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GUIDELINE ON 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.

Document History

Final Version	Reason for Amendment	Effective Date
1	First issue, public comments incorporated and published for implementation	March 2013
2	<ul style="list-style-type: none"> - 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.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.BP10; 20.1, 20.4, 20.BP9, 19.BP10; 21.BP1, 21.BP2 - Clarification of rules 9.BP1, 2, 3, 8, 9 - Correction of filename in section 3.2.R.1.2 	October 2016
3	Revised and implemented.	April 2017
4	<ul style="list-style-type: none"> - Content revised on the latest SAHPRA guideline template - Old document number 2.22 changed to SAHPGL-HPA-03 	November 2022

DR BOITUMELO SEMETE-MAKOKOTLELA
CHIEF EXECUTIVE OFFICER

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Glossary

Abbreviation/ Term	Meaning
API	Active Pharmaceutical Ingredient (also known as Drug Substance)
CD	Compact Disc
CD-ROM	Compact Disc Read-Only Memory
CTD	Common Technical Document
DTD	Document Type Definition
DVD	Digital Video Disc
ICH	International Council for Harmonisation (of Technical Requirements for Registration of Pharmaceuticals for Human Use)
MD5	Message-Digest algorithm 5
Util	Utility folder in the eCTD Sequence. Contains technical files
XML	Extensible Markup Language
ZA/SA	South Africa
PDF	Portable Document Format

1. INTRODUCTION

This guideline provides the technical requirements to applicants on the electronic Common Technical Document (eCTD). It is to be used in the preparation and submission of applications for registration and variation of medicines to SAHPRA, in the eCTD format established by the International Council for Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use.

Applicants who apply in the eCTD format must comply with the requirements for such submissions; these are:

- the requirements defined in this guideline
- the South African Specification for eCTD Module 1
- the Electronic Common Technical Document Specification (v3.2.2), developed by the ICH M2 Expert Working Group (EWG)
- the Guidance for the Submission of Regulatory information in eCTD Format

1.1 Purpose

The eCTD is intended as an electronic-only submission.

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.

1.2 Scope

This guideline applies to all human medicines (pharmaceutical and biological). It does not apply to veterinary medicinal products or complementary medicines.

Once an applicant submits an application in the eCTD format, all responses to recommendations, additional information, and variations for the same medicine should be submitted in the eCTD format. Applicant cannot revert to the paper based CTD or eSubmission format for subsequent submissions for the same medicine.

2. LEGAL PROVISION

There are no legal provisions for this guideline.

3. eCTD VALIDATION CRITERIA

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	Not for submission types Withdrawal and Cancellation. 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	Not for submission types Withdrawal and Cancellation. 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	Not for submission types Withdrawal and Cancellation. 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	BP	Only for submission type "New application".

		Information Leaflet in section 1.3.2 should be hyperlinked to the package insert in section 1.3.1.1.		For more information, please refer to the Guidance for the Submission of Regulatory Information in eCTD format.
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ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
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 and Guidance for the Submission of Regulatory Information in eCTD format

9.BP9	ZA Module 1	A Tabulated Schedule of Amendments must exist in section 1.5.2.1.	BP	Only for some submission types of pharmaceutical responses and amendments. For more information, please refer to the Guidance for the Submission of Regulatory Information in eCTD format, section 5.6
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	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
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 zaleaf.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	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
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	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
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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	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
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

				<p>criterion can only be validated in the lifecycle (not part of a stand-alone validation).</p>
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	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
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, and 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	

ZA rule no. (V2.0)	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)
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 preregistration 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	

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)
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	P/F

							published reference DTDs if available. Please refer to document 2.27 eCTD Checksums for the checksum of the ZA DTD.	
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	P/F					

		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.						
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	P/F

							present and is placed in a correct position (i.e., ensure there is a ZA Module 1 backbone file named za-regional.xml in the folder xxxx/m1/za)	
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 a ZA Module 1 backbone file named za-regional.xml in the folder xxxx/m1/za)	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)
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
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	P/F

							the DTD versions provided in the 'util/dtd' folder	
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
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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)
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.	P/F

							Please refer to document 2.27 eCTD Checksums for the checksum of the ZA DTD.	
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	P/F					

		the ZA M1 DTD used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle.						
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 a 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	P/F

							formed and valid when compared to the DTD versions provided in the 'util/dtd' folder	
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	P/F					

		to the stylesheet provided in the util folder.						
--	--	--	--	--	--	--	--	--

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. 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.				
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. 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	Not for submission types Withdrawal and Cancellation. 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	Not for submission types Withdrawal and Cancellation. 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.				

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.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	BP	See "Amendments" guideline and Guidance for the Submission of				

		hyperlinked to the relevant documents dealing with the recommendations and responses.		Regulatory Information in eCTD format				
9.BP9	ZA Module 1	A Tabulated Schedule of Amendments should exist in section 1.5.2.1.	BP	Only for some submission types of pharmaceutical responses and amendments. For more information, please refer to the Guidance for the Submission of Regulatory Information in eCTD format, section 5.6				
				Rule 22 is replaced by rule 1.2 and 2.2	22	Util Folder	A 'util' folder exists and is in the correct location (xxxx/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	P/F

							checksum of the ZA DTD.	
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					

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)
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	P/F

							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.	
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	P/F					

		checksum for the stylesheet associated with the DTD used for the sequence.						
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

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)
14.5	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 indexmd5.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					
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

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. 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	<p>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> <p>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.</p> <p>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>	P/F

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

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)
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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.				
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	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 delete , the eCTD Validator verifies that: the modified file must exist / the title is required / href must not exist.	P/E

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)
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				New rule 17.3	14	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-litref 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
20.BP7	PDF Files	All PDF links and Hyperlinks are relative	BP		34	PDF	All PDF links and Hyperlinks are	BP

		(are not absolute or rooted).					relative (are not absolute or rooted)	
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					

ZA rule	Category (V2.0)	VALIDATION CRITERIA ZA V2.0	Severity (V2.0)	Comment (V2.0)	ZA rule	Category (V1.0)	VALIDATION CRITERIA ZA (V1.0)	Severity (V1.0)
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no. (V2.0)					no. (V1.0)			
21· Envelope Attributes								
21.BP1	Envelope Attributes	If the submission type is a Response to a preregistration recommendation or postregistration, 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 file names below are entirely variable. If the folder name does not start with this word, then the fixed filenames should be followed.

Bold, no file extension These entries indicate folder names, and are coloured in accordance with the legend above.

Regular, with file extension(.pdf) 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)

folder required and

but files can also be placed directly at this location. The subfolders and at these locations, there must be a subfolder if

additional folders optional

content is provided. Optional additional subfolders:

product-name**0000**

index.xml

index-md5.txt

m1**za**

za-regional.xml

10-application-letter

application-letter-**var**.pdf

12-application**121-application-form**

application-form-**var**.pdf

122-annexes**1221-proof-of-payment**

proof-of-payment-**var**

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

2s1-gen-info

nomenclature-**var**.pdf

structure-**var**.pdf

general-properties-**var**.pdf

32s2-manuf

manufacturer-**var**.pdf

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

control-of-materials-**var**.pdf

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

process-validation-**var**.pdf

manuf-process-development-**var**.pdf

32s3-charac

elucidation-of-structure-**var**.pdf

impurities-**var**.pdf

32s4-contr-drug-sub

ctrlstrat-**var**.pdf

32s41-spec

specification-**var**.pdf

32s42-analyt-proc

analytical-procedure.pdf

32s43-val-analyt-proc

validation-analyt-procedure.pdf

32s44-batch-analys

batch-analyses-**var**.pdf

32s45-justif-spec

justification-of-specification-**var**.pdf

32s5-ref-stand

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

reference-standards-**var**.pdf

32s6-cont-closure-sys

container-closure-system-**var**.pdf

32s7-stab

stability-summary-**var**.pdf

postapproval-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

multiple branches possible

excipient

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

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

32p5-contr-drug-prod

ctrlstrat-var.pdf

32p51-spec

specifications-var.pdf

32p52-analyt-proc

analytical-procedure.pdf

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

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 folder	multiple branches possible
substance.pdf	
32r-reg-info	optional folder
32r1-availabilit	folder required
32r11-overview	folder required
overview-var.pdf	
32r12-ref	folder required
ref-prd-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	

In line with ICH eCTD specification, "The directory/file structure would typically follow that of the drug substance section in Module 3.2.S."

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	
study-report.pdf	optional folder
4214-pd-drug-interact	
study-report	
study-report.pdf	optional folder
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 study-report.pdf	optional folder
4226-pk-drug interact study-report study-report.pdf	optional folder
4227-other-pk-stud study-report study-report.pdf	optional folder
423-tox 4231-single-dose-tox study-report study-report.pdf	optional folder
4232-repeat-dose-tox study-report study-report.pdf	optional folder
4233-genotox 42331-in-vitro study-report study-report.pdf	optional folder
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	
study-report	optional folder
study-report.pdf	
4235-repro-dev-tox	
42351-fert-embryo-dev	
study-report	optional folder
study-report.pdf	
42352-embryo-fetal-dev	
study-report	optional folder
study-report.pdf	
42353-pre-postnatal-dev	
study-report	optional folder
study-report.pdf	

42354-juv**study-report**

optional folder

study-report.pdf

4236-loc-tol**study-report**

optional folder

study-report.pdf

4237-other-tox-stud**42371-antigen****study-report**

optional folder

study-report.pdf

42372-immunotox**study-report**

optional folder

study-report.pdf

42373-mechan-stud**study-report**

optional folder

study-report.pdf

42374-dep**study-report**

optional folder

study-report.pdf

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	folder required and additional folders optional
study-report	
study-report.pdf	
5312-compar-ba-be-stud-rep	
study-report	folder required and additional folders optional
study-report.pdf	

5313-in-vitro-in-vivo-corr-stud-rep study-report study-report.pdf	folder required and additional folders optional
5314-bioanalyt-analyt-met study-report study-report.pdf	folder required and additional folders optional
532-rep-stud-pk-human-biomat 5321-plasma-prot-bind-stud-rep study-report study-report.pdf	folder required and additional folders optional
5322-rep-hep-metab-interact-stud study-report study-report.pdf	folder required and additional folders optional
5323-stud-other-human-biomat study-report study-report.pdf	folder required and additional folders optional
533-rep-human-pk-stud 5331-healthy-subj-pk-init-tol-stud-rep study-report study-report.pdf	folder required and additional folders optional
5332-patient-pk-init-tol-stud-rep	

study-report study-report.pdf	folder required and additional folders optional
5333-intrin-factor-pk-stud-rep study-report study-report.pdf	folder required and additional folders optional
5334-extrin-factor-pk-stud-rep study-report study-report.pdf	folder required and additional folders optional
5335-popul-pk-stud-rep study-report study-report.pdf	folder required and additional folders optional
534-rep-human-pd-stud 5341-healthy-subj-pd-stud-rep study-report study-report.pdf	folder required and additional folders optional
5342-patient-pd-stud-rep study-report study-report.pdf	folder required and additional folders optional
535-rep-effic-safety-stud indication	multiple branches possible
5351-stud-rep-contr	

<p>study-report study-report.pdf</p>	<p>folder required and additional folders optional</p>
<p>5352-stud-rep-uncontr study-report study-report.pdf</p>	<p>folder required and additional folders optional</p>
<p>5353-rep-analys-data-more-one-stud study-report study-report.pdf</p>	<p>folder required and additional folders optional</p>
<p>5354-other-stud-rep study-report study-report.pdf</p>	<p>folder required and additional folders optional</p>
<p>536-postmark-exp folder study-report.pdf</p>	<p>optional folder</p>
<p>537-crf-ipl study filename.pdf</p>	<p>optional folder</p>
<p>54-lit-ref folder reference.pdf</p>	<p>optional folder</p>

util

dtd

za-regional.dtd

za-envelope.mod

za-leaf.mod

ich-ectd-3-2.dtd

style

ectd-2-0.xsl

za-regional.xsl

4. REFERENCES

The following related documents are referenced:

- 4.1 Guideline for Submission in eCTD format.
- 4.2 General Information.

5. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the old guideline number 2.22 for eCTD Validation Criteria. It will be reviewed on this timeframe or as and when required.