DRAFT FOR COMMENTS:

Guideline on eCTD Preparation and Submission for Medicinal Product Registration

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Guideline on eCTD Preparation and Submission for Medicinal Product Registration

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41 ## Acronyms:

ATC	Anatomical Therapeutic Chemical
CTD	Common Technical Document
DSC	Drug Safety Center
DTD	Document Type Definition
eCTD	Electronic Common Technical Document
EMA	European Medicine Agency
GVP	Good Pharmacovigilance Practice
ICH	International Conference on Harmonization
INN	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
PSMF	Pharmacovigilance System Master File
Q&A	Question and Answer documents
SFDA	Saudi Food & Drug Authority

TCR&P	Technical Committee of Registration of Pharmaceutical Companies and Products of Human Medicine and Pricing
TOC	Table of Contents
UTIL	Utility folder in the eCTD Sequence contains technical files XML “Extensible Mark-up Language”.

Definitions

Application number	official reference number assigned to an application submission.
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.
Common Technical Documents	is a Common Technical Documents format, which consist of 5 modules (M1-M5).
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.
Document Type Definition	Document Type Definition. It is 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 guidelines in order to seek Marketing Authorization for a medicine, or any amendments thereof. An eCTD application may comprise a number of eCTD Sequences. In MOH-DSC an eCTD application may comprise several strengths, each with a unique proprietary name. Such a collection may also be described as dossiers.
eCTD Sequence	All files and folders in a submission in eCTD format are to be placed under the eCTD-Sequence number folder.
eCTD Submission	is an electronic-only submission in the eCTD format supported by an electronic application form.
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-DSC 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 and possibly additional describing information (eCTD attributes). In contrast to a leaf element, no document is associated to a heading.
Lifecycle Management (LCM)	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.
Medicine	Any substance or combination of substances intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.
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.

Optical Character Recognition (OCR)	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	it 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	it is the table created by the applicant in order to track the sequence. It provides information about the content of an eCTD sequence including the date when it was submitted to the MOH-DSC. 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)”.
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	also known as 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.

CHAPTER ONE

Introduction

This guideline supports applicants in preparing eCTD submissions in compliance with national and international regulatory standards.

It is intended for Registration, re-registration & Variation applications for medicine and biological 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.

Legal Basis

ROYAL DEGREE 35/2015, Ministerial decision number 113/2020, Articles no. 62-75, for registering medicines (pharmaceutical, health and herbal).

Purpose

The purpose of this guideline is to provide clear and standardized instructions for the preparation and submission of medicine registration dossiers in eCTD formats through MOH-portal.

Scope

This guideline applies to all medicine marketing authorization holders (MAHs) and regulatory affairs consultants submitting applications for the registration, re-registration, or variation of medicine in the Sultanate of Oman.

It covers the requirements and structure for preparing dossiers in eCTD (electronic Common Technical Document) formats.

Structure

This is the first version of this guideline and is organized into four chapters. CHAPTER ONE covers the Introduction, Purpose, Scope, and Structure. CHAPTER TWO outlines the detailed procedures. CHAPTER THREE defines responsibilities in relation to this guideline. CHAPTER FOUR includes the document history and version control table, references, and the Annex.

CHAPTER TWO

Electronic- Common Technical Document (eCTD):

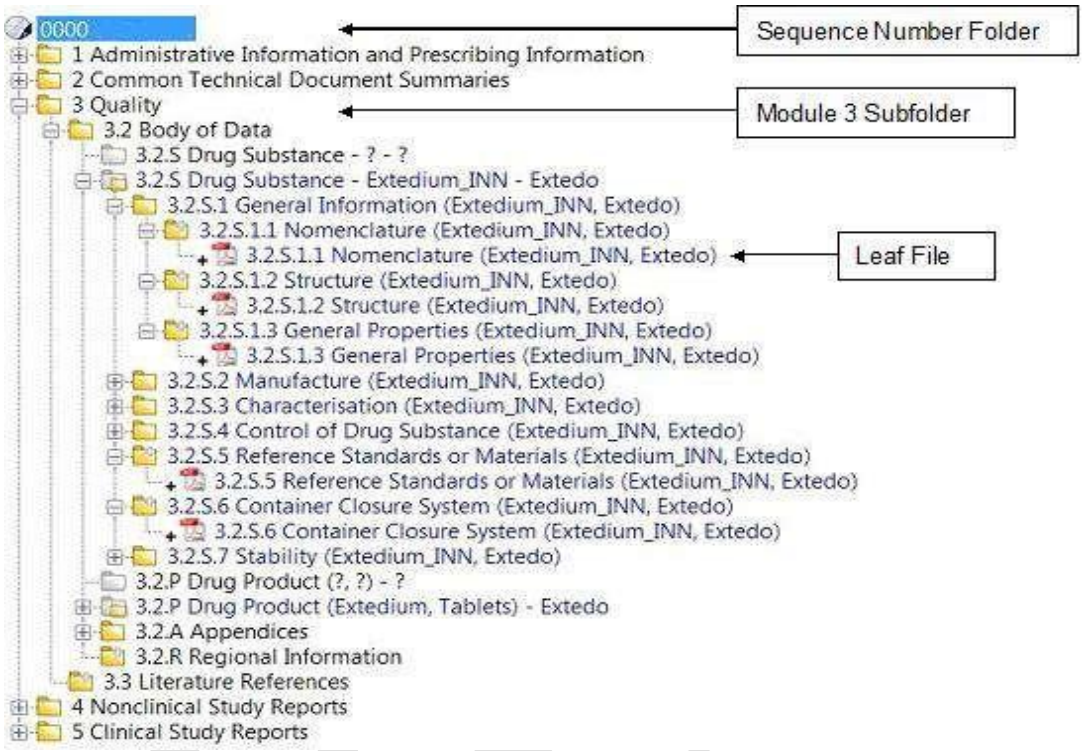
1. **Types of submissions:**
    - New registration.
    - Re-registration.
    - Variations.
2. **Types of products:**
    - All medicine.

3. **Content and Structure of eCTD Submissions:**

The compiled scientific information enclosed in an eCTD is identical to that of CTD submissions i.e., (Module1 to Module 5). The data requirements for each application will differ depending on the drug type. Where the full modules will be required (M1-M5) for a New Chemical Entity (NCE), Biologicals and Vaccines products while some modules may not be applicable in applications for generic products where they should be clearly marked in this case and shouldn't be left empty.

The full structural content of module 1 to 5 is available in (Appendix-I) as it combines regional (Module 1) and international standards (Module 2-5) as per ICH M2 EWG.

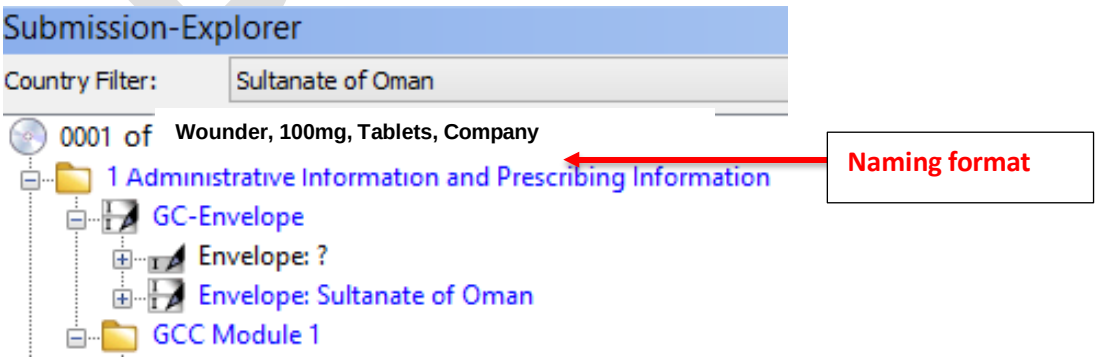
The structure of an eCTD dossier is viewed graphically via an XML viewing tool as seen in the graph below.



(Figure2): Structure of eCTD dossier

Labeling of the Sequence Number Folder (0000)

The Sequence Number Folder (0000) must be labeled in the following format: **"Trade Name, Strength, Dosage Form, and Company Name"**



(Figure3): Naming format for product dossier

4. Presentation of the Product Application in MOH-Portal:

The product application will consist of 4 parts:

- **Application form:** product pharmaceutical information to be filled by the applicant (all mandatory fields must be provided).
- **Product Pricing details.**
- **Attachment:**
  - eCTD file filled in a format that is easy for download without any pass code.
- **Payment:** fees should be paid upon submission.

5. SPECIFICATIONS:

Application form information filled by the applicant must be identical to the information in eCTD files attached.

a. Language:

Information and documents supporting the drug application such as certificates and approval letters must be either in Arabic or English. If documents are there in other languages, they should be translated to English by an authorized translation office.

b. Authentication:

Authentication also known as legalization refers to the process whereby the origins of the document are attested at the competent authority and then by the Ministry of Foreign affairs in the country of origin, in addition to Oman Embassy/Consulate or its representative according to the prescribed rules, otherwise by an apostille. Documents that should be authenticated are shown in (Appendix-II).

c. Online application Requirements:

The applicant should submit full eCTD file without any pass code. In case if link was provided for file download the title should include:

- The company name (Manufacturer name and/or MAH).

- The product Trade name.
- The submission type (new, follow-up, re-reg., variation)
- The sequence number of the submissions (e.g. 0002).

d. Media:

The electronic submission of the file in the attached link can be as a single or multi strength.

6. SECURITY:

There are various aspects related to security. The security of the submission during transportation/transmission is the responsibility of the applicant. Once received by MOH-DSC, security and submission integrity will become the sole responsibility of the Center. 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 the electronic application and the attachment.

7. 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-DSC. 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-DSC maintain the integrity of the submitted files.

8. SUBMISSION CONSIDERATIONS FOR ELECTRONIC VERSION OF MODULE I:

a. Handling of Empty or Missing eCTD Sections:

In Marketing Authorization applications for NCE, the full content of Modules 1 to 5 should be submitted, while some of them may not be applicable on case of MAAs for a multisource product where the applicant should in justify that in the relevant sections including Quality Overall Summary and/or Non-Clinical/Clinical Overviews (Module 2.3, 2.4, 2.5). Appendix-I demonstrates the required sections for each category.

b. 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 documents included in electronic submissions should be in PDF format.
- "ZIP files" submission will not be accepted
- The relevant information must be structured according to the requirements of the Common Technical Document (CTD).
- 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- working documents' on the same media containing the electronic dossier, where the number (xxxx) matches the number of the eCTD sequence being submitted.

c. 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, the following points should be considered:

- Files must be legible with PDF version 1.4 or higher
- Each PDF file should not exceed 100 megabytes.
- PDF files produced from an electronic source document are highly preferred over PDF files produced from scanned paper since they 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 was unavoidable, readability and file size must be balanced; the following are recommended (resolution 300 dpi (photographs up to 600 dpi), avoid gray scale or color where possible, use only lossless compression techniques).
- If colors were 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 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.

d. 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, w h e r e they aid in the navigation around the document content.

In general terms, bookmarks and hyperlinks should be used to aid navigation.

e. 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.

- **DOCUMENTS THAT MUST ALWAYS 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.
- **DOCUMENTS NOT REQUIRED 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 Certificates like (CPP, GMP, free from BSE/TSE certificate, CoA, Manufacturer's license, certificates of suitability, etc.)
- 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.

f. Letter of Application (Cover letter):

Submissions in eCTD format should be accompanied by a cover letter. The PDF should be a scan of the originally signed document, do refer to Appendix-III for the format of cover letter and the following statements must be included:

Since the eCTD viewing tools displays 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	Submission Description	Related e- CTD Sequence	Regulatory Activity

					Status

The Tracking table should include all the previous sequences (if any). Otherwise, the application can be subjected to rejection.

The letter should not contain any scientific information. Responses to questions raised by MOH-DSC should not be included in the cover letter, since they have been assigned a specific location in Module 1.9.

New Application:

The application shall be submitted in eCTD format, encompassing dossier preparation, structure, submission route, and validation requirements. Product designation and applicable regulatory pathways, including reliance approaches, shall be in accordance with the Oman Regulatory Framework for Medicinal company and Products Approval.

Re-Registration:

Re-registration is the renewal of marketing authorization for a medicinal product. 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, otherwise the medicine registration will be considered cancelled.

The Re-registration process follows the same procedure for registration of new product.

The required documents should be submitted as per (Appendix-IV). In addition, the following documents must be included within additional data folder:

a. Declaration letter or part of the cover letter mentioning that there are no changes on the product other than what have been approved by MOH-DSC.
b. In case of any changes, a table of comparison between the previous approved specification with the proposed changes.
c. Importation status; proof that the product was regularly imported during the last 5 years. In case of no importation, a justification letter should be provided.

Variations:

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

- An application form may contain several variations for one submission, refer to the application form in the variation guideline for medicinal product.
- Parallel submissions are acceptable only if variations were not related.
- Variation process and required documents follows the variation guideline for medicinal product.
- There should not be any changes other than those identified in this application (except for other variations addressed in other applications submitted in parallel)

Validation:

To verify that the application dossier is technically complete, correctly formatted, compliant with eCTD system requirements before scientific review. Validation will be performed in accordance with the Oman Regulatory Framework for Medicinal company and Products.

It includes:

- Compliance with eCTD structure (Modules 1–5)
- Correct XML backbone, file naming, and folder hierarchy
- Acceptable file formats (PDF, XML, etc.)
- File integrity (readability, hyperlinks, bookmarks)
- Completion of mandatory documents in Module 1
- Successful upload and system acceptance through the submission portal
- Absence of corrupted or password-protected files

MOH feedback on submissions will be sent through MOH-Portal.

General Notes:

- Once an eCTD submission was received, switching back to non-eCTD format would not be accepted.
- Responses to questions should always be submitted in eCTD format, as

well as any correspondence that relates directly to the content of the dossier.

- response to queries should follow the same basic principles as the first submission. Each inquiry should be followed with its respective section name and a hyperlink to the module containing the answer as it can greatly enhance the review process.
- Submission during an ongoing regulatory activity will not be accepted, except in variation with other submissions (i.e., parallel variation submissions).
- It is advisable that applicants would submit the full eCTD modules (M1-M5) for Re-registration submission, but M1 and M3 can only submitted.
- Different presentations or dosage form of a product e.g. (Prefilled Syringes, Vials) should be submitted as separate submissions.
- Different pack sizes of one presentation or dosage form should be submitted in one submission.
- For a multi strength product, the follow up, responses, variations, etc., can be submitted either in one or separate sequences.
- In case if a particular section was not applicable, the applicant must submit a justification for the same in the allocated section.

CHAPTER THREE

Responsibilities:

Pharmaceutical companies	

Marketing Authorization Holders (MAHs) Regulatory Affairs Professionals/Applicants Pharmaceutical Consultancy Service Companies	• To adhere to the guidelines and the regulations for all application submission. • To reply for any further quires.
Technical Committees of Registration	• Decision making based on the cases and conditions.
Sections of Medicinal & Biological products section	• Verification of the application submitted for registration. • Issue the letters with quires. • Issuance of the notification's letters based on committees' decisions. • Issuance of the registration certificate /variation approval letters.

CHAPTER FOUR

Document History and Version Control

Version	Description	Review Date
1	**Initial Release**	**August 2025**
2		
3		

References:

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Annexes

Appendix 1:

eCTD Structure for Medicinal and Biological Products

Module 1	Regional Administrative Information	
Section	**Requirements**	
1.0	Cover letter	
1.1	Comprehensive Table of content	
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 /French leaflet	
1.3.4	Artwork (Mock-ups)	
1.3.5	Samples	
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	
1.7.3	Certificate of analysis – Drug Substance	
1.7.4	Certificate of analysis – Excipients	
1.7.5	Alcohol-free declaration	
1.7.6	Pork-free declaration	
1.7.7	Certificate of suitability for 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 certificate	
1.8.2	Other documents related – Pricing list	
1.9	Responses to questions	

- Statement of out of patency must be submitted for first generic product.

Module 2	Common Technical Document Summaries	
2.1	Table of Contents of Module 2-5	
2.2	Introduction	
2.3	Quality Overall Summary	
	Introduction	
2.3.S	Drug substance	
2.3.S.1	General Information	
2.3.S.2	Manufacture	
2.3.S.3	Characterization	
2.3.S.4	Control of Drug Substance	
2.3.S.5	Reference Standards or Materials	
2.3.S.6	Container/Closure System	
2.3.S.7	Stability	
2.3.P	Drug Product	
2.3.P.1	Description and Composition of the Drug Product	
2.3.P.2	Pharmaceutical Development	
2.3.P.3	Manufacture	
2.3.P.4	Control of Excipients	
2.3.P.5	Control of Drug Product	
2.3.P.6	Reference Standards or Materials	
2.3.P.7	Container/Closure System	
2.3.P.8	Stability	
2.3.A	Appendices	
2.3.A.1	Facilities and Equipment	
2.3.A.2	Adventitious Agents Safety Evaluation	
2.3.A.3	Novel Excipients	
2.3.R	Regional Information	
2.4	Nonclinical Overview **FOR ORIGINATORS ONLY**	
2.5	Overview of the Nonclinical Testing Strategy	
2.5.1	Product Development Rationale	
2.5.2	Overview of Biopharmaceutics	
2.5.3	Overview of Clinical Pharmacology	
2.5.4	Overview of Efficacy	
2.5.5	Overview of Safety	
2.5.6	Benefits and Risks Conclusions	
2.5.7	References	
2.6	Non clinical written and tabulated summaries: Pharmacology, pharmacokinetics Toxicology **FOR ORIGINATOR ONLY**	
2.6.1	Introduction	
2.6.2	Pharmacology Written Summary	
2.6.2.1	Brief Summary	
2.6.2.2	Primary Pharmacodynamics	
2.6.2.3	Secondary Pharmacodynamics	
2.6.2.4	Safety Pharmacology	
2.6.2.5	Pharmacodynamic Drug Interactions	
2.6.2.6	Discussion and Conclusions	

Module 2 should reflect the information provided in modules 3, 4 and 5

Module 2	Quality	
2.6.2.7	Tables and Figures	
2.6.3	Pharmacology Tabulated Summary	
2.6.4	Pharmacokinetics Written Summary	
2.6.4.1	Brief Summary	
2.6.4.2	Methods of Analysis	
2.6.4.3	Absorption	
2.6.4.5	Metabolism (interspecies comparison)	
2.6.4.6	Excretion	
2.6.4.7	Pharmacokinetic Drug Interactions	
2.6.4.8	Other Pharmacokinetic Studies	
2.6.4.9	Discussion and Conclusions	
2.6.4.10	Tables and Figures	
2.6.5	Pharmacokinetics Tabulated Summary	
2.6.6	Toxicology Written Summary	
2.6.6.1	Brief Summary	
2.6.6.2	Single-Dose Toxicity	
2.6.6.3	Repeat-Dose Toxicity	
2.6.6.4	Genotoxicity	
2.6.6.5	Carcinogenicity	
2.6.6.6	Reproductive and Developmental Toxicity	
2.6.6.7	Local Tolerance	
2.6.6.8	Other Toxicity Studies (if available)	
2.6.6.9	Discussion and Conclusions	
2.6.6.10	References	
2.6.7	Toxicology Tabulated Summary	
2.7	Clinical Summary	
2.7.1	Summary of Biopharmaceutic and Associated Analytical Methods	
2.7.1.1	Background and Overview	
2.7.1.2	Summary of Results of Individual Studies	
2.7.1.3	Comparison and Analyses of Results Across Studies	
2.7.1.4	Appendix	
2.7.2	Summary of Clinical Pharmacology Studies	
2.7.2.1	Background and Overview	
2.7.2.2	Summary of Results of Individual Studies	
2.7.2.3	Comparison and Analyses of Results Across Studies	
2.7.2.4	Special Studies	
2.7.2.5	Appendix	
2.7.3	Summary of Clinical Efficacy	
2.7.3.1	Background and Overview of Clinical Efficacy	
2.7.3.2	Summary of Results of Individual Studies	
2.7.3.3	Comparison and Analyses of Results Across Studies	
2.7.3.3.1	Study Populations	
2.7.3.3.2	Comparison of Efficacy Results Across All Studies	
2.7.3.3.3	Comparison of Results in Sub-Populations	
2.7.3.4	Analysis of Clinical Information Relevant to Dosing Recommendations	
2.7.3.5	Persistence of Efficacy and/or Tolerance Effects	
2.7.3.6	Appendix	
2.7.4	Summary of Clinical Safety	
2.7.4.1	Exposure to the Drug	

2.7.4.1.1	Overall Safety Evaluation Plan and Narratives of Safety Studies	
2.7.4.1.2	Overall Extent of Exposure	
2.7.4.1.3	Demographic and Other Characteristics of Study Population	

2.7.4.2	Adverse Events	
2.7.4.2.1	Analysis of Adverse Events by Organ System or Syndrome	
2.7.4.2.2	Narratives	
2.7.4.3	Clinical Laboratory Evaluations	
2.7.4.4	Vital Signs, Physical Findings, Observations Related to Safety	
2.7.4.5	Safety in Special Groups and Situations	
2.7.4.5.1	Intrinsic Factors	
2.7.4.5.2	Extrinsic Factors	
2.7.4.5.3	Drug Interactions	
2.7.4.5.4	Use in Pregnancy and Lactation	
2.7.4.5.5	Overdose	
2.7.4.5.6	Drug Abuse	
2.7.4.5.7	Withdrawal and Rebound	
2.7.4.5.8	Effects on Ability to Drive or Operate Machinery or Impairment of Mental Ability	
2.7.4.6	Post-Marketing Data	
2.7.4.7	Appendix	
2.7.5	References	
2.7.6	Synopses of Individual Studies	

Module 3	Quality	
3.1	Table of Contents of Module 3	
3.2	Body of data	
3.2.S	Drug Substance	
3.2.S.1	General Information	
3.2.S.1.1	Nomenclature	
3.2.S.1.2	Structure	
3.2.S.1.3	General Properties	
3.2.S.2	Manufacture	
3.2.S.2.1	Manufacturer(s)	
3.2.S.2.2	Description of Process and Process Controls	
3.2.S.2.3	Control of Materials	
3.2.S.2.4	Control of Critical Steps and Intermediates	
3.2.S.2.5	Process Validation and/or Evaluation	
3.2.S.2.6	Manufacturing Process Development	
3.2.S.3	Characterization	
3.2.S.3.1	Elucidation of Structure and Other Characteristics	
3.2.S.3.2	Impurities	
3.2.S.4	Control of Drug Substance	
3.2.S.4.1	Specifications	
3.2.S.4.2	Analytical Procedures	
3.2.S.4.3	Validation of Analytical Procedures	
3.2.S.4.4	Batch Analyses	
3.2.S.4.5	Justification of Specification	
3.2.S.5	Reference Standards or Materials	
3.2.S.6	Container/Closure Systems	
3.2.S.7	Stability	
3.2.S.7.1	Stability Summary and Conclusions	
3.2.S.7.2	Post-approval Stability Protocol and Commitment	
3.2.S.7.3	Stability Data	

3.2.P	Drug Product	
3.2.P.1	Description and Composition of the Drug Product	
3.2.P.2	Pharmaceutical Development	
3.2.P.2.1	Components of the Drug Product	
3.2.P.2.1.1	Drug substance	
3.2.P.2.1.2	Excipients	
3.2.P.2.2	Drug Product	
3.2.P.2.2.1	Formulation Development	
3.2.P.2.2.2	Overages	
3.2.P.2.2.3	Physiochemical and Biological Properties	
3.2.P.2.3	Manufacturing Process Development	
3.2.P.2.4	Container Closure System	
3.2.P.2.5	Microbiological Attributes	
3.2.P.2.6	Compatibility	
3.2.P.3	Manufacture	
3.2.P.3.1	Manufacturer(s)	
3.2.P.3.2	Batch Formula	
3.2.P.3.3	Description of Manufacturing Process and Process Controls	
3.2.P.3.4	Controls of Critical Steps and Intermediates	
3.2.P.3.5	Process Validation and/or Evaluation	
3.2.P.4	Control of Excipients	
3.2.P.4.1	Specifications	
3.2.P.4.2	Analytical Procedures	
3.2.P.4.3	Validation of Analytical Procedures	
3.2.P.4.4	Justification of Specifications	
3.2.P.4.5	Excipients of Human or Animal Origin	
3.2.P.4.6	Novel Excipients	
3.2.P.5	Control of Drug Product	
3.2.P.5.1	Specifications	
3.2.P.5.2	Analytical Procedures	
3.2.P.5.3	Validation of Analytical Procedures	
3.2.P.5.4	Batch Analyses	
3.2.P.5.5	Characterization of Impurities	
3.2.P.5.6	Justification of Specifications	
3.2.P.6	Reference Standards or Materials	
3.2.P.7	Container/Closure System	
3.2.P.8	Stability	
3.2.P.8.1	Stability Summary and Conclusions	
3.2.P.8.2	Post-Approval Stability Protocol and Stability Commitments	
3.2.P.8.3	Stability Data	
3.2.A	Appendices	
3.2.A.1	Facilities and Equipment	
3.2.A.2	Adventitious Agents Safety Evaluation	
3.2.A.3	Excipients	
3.2.R	Regional Information	
3.2.R.1	Alcohol Content Declaration	
3.2.R.2	Porcine/Pork – content/origin	
3.2.R.3	The diluents and colouring agents in the product formula	
3.3	Literature References	

Module 4	Non-Clinical Study Reports	
4.1	Table of Contents of Module 4	
4.2	Study Reports	
4.2.1	Pharmacology	
4.2.1.1	Primary Pharmacodynamics	
4.2.1.2	Secondary Pharmacodynamics	
4.2.1.3	Safety Pharmacology	
4.2.1.4	Pharmacodynamic Drug Interactions	
4.2.2	Pharmacokinetics	
4.2.2.1	Analytical Methods and Validation Reports	
4.2.2.2	Absorption	
4.2.2.3	Distribution	
4.2.2.4	Metabolism	
4.2.2.5	Excretion	
4.2.2.6	Pharmacokinetic Drug Interactions	
4.2.2.7	Other Pharmacokinetic Studies	
4.2.3	Toxicology R	
4.2.3.1	Single-Dose Toxicity	
4.2.3.2	Repeat-Dose Toxicity	
4.2.3.3	Genotoxicity	
4.2.3.3.1	In vitro Studies	
4.2.3.3.2	In vivo Studies	
4.2.3.4	Carcinogenicity	
4.2.3.4.1	Long Term Studies	
4.2.3.4.2	Short- or medium-term studies	
4.2.3.4.3	Other studies	
4.2.3.5	Reproductive and Development Toxicity	
4.2.3.5.1	Fertility and Embryonic Development	
4.2.3.5.2	Embryo-Fetal Development	
4.2.3.5.3	Pre- and Post-natal Development & Maternal Function	
4.2.3.5.4	Offspring, Juvenile, Second & Third-Generation Studies	
4.2.3.6	Local Tolerance	
4.2.3.7	Other Toxicity Studies	
4.2.3.7.1	Antigenicity	
4.2.3.7.2	Immunogenicity	
4.2.3.7.3	Mechanistic Studies (not included elsewhere)	
4.2.3.7.4	Dependence	
4.2.3.7.5	Metabolites	
4.2.3.7.6	Impurities	
4.2.3.7.7	Other	
4.3	Literature References	

Module 5	Clinical Study Reports	
5.1	Table of Contents of Module 5	
5.2	Tabular Listing of All Clinical Studies	
5.3	Clinical Study Reports	
5.3.1	Reports of Biopharmaceutics Studies	
5.3.1.1	Bioavailability (BA) Study Reports	
5.3.1.2	Comparative BA & BE Study Reports	
5.3.1.3	In vitro/In vivo Correlation (IV/IVC) study reports	
5.3.1.4	Reports of Bioanalytical and Analytical Methods for Human studies	
5.3.2	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	
5.3.2.1	Plasma Protein Binding Study Reports	
5.3.2.2	Reports of Hepatic Metabolism and Drug Interactions studies	
5.3.2.3	Reports of Studies Using other Human Biomaterials	
5.3.3	Reports of Human Pharmacokinetic Studies	
5.3.3.1	Healthy Subject PK and Tolerability	
5.3.3.2	Patient PK and Initial Tolerability	
5.3.3.3	Intrinsic Factor PK Study Reports	
5.3.3.4	Extrinsic Factor PK Study Reports	
5.3.3.5	Population PK Study Reports	
5.3.4	Reports of Human Pharmacodynamics (PD) Studies	
5.3.4.1	Healthy Subject PD and PK/PD Study Reports	
5.3.4.2	Patient PD and PK/PD Study Reports	
5.3.5	Reports of Efficacy and Safety Studies	
5.3.5.1	Study reports of Controlled Clinical Studies pertinent to the claimed Indication	
5.3.5.2	Study reports of Uncontrolled Clinical Studies	
5.3.5.3	Reports of Analyses of Data from More than One Study	
5.3.5.4	Other Study Reports	
5.3.6	Reports of Post-Marketing Experience (PSURs, ICSRs)	
5.3.7	Case Report Forms and Individual Patient Listings	
5.4	Literature References	

Appendix 2:

Module 1:

Regional Administrative Information for New Submission

Section	Requirements	1	2	3
1.0	Cover Letter	□	□	
1.1	Comprehensive Table of Content			
1.2	Application Form*	□	□	
1.3				
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	Information on the experts			
1.3.5	Samples [a]			
1.4				
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				
1.6.1	Pharmacovigilance System			
1.6.2	Risk Management Plan			
1.7				
1.7.1	GMP Certificate			
1.7.2	CPP or Free-sales [b]			□
1.7.3	Certificate of analysis – Drug Substance & Finished Product	□c	□c	
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 [e]			
1.7.10	Letter of access or acknowledgment to DMF			
1.8				
1.8.1	Price list**	□	□	□
1.8.2	Other document related			
1.9	Responses to questions			
	Additional data			

1. Signature of Authorized person
2. Company official stamp
3. Authentication
    a. Physical sample
    b. Not required for local manufacturers
    c. Only for Finished Products
    d. Summary of PSMF
    e. Out of patency statement (first generic only)

*Refer to Appendix-V

**Refer to Appendix-VI

Appendix 3:

Cover Letter

The following points are to be included in a cover letter in addition to any further details that the applicants believe to be of importance:

Local Agent:

Company Name and Address:

Trade Name:

ATC code:

Dosage Form:

Dosage Strength:

International Non-proprietary Name (INN):

Validation Tool used:

Validation Specification:

MD5 checksum:

Sequence Tracking Table:

Date of submission	Sequence Number	Submission Type	Regulatory activity/ Submission Description	Related e-CTD Sequence	Regulatory Status (Submitted/ Approved/ Rejected)

Appendix 4:

Module 1:

Regional Administrative Information for Re-Registration

Section	Requirements of Module 1	Re-Reg.
1.0	Cover letter	☐
1.2	Application Form	☐
1.3		
1.3.1	Summary of Product Characteristics (SPC)	☐[a]
1.3.2	Labeling	☐[a]
1.3.3	Patient information leaflet (PIL)	☐[a]
1.3.4	Artwork (Mock-ups)	☐[a]
1.7	Certificates and Documents	
1.7.2	CPP or Free-sales	☐
1.7.7	Certificate of suitability (EDQM) + TSE	☐[a]
1.8	Pricing	
1.8.1	Price list	☐[b]
	Additional data	☐
Section	Requirements of Module 3	
3.2.S	Drug Substance	☐[a]
3.2.P	Drug Product	☐[a]
3.2.A	Appendices	☐[a]

a. Should be submitted only, if there are changes from the previously submitted
b. In the initial submission, the certificate without authentication can be submitted, but must be provided upon request

Appendix 5:

نموذج شهادة الأسعار (نموذج 18 بلد)

Price Certificate Form (form 18)

GENERAL INFOR	Product Name		Concentration		Pack Size
	Pharmaceutical Form		Company Name &Nationality		
COUNTRY OF ORIGIN	**Ex-Factory Price** (In Country of Origin's currency)	**Wholesale Price** (In Country of Origin's currency)	**Public Price** (In Country of Origin's currency)	***Proposed CIF in USD**	**NOTE**

THE OTHER PRICE IN COUNTRIES WHERE THE PRODUCT IS MARKETED

No.	Country Name	Pack Size	Ex-Factory price	currenc	CIF PRICE	currenc	PUBLIC PRICE	currenc	NOTES
1	Austria								
2	Australia								
3	Belgium								
4	Canada								
5	Denmark								
6	France								
7	Germany								
8	Holland								
9	Hungary								
10	Ireland								
11	Italy								
12	Japan								
13	Portugal								
14	South Korea								
15	Spain								
16	Sweden								
17	Switzerland								
18	U.K								

WE:		**تشهد شركة:**
Certify that all prices in this form are correct and accurate.		**ان جميع الأسعار في هذا النموذج صحيحة.**
Name of the person authorized to sign on behalf of the company		**اسم الشخص المفوض بالتوقيع عن الشركة**
Stamp		**ختم الشركة**

In case of registering multiple package sizes, each pack must have a separate stamped form.

في حال وجود أكثر من عبوة مسوقة يُذكر سعر كل عبوة والبلدان المسوق بها في نموذج مستقل مختوما بختم الشركة

***Proposed CIF for local manufacturer should be in Omani Rial**