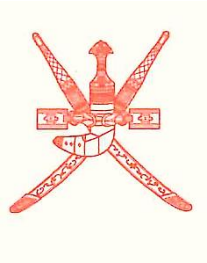
Sultanate of Oman
Ministry of Health
Directorate General of Pharmaceutical Affairs
and Drug Control
MUSCAT



سلطنة عمان
وزارة الصحة
المديرية العامة للصيدلة
والرقابة الدوائية
مسقط

Oman Guidance for eCTD Submission

July 2015

Version 02

Directorate General of Pharmaceutical Affairs & Drug Control

(MOH-DGPA&DC)

This guidance is intended to provide recommendations to applicants wishing to register medicines in eCTD (electronic Common Technical Document) format. It reflects the current position and will be regularly updated with changes in legislation and policies. It is important that applicants adhere to administrative requirements to avoid delays in processing and evaluating applications.

Guidance and application forms are available on the Ministry website (www.moh.gov.om)

Version Control

Version	Date	Approved by	Update
1.0	September, 2014	Drug Control Department	First Published Version
2.0	July, 2015	Drug Control Department	-Revision of Chapter 5.0 -Addition of Chapter 5.1, Section 5.2 -Revision of Chapter 6.0 -Revision of Chapter 8.0 -Revision of Chapter 10.0, Section 10.2 -Addition of Chapter 15.0 (FAQs) -Addition of Appendix III (Cover Letter)

TABLE OF CONTENTS

Abbreviations and acronyms:

ATC	Anatomical Therapeutic Chemical
CD	Compact Disc.
CD-ROM	Compact Disc Read-Only Memory CMC "Chemistry, Manufacturing and Control".
CTD	Common Technical Document.
DGPA&DC	Directorate General of Pharmaceutical Affairs & Drug Control.
DTD	Document Type Definition.
DVD	Digital Video Disc.
eCTD	electronic Common Technical Document.
EMA	European Medicine Agency
ICH	International Conference on Harmonization.
INN	The International Non-proprietary Name.
ISO	International Standards Organization.
IT	Information technology.
LCM	Life cycle management.
MD5	Message-Digest algorithm 5.
MOH	Ministry of Health
OCR	Optical Character Recognition.
PDF	Portable Document Format.
PI	Package Insert.
PIL	Patient Information Leaflet.
Q&A	Question and Answer documents.
SFDA	Saudi Food & Drug Authority
TOC	Table of Contents.
Util	Utility folder in the eCTD Sequence, contains technical files XML "Extensible Markup Language".

Glossary:

Application number:	The application number is the official reference number assigned to the dossier or eCTD application by the MOH-DGPA&DC.
Backbone	The backbone is similar to a container that holds pointers (called leaf elements) to the files that are part of the submission. The backbone is based on a XML Document Type Definition (DTD).
Bookmark	Bookmarks are navigational links listed in the Bookmarks pane that when clicked - display corresponding page content in the Document pane. Bookmarks are organized in a hierarchical order. It is strongly recommended to provide bookmarks within larger submission documents and especially in key regulatory documents. The bookmarks should reflect the entries of the table of contents or - if a table of contents is not available - the main headings.
Dossier:	A collection of documents compiled by an applicant in compliance with Oman MOH legislation and guidelines in order to seek registration of a medicine, or any amendments thereof. An application may comprise a number of submissions.
DTD	Document Type Definition. Schema language defining the structure of a XML document including element names, hierarchy and attributes. In the eCTD the DTD file(s) are located under <sequence>\util\dtd or <sequence>\m1\<region>\util\dtd, respectively. A DTD can be declared inline in the XML document, or as an external reference.
eCTD Application:	A collection of electronic documents compiled by an applicant in compliance with Oman MOH legislation and guidelines in order to seek registration of a medicine, or any amendments thereof. An eCTD application may comprise a number of eCTD Sequences. In MOH-DGPA&DC an eCTD application may comprise several strengths, each with a unique proprietary name. Such a collection may also be described as a dossier.
eCTD Identifier:	An eCTD identifier is the application number used as the directory name in the top-level directory.

eCTD Sequence:	All files and folders in a submission in eCTD format are to be placed under the eCTD-Sequence number folder
eCTD Submission:	An eCTD Submission is an electronic-only submission in the eCTD format that is supported by paper documents (e.g. some documents from Module 1).
Envelope:	The "envelope" element is designed to be used for all types of submissions (registration, re-registration, variations) for a given medicinal product and will mainly be used for the first simple processing at the MOH-DGPA&DC level. The envelope provides meta-data at the submission level. The elements of the "envelope" are defined in the GCC Module 1 specification.
Heading element:	XML component. The heading element contains the title of a heading and possibly additional describing information (eCTD attributes). In contrast to a leaf element, no document is associated to a heading.
LCM:	Lifecycle Management: In the context of the eCTD, LCM represents the evolution of the regulatory application including post marketing activities. Technically, the lifecycle is represented by eCTD sequences and operation attributes.
Leaf element:	XML component. The information for an individual file is contained in the leaf element, its attributes and its title element. The <leaf> element is used repeatedly throughout the eCTD backbone file to provide individual information for each submitted file. The eCTD content is made up of multiple files. The eCTD contains a <leaf> element for each of these files. Each <leaf> element has associated attributes that provide important information on the file to which the element relates, including the location of the file in the folder structure.
MD5 checksum:	Message Digest 5 algorithm: that calculates unique 128 bit hash values of electronic files. A MD5 checksum is calculated for each physical referenced in the eCTD backbone (available in the leaf element) and for the backbone itself (available in file index-md5.txt). The checksums are used to verify that the information was transmitted and received without being modified or corrupted.
Metadata:	In the eCTD context the term metadata (or meta-data) is used synonymously for attributes of the XML backbone. This includes information assigned at submission level (M1 envelope) and at section level (heading elements e.g. 3.2.P -> product, dosage form, and manufacturer). The information about individual documents is presented by attributes of the leaf elements (e.g. document ID, file name, checksum, and lifecycle operation).

Modified-file attribute**:**	XML component. The purpose of the modified-file attribute is to provide the location of the leaf that is being modified (i.e. appended, replaced, or deleted) by the current leaf element. The modified-file attribute should have a value when the operation attribute has a value of append, replace or delete.
OCR:	Optical Character Recognition. Mechanical or electronic translation of images of handwritten, typewritten or printed text (usually captured by a scanner) into machine-editable text Generally, PDF documents of an eCTD should be created from the electronic source file by PDF rendition.
Operation attribute:	XML component. The operation attribute provides information about the lifecycle of a leaf element (document in the eCTD). The values for the operation attribute are limited to "new", "replace", "append", or delete".
Regulatory activity:	In the context of the eCTD, a "Regulatory Activity" comprises a collection of eCTD lifecycle sequences covering the start to the end of a specific submission process, (e.g. registration, re-registration, variations). It is a concept used in some review tools to group together several business related sequences.
Sequence:	In the context of the eCTD, a sequence represents a single set of information/documents that are submitted in 1 lifecycle step of the eCTD at one particular time. Sequences are consecutively numbered in 4 digits, starting with sequence 0000 and followed by subsequent sequences (0001, 0002, 000n).
Tracking table:	A sequence tracking table is requested for a submission procedures. It provides information about the content of an eCTD sequence including the date when it was submitted to the MOH-DGPA&DC. Tracking tables can be submitted in XML or PDF format in the cover letter section of Module 1.
Validation:	Technical validation: The technical validation is a validation by an automated tool, checking the DTD and other technical components of the eCTD. Two categories of validation rules apply: "Pass/Fail (P/F)" and "Best Practice (BP)".
XML	**"**Extensible Markup Language**":** XML is used for defining data elements on a Web page and business-to-business documents; it contains both the data and the description of the data. The backbone of the eCTD (index.xml) and the regional.xml (Module 1) are presented in XML format.
XML attributes:	XML attributes (or heading element attributes) are used to provide additional information for specific sections of the eCTD as defined by the ICH eCTD specification and local Module 1 specifications

1.0 Introduction:

This guidance document is intended to provide assistance with the submission of regulatory information in electronic Common Technical Document format (eCTD) to the Directorate General of Pharmaceutical Affairs & Drug Control (MOH-DGPA&DC).

The document covers general guidance on how to organize electronic application information submitted to the Directorate in accordance with eCTD specifications. Guidance on the information to be included in each section of the applications and submissions is based on the International Conference of Harmonization (ICH) and Oman MOH Regulatory framework for drug approval. This guidance is intended for Registration, Re-registration & Variation applications for human pharmaceutical products. It should be stressed that it reflects the current situation and will be regularly updated in light of changes.

Applicants submitting eCTD applications must comply with this guidance documents as well as the "GCC Module 1 Specifications for eCTD" made available on the Ministry website.

It should be noted that the MOH-DGPA&DC has the right to request any further information and data in order to assess adequately the safety, efficacy and quality of the medicinal products. The MOH-DGPA&DC is committed to ensuring that such requests are justifiable and decisions are clearly documented.

2.0 Purpose and Scope:

The scope of this guidance is to provide detailed information on how to submit eCTD applications of cover the submission of electronic regulatory information in eCTD format for all human medicinal products within the MOH-DGPA&DC registration framework.

The hierarchal structure of the eCTD follows that of the CTD. All modules must be submitted electronically along with some selected documents in Module 1 that must be submitted in both soft and hard copy formats (Refer to Appendix-I).

3.0 Types of submissions:

- **New registration.**
- **Re-registration.**
- **Variations.**

4.0 Types of products:

The scope of products to be submitted in eCTD format are the following:

a . New Chemical Entities.

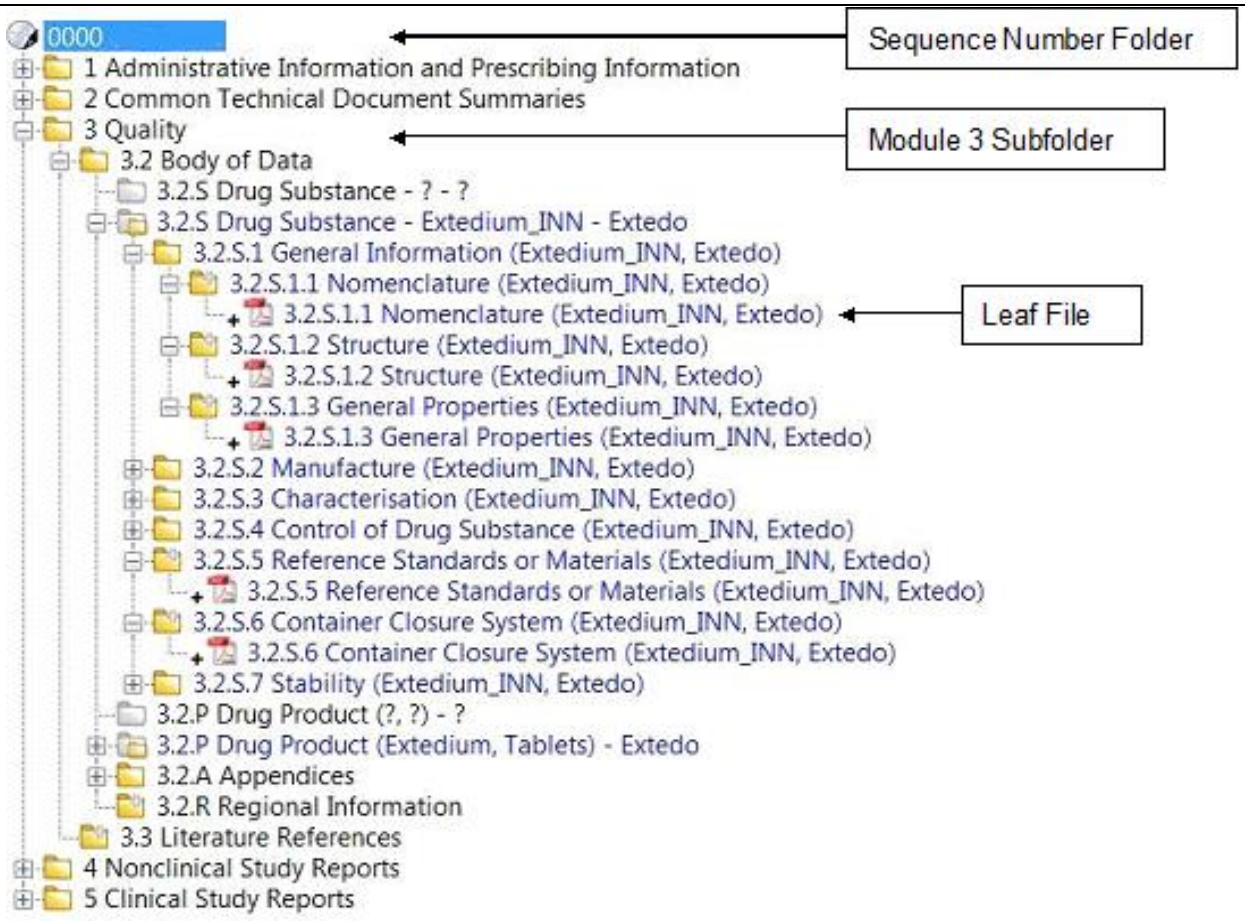
b. Generics.

c. Biologics.

5.0 Content and structure of eCTD Submissions:

5.1 Structure:

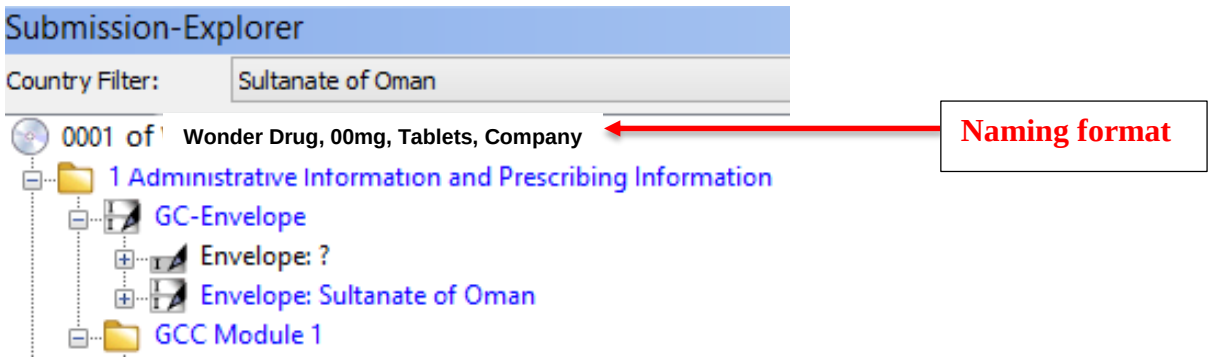
In terms of dossier content, the compiled scientific information enclosed in an eCTD is identical to that of CTD submissions. The difference between CTDs and eCTDs lies in the type of media used, and the method of structuring documents. An eCTD submission is an electronic dossier built using an XML backbone with a unified pattern of arranging documents into branches and leaves. It allows better accessibility and therefore improving the overall review process. The structure of an eCTD dossier is viewed graphically via an XML viewing tool as seen in the graph below.



5.2 Labeling of the Sequence Number Folder |(0000):

The Sequence Number Folder (0000) must be labeled in the following format:

"Trade Name, Strength, Dosage Form, Company Name"



6.0 Hard Copies for Module I:

eCTD dossiers are submitted electronically. Nonetheless, for legal reasons, specific documents of Module 1 that are listed in Appendix I must be available in hard and soft copies. Both copies must be identical,

7.0 Specifications of hard copy Documents:

7.1 Legibility and Size:

All documents including tables should be legible and the page size should be A4 Norm.

7.2 Page divider/tab:

A page divider or tab (with the header of the section printed) should be used to separate selected section in module 1.

7.3 Language:

Information and documents supporting a drug application-such as certificates and approval letters must be either in Arabic or English. If documents are neither in Arabic nor English, a translation to English (from an authorized translation office) are required.

7.4 Authentication:

Authentication also known as legalization- refers to the process whereby the origins of the document are attested. Authentications of documents are made to MOH-DGPA&DC by the Health authority and/or the Ministry of Foreign affairs in the country of origin, in addition to Oman Embassy or Consulate where the document was issued, refer to appendix- I.

8.0 Letter of Application (Cover letter):

Submissions as well as additional information in eCTD format should be accompanied by a cover letter of application in both paper and portable document format (PDF). The PDF should be a scan of the originally signed document and must be searchable (OCR scanned) including the following:

- Local Agent:
- Company Name and address
- ATC code(if available)
- Dosage form
- Dosage strength(s)
- The International Non-proprietary Name (INN) of the product
- Number of CDs/DVDs provided
- Application Number
- Validation Tool used
- Validation Specification Version
- MD5 checksum:
- The tracking table of the submitted sequences.

The following statements must be included:

1. "We confirm that the CD/DVD-burning session is closed and the submission is

   Checked with an up-to-date and state-of-the art virus checker".

2. "We confirm that the documents submitted in electronic form and the corresponding paper version of parts of module 1 are identical."

As eCTD viewing tools will display all "new" leaf elements in a current or cumulative view, it is recommended that additional descriptive text be included in the leaf title to assist with identification of specific letters (e.g. new letter of re-registration / new letter of variation). This will help identify each letter of application leaf and the submission it is in, rather than having the letters named the same in each sequence.

The tracking table of the submitted sequences, as mentioned above, should be included in the letter of application or as an annex to the letter, as per the following example:

Date of submission	Sequence number	Submission type	Related eCTD sequence	Regulatory activity/ Submission description	Regulatory status (submitted / approved / rejected)

- The letter (paper version) must be signed.
- The letter should not contain any scientific information. Responses to questions raised by MOH-DGPA&DC should not be included in the cover letter, since they have been assigned a specific location in Module 1.9.
- Refer to Appendix IV for details to be included in the cover letter along with the tracking table

9.0 Qualifications of the Product File:

9.1 Softcopy Requirements:

For the softcopy, each CD or DVD and its hard plastic cover submitted should include the following label information, clearly presented and printed on the media with font size "12 Times New Roman":

- The company name (Manufacturer name and/or MAH).
- The product Trade name.
- INN name.
- The submission type.
- The sequence number of the submissions contained on the CD/DVD (e.g. 0002).

9.2 Media:

The electronic submission may only be submitted in CD or DVD (single or dual layer). The disc must not be bootable or have auto-start programs. Currently both CD-ROM and DVD ISO 9660 are considered an acceptable media standard.

9.3 System compatibility:

The electronic submission (as provided) must be directly readable and usable on MOH-DGPA&DC hardware and software.

9.4 Validation confirmation

It is the Applicant's responsibility to ensure that their electronic submission is free of viruses. The applicant must scan the submission via a competent antivirus software and produce a certificate proving that the submission is free of viruses. Applicants must use an eCTD validation tool that checks the submission for technical interoperability before submission. The applicant must submit the results of the validation report along with the number generated by the MD5 checksum.

9.5 Security:

There are various aspects related to security. The physical security of the submission during transportation/transmission is the responsibility of the applicant. Once received by MOH-DGPA&DC, security and submission integrity will become the sole responsibility of the Directorate. In this respect, it should be noted that we will take appropriate measures to prevent loss, unauthorized duplication and/or access or theft of regulatory information presented both on paper and electronic media that are distributed throughout the Directorate.

9.6 Password protection:

One-time security settings or password protection of electronic Submissions for security purposes is not acceptable during transportation/transmission from the applicant to MOH-DGPA&DC. Applicants should also not include any file level security settings or password protection for individual files in the electronic submission. Applicants should allow printing, annotations to the documents, and selection of text and graphics. The Internal security and access control processes in MOH-DGPA&DC maintain the integrity of the submitted files.

10.0 Registration Process (New):

10.1 Appointments for submitting applications:

The applicant must submit an appointment letter to MOH-DGPA&DC to schedule **Registration and Re-registration** appointments. Appointments will be given to applicants to submit products that are manufactured/batch released by companies already registered by MOH-DGPA&DC. The applicant will then be contacted by an assigned staff member to be informed of the designated date and time of submission. **In case the applicant did not appear on the scheduled date (no show), a new appointment request has to be made** (refer to Appendix II for the format of the appointment request). **It is important to note that Variations do not require prior appointments. Applications for variations are received weekly on Tuesdays from 9:00 am till 11:59 Am.**

10.2 Submission of Application:

On the scheduled day of submission, the applicant must be present at the specified time slot. Submitted dossiers are verified against a checklist of all required documents according to MOH-DGPA&DC submission criteria.

10.3 Phase- I (Validation):

The submission will be rescanned by MOH-DGPA&DC for viruses. Technical validation of the dossier will be carried out via the Importation tool and the generated 32 digit MD5 checksum will be matched with the one submitted by the applicant. Refer to section 14.0.

10.4 Post Phase- I (Validation):

Upon completion of validation, the outcome is either one of the followings:

10.4.1 Valid Drug Applications:

The applicant will receive an Acknowledgement letter with the assigned eCTD application number and the validation report attached. The dossier is then forwarded for evaluation and assessment.

10.4.2 Invalid Drug Applications:

- A failure letter is issued to the applicant attached to a detailed validation report with all the errors. The applicant is allowed a period of 90 days to rectify the errors from the date of the letter.
- The applicant shall contact the MOH-DGPA&DC requesting an appointment to resubmit the dossier once the errors have been rectified
- If the applicant has provided the requested information within 90 days. The application will forward to the concerned staff member for further processing and assessment.
- If the applicant has provided the requested information within 90 days, but it was found to be still incomplete, the applicant can complete the missing within the rest of the 90 days.
- In case of failure to submit within 90 days, the drug application will be rejected.

10.5 Phase II (Evaluation & Assessment):

After successful completion of both validations, technical and content, the submitted dossier will be forwarded for assessment. If deficiencies are identified during assessment, a request is sent to the applicant to provide the required documents within 90 days from the date of the request. Depending on the applicant's response, the subsequent outcomes are:

1. **Applicant responds within 90 days**: submitted documents are assessed.

2. **Applicant provides the requirements within 90 days but the response is deemed unsatisfactory:** MOH-DGPA&DC will study the case and decide whether to reject the application or grant an extension period not exceeding 30 days.

3. **Applicant fails to respond within 90 days**: Rejection of application.

11.0 Re-Registration:

Applicants must submit a renewal request every five years for drug products that have already received marketing authorization – **at least six months prior to the end of the 5 year registration period.** The followings are required:

- CD/DVD of the required documents in eCTD format (refer to "Sections 14.0").
- Hardcopy consisting of the documents selected in Appendix-I.
- The requirements for re-registration are made available on the MOH/MOH-DGPA&DC website.

12.0 Variations:

An applicant can submit a variation application – on drug products that have already received a marketing authorization from MOH-DGPA&DC – through submitting the following:

- CD/DVD of the required documents in eCTD format (refer to "Sections 14.0").
- Cover letter and Hard copies of legalized documents (In case the variation involves legalized documents).
- The requirements variations are made available on the MOH-DGPA&DC/MOH website

13.0 Correspondence:

The eCTD is designed to ensure that assessors have a current view of the submitted information in their designated place in the dossier at all times. Therefore, formal responses to questions should always be submitted in eCTD format, as well as any correspondence that relates directly to the content of the dossier.

14.0 Submission Considerations for Electronic Version of Module I:

14.1 Handling of Empty or Missing eCTD Sections:

For new applications (Registration) (including generic applications), detailed statements justifying the absence of data or specific eCTD sections should be provided in the relevant Quality Overall Summary and/or Non-Clinical/Clinical Overviews (Module 2.3, 2.4, 2.5).

14.2 File formats (General requirements):

Detailed guidance on the specific file formats can be found in the ICH eCTD specification document and GCC Module 1 specifications. The following points have to be taken into consideration:

- The relevant information must be structured according to the requirements of the Common Technical Document (CTD).
- The documents included in electronic submissions should be in **PDF** format.
- Each PDF file should not exceed 100 megabytes.
- Files must be legible with PDF version 1.4 or higher.
- For graphics: Joint Photographic Experts Group (JPEG), Portable Network Graphics (PNG), Scalable Vector Graphics (SVG) or Graphic Interchange Format (GIF).
- The files referred to above should not be added as leaf elements within the eCTD structure. They should always be provided in a separate folder called 'xxxx-workingdocuments' on the same media containing the electronic dossier, where the number (xxxx) matches the number of the eCTD sequence being submitted (e.g. 0000-workingdocuments)" with a substructure as follows:

14.2.1 Portable Document Format "PDF":

PDF is accepted as a standard for documents defined in this guidance. To ensure that PDF files can be accessed efficiently, **each PDF file should not exceed 100 megabytes**.

For PDF files, the following points must be taken into consideration:

- Files must be legible with PDF version 1.4 or higher

- PDF files produced from an electronic source document are highly preferred over PDF files produced from scanned paper, since those 'electronic' PDF files provide the maximum functionality to the reviewers in terms of search and print capabilities, and copy and paste functionality. The overviews/summaries in the CTD Module 2 should always be generated from an electronic source document.

- If scanning is unavoidable, readability and file size must be balanced; the following is recommended: resolution 300 dpi (photographs up to 600 dpi), avoid gray scale or color where possible, use only lossless compression techniques.

- If colors other than black are used, the colored pages must be tested on a black and white printer for acceptable reproduction and legibility prior to submission.

- Print area for pages must fit on an A4 sheet of paper; margins must allow binding in multi-ring binders without affecting readability.

- Landscape-oriented tables must automatically appear in landscape on screen.

14.2.2 Bookmarks and hypertext links:

Navigation through an electronic submission is greatly enhanced by the intelligent use of bookmarks and hypertext links. ICH guidance states “It is expected that any document that has a Table of Contents (TOC) will have bookmarks".

Documents without TOCs should have bookmarks included where it aids in the navigation around the document content.
In general terms, bookmarks and hyperlinks should be used to aid navigation.

14.3 Text Searchable Files:

Applicants are requested to ensure that all submissions contain the maximum amount of text searchable content. Documents with searchable text will aid the assessor, or any other user, in searching for specific terms and also in copying and pasting information into another document, such as an assessment report. This appendix provides some guidance about what must be text searchable and the ways to ensure that files are created appropriately.

14.3.1 Documents that must be text searchable:

- The PDF should be produced wherever possible from a text source, such as MS Word, but if sourced from a scanned original then they **must be** OCR'd.
- Key administrative documents in Module 1 including, the cover letter, application form, SPC, labeling and PIL documents
- The main body of text of Risk Management Plans
- Any document in Module 2 of the submission (QOS, Nonclinical Overview and Summaries, Clinical Overview and Summaries).
- The main body of text in any reports, methods, analytical procedures, etc. supplied in Module 3 of the submission
- The main body of text and main tables in modules 4 and 5.

14.3.2 Documents that are recommended to be text searchable:

- The PDF should be produced wherever possible from a text source, such as MS Word, but if sourced from a scanned original then there is no need for OCR.
- Any original Certificate of Pharmaceutical Product.
- Any original Certificate that confirm that the product is free from BSE/TSE.
- Any original GMP certificate.
- Any original certificate of analysis.
- Any manufacturer's licenses.
- Any certificates of suitability.
- Any Manufacturing Authorization.
- Any literature references sourced from journals, periodicals and books (except when these are used in a bibliographic application so support the main claims of the application).
- Any page with a signature that does not contain other information key to the understanding of the submission
- Applicants should consider providing signatures on separate pages from key text in reports, overviews, etc.

14.4 Module 1: 1.9 Responses to questions

The organization of the submission of electronic information in response to a list of questions should follow the format of the first submission.

15.0 Frequently Asked Questions:

Prior to scheduling a submission appointment, all applicants must go through the Frequently Asked Questions mentioned below:

Q1. What is an Application number?

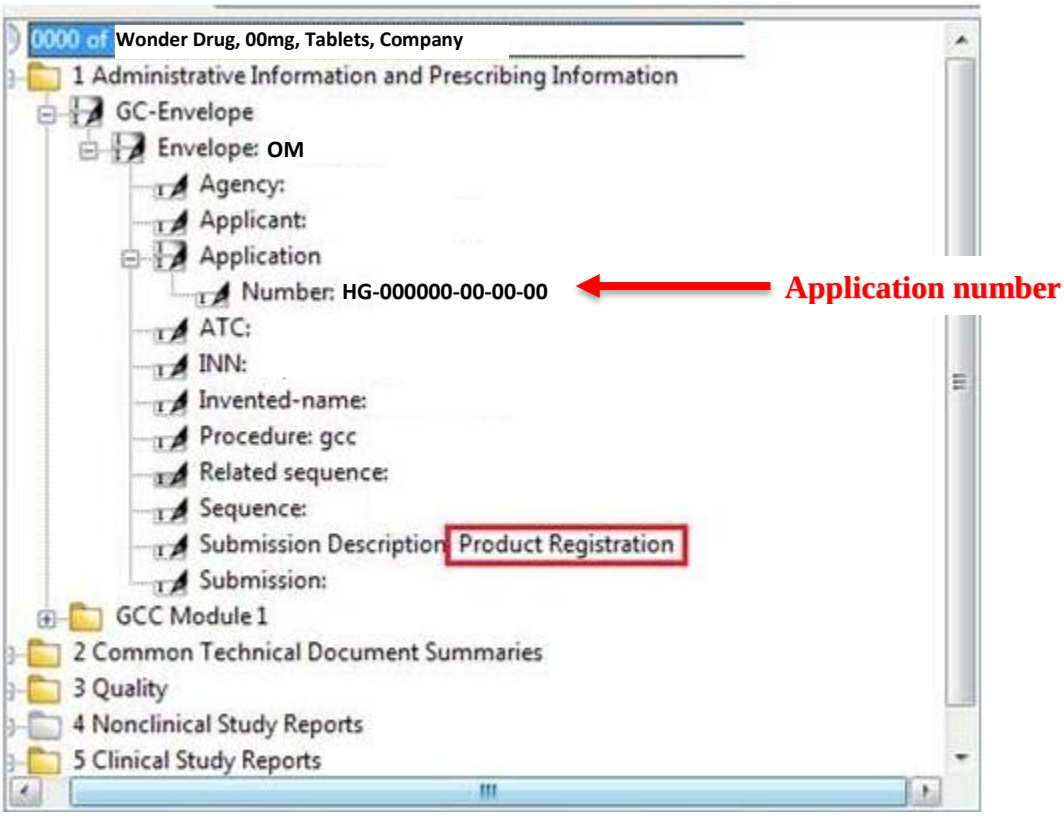
A1. An Application number is also known as an eCTD identifier number. It replaces the current Registration number for all eCTD applications.

Q2. When is the Application number issued?

A2. An Application number is issued by DGPA&DC once an appointment is scheduled to receive a product dossier. Applicants will be informed about the assigned application number and the scheduled date for receiving the product dossier.

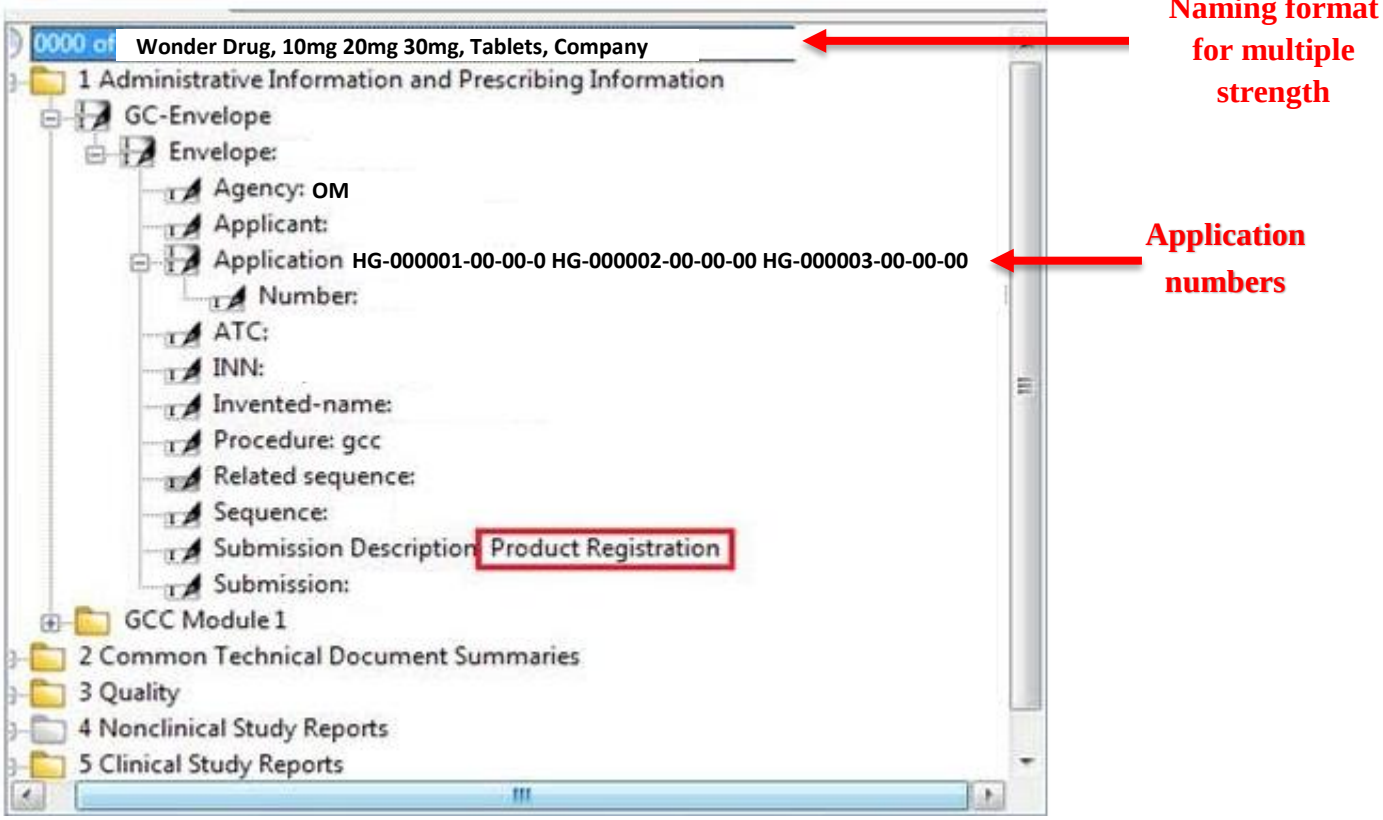
Q3. Where is the Application number reflected in an eCTD submission?

A3. The application number is reflected under the Envelope file as shown in the figure below



Q4. How is the application number reflected for products with multiple strengths in a single submission?

A4. Each strength and each application number must be mentioned. The Example below is for a product with 3 strengths:



Q5. In which Section of Module 1 shall I place the Certificate of Suitability for compliance with Ph. Eur. Issued by EDQM for the API manufacturer?

A5. It must be placed in Section 1.7.7, "Certificate of suitability (EDQM) + TSE".

Q6. In which Section of Module 1 shall I place the TSE/BSE free certificate?

A6. It must be placed in Section 1.7.7, "Certificate of suitability (EDQM) + TSE".

Q7. In which Section of Module 1 shall I place the GMP certificate for the API manufacturer?

A7. It must be placed in Section 1.7.1, "GMP".

Q8. In which Section of Module 1 shall I place the list of countries where the product is registered (Worldwide Registration Status)?

A8. It must be placed in Section 1.8.2, "Other documents related-Pricing list"

Q9. In which Section of Module 1 shall I place the copies of registration certificates if the product is registered in GCC countries?

A9. It must be placed in Section 1.8.2, "Other documents related-Pricing list"

Q10. How to prepare the tracking table enclosed with the cover letter?

A10. The tracking table format is the following:

Date of submission	Sequence number	Submission type	Related eCTD sequence	Regulatory activity/ Submission description	Regulatory status (submitted / approved / rejected)

Date of Submission: The submission appointment date.

Sequence number: The four digit sequence number e.g 0000.

Submission Type: (New / Replace / Delete).

New: New documents submitted for the first time.

Replace: Documents submitted to replace previously submitted documents.

Delete: A submission with deleted documents that were submitted previously.

Related eCTD sequence: Refer to the initial sequence related to the submission. It will always be left blank in cases of New submissions (0000).

Regulatory activity/ Submission description: A brief description of the type of submission. E.g. ("New product application", "Variation", "Re-registration", "Response to Questions").

Regulatory status (Submitted/ Approved/ Rejected): It reflects the current status of the application with the Directorate.

Q11. What to be included in a Cover Letter?

A11. Please refer to ***Appendix III***

Appendix-I

Module 1 documents that are requested additionally in paper format:

Section	Requirements	1*	2*	3*	4*	HC [a]
1.0	Cover letter	✓	✓	✓		✓
1.1	Comprehensive Table of contents					
1.2	Application Form		✓	✓		✓
1.3	Product Information					
1.3.1	Summary of Product Characteristics (SPC)					
1.3.2	Labeling					
1.3.3	Patient information leaflet (PIL)					
1.3.3.1	Arabic leaflet					
1.3.3.2	English leaflet					
1.3.4	Artwork (Mock-ups)					
1.3.5	Samples					♦[b]
1.4	Information on the experts					
1.4.1	Quality					
1.4.2	Non-Clinical					
1.4.3	Clinical					
1.5	Environmental Risk Assessment					
1.5.1	Non-Genetically Modified Organism (Non-GMO)					
1.5.2	GMO					
1.6	Pharmacovigilance					
1.6.1	Pharmacovigilance System	✓				
1.6.2	Risk Management Plan	✓				
1.7	Certificates and Documents					
1.7.1	GMP Certificate					
1.7.2	CPP or Free-sales[c]				✓	✓
1.7.3	Certificate of analysis – Drug Substance & Finished Product	✓[d]	✓[d]	✓[d]		
1.7.4	Certificate of analysis – Excipients					
1.7.5	Alcohol-content declaration	✓	✓	✓		
1.7.6	Pork-content declaration	✓	✓	✓		
1.7.7	Certificate of suitability (EDQM) + TSE					
1.7.8	The diluents and coloring agents in the product formula	✓	✓	✓		
1.7.9	Patent Information					
1.7.10	Letter of access or acknowledgment to DMF					✓
1.8	Pricing					
1.8.1	Price list	✓	✓	✓	✓	✓[e]
1.8.2	Other documents related-Pricing list					
1.9	Responses to questions					
	Additional data					

- ✸ **1:** Company original paper (original hard copy)
- ✸ **2:** Signature of authorized person
- ✸ **3:** Company official stamp
- ✸ **4:** Authentication

a. Hard-copy (HC)
b. Physical Sample
c. Not required for local manufacturers
d. Only for finished products
e. In the initial submission, a price list without authentication can be accepted, but must be provided if requested later on

Appendix-II

Appointment Letter

Ref. No.
Date:

Director of Drug Control

Directorate General of Pharmaceutical Affairs & Drug Control

Ministry of Health

Subject: Submission of registration files

After compliments,

We kindly request from you to grant us an appointment for submitting Registration / Re-registration applications for the following product/s:

Sr.#	Type of Application	Trade name, Strength, Dosage form	Generic name	Pack Size	Manufacturer, COO	MAH, COO	GCC Registration status

Yours Faithfully,

Local Agent signature & stamp

Appendix III

Points to be included in a cover letter:

Local Agent:

Company Name and Address:

Trade Name:

ATC code:

Dosage Form:

Dosage Strength:

International Non-proprietary Name (INN):

Number of CDs/DVDs provided:

Application Number:

Validation Tool used:

Validation Specification:

MD5 checksum:

Sequence Tracking Table:

Date of submission	Sequence number	Submission type	Related eCTD sequence	Regulatory activity/ Submission description	Regulatory status (submitted / approved / rejected)

"We confirm that the CD/DVD-burning session is closed and the submission is checked with an up-to-date and state-of-the art virus checker".

"We confirm that the documents submitted in electronic form and the corresponding paper version of parts of module 1 are identical".

Appendix-IV

References

GCC Reference document

- GCC Module 1 Specifications

SFDA Reference document

- Guidance for Submission

Thailand FDA

- TH eCTD Specification Module 1 and Regional Information

Swissmedic

- Guidance for Industry on Providing Regulatory Information in eCTD Format

US FDA

- Guidance for Industry Providing Regulatory Submissions in Electronic Format — Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

South Africa Medicines Control Council

- South African Specification1 for eCTD2 Regional - Module 1

EMA

- TIGes Harmonised Guidance for eCTD Submissions in the EU

ICH Reference Documents:

- ICH electronic Common Technical Document (eCTD)
- ICH Specification 3.2 (Modules 2 - 5) (Notice to Applicants Vol 2B)
- ICH Q&As
- ICH M4 Granularity