration, then the related sequence attribute is a four digit number.	BP					
21.BP2	Envelope Attributes	If the submission type is not a Response to a pre-registration recommendation or post-registration, then the related sequence attribute must be "none".	BP					

LEGEND

Black

These entries are fixed text for folder and file names according to the ZA and ICH specifications. The level of adherence to these names is specified in the eCTD validation criteria.

Red

These entries are variable text for folder and file names according to the ZA and ICH specifications. In all folder locations containing file names entirely in red text or files with **-var**

Blue (compendial)

If the folder name starts with this text, then component filenames below are entirely variable. If the foldername does not start with this word, then the fixed filenames should be followed.

Black, no file extension

Regular, with file extension (.pdf)

These entries indicate folder names, and are coloured in accordance with the legend above

These entries indicate file names, and are coloured in accordance with the legend above

Use of Additional Folders

multiple branches possible

At these locations, a complete branch of the table of contents can be added

optional folder

At these locations, one or more optional subfolders may be used, (also as nested folders, i.e. folders within folders) but files can also be placed directly at this location. The subfolders and

folder required and

At these locations, there must be a subfolder if content is provided. Optional additional subfolders

additional folders optional

product-name**0000**

index.xml

index-md5.txt

m1**za**

za-regional.xml

10-application-letterapplication-letter-**var**.pdf**12-application****121-application-form**application-form-**var**.pdf**122-annexes****1221-proof-of-payment**proof-of-payment-**var**.pdf

- 1222-letter-of-authorisation**
 - letter-of-authorisation-**var**.pdf
- 1223-dossier-product-batch-information**
 - dossier-product-batch-information-**var**.pdf
- 1224-electronic-copy-declaration**
 - electronic-copy-declaration-**var**.pdf
- 1225-cv-pharmacovigilance**
 - cv-pharmacovigilance-**var**.pdf
- 1226-api-change-control**
 - api-change-control-**var**.pdf
- 1227-vamf-certificate**
 - vamf-certificate-**var**.pdf
- 1228-pmf-certificate**
 - pmf-certificate-**var**.pdf
- 13-za-labelling-packaging**
 - 131-sapi**
 - 1311-pi**
 - pi-**var**.pdf
 - 1312-stdrefs**
 - stdrefs-**var**.pdf
 - 132-pil**
 - pil-**var**.pdf
 - 133-labels**
 - label-**var**.pdf
 - 134-braille**
 - braille-**var**.pdf
- 14-expert-information**
 - 141-quality**
 - quality-**var**.pdf
 - 142-non-clinical**
 - non-clinical-**var**.pdf
 - 143-clinical**
 - clinical-**var**.pdf
- 15-specific-requirements**
 - 151-literature-based**
 - literature-based-**var**.pdf

- 152-amendment**
 - 1521-amendment-schedule**
 - amendment-schedule-**var**.pdf
 - 1522-medicine-register**
 - medicine-register-**var**.pdf
 - 1523-affidavit**
 - affidavit-**var**.pdf
- 153-proprietary-name**
 - proprietary-name-**var**.pdf
- 154-gmo**
 - gmo-**var**.pdf
- 155-pi-amendment**
 - pi-amendment-**var**.pdf
- 16-environ-risk-assessment**
 - 161-nongmo**
 - nongmo-**var**.pdf
 - 162-gmo**
 - gmo-**var**.pdf
- 17-gmp**
 - 171-last-inspection**
 - last-inspection-**var**.pdf
 - 172-inspection-report-or-equivalent**
 - inspection-report-**var**.pdf
 - 173-gmp-certificate**
 - gmp-certificate-**var**.pdf
- 174-release**
 - 1741-api**
 - api-**var**.pdf
 - 1742-ipi**
 - ipi-**var**.pdf
 - 1743-fprc-tests**
 - fprc-tests-**var**.pdf
 - 1744-fprc-criteria**
 - fprc-criteria-**var**.pdf
- 175-contract-confirmation**
 - contract-confirmation-**var**.pdf

- 176-cpp**
 - cpp-**var**.pdf
- 177-sapc-reg**
 - sapc-reg-**var**.pdf
- 178-comp-reg**
 - comp-reg-**var**.pdf
- 179-docs-phcr**
 - phcr-**var**.pdf
- 1710-sample-documents**
 - 17101-sample-submission-confirmation**
 - confirmation-sample-**var**.pdf
 - 17102-sample-bmr**
 - sample-bmr-**var**.pdf
 - 17103-sample-coa**
 - sample-coa-**var**.pdf
- 1711-manufacturing-permit**
 - manufacturing-permit-**var**.pdf
- 1712-inspection-flow-diagram**
 - inspection-flow-diagram-**var**.pdf
- 1713-organogram**
 - organogram-**var**.pdf
- 18-compliance-screening**
 - compliance-screening-**var**.pdf
- 19-indiv-patient-data**
 - indiv-patient-data-**var**.pdf
- 110-foreign-reg-status**
 - 1101-countries-same-appl**
 - countries-same-appl-**var**.pdf
 - 1102-foreign-reg-certif-or-ma**
 - foreign-reg-cert-or-ma-**var**.pdf
 - 1103-foreign-pi**
 - foreign-pi-**var**.pdf
 - 1104-data-set-similarities**
 - data-set-similarities-**var**.pdf
- 111-be-trial-info**
 - be-trial-info-**var**.pdf

112-paediatric-dev-program

paediatric-dev-program-**var**.pdf

113-risk-management-plan

risk-management-plan-**var**.pdf

m2

22-intro

introduction-**var**.pdf

23-qos

qos-**var**.pdf

OR

introduction-**var**.pdf

drug-substance-**var**.pdf

drug-product-**var**.pdf

appendices-**var**.pdf

regional-information-**var**.pdf

24-nonclin-over

nonclinical-overview-**var**.pdf

25-clin-over

clinical-overview-**var**.pdf

26-nonclin-sum

introduction-**var**.pdf

pharmacol-written-summary-**var**.pdf

pharmacol-tabulated-summary-**var**.pdf

pharmkin-written-summary-**var**.pdf

pharmkin-tabulated-summary-**var**.pdf

toxicology-written-summary-**var**.pdf

toxicology-tabulated-summary-**var**.pdf

27-clin-sum

summary-biopharm-**var**.pdf

summary-clin-pharm-**var**.pdf

summary-clin-efficacy-**var**.pdf

summary-clin-safety-**var**.pdf

literature-references-**var**.pdf

synopses-indiv-studies-**var**.pdf

m3

32-body-data

32s-drug-sub**drug-substance**

multiple branches possible

32s1-gen-infonomenclature-**var**.pdfstructure-**var**.pdfgeneral-properties-**var**.pdf**32s2-manuf**manufacturer-**var**.pdfmanuf-process-and-controls-**var**.pdfcontrol-of-materials-**var**.pdfcontrol-critical-steps-**var**.pdfprocess-validation-**var**.pdfmanuf-process-development-**var**.pdf**32s3-charac**elucidation-of-structure-**var**.pdfimpurities-**var**.pdf**32s4-contr-drug-sub**ctrlstrat-**var**.pdf

Refer to ICH eCTD Q&A 81, additional files are now allowed for control strategy summary.

32s41-specspecification-**var**.pdf**32s42-analyt-proc**

analytical-procedure.pdf

32s43-val-analyt-proc

validation-analyt-procedure.pdf

32s44-batch-analysbatch-analyses-**var**.pdf**32s45-justif-spec**justification-of-specification-**var**.pdf**32s5-ref-stand**reference-standards-**var**.pdf**32s6-cont-closure-sys**container-closure-system-**var**.pdf**32s7-stab**stability-summary-**var**.pdfpostapproval-stability-**var**.pdf

stability-data-**var**.pdf

32p-drug-prod

drug-product

multiple branches possible

32p1-desc-comp

description-and-composition-**var**.pdf

32p2-pharm-dev

pharmaceutical-development-**var**.pdf

32p3-manuf

manufacturers-**var**.pdf

batch-formula-**var**.pdf

manuf-process-and-controls-**var**.pdf

control-critical-steps-**var**.pdf

process-validation-**var**.pdf

32p4-contr-excip

excipients.pdf

Refer to ICH eCTD Q&A 73, options 1 & 2, file name entirely variable, multiple files allowed.

excipient

multiple branches possible

specifications-**var**.pdf

analytical-procedures-**var**.pdf

validation-analyt-procedures-**var**.pdf

justification-of-specifications-**var**.pdf

compendial-excipients

multiple branches possible

specifications.pdf

analytical-procedures.pdf

validation-analyt-procedures.pdf

justification-of-specifications.pdf

excipients-human-animal-**var**.pdf

novel-excipients-**var**.pdf

32p5-contr-drug-prod

ctrlstrat-**var**.pdf

Refer to ICH eCTD Q&A 81, additional files are now allowed for control strategy summary.

32p51-spec

specifications-**var**.pdf

32p52-analyt-proc

analytical-procedure.pdf

32p53-val-analyt-proc

	validation-analytical-procedures.pdf	
32p54-batch-analys	batch-analyses-var.pdf	
32p55-charac-imp	characterisation-impurities-var.pdf	
32p56-justif-spec	justification-of-specifications-var.pdf	
32p6-ref-stand	reference-standards-var.pdf	
32p7-cont-closure-sys	container-closure-system-var.pdf	
32p8-stab	stability-summary-var.pdf	
	postapproval-stability-var.pdf	
	stability-data-var.pdf	
32a-app		
32a1-fac-equip		
manufacturer	optional folder	
	facilities-and-equipment-report.pdf	
32a2-advent-agent		
substance	optional folder	
	adventitious-agents-report.pdf	
32a3-excip-substance	multiple branches possible	In line with ICH eCTD specification, "The directory/file structure would typically follow that of the drug substance section in Module 3.2.S."
folder	optional folder	
	substance.pdf	
32r-reg-info		
32r1-availability	folder required	
32r11-overview	folder required	
	overview-var.pdf	
32r12-ref	folder required	
	ref-pdr-var.pdf	
32r13-coa	folder required	
	coa-var.pdf	
32r14-availability	folder required	

avail- var .pdf	
32r2-parent-api-diff-sites	folder required and additional folders optional
statement- var .pdf	
32r3-cep	folder required and additional folders optional
cep- var .pdf	
32r4-multiple-api-mnf	folder required and additional folders optional
comp-rep- var .pdf	
comp-results- var .pdf	
compliance-guidelines- var .pdf	
coa- var .pdf	
32r5-med-dev	folder required and additional folders optional
med-dev- var .pdf	
32r6-animal-human-orig	folder required and additional folders optional
origin- var .pdf	
32r7-bmr	folder required and additional folders optional
bmr- var .pdf	
32r8-other	folder required and additional folders optional
other- var .pdf	
33-lit-ref	
folder	optional folder
reference.pdf	
m4	
42-stud-rep	
421-pharmacol	
4211-prim-pd	
study-report	optional folder
study-report.pdf	
4212-sec-pd	
study-report	optional folder
study-report.pdf	
4213-safety-pharmacol	
study-report	optional folder
study-report.pdf	
4214-pd-drug-interact	
study-report	optional folder
study-report.pdf	

422-pk	
4221-analyt-met-val	
study-report	optional folder
study-report.pdf	
4222-absorp	
study-report	optional folder
study-report.pdf	
4223-distrib	
study-report	optional folder
study-report.pdf	
4224-metab	
study-report	optional folder
study-report.pdf	
4225-excr	
study-report	optional folder
study-report.pdf	
4226-pk-drug-interact	
study-report	optional folder
study-report.pdf	
4227-other-pk-stud	
study-report	optional folder
study-report.pdf	
423-tox	
4231-single-dose-tox	
study-report	optional folder
study-report.pdf	
4232-repeat-dose-tox	
study-report	optional folder
study-report.pdf	
4233-genotox	
42331-in-vitro	
study-report	optional folder
study-report.pdf	
42332-in-vivo	
study-report	optional folder
study-report.pdf	

4234-carcigen	
42341-lt-stud	
study-report	optional folder
study-report.pdf	
42342-smt-stud	
study-report	optional folder
study-report.pdf	
42343-other-stud	
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study-report.pdf	
4235-repro-dev-tox	
42351-fert-embryo-dev	
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study-report.pdf	
42352-embryo-fetal-dev	
study-report	optional folder
study-report.pdf	
42353-pre-postnatal-dev	
study-report	optional folder
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42354-juv	
study-report	optional folder
study-report.pdf	
4236-loc-tol	
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study-report.pdf	
4237-other-tox-stud	
42371-antigen	
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study-report.pdf	
42372-immunotox	
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study-report.pdf	
42373-mechan-stud	
study-report	optional folder
study-report.pdf	

42374-dep		
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42375-metab		
study-report	optional folder	
study-report.pdf		
42376-imp		
study-report	optional folder	
study-report.pdf		
42377-other		
study-report	optional folder	
study-report.pdf		
43-lit-ref		
folder	optional folder	
reference.pdf		
m5		
52-tab-list		
tabular-listing-var.pdf		
53-clin-stud-rep		
531-rep-biopharm-stud		
5311-ba-stud-rep		
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5312-compar-ba-be-stud-rep		
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5313-in-vitro-in-vivo-corr-stud-rep		
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5314-bioanalyt-analyt-met		
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532-rep-stud-pk-human-biomat		
5321-plasma-prot-bind-stud-rep		
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5322-rep-hep-metab-interact-stud	
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study-report.pdf	
5323-stud-other-human-biomat	
study-report	folder required and additional folders optional
study-report.pdf	
533-rep-human-pk-stud	
5331-healthy-subj-pk-init-tol-stud-rep	
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5332-patient-pk-init-tol-stud-rep	
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5333-intrin-factor-pk-stud-rep	
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5334-extrin-factor-pk-stud-rep	
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5335-popul-pk-stud-rep	
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534-rep-human-pd-stud	
5341-healthy-subj-pd-stud-rep	
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study-report.pdf	
5342-patient-pd-stud-rep	
study-report	folder required and additional folders optional
study-report.pdf	
535-rep-effic-safety-stud	
indication	multiple branches possible
5351-stud-rep-contr	
study-report	folder required and additional folders optional
study-report.pdf	
5352-stud-rep-uncontr	
study-report	folder required and additional folders optional

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UPDATE HISTORY

Date	Reason for update	Version & publication
Feb 2013	First publication as working document	v1_7 working document Feb 2013
March 2013	Publication for pilot implementation and comment	v1 March 2013
September 2016	Rules revised in line with the EU. New rules included: 1.4, 1.5 2.1, 2.2, 2.3 3.6 4.1, 4.2 7.4, 7.5 8.6 9.1, 9.2, 9.3, 9.4, 9.5, 9.BP1 to 10 10.1, 10.2 11.1, 11.2 12.1, 12.2, 12.3 14.7, 14.8, 14.10, 14.BP2, 14.BP3, 14.BP5 19.1, 19.BP1 20.1, 20.4, 20.BP9, 19.BP10 21.BP1, 21.BP2	v2 Oct 2016
01 May 2017	Implementation	