World Health Organization

WHO-PQT Module 1 eCTD Specification

Version 1.0

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Approved by [WHO]

1 DOCUMENT CONTROL

1.1 *Change Record*

Version	Date	Author(s)	Comments
1,0	January, 2023	WHO	First Approved Version

1.2 Reviewers

Version	Name	Organisation
1.0	WHO	

2 CONTENT

3 GLOSSARY OF TERMS AND ABBREVIATIONS

Term	Definition
Applicant	A pharmaceutical company or its agent that is submitting information in support of an ***application***.
Applicant's Information	Regulatory information submitted by an ***applicant*** for, or to maintain, a marketing authorization that falls within the scope of this guidance document.
APIMF	Active Pharmaceutical Ingredient Master File
Application Type	The application type describes the ***regulatory activity*** to which the content will be submitted.
Backbone	eCTD backbone contains the table of content in XML format based on a DTD.
eCTD	Electronic Common Technical Documentation
eCTD application or also known as a dossier	A collection of electronic documents compiled by a pharmaceutical company or its agent in compliance with the WHO guidelines in order to seek a marketing authorization or any amendments thereof. An ***eCTD application*** may comprise a number of ***regulatory activities***. An eCTD application to the WHO may only comprise one dosage form and strength, under one invented product name.
Envelope	The envelope of Module 1 contains the metadata of the submission.
DTD	Document Type Definition
Leaf	A leaf element in eCTD is a document within the submission.
MA	Marketing Authorization. This is common term used in Industry. This is equivalent in WHO-PQT to the successful acceptance or prequalification of an application for a product
MAH	Marketing Authorization Holder. This is common term used in Industry. This is equivalent in WHO-PQT to the Applicant of a product.
OP	Open Part of an APIMF
RP	Restricted Part of an APIMF
Regulatory Activity	A ***single sequence or a collection of sequences*** covering the start to the end of a specific business process, e.g. a new application or a type IN change. To allow a more precise handling, the regulatory activity will be classified using a controlled vocabulary (application type or regulatory activity type) and a free text field for a short narrative description.
Sequence	A single set of information and / or electronic documents submitted at one particular time by the applicant as a part of, or the complete application. Any collection of content assembled in accordance with the eCTD specification (ICH and WHO) will be described using metadata as defined by the WHO-PQT envelope.
Submission Unit Type	The submission unit type element of the envelope metadata set describes the content at a lower level (a "sub-activity") which is submitted in relation

	to a defined regulatory activity such as the initial submission, the applicant response to validation issues or list of questions or any other additional information.

4 INTRODUCTION

This document specifies Module 1 of the electronic Common Technical Document (eCTD) for applications to the World Health Organization (WHO) PQT Unit. eCTD format will be used for four product types FPP (Finished Pharmaceutical Product), FVP (Finished Vaccine Product), APIMFs (Active Pharmaceutical Ingredient Master File), and APIPQ (Active Pharmaceutical Ingredient Prequalification).

This document should be read together with the ICH eCTD Specification 3.2.2 to prepare a valid eCTD submission to the WHO PQT unit. The latest version of the ICH eCTD Specification can be found at: https://www.ich.org/page/electronic-standards-estri.

4.1 eCTD Workflow

The eCTD specification currently only regulates one-way transmission from applicants to the agency and focuses on the data submission. Applicants shall establish an eCTD package to initiate the process.

During the entire life cycle, once submitted in an eCTD format, the dossier and subsequent applications must remain in an eCTD format and must not be submitted in a non-eCTD format, this includes any future post-marketing changes.

For applications against an already prequalified product, section 10 describes how to transfer a non-eCTD submission to an eCTD submission.

The eCTD workflow describes regulatory activities with the attribute values of sequence and related sequence. This information is provided as envelop attribute and referred to Appendix 13.1. The correct use of sequence and related sequence is explained in Appendix 13.2.

4.2 eCTD structure

The structure of the WHO-PQT M1 eCTD is shown in Appendix 13.2 which includes the technical files and folders from module 1. Besides the Util folder including both DTD's, one index.xml file and one MD5 file (index-md5.txt) are part of the module.

5 WHO-PQT MODULE 1 INFORMATION

The eCTD module 1 of WHO-PQT is designed to cover API, APIMF, FFP and FVP applications in a single module. Each of these applications require individual dossiers. Based on the ICH Common Technical Document ("CTD") specifications thus module 1 should contain WHO-specific administrative information, product information, mandatory and optional documents and regulatory business information.

Published on the WHO-PQT webpage, required business content and structure is public available in legally binding guidance documents at the WHO-PQT webpage (LINK).

A mandatory document shall be included for all application types is a cover letter.

The applicant creates the application on the ePQS portal and includes the application form and cover letter in the eCTD dossier.

6 GENERAL MODULE 1 DESIGN

6.1 General Architecture of Module 1

The WHO Module 1 architecture is similar to that of Modules 2 to 5 of the eCTD, comprising a directory structure and a backbone with leaves. The backbone must be a valid XML document according to the WHO Document Type Definition (DTD). The backbone (whopqt-regional.xml) contains metadata for the leaves, including pointers to the files in the directory structure. In addition, the WHO DTD defines metadata at the submission level in the form of an envelope. The root element is „`whopqt-backbone`" and contains two elements: „`whopqt-envelope`" and "`m1-whopqt`".

The WHO-PQT DTD is modularized, i.e. the envelope and leaves are referenced from the main part of the DTD as external entities called respectively *whopqt-envelope.mod* and *whopqt-leaf.mod*. The WHO-PQT "`leaf`" is identical to the leaf element described in the ICH eCTD DTD; reference is made to Table 6-8 of the ICH eCTD Specification 3.2.2.

Files can be referred to across modules (e.g., from Module 1 to Module 2) or across sequences within the same eCTD application; When referring to files across modules or across sequences, the reference must always be relative, starting from the location of the XML file.

The eCTD contains more than documents and requires the applicant to deliver technical information such as the DTD, the MD5 checksum, additional metadata, and other information. The files that are required by WHO-PQT in addition to the documents are as follows:

Top level folder:

- index.xml: eCTD backbone file, the table of content
- index-md5.txt the MD5 checksum file

Util folder:

- dtd folder File folder for document type definition files

DTD folder:

- whopqt-envelope.mod
- whopqt-leaf.mod
- whopqt-regional.dtd WHO regional DTD
- ich-ectd-3-2.dtd ICH DTD

6.2 Envelope

The „`whopqt-envelope`" element is designed to be used for all types of applications for a given medicinal product and will mainly be used for the initial processing at the WHO Prequalification Team level. The envelope provides metadata at the submission level. A description of each envelope element is provided in Appendix 13.1 of this specification.

6.3 m-1-whopqt

The "`m1-whopqt`" element of the WHO-PQT regional DTD is based on the same conceptual approach as the common part of the ICH eCTD DTD. It provides an XML catalogue with meta-data at the leaf level including pointers to the location of files in a directory structure. As for the ICH eCTD DTD, the "`m1-whopqt`" element maps to the directory structure. A tabular overview of the directory is contained Appendix 2: WHO-PQT M1 Element, Files and Folders of this specification.

7 FILE AND FORMAT SPECIFICATION

7.1 PDF File Format

Version

The currently recommended PDF version (v1.4 to v1.7) is listed on the ICH website. Submitted PDF files should be readable by Adobe Reader or Adobe Acrobat DC (or higher) without the requirement for additional software or components. If other programs or software were used during the creation of the PDF file, applicants should make sure that no need for additional programs or software before opening, viewing, or positioning the file.

Limitation

PDF files must not contain JavaScript, dynamic content (such as sound effects, videos, special effects, animations, or 3D objects); nor must they contain comments. Also make sure that all hyperlinks in the document are still valid.

Safety

PDF files must not have security settings or password protection. The text should be set to allow printing, select text/ graphics, add/ change comments, and form fields.

File Size

The size of a single PDF file should not exceed 500 MB.

Font

If the font used to create the text is not provided in the PDF, or if it is not available on the examiner's computer, the PDF reader will automatically replace the font that displays the text. Font substitution may affect the appearance and results of the file, and in some cases, the image of the file contents. Therefore, avoid using custom fonts when creating PDF files.

Font Size

Font size 12 should be used for narrative texts. Font sizes 9 to 12 can be used for other text, e.g captions of tables and figures. When choosing the font size, consider providing enough information on a single page to make it easier for reviewers to compare data, while maintaining clarity and readability. The commonly accepted font size in the table is Times New Roman font size 9-10, or other recommended fonts of considerable size. Avoid using smaller fonts. When creating a file containing scanned image, make sure that after resizing the image, the effective font size will not be reduced below the recommended size.

Font color

It is recommended to submit documents with words in black, hyperlinks can be marked in blue. Light colors may cause difficulty reading on the screen and should be avoided. The use of background shadows can also cause

reading difficulties and should be avoided, too. Applicants can also use the printer to print a sample page from a document to preview before sending it.

Orientation

The page should be displayed in the proper orientation for reading. The correct page orientation prevents reviewers from rotating the page. For this reason, before storing the PDF file in its final form, the page orientation of landscape pages should be exactly set to landscape to ensure correct page display.

Page size and border

The print area of the page should fit both A4 paper (21.0x29.7cm) and letter paper (21.6x27.9 cm). Binding margins should be at least 2.5cm (such as the left side of each page in portrait pages and the top side of each page in landscape pages) to avoid obscuring information. The remaining margins should be at least 1.0 cm. Header and footer information and page numbers must not appear in the margins.

Header and footer

ICH M4 stipulates that all pages of the document should include a header and footer that briefly describe the subject for reviewers to identify the document by a large amount of interpretation data. Also, each page (header or footer) of the document should have a unique label for easy identification when reviewing multiple documents on the screen at the same time. The unique label does not necessarily include CTD chapters or other interpretive materials but should be a general subject sufficient to identify the document. (Such as research label or lot number ... etc.)

Page number

The first page of the document shall be numbered as page 1, and all subsequent pages (including appendices and attachments) shall be numbered consecutively in Arabic numerals. Page numbers should not use Roman numerals (for example: title page, table of contents) and pages should not be unnumbered (for example: title page).

Document resource

Avoid using image-based PDF documents whenever possible. Scanning paper to generate a PDF document usually leads to a lower image resolution in comparison to a PDF document generated from other sources such as word files. Scanned documents are often difficult to read, and content is not allowed to be searched, copied or edited. If scanned documents must be sent, the text should be made searchable as much as possible, e. g. using Optical Character Recognition (OCR) to convert documents.

Paper should be scanned using the dpi settings listed in the table below. Scan documents at a resolution of 300 dots per inch (dpi) to ensure that document pages are legible both on the computer screen and printing, while minimizing file size. Avoid reprinting the scanned documents, which always reduce the resolution again. The scanned image must not be resized. See the table below for the resolutions of various types of images.

Recommended resolutions

Document types	Resolution
Handwritten notes	300 dpi （Black ink）
Output graphics from drawing	300 dpi
Black and white photo	600 dpi （8-bit gray scaling）
Color photo	300 dpi （24-bit RGB）
Gel, Karyotype	600 dpi （8-bit gray scaling）
HPLC	300 dpi

Compress images and reduce file size

Colour or grey scaling images should be compressed using JPEG 2000 and monochrome images should be compressed using JBIG2. Compressing images is a way to reduce file size. Some compression methods cause data loss and may cause compression distortions that affect the information, but both methods mentioned in this section have lossless compression options.

Colour of Image

It is difficult to ensure that the colours seen by the reviewers are the same as those in the original image. To avoid this difference, ICC profiles should be used for colour matching (for more information, see International Color Consortium, ICC; www.color.org).

Navigation

Hyperlinks and bookmarks improve the positioning of documents. Hyperlinks can be underlined and marked with blue text. Even if there is no table of contents (TOC) in the file, bookmarks should still be created or marked.

Documents over 5 pages should include hyperlinked TOC and bookmarks, except for references. (e.g., m2.7.5, m3.3, m4.3, m5.4)

In general, for documents with TOC, bookmark each item listed. Bookmarks should include all tables, figures, publications, references, and appendices. These bookmarks are especially important for improving the positioning of documents. A hierarchy of no more than 4 levels is recommended, but more levels can be established if it helps positioning. The hyperlinks link related chapters, tables, figures, references, and appendices that are not on the same page, which also helps improve the efficiency of document positioning.

When establishing cross-document hyperlinks, relative paths should be considered to minimize the chance of losing hyperlink functionality when documents are moved between storage devices. When creating bookmarks and hyperlinks, applicants should make sure that target pages is displayed at the same magnification as source pages.

Preview

The preview of the PDF file should be set to bookmarks or pages. If there is no bookmark, preview should be set as a single page. Magnification and page format should be set to default values.

Optimization

To ensure that PDF files can be reviewed at high speed, it should be set to optimize the PDF file with web view.

XML

A working group of the World Wide Web Consortium (W3C) has developed Extensible Markup Language (XML). This is a non-proprietary language used to improve upon previous markup languages, including Standard Generalized Markup Language (SGML) and Hypertext Markup Language (HTML).

XML is currently used for some content of eCTD. Applicants should contact the health authority in the applicant's area to find out whether to accept these XML files. For more information on XML standards, visit the W3C website.

SVG

Scalable Vector Graphics (SVG) is a language for describing two-dimensional graphics in XML. SVG supports three types of graphics: vector graphics (for example, paths composed of lines and curves), raster images and text. Graphical objects can group, style, transform and combine previously rendered objects. The text can be located in any XML namespace suitable for the application, which enhances the searchability and browsability of SVG graphics. The feature set includes transformation, clipping paths, alpha channels, filter effects, template objects and extensibility.

SVG images can be dynamic and interactive. SVG's Archive Object Model (DOM) includes a complete XML DOM, which enables simple and effective vector graphics animation through scripting. Users can assign a rich set of event handlers to any SVG graphic object, such as on mouseover and onclick. Because of its compatibility and use of other Web standards, users can perform functions such as scripting on SVG elements and other XML

elements from different namespaces in the same Web page. SVG files must not contain JavaScript. For more information about the SVG specification, please visit the W3C website.

7.2 Other File Formats

The use of PDF is currently mandatory, other file formats for Module 1 content are allowed in the following sections:

1.3.1 Summary of Product Characteristics (SmPC)

1.3.3 Package Leaflet

1.15 Response to questions

See following table:

File Format	Format Name	File Format	Format Name
.doc	Microsoft Windows Word document	.docx	Microsoft Word Open XML document

1.3.2 Labelling Text and Mockups – see following table:

File Format	Format Name	File Format	Format Name
.doc	Microsoft Windows Word document	.docx	Microsoft Word Open XML document
.jpg, jpeg	Joint Photographic Expert Group	.gif	Graphics Interchange Format
.png	Portable Network Graphics	.svg	Scalable Vector Graphics

1.4.1 Bioequivalence trial information form (BTIF) – see following table

File Format	Format Name	File Format	Format Name
.doc	Microsoft Windows Word document	.docx	Microsoft Word Open XML document
.xls	Microsoft Excel document	.xlsx	Microsoft Excel Open XML document
.bmp	Bitmap Graphics	.gif	Graphics Interchange Format
.jpg, jpeg	Joint Photographic Expert Group	.png	Portable Network Graphics

1.5 Editable review documents – no PDF document allowed, allowed file formats see following table

File Format	Format Name	File Format	Format Name
.doc	Microsoft Windows Word document	.docx	Microsoft Word Open XML document

For data requested by the WHO which needs to be provided in any other format than specified above, please follow the instructions given by requestor.

7.3 *File Naming Convention*

File names in Module 1 follow one of two conventions.

FIXED is a defined component of the filename based on the CTD section and VAR is an additional optional variable component. EXT represents the file extension. Components are separated by a hyphen (except the dot for the file extension). No spaces should be used within each component, but hyphens can be used in the variable part to separate several words.

Fixed components shall be used. The variable component is optional and should be used as appropriate to further define these files. The variable component, if used, should be a meaningful concatenation of words with the option of hyphens for separators and should be kept as brief and descriptive as possible to avoid exceeding the maximum path length. File extensions in line with this specification should be applied as applicable.

There are no recommendations for variable components in this specification. The format of the file is indicated by the file extension. File names should always be in lowercase, in line with the ICH eCTD specification.

Examples:

cover.pdf
form-xxx.pdf
form-annex-01.pdf
mockups-tablet10mg.pdf
packaging-tablet1-5mg.pdf

7.4 Directory naming Convention

The WHO-PQT Module 1 Specification provides a directory and file structure that is strongly recommended. For details, please see Appendix 13.2. The same high-level directory structure is used for all 4 product types.

7.5 *Folder and File Name Path Length*

The overall folder and file name path length starting from the sequence number should not exceed 180 characters, for any file in any module. This is WHO-PQT requirement, and it is acknowledged that this is less than the ICH agreed overall path length.

7.6 *Node Extensions*

Node extensions are a way of providing extra organizational information to the eCTD. The node extension

should be visualized as an extra heading in the eCTD and should be displayed as such when the XML backbone is viewed.

8 HANDLING OF EMPTY OR MISSING ECTD SECTIONS

Placeholder documents highlighting 'no relevant content' should not be included in the eCTD. These files would create a document lifecycle for non-existent documents, and unnecessary complication and maintenance of the eCTD lifecycle. So, sections without information should be left empty and justified in the respective Module 2 document, as relevant.

9 APIPQ AND APIMF HANDLING

The main objective of the APIMF is to allow valuable confidential intellectual property or 'know-how' of the manufacturer of the active pharmaceutical ingredient (API) to be protected, while at the same time allowing the applicant or Marketing Authorization Holder (MAH) of the finished pharmaceutical product to take full responsibility for the medicinal product and the quality and quality control of the active substance. The WHO thus must have access to the complete information that is necessary for an evaluation of the suitability of the use of the active substance in the medicinal product.

The Applicant/MAH of the FPP is responsible for ensuring that they have access to all relevant information concerning the current manufacturer of the active substance, in order to ensure that they are capable of taking full responsibility for the quality of the API in the medicinal product.

The Applicant/MAH should include a copy of the OP (open part) in the FPP dossier (CTD format section 3.2.S). The version of the OP in the FPP dossier should be the most recent and it should be identical to the OP as supplied by the APIMF holder to the WHO-PQT as part of the APIMF.

The scientific information in the APIMF should be physically divided into two separate parts, namely the Open (Applicant's) Part (OP) and the Restricted Part (RP). The OP contains the information that the APIMF holder regards as non-confidential to the Applicant/MA holder, whereas the RP contains the information that the APIMF holder regards as confidential. It is emphasized that the OP is still a confidential document.. In all cases the OP should contain sufficient information to enable the Applicant/MA holder to take full responsibility for an evaluation of the suitability of the specification for the active substance to control the quality of this active substance for use in the manufacture of a specified medicinal product.

The RP may contain the remaining information, such as detailed information on the individual steps of the manufacturing method (reaction conditions, temperature, validation, and evaluation data of critical steps) and the quality control during the manufacture of the active substance. The WHO may not accept that information has not been disclosed to the Applicant/MA holder. In such cases, the WHO may ask for an amendment to the OP.

In addition to the OP and RP, the APIMF should contain a separate summary for both the OP and the RP. Each version of the OP and RP should have unique and independent version control numbers.
Since an APIPQ application (like an FPP application) only ever refers to the corresponding APIMF product's

documentation, a separate document repository for APIPQ products will not be put in place. Rather, all CTD documents will be filed under the associated APIMF product record.

10 TRANSITION FROM NON-ECTD TO ECTD

A baseline submission is a compiled submission of the current status of the dossier, i.e., resubmission of all currently valid documents that have already been provided to WHO for registration but in another format. A baseline is the start of an eCTD when changing from paper or any other electronic format.

- The baseline would preferably consist of high-quality electronic source documents.
- The baseline should normally be submitted as sequence 0000 or with the next subsequent number of the dossier.
- The application type “Post-PQ change”, application sub-type “eCTD-Baseline” and submission unit type “reformat” should be used in the envelope
- The baseline should always be a separate submission and should never include new applications.

A baseline must pass the technical eCTD validation without any issue. In addition, the applicant has to state in the cover letter that the provided submission in eCTD format is a digital copy based on the last registered submission at WHO-PQT.

11 UNIVERSAL UNIQUE IDENTIFIER (UUID)

Although the eCTD envelope contains several pieces of information about the eCTD application that the sequence belongs to, such as the generic name and the product name, all eCTD sequences built in accordance with this specification must contain a UUID, linking the sequence to the eCTD application to which dossier it belongs.

The UUID is used by WHO to facilitate archiving the sequence with the correct eCTD lifecycle and for automated sorting of incoming eCTD submissions to the correct eCTD lifecycle. It is important that the UUID for each eCTD lifecycle is unique, and it should therefore always be machine generated, i.e. be created by the eCTD building tool or, if not possible, by using an online UUID generator. Creating the UUID with uppercases or lowercases is not restricted but needs be kept as chosen during the full lifecycle.

The applicant should generate a UUID based on ISO/IEC 11578:1996 and ITU-T Rec X.667 | ISO/IEC 9834-8:2005. It is a hexadecimal number in the form of xxxxxxxx-xxxx-xxxx-xxxx-xxxxxxxxxxxx, showing 32 digits and 4 hyphens. The ‘x’ will be replaced by a number or a letter. It is recommended to use randomly generated sections (version 4 of UUID types).

Such UUID would for example look like: 46595546-4550-4a3c-9535-fc6380f4f468.
This structure guarantees uniqueness across applicants and applications. The UUID will be generated for the first time when creating the first sequence following the implementation of the UUID requirement in the specification and will be provided in the eCTD envelope. All subsequent sequences for that same eCTD lifecycle should contain the same UUID. In this way, sequences can be allocated automatically to the correct eCTD lifecycle by the WHO.

Beside the technical validation checking the correct UUID, the WHO can also check that the UUID is not the same as in another already existing eCTD lifecycle in the WHO's eCTD repository. Since the UUID is used in the automatic processing of eCTD sequences, it is important that each UUID in the eCTD repository is unique. Therefore, even if this is not part of the eCTD technical validation criteria, in such cases, WHO will contact the applicant/MAH and request an updated eCTD sequence with a new UUID. If this is not the first sequence of the eCTD lifecycle, the applicant/MAH must also update all previously submitted sequences in the eCTD lifecycle that have been assigned this same UUID.

12 CHANGE CONTROL

The WHO-PQT Module 1 specification is likely to change with time. Factors that could affect the content of the specification include, but are not limited to:

- Change in the content of the Module 1 for the CTD, either through the amendment of information, at the same level of detail, or by provision of more detailed definition of content and structure
- Change to the WHO specific requirements for applications that are outside the scope of the CTD
- Update of standards that are already in use within the eCTD
- Identification of new standards that provide additional value for the creation and/or usage of the eCTD
- Identification of new functional requirements
- Experience of use of the eCTD by all parties, in particular Module 1.

13 APPENDIX

13.1 Appendix 1: The WHO-PQT Envelope Elements

XML Element	XML Attribute	Description/Instructions	Example	Constraint	Occurrence	Valid Value Reference
whopqt-envelope		Root element that provides meta-data for the submission.	N/A	**Mandatory**	**single value**	
identifier		Fill in an UUID. The same UUID will be used for all sequences of an eCTD application	123e4567-e89b-12d3-a456-426614174000 (Please do not use)	**Mandatory**	**single value**	
product		Product provides the information for which product the submission shall be. It is descriped by attributes type and subtype	N/A	Mandatory	single value	
	type	Product code for type of product See Attribute Type List	FPP	**Mandatory**	**single value**	**Product Type.xml**
	subtype	Closer description of the type of the product See Attribute Type List	FPP, BTP	**Mandatory for FPP only**	**single value**	**Product Sub-Type.xml**
product-name		For FPPs this equates to the SF field Generic Name. For FVPs this equates to the SF field WHO vaccine name (full). For APIMFs and APIPQs this equates to the SF field Active Pharmaceutical Ingredient for publishing	WonderPill	**Mandatory**	**single value**	
application		Provides administrative information associated with the submission. The type of regulatory activity to which the content will be submitted. Each should be multiple choices.	N/A	Mandatory	single value	

	type	See Attribute Type List		**Mandatory**	**single value**	**Application Type.xml**
	subtype	See Attribute Type List		**mandatory for FPP. Optional for FVP, API and APIMFs**	**single value**	**Application Sub-Type.xml**
submission-unit		Provides administrative information associated with the regulatory activity.	N/A	Mandatory	single value	
	type	Submission unit type describes the content at a lower level (a sub-category for the activity) which is submitted in relation to a defined regulatory activity See Attribute Type List		**Mandatory**	**single value**	**Submission Unit Type.xml**
applicant-organisation		The name of the company submitting the eCTD.		**Mandatory**	**single value**	
contact-email		Email Address of the Contact from Applicant		**Optional**	**multi-value**	
whopqt-prod-id		WHO Product ID: Issued by Salesforce		**Mandatory**	**single value**	
sf-case-id		SF Case ID: Issued by Salesforce		**Mandatory**	**single value**	
sequence-number		This is the sequence number of the submission – this should start at 0000 for the initial submission, and then increase incrementally with each subsequent submission related to the same product, e.g. 0000, 0001, 0002, 0003, etc.		**Mandatory**	**single value**	
related-sequence		This is the sequence number of previous submission(s) to which this submission relates, e.g. the responses to questions to a particular post qualification change. In the case of submission unit types 'initial' and 'reformat', related sequence is identical to the sequence number.		**Mandatory**	**multi-value**	
description		Application description: this element is used to provide a free text description of the submission		**Optional**	**single value**	

13.2 Appendix 2: WHO M1 Element, Files and Folders

The WHO-PQT Module 1 XML Submission contains an element for each Table of Contents entry of the Notice to Applicants Module 1. The following sections describe information that is captured within the Module 1 XML submission in an eCTD, but which is not captured within the M4 common technical document (CTD) of ICH (https://www.ich.org/page/ctd) for Module 1.

Sequential number	Number	CTD section number
	Title	CTD title
	Element	Element name in the WHO Backbone
	File	File/Directory name from m1/whopqt – should be relative path from m1/whopqt e.g. xxxx.pdf. This is consistent with ICH standards. The file extension corresponds to the file type; i.e. the “pdf” extension is only illustrative.
	Comment	

1	Number	
	Title	Module 1 WHO
	Element	m1-whopqt
	Directory	m1/whopqt
	Comment	Top level directory for the WHO Module 1 as per ICH eCTD Specification
2	Number	
	Title	
	Element	
	File	m1/whopqt/whopqt-regional.xml
	Comment	The WHO-PQT Regional XML instance including the envelope information. Note that the operation attribute for the whopqt-regional.xml should always be set to ‘new’.
3	Number	1.0
	Title	Cover Letter
	Element	m1-0-cover
	File	m1/whopqt/10-cover/cover-VAR.EXT
	Comment	

4	Number	1.2
	Title	Application information
	Element	m1-2-appinfo
	Directory	m1/whopqt/12-appinfo
	Comment	
5	Number	1.2.1
	Title	Application Form
	Element	m1-2-1-appform
	File	m1/whopqt/12-appinfo/121-appform/appform-VAR.EXT
	Comment	
6	Number	1.2.2
	Title	Manufacturing Authorisations/Registrations/CPPs
	Element	m1-2-2-maa
	File	m1/whopqt/12-appinfo/122-maa/maa-VAR.EXT
	Comment	
7	Number	1.2.3
	Title	Copy of certificate(s) of suitability of the European Pharmacopoeia (CEP) (including any annexes)
	Element	m1-2-3-cep
	File	m1/whopqt/12-appinfo/123-cep/cep-VAR.EXT
	Comment	
8	Number	1.2.4
	Title	Letters of access for active pharmaceutical ingredient master files (APIMFs)
	Element	m1-2-4-loa
	File	m1/whopqt/12-appinfo/124-loa/loa-VAR-EXT
	Comment	
9	Number	1.2.5
	Title	Good manufacturing practices (GMP) information
	Element	m1-2-5-gmp
	File	m1/whopqt/12-appinfo/125-gmp/gmp-VAR.EXT
	Comment	

10	Number	1.2.6
	Title	Biowaiver requests in relation to conducting a comparative bioavailability study
	Element	m1-2-6-bw
	File	m1/whopqt/12-appinfo/126-bw/bw-VAR.EXT
	Comment	
11	Number	1.2.7
	Title	Confirmation of API prequalification document (CPQ)
	Element	m1-2-7-cpq
	File	m1/whopqt/12-appinfo/127-cpq/cpq-VAR.EXT
	Comment	
12	Number	1.2.8
	Title	Contract manufacturing/testing/licensing agreements
	Element	m1-2-8-contracts
	File	m1/whopqt/12-appinfo/128-contracts/contracts-VAR.EXT
	Comment	
13	Number	1.2.9
	Title	Technology transfer protocol and reports/technology packs
	Element	m1-2-9-techpack
	File	m1/whopqt/12-appinfo/129-techpack/techpack-VAR.EXT
	Comment	
14	Number	1.2.10
	Title	Biosimilarity Claim
	Element	m1-2-10-biosim
	File	m1/whopqt/12-appinfo/1210-biosim/biosim-VAR.EXT
	Comment	
15	Number	1.2.11
	Title	Summary of Changes Document
	Element	m1-2-11-chansum
	File	m1/whopqt/12-appinfo/1211-chansum/chansum-VAR.EXT
	Comment	

16	Number	1.2.12
	Title	Previous Commitments
	Element	m1-2-12-commit
	File	m1/whopqt/12-appinfo/1212-com/com-VAR.EXT
	Comment	
17	Number	1.2.13
	Title	NRA approval
	Element	m1-2-13-nraapprov
	File	m1/whopqt/12-appinfo/1213-nraapprov/nraapprov-VAR.EXT
	Comment	
18	Number	1.3
	Title	Product Information
	Element	m1-3-pi
	Directory	m1/whopqt/13-pi/
	Comment	
19	Number	1.3.1
	Title	Summary of Product Characteristics (SmPC)
	Element	m1-3-1-smpc
	File	m1/whopqt/13-pi/131-smpc/smpc-VAR.EXT
	Comment	
20	Number	1.3.2
	Title	Labelling Text and Mockups
	Element	m1-3-2-label
	File	m1/whopqt/13-pi/132-label/mockups-VAR.EXT m1/whopqt/13-pi/132-label/labels-VAR.EXT
	Comment	
21	Number	1.3.3
	Title	Package Leaflet
	Element	m1-3-3-pil
	File	m1/whopqt/13-pi/133-pil/pil-VAR.EXT
	Comment	

22	Number	1.3.4
	Title	Description of immunization /administration devices to be delivered with the vaccine
	Element	m1-3-4-imd
	File	m1/whopqt/13-pi/134-imd/imd-VAR.EXT
	Comment	
23	Number	1.3.5
	Title	Recommended schedule and route of administration
	Element	m1-3-5-rsra
	File	m1/whopqt/13-pi/135-rsra/rsra-VAR.EXT
	Comment	
24	Number	1.4
	Title	Regional summaries
	Element	m1-4-regsum
	Directory	m1/whopqt/14-regsum/
	Comment	
25	Number	1.4.1
	Title	Bioequivalence trial information form (BTIF)
	Element	m1-4-1-btinfo
	File	m1/whopqt/14-regsum/141-btinfo/btinfo-VAR.EXT
	Comment	
26	Number	1.4.2
	Title	Quality information summary (QIS)
	Element	m1-4-2-qis
	File	m1/whopqt/14-regsum/142-qis/qis-VAR.EXT
	Comment	
27	Number	1.5
	Title	Editable review documents
	Element	m1-5-erd
	File	m1/whopqt/15-erd/erd-VAR.EXT
	Comment	e.g., product information, BTIF, QIS, QOS-BTP, QOS–PD, biowaiver forms

28	Number	1.6
	Title	Product Samples Details
	Element	m1-6-sample
	File	m1/whopqt/16-sample/sample-VAR.EXT
	Comment	e.g. FPP, device(s), certificates of analysis
29	Number	1.7
	Title	Biosimilarity information summary
	Element	m1-7-bis
	File	m1/whopqt/17-bis/bis-VAR.EXT
	Comment	
30	Number	1.8
	Title	Information relating to pharmacovigilance and post-marketing safety documentation
	Element	m1-8-phv
	Directory	m1/whopqt/18-phv/
	Comment	
31	Number	1.8.1
	Title	Pharmacovigilance system (Medicines)
	Element	m1-8-1-pvs
	File	m1/whopqt/18-phv/181-pvs/pvs-VAR.EXT
	Comment	
32	Number	1.8.2
	Title	Risk-management system and prequalification-specific addendum to the risk management plan (Medicines)
	Element	m1-8-2-rmpm
	File	m1/whopqt/18-phv/182-rmpm/rmpm-VAR.EXT
	Comment	
33	Number	1.8.3
	Title	Post-marketing pharmacovigilance or Risk Management Plan (Vaccines)
	Element	m1-8-3-rmpv
	File	m1/whopqt/18-phv/183-rmpv/rmpv-VAR-EXT
	Comment	

34	Number	1.8.4
	Title	Initial evaluation of vaccines that have been in the market for more than five years or reassessment of already prequalified vaccines
	Element	m1-8-4-inieva
	File	m1/whopqt/18-phv/184-inieva/inieva-VAR-EXT
	Comment	
35	Number	1.8.5
	Title	Ongoing clinical studies for vaccines licensed within the last five years
	Element	m1-8-5-ogcsv
	File	m1/whopqt/18-phv/185-ogcsv/ogcsv5-VAR-EXT
	Comment	
36	Number	1.9
	Title	Presubmission/scientific advice information
	Element	m1-9-presub
	Directory	m1/whopqt/19-presub/
	Comment	
37	Number	1.9.1
	Title	Presubmission meeting minutes
	Element	m1-9-1-premtg
	File	m1/whopqt/19-presub/191-premtg/premtg-VAR.EXT
	Comment	
38	Number	1.9.2
	Title	Scientific advice information
	Element	m1-9-2-sciadv
	File	m1/whopqt/19-presub/192-sciadv/sciadv-VAR.EXT
	Comment	
39	Number	1.9.3
	Title	Letter of Intention
	Element	m1-9-3-loi
	File	m1/whopqt/19-presub/193-loi/loi-VAR.EXT
	Comment	

40	Number	1.10
	Title	Compliance Info
	Element	m1-10-compliance
	Directory	m1/whopqt/110-compliance
	Comment	
41	Number	1.10.1
	Title	Certificate of Establishment Licensing
	Element	m1-10-1-estcert
	File	m1/whopqt/110-compliance/1101-estcert/estcert-VAR.EXT
	Comment	
42	Number	1.10.2
	Title	Policy for assignment of date of manufacture
	Element	m1-10-2-poliassig
	File	m1/whopqt/110-compliance/1102-poliassig/poliassig-VAR.EXT
	Comment	
43	Number	1.10.3
	Title	Environmental Risk Assessment
	Element	m1-10-3-environrisk
	File	m1/whopqt/110-compliance/1103-environrisk/environrisk-VAR.EXT
	Comment	
44	Number	1.11
	Title	Vaccine composition, presentations and scheduling information
	Element	m1-11-vac-comp
	Directory	m1/whopqt/111-vac-comp/
	Comment	
45	Number	1.11.1
	Title	Presentations available to UN agencies
	Element	m1-11-1-unpress
	File	m1/whopqt/111-vac-comp/1111-unpress/unpress-VAR.EXT
	Comment	

46	Number	1.11.2
	Title	Vaccine temperature stability profile to support prequalification
	Element	m1-11-2-vacstab
	File	m1/whopqt/111-vac-comp/1112-vacstab/vacstab-VAR.EXT
	Comment	
47	Number	1.11.3
	Title	Template of lot summary protocol
	Element	m1-11-3-sumprot
	File	m1/whopqt/111-vac-comp/1113-sumprot/sumprot-VAR.EXT
	Comment	
48	Number	1.11.4
	Title	PSPQ Self-assessment
	Element	m1-11-4-pspqs
	File	m1/whopqt/111-vac-comp/1114-pspqs/pspqs-VAR.EXT
	Comment	
49	Number	1.12
	Title	Supplemental pre-clinical and clinical Information (Pre-marketing)
	Element	m1-12-supplement
	Directory	m1/whopqt/112-supplement/
	Comment	
50	Number	1.12.1
	Title	Pre-clinical trials sponsored by the applicant
	Element	m1-12-1-preclinpqt
	File	m1/whopqt/112-supplement/1121-preclinpqt/preclinpqt-VAR.EXT
	Comment	
51	Number	1.12.2
	Title	Clinical trials sponsored by the applicant
	Element	m1-12-2-clinpqt
	File	m1/whopqt/112-supplement/1122-clinpqt/clinpqt-VAR.EXT
	Comment	

52	Number	1.12.3
	Title	Final approved protocol by ERC and NRA
	Element	m1-12-3-prot-ercnra
	File	m1/whopqt/112-supplement/1123-prot-ercnra/prot-ercnra-VAR.EXT
	Comment	
53	Number	1.12.4
	Title	Clinical trials currently ongoing
	Element	m1-12-4-ong-clinpqt
	File	m1/whopqt/112-supplement/1124-ong-clinpqt/ong-clinpqt-VAR.EXT
	Comment	
54	Number	1.12.5
	Title	Other studies with applicant product for which the applicant is not the sponsor
	Element	m1-12-5-oth-clinpqt
	File	m1/whopqt/112-supplement/1125-oth-clinpqt/oth-clinpqt-VAR.EXT
	Comment	
55	Number	1.12.6
	Title	Complementary Clinical summary
	Element	m1-12-6-sum-clin
	File	m1/whopqt/112-supplement/1126-sum-clin/sum-clin-VAR.EXT
	Comment	
56	Number	1.12.7
	Title	NRA(s) Assessment Report
	Element	m1-12-7-assessnra
	File	m1/whopqt/112-supplement/1127-assessnra/assessnra-VAR.EXT
	Comment	
57	Number	1.12.8
	Title	Clinical Independent expert report
	Element	m1-12-8-cierpt
	File	m1/whopqt/112-supplement/1128-cierpt/cierpt-VAR.EXT
	Comment	

58	Number	1.13
	Title	Regulatory actions
	Element	m1-13-reg-act
	Directory	m1/whopqt/113-reg-act/
	Comment	
59	Number	1.13.1
	Title	Information on refusals, withdrawals, suspensions
	Element	m1-13-1-infrws
	File	m1/whopqt/113-reg-act/1131-infrws/infrws-VAR.EXT
	Comment	
60	Number	1.13.2
	Title	List of lots rejected by an NRA
	Element	m1-13-2-lotsrej
	File	m1/whopqt/113-reg-act/1132-lotsrej/lotsrej-VAR.EXT
	Comment	
61	Number	1.13.3
	Title	Restrictions on distributions and recalls of lots
	Element	m1-13-3-rest
	File	m1/whopqt/113-reg-act/1133-rest/rest-VAR.EXT
	Comment	
62	Number	1.13.4
	Title	Clinical trial suspensions
	Element	m1-13-4-clinsusp
	File	m1/whopqt/113-reg-act/1134-clinsusp/clinsusp-VAR.EXT
	Comment	
63	Number	1.13.5
	Title	Dosage or schedule changes since initial marketing authorization
	Element	m1-13-5-dosage
	File	m1/whopqt/113-reg-act/1135-dosage/dosage-VAR.EXT
	Comment	

64	Number	1.13.6
	Title	Changes in target populations since the initial marketing authorization
	Element	m1-13-6-chantag
	File	m1/whopqt/113-reg-act/1136-chantag/chantag-VAR.EXT
	Comment	
65	Number	1.14
	Title	Distribution Information
	Element	m1-14-distrinfo
	Directory	m1/whopqt/114-distrinfo/
	Comment	
66	Number	1.14.1
	Title	Quantity of finished product distributed in the domestic market
	Element	m1-14-1-qfp
	File	m1/whopqt/114-distrinfo/1141-qfp/qfp-VAR.EXT
	Comment	
67	Number	1.14.2
	Title	Countries where the product has received a Marketing Authorization
	Element	m1-14-2-maaothers
	File	m1/whopqt/114-distrinfo/1142-maaothers/maaothers-VAR.EXT
	Comment	
68	Number	1.14.3
	Title	Release process by the NRA/NCL and recording system for distribution
	Element	m1-14-3-release
	File	m1/whopqt/114-distrinfo/1143-release/release-VAR.EXT
	Comment	
69	Number	1.14.4
	Title	Summary of the packaging procedures for international shipments for UN agencies and the validation
	Element	m1-14-4-intship
	File	m1/whopqt/114-distrinfo/1144-intship/intship-VAR.EXT
	Comment	

70	Number	1.15
	Title	Response to questions
	Element	m1-15-resp
	File	m1/whopqt/115-resp/resp-VAR.EXT
	Comment	
71	Number	1.16
	Title	Other documents
	Element	m1-16-other
	File	m1/whopqt/116-other/other-VAR.EXT
	Comment	

13.3 Appendix 3: Example of the use of the Related Sequence and the Submission Unit type elements

The related-sequence element is used to identify sequences belonging to the same ‘regulatory activity’. A 'regulatory activity' is a logical unit of submission activity (e.g., Mx FPP New Prequalification Application or a Type IN Change) with a defined start and end point. In eCTD, this will consist of all the sequences that together make up the lifecycle of that particular 'regulatory activity’. The Submission Unit Type element describes the stage within the regulatory activity, such as “initial”, “response”, or “additional-info”.

For new regulatory activities, the related sequence attribute should always be equal to the current sequence number. When submitting lifecycle sequences within an existing activity, the related-sequence attribute should be populated with the sequence number the regulatory activity has been started with. The Submission Unit Type should be populated with the respective term describing the content of the sequence to be filed at that point in time. See the table below for some illustrative examples.

It is generally expected that there is usually just one related sequence, but there are occasions where more than one related sequence should be provided: e.g. there are two post-PQ changes (sequence 0050 and sequence 0060) and a single response (sequence 0070) is produced that relates to both post-PQ changes.

For any of the Application Types (regulatory activities), an initial and any of the additional submission unit types can be used, e.g. ‘response’ in case of responses to the list of questions or out- standing list of issues. The post-PQ change may have an initial and additional-info Submission Unit Type. The submission description may describe details if this content is related to, e.g. an earlier defined obligation or to which day in the procedure the response is assigned to.

Sequence	Submission description	Product Type-Application type-Application Sub Type	Related sequence	Submission unit type	Comment
0000	FPP New Prequalification Application	FPP-PQP-FULL	0000	initial	This is the beginning of a new regulatory activity and so the submission unit type is 'initial'. The related sequence will be identical with the sequence number (i.e. 0000 in this example).
0001		FPP-PQP-FULL	0000	response	This is a continuation of the regulatory activity 'FPP-NPQA-F initiated in 0000 and so the related sequence points to the beginning of that activity. The submission unit type describes the actual contribution 'response' being submitted within FPP-NPQA-F regulatory activity
0002		FPP-PQP-FULL	0000	response	This is a continuation of the regulatory activity 'FPP-NPQA-F ' initiated in 0000 and so the related sequence points to the beginning of that activity The submission unit type describes the actual contribution 'response' being submitted within the FPP-NPQA-F regulatory activity
0003	FPP Post-PQ	FPP-PPQ-AN	0003	initial	This is the beginning of a new regulatory activity, a change with the type 'FPP-PPQ-AN' so the submission unit is 'initial'. The related sequence will be identical with the sequence number 0003.
0004	FPP Post-PQ	FPP-PPQ-IN	0004	initial	This is the beginning of another new regulatory activity, a change with the type FPP-PPQ-IN. So the submission unit is 'initial'. Again, the related sequence will be identical with the sequence number 0004.
0005	FPP Post-PQ	FPP-PPQ-AN	0003	response	This is a continuation of the regulatory activity 'FPP-NPQA-AN' initiated in 0003 and so the related sequence points to the beginning of that activity. The submission unit type describes the actual contribution 'response' being submitted within FPP-NPQA-AN regulatory activity

For a new regulatory activity, the appropriate application type should be used. Applicants should refer to the application type descriptions in the WHO Module 1 specification.