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 on eCTD Submissions

Version 3.0

March 2018

Ministry of Health

Directorate General of Pharmaceutical Affairs & Drug Control

(MOH-DGPA&DC)

This guidance is intended to provide assistance and advice to applicants about different aspects related to Marketing Authorizations in eCTD (electronic Common Technical Document) format. It reflects the current practice and will be regularly updated in case of changes in legislation and policies. It is important for applicants to adhere to the administrative requirements in order to avoid un necessary delays in the process.

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

Document 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 – Revision 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)
3.0		Drug Control Department	– Addition of Fast Track. – Addition of Baseline. – Updating Registration process (new MAAs) – Updating of re-registration. – Updating Variations. – Addition of Important Notes. – Updating FAQs.

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 Age
GVP	Good Pharmacovigilance Practice
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
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".

Glossary:

Application number: it is the official reference number assigned to an application for Marketing Authorization to 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. 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-DGPA&DC an eCTD application may comprise several strengths, each with a unique proprietary name. Such a collection may also be described as dossiers.

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: 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 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.

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-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)”.

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.

1 Introduction:

This guidance 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 DGPA&DC 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, Baseline, 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 additional 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 Scope:

The scope of this guidance is to provide detailed information on how to submit eCTD applications to 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 specific documents in Module 1 that must be submitted in both soft and hard copy formats.

3 Types of submissions:

- New registration.
- Baseline
- Re-registration.
- Variations.

4 Types of products:

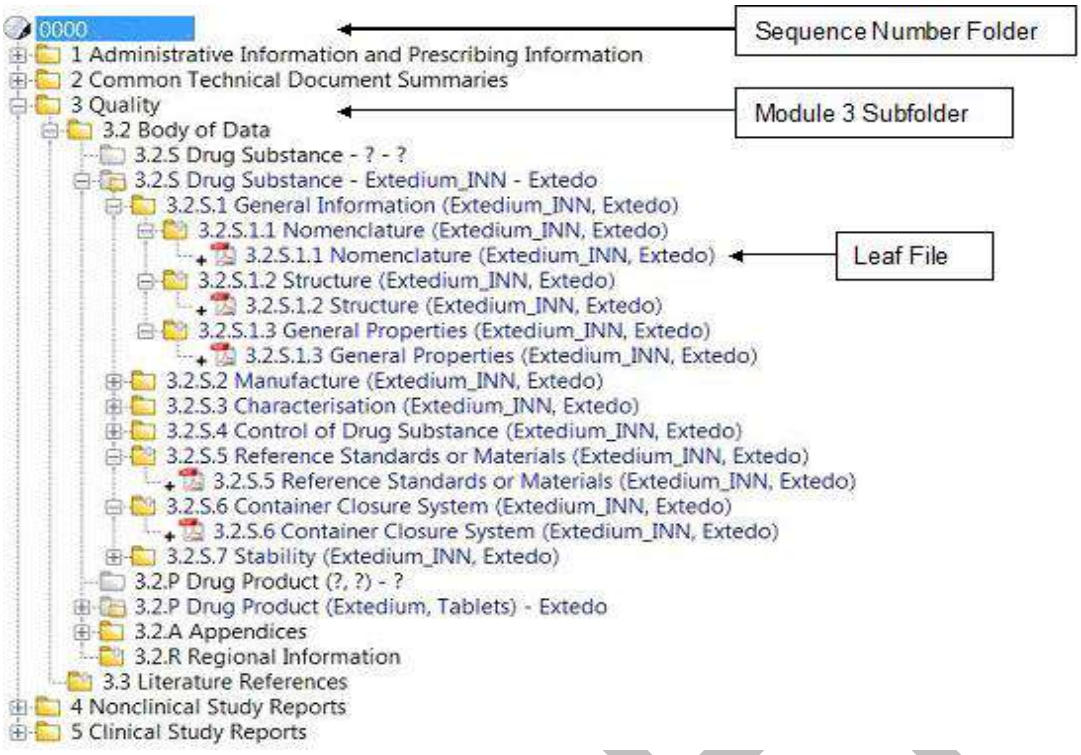
- New Chemical Entities.
- Generics.
- Biologics**.**

5 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 Biosimilar 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

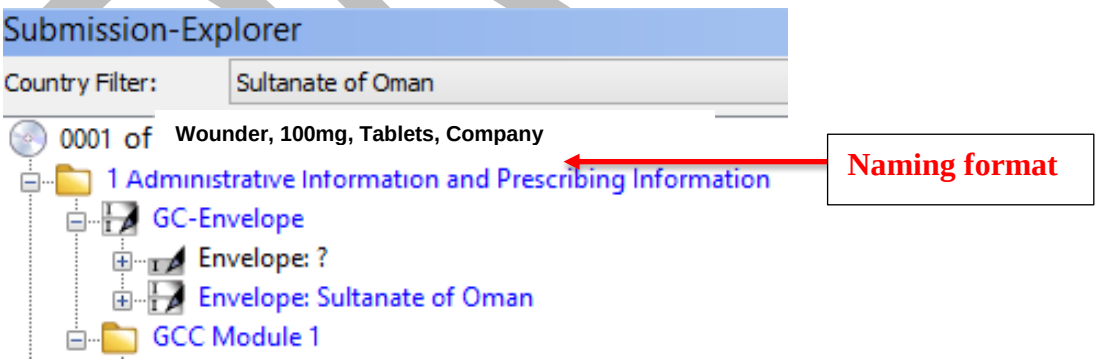
The difference between CTD and eCTD lies in the type of media used, and the method of structuring documents. An eCTD submission is an electronic dossier built using an XML backbone with a unified pattern of arranging documents into branches and leaves. It allows better accessibility and therefore improving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



(Figure1): Structure of eCTD dossier

6 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"**



(Figure2): Naming format for product dossier

7 Presentation of the Product File:

The product dossier will consist of 2 parts:

- Hard copy part: a file containing some hard copies of M1. In case of multiple strengths, one hard copy file should be submitted for each.
- Soft copy part: CD/DVD of M1-M5 for a product. Combined submission will be required for a multiple strength product.

7.1 Hard Copies for Module I:

Module 1 follows the same GCC specifications. However, for legal reasons, specific documents of Module 1 that are listed in Appendix-II must be available in hard and soft copies. In addition, the CD validation report can be submitted in either hard or soft copy.

7.1.1 SPECIFICATIONS:

Hard copy documents must be identical to the soft copy in eCTD submission.

7.1.2 LEGIBILITY AND SIZE:

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

7.1.3 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.

7.1.4 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.

7.1.5 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) .

7.2 Softcopy Requirements:

The applicant should submit 2 CD's or DVD's along with the validation report, each CD should be submitted in a hard plastic cover and must include the following label information, clearly and well presented on the media":

- 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).

7.2.1 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.

7.2.2 SYSTEM COMPATIBILITY:

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

7.2.3 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 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, by using the GCC validation criteria 1.2 or 1.4. Although it is recommended to use validation criteria 1.4, it is also important to note that applicant shouldn't downgrade the validation criteria of the submission if the product was already submitted in 1.4. The results of the validation report along with the number generated by the MD5 checksum should also be submitted.

7.2.4 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.

7.2.5 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.

8 Submission Considerations for Electronic Version of Module I:

8.1 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.

8.2 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 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 (e.g. 0000-workingdocuments)" with a substructure as follows:

8.3 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.

8.4 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 they aid in the navigation around

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

8.5 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.

8.5.1 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.

8.5.2 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.

8.6 Letter of Application (Cover letter):

Submissions in eCTD format should be accompanied by a cover letter of application in both hard copy and soft copy. 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 letter (paper version) must be signed & stamped.

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-DGPA&DC should not be included in the cover letter, since they have been assigned a specific location in Module 1.9.

9 Registration Process (New MAAs):

9.1 Appointments for submitting applications:

The applicant should submit a request for an appointment to submit the application to MOH-DGPA&DC. Appointments will be given for products that are manufactured/batch released by companies registered by MOH-DGPA&DC. The applicant will be informed with the appointment day and time.

In case the applicant did not appear on the scheduled date (no show), a new appointment request has to be made refer to (Appendix IV) for the format of the appointment request). It is important to note that Variations do not require prior appointments.

If the product was registered in any GCC country, the applicant should attach a copy of a Certificate of Analysis along with the appointment letter. The same should also be enclosed in the dossier.

9.2 Submission of Application:

On the submission day, the applicant must be present at the specified time slot. Submitted dossiers along with the two CD's/DVD's will be verified against a checklist of all required documents according to MOH-DGPA&DC submission criteria.

9.3 Phase- I (Validation):

The submission will be rescanned by MOH-DGPA&DC for viruses. Technical validation of the dossier will be carried out using an Importation tool and the generated 32 digits MD5 checksum should match with the one submitted by the applicant.

9.4 Post Phase- I (Validation):

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

9.4.1 VALID DRUG APPLICATIONS:

The applicant will receive a copy of the application form with the assigned eCTD application number. The dossier is then forwarded for evaluation and assessment.

9.4.2 INVALID DRUG APPLICATIONS:

The dossier and the samples will be returned back to the agent along with the validation report presenting all the errors. The applicant is allowed a period of 30 days to rectify the errors from the date of submission.

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 30 days. The application will forward to the concerned staff member for further processing and assessment.

If the applicant has provided the requested information within 30 days, but it was found to be still incomplete, the applicant can complete the missing within the rest of the 30 days.

In case of failure to submit within 30 days, the drug application will be rejected.

9.5 Phase II (Review):

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. The response must be in eCTD format with appropriate sequence number. Depending on the applicant's response, the subsequent outcomes are:

1. **Applicant responds within 90 days**: submitted documents will be assessed and if the response was unsatisfactory, the requirements will be sent to the applicant and another 90 days will be given.
2. **Failure to respond within the timeline**: such applications will be forwarded to TCR&P for decision-making.

9.6 Phase III (Decision)

Decision on application will be taken by the TCR&P.

10 Fast Track

Fast track is a designation given by the MOH-DGPA&DC to a pharmaceutical product for expedited review to facilitate product registration and as such they are intended for products that treat a serious or life-threatening condition or fill an unmet medical needs.

The applicant, along with the appointment request and not after receiving the product file, should indicate if the product was legible for Fast Track process.

11 Baseline

A baseline is the re-submission, in electronic format, of all current valid documents of a registered product that have been previously submitted to MOH-DGPA&DC in other formats. Baseline submission is necessary to switch from a non-electronic to an electronic format before starting further lifecycle activities. Therefore, it is mandatory before submitting a re-registration and/ or variation applications in eCTD format.

It is preferred that baseline submission should include full modules (M1-M5). However, if not applicable, specific documents of (M1 & M3) can be submitted as minimum requirements as per (Appendix- V). It is recommended that baseline submissions not to include any updated information and to be limited to resubmission of current approved specifications. In case of changes, the applicant should submit a declaration letter in both hard and soft copies, describing those changes and to state if any variation applications were submitted or not and their status. In addition, baseline submissions are not going to be evaluated by DGPA&DC. Therefore, valid submissions do not necessary mean the approval of the content.

Baseline submissions should always have sequence number (0000). However, in some circumstances it can be submitted as (0001,0002,0003, etc.) this is typically in case if the registration was valid for strength at the time when renewal application for another strength was submitted in an e-CTD format. An example is demonstrated in FAQs.

12 Re-Registration:

Re-registration is the renewal of marketing authorization for a pharmaceutical 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.

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

The required documents should be submitted as per (Appendix-V). 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-DGPA&DC.
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.

12.1 (3.2. S Drug Substance):

The drug substance information should be submitted in one of the following options:

a. Complete section 3.2.S, or
b. Drug Master File (DMF), or
c. Certificate of suitability (CEP) with the followings sections; 3.2.S.1.3 (General properties), 3.2.S.3.1 (Elucidation of structure and other characteristics), 3.2.S.4.2 (Analytical procedures), 3.2.S.4.3 (validation of analytical procedures) and 3.2.S.6 (Container closure system).

In case the finished product contains plasma derivatives, complete Plasma Master File (PMF) or a commitment letter from the manufacturer showing that the source of plasma did not changed from the previously approved source should be submitted.

12.2 (3.2. S.4.1 Specifications):

Copies of the current API specifications, duly signed and dated, should be provided, including the test methods. The specifications should indicate the reference number, version number, effective date and change history if any.

12.3 (3.2. P.5.1 Specifications):

Copies of the current drug product specifications, duly signed and dated, should be provided, including the test methods. The specifications should indicate the reference number, version number, effective date and change history if any**.**

12.4 (3.2. P.8 Stability):

Stability data on two production batches in accordance with the "GCC Guidelines for Stability Testing of Active Pharmaceutical Ingredients (APIs) and Finished Pharmaceutical Products (FPPs)" to support the current Finished Pharmaceutical Product Specifications (FPPs) and analytical procedures and it should cover the claimed shelf-life.

13 Variations:

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

- The application form for variation is as per (Appendix –VI).
- An application form may contain several variations for one submission.
- Parallel submissions are acceptable only if variations were not related.
- Applications for variations are received weekly on Tuesdays from 9:00 am till 11:59 Am.
- Variation process and required documents follows the current GCC guidelines for variation.
- CD/DVD of the required documents in eCTD format along with the validation report.
- Cover letter and Hard copies of legalized documents and it must be identical to those made available in soft copy (In case the variation involves legalized documents).
- There should not be any changes other than those identified in this application

(except for other variations addressed in other applications submitted in parallel)

14 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.

15 Responses to Questions

The organization related to submission of electronic information in response to a list of questions should follow the same basic principles as the first submission. This section should not contain any technical documents since they should be uploaded in the relevant modules. This section should list the inquiries with a corresponding narrative text for each question. 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.

16 Important Notes:

- Once an eCTD submission was received, switching back to non-eCTD format would not be accepted.
- Submission during an ongoing regulatory activity will not be accepted, except in two cases one is for baseline submissions during an ongoing none-CTD variation the second is in case of submitting a variation that is different from other variations addressed in other submissions (i.e, parallel variation submissions).
- It is advisable that applicants would submit the full eCTD modules (M1-M5) for baseline & Re-registration submission.
- Products with multiple strengths should be submitted in one submission (Combined)
- 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.

17 Frequently Asked Questions (FAQs):

Prior to prepare a submission, the applicants are highly advised to go through this part as it can greatly facilitate in understanding several concerns with their applications.

Q1. What is the Application number?

An Application number is also known, as an eCTD identifier number is the number generated by the DGPA&DC and given against each product or strength. It consists of twelve digits and two letters each indicates something as follows:

e.g.: **HG-000000-00-00-00**

HG: Human Generic
HN: Human N.C.E
First Six digits "000000": Serial number
Second two digits "00": Renewal
Third two digits "00": Type 1 Variations
Fourth two digits "00": Type 2 Variations

Q2. When is the Application number issued?

An Application number is issued by DGPA&DC once the dossier passes technical validation as it is documented in the application form.

Q3. What should I place in section 1.6.1 "pharmacology system"?

You are only requested to submit a summary of the PSMF (Pharmacovigilance System Master File) according to the Guidelines on good Pharmacovigilance practice (GVP) for Arab countries (version 2) and Guidelines on good Pharmacovigilance practices in Oman for MAH/Pharmaceutical companies (version 1).

Q4. 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?

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

Q5. In which Section of Module 1 shall I place the GMP certificate for the API manufacturer?

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

Q6. Is it important to attach the company local registration certificate and where?

Yes, it is mandatory to attach the local registration certificate of the company for the submitted product and it should be placed in 1.7.1 "GMP".

Q7. In which Section of Module 1 shall I place the list of countries where the product is registered (Worldwide Registration Status)?

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

Q8. In which Section of Module 1 shall I place the copies of registration certificates if the product is registered in GCC countries?

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

Q9. Are there any special considerations for the price list?

Yes, there are several issues to be considered such as:

- To fill in all the fields related to the price details in the country of origin.
- The proposed CIF price must be in USD.

- The validity of the certificate should not exceed 6 months from its date of issue.
- The prices in other countries should be mentioned with respect to the list of countries where the product is registered.

Q10. Is it possible to submit price certificate without it being legalized?

Price certificate (Form 30) must be legalized for new marketing authorizations during submission. However, unauthenticated certificate is acceptable for renewal applications.

Q11. Can I submit an appointment while the application is not ready?

No, the applicant should submit an appointment request only when the dossier is ready.

Q12. If my product is legible for fast track, what type of documents should I attach to the appointment request?

The applicant should submit any documents to support the stated request such as: scientific publications, Summery of clinical studies, Approval by respected regulatory authorities such as: US FDA and EMA as fast track application… etc.

Q13. Do I have to submit a new appointment request for a re-submission?

No, the applicant should only inform the staff verbally once the application is ready for resubmission within one month.

Q14. How to prepare a sequence-tracking table within the cover letter?

The tracking table format is as following:

Date of Submission	Sequence Number	Submission Type	Submission Description	Related e-CTD Sequenc	Regulatory Activity Status
12/1/2016	0000	New	New Product Application	_	Approved
4/6/2016	0001	Response	Response to Question	0000	Approved
6/3/2017	0002	Variation	Variation-Type2 (addition of new Indication)	0000	Approved
15/5/2017	0003	Response	Response to Question	0002	Approved
23/9/2017	0004	Variation	Variation-Type2 (Addition of new Indication)	0002	Under review
1/10/2017	0005	Variation	Variation-Type 1B	0000	Submitted
19/12/2017	0006	Variation	Variation-Type 2 (extension of shelf life)	0000	Rejected
12/1/2018	0007	Response	Appeal to Rejection Decision	0006	Submitted

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

Submission Type: (New / Re-registration / Variation / Baseline/ Response).

Submission description: a brief description of the type of submission e.g. ("New product application, reformat, variation Type, Re-registration, Response to requirement, Reformat, and appeal..etc).

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

Q15. How to prepare a sequence-tracking table for a baseline submission for a product that was registered against a non-eCTD format?

Date of Submission	Sequence Number	Submission Type	Submission Description	Related e-CTD Sequence	Regulatory Activity Status
	0000	Baseline	Reformat for Product X (10mg and20mg)	–	Submitted

Q16. How many submissions are required for one product with multiple strengths?

The applicant should submit multiple strengths product in one submission CD or DVD. However, hard copies will be required to be submitted separately for each.

Q17. How can I deal with the renewal application of a product, registered in non-eCTD format, having multiple strengths where 2 strengths are expiring soon and another is still valid?

At first, the applicant should submit a baseline submission with a sequence (0000). This submission should include all multiple strengths and all registered pack sizes regardless to the expiry dates of their registration certificates. Then, a renewal submission with sequence (0001) for strength(s) that are due for renewal should be submitted. As it shows in the following example:

Date of Submission	Sequence Number	Submission Type	Submission Description	Related e-CTD Sequence	Regulatory Activity Status
	0000	Baseline	Reformat (product X 375mg, 625mg &1g)	–	Approved
	0001	Re-Registration	Re-Registration of (product X 375mg, 625mg)	0000	Approved

	0002	Variation	Variation-Type2 (Pack insert update)(product X 375mg, 625mg)	0001	Approved
	0003	Variation	Variation-Type2 (Change of specification)(product X 1g)	0000	Approved
	0004	Re-Registration	Re-Registration of (product X 1g)	0000	Submitted

Q18. Can I submit a baseline application while non-eCTD variation is under review?

In order to facilitate switching to eCTD, baseline submissions during an ongoing none-CTD variation review is acceptable.

Q19. How about submitting a baseline while non e-CTD re-registration is under process?

In this case, baseline submissions are not accepted unless the renewal was finalized. The applicant may submit the baseline after issuing the registration certificate

Q20. I previously submitted a combined (baseline with renewal submission for one strength and it got approved. Now how can I proceed with renewal applications for other strengths?

The applicant should submit the baseline for the remaining strengths. In this case the baseline sequence number will continue from the last one and it must not be (0000). As shown in below example:

Date of Submission	Sequence Number	Submission Type	Submission Description	Related e-CTD Sequenc	Regulatory Activity Status
	0000	Re-registration	Renewal for product X (250 mg)	_	Approved
	0001	Response	Response to QCL requirements	0000	Approved
	0002	Variation	Type 1a variation	0000	Approved
	0003	Baseline	Baseline reformat for product X (500 mg).	-	Approved
	0004	Re-registration	Renewal for product X (500 mg)	0003	Approved
	0005	Response	Response to M1 requirements	0004	Approved
	0006	Variation	Type 2 (change in shelf life from 3-5 years) for products 250 mg and 500 mg	0000 and 0004	Submitted

Q21. Can you advise me how to prepare a renewal application for product X which has 2 different pack sizes, registration number (D0123A and D0123B), with 2 different validity dates?

The applicant should submit baseline submission with sequence (0000). The baseline should include all registered pack sizes (pack A and B) regardless to the expiry dates of their registration certificates. Then, a Re-registration application with sequence (0001) should be submitted. After approval, the validity dates of both packs will be unified and the date of the smallest pack size (A) will be applied for both packs.

Q22. If I submitted for an additional pack size to a registered product, will it have validity of 5 years?

The expiry dates of the additional pack sizes will always be equal to the date of the first pack registered.

Appendix-I

eCTD Structure for Human Medicine

Generic Products

R: Required O: Optional

Module 1	Regional Administrative Information	
Section	**Requirements**	**G**
1.0	Cover letter	R
1.1	Comprehensive Table of content	R
1.2	Application Form	R
1.3	Product Information	
1.3.1	Summary of Product Characteristics (SPC)	R
1.3.2	Labeling	R
1.3.3	Patient information leaflet (PIL)	
1.3.3.1	Arabic leaflet	R
1.3.3.2	English leaflet /French leaflet	R
1.3.4	Artwork (Mock-ups)	R
1.3.5	Samples	R
1.4	Information on the experts	
1.4.1	Quality	O
1.4.2	Non-Clinical	O
1.4.3	Clinical	O
1.5	Environmental Risk Assessment	
1.5.1	Non-Genetically Modified Organism (Non-GMO)	O
1.5.2	GMO	O
1.6	Pharmacovigilance	
1.6.1	Pharmacovigilance System	R
1.6.2	Risk Management Plan	O
1.7	Certificates and documents	
1.7.1	GMP Certificate	R
1.7.2	CPP or Free-sales	R
1.7.3	Certificate of analysis – Drug Substance	R
1.7.4	Certificate of analysis – Excipients	R
1.7.5	Alcohol-free declaration	R
1.7.6	Pork-free declaration	R
1.7.7	Certificate of suitability for TSE	R
1.7.8	The diluents and colouring agents in the product formula	R
1.7.9	Patent Information	R
1.7.10	Letter of access or acknowledgment to DMF	R
1.8	Pricing	
1.8.1	Price certificate	R
1.8.2	Other documents related – Pricing list	O
1.9	Responses to questions	O

- Blank fields are not required at this stage or not applicable for that specific drug submission type
- Optional means that it might not be needed at this stage.
- Statement of out of patency must be submitted for first generic product.

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

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

Module 4	Non-Clinical Study Reports	G
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	O

Module 5	Clinical Study Reports	G
5.1	Table of Contents of Module 5	R
5.2	Tabular Listing of All Clinical Studies	R
5.3	Clinical Study Reports	
5.3.1	Reports of Biopharmaceutics Studies	
5.3.1.1	Bioavailability (BA) Study Reports	R
5.3.1.2	Comparative BA & BE Study Reports	R
5.3.1.3	In vitro/In vivo Correlation (IV/IVC) study reports	R
5.3.1.4	Reports of Bioanalytical and Analytical Methods for Human studies	R
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)	R
5.3.7	Case Report Forms and Individual Patient Listings	R
5.4	Literature References	R

Appendix- II

Module 1: Regional Administrative Information for New Submission

Section	Requirements	1	2	3	4	5
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					
1.3.4	Information on the experts					
1.3.5	Samples					✓[a]
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	✓[d]				
1.6.2	Risk Management Plan	✓				
1.7	Certificates and Documents					
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]	✓[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	Pricing					
1.8.1	Price list**	✓	✓	✓	✓	✓
1.8.2	Other document related					
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
5: Hard Copy

*****Refer to Appendix-VII

** Refer to Appendix-VII

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)

Appendix-III

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):

Number of CDs/DVDs provided:

Application Number:

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)

- "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 versions of parts of module 1 are identical".
- The content of the previously submitted dossier has not been changed only the format. (Only applicable for baseline)

Appendix- IV

Director of Drug Control
Directorate General of Pharmaceutical Affairs & Drug Control
Ministry of Health
Appointment Request Form

Ref. No.: Date:

1. Submission Type
   - ☐ Registration
   - ☐ Baseline
   - ☐ Re-Registration

2. Fast track
   - ☐ Yes
   - ☐ No

(*If yes, applicant must attach the necessary documents to support the request)*

Sr.#	Trade name, Strength, Dosage form	Generic name	Pack Size	Manufacturer, CoO	MAH, CoO	GCC Registration status
1						
2						
3						
4						
5						

If the product was registered in any GCC country, a copy of a valid registration certificate and CoA if available should be attached along with the request.

Local Agent Signature: Stamp:

Appendix- V
Module 1: Regional Administrative Information for Re-Registration & Baseline

Section	Requirements of Module 1	Re-Reg.	Base.
1.0	Cover letter	✓	✓
1.2	Application Form	✓	✓
1.3	Product Information		
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 approved document
b. In the initial submission, the certificate without authentication can be submitted, but must be provided upon request

Appendix-VI

Application Form for Post Approval Changes (variation) of a Registered Pharmaceutical Product

<u>This form should be filled by the company.</u>

1. This application concerns:

- ☐ New Drug
- ☐ Generic (Multisource)
- ☐ Biological:
  - Biosimilar
  - Blood Product
  - Vaccine
- ☐ Others (specify):

Product Information:

Registration No.:	Application No.:
Trade Name:	
Active Ingredient(s):	
Dosage Form:	
Strength/Unit:	
Package Size(s):	
Route of Administration:	
Primary Packaging:	
Secondary Packaging:	
Approved Shelf Life:	
Approved Storage Condition:	
Marketing Authorization Holder:	
Name:	Address:
Batch Releaser:	
Name:	Address:
Manufacturer:	
Name:	Address:

2. **Variation(s) type:**

   a. Copy of the relevant page(s) from the Variation Guidelines for this/these change(s) are attached and the relevant boxes for conditions and documentation.
   b. This Application includes the following variations.

Sr. No.	Variation Description as per GCC guidelines for variation	Variation Type	Date of Implementation*

*Date of implementation of Type IA variation should be specified as this variation could be implemented prior to this submission.

3. **Variation Description:**

   Full description of proposed changes

Proposed*	Current*

*Specify the precise present and proposed wording or specification, including dossier section number(s) at the lowest possible level.

For SPC, labeling and package leaflet changes, underline or highlight the changed words presented in the table above or provide as a separate Annex.

Declaration:

I hereby confirm that the submitted application for the above Marketing Authorization to be varied in accordance with the proposals given above. I declare that:

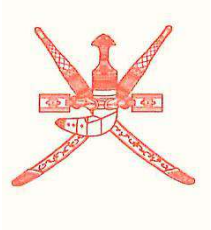
- ☐ The submitted information is true and accurate
- ☐ There are no changes other than those identified in this application (except for other variations addressed in other applications submitted in parallel)
- ☐ No other applications will be submitted for the same variations addressed in this application unless they are finalized by DGPA&DC. Otherwise, withdrawal request form will be requested
- ☐ Where applicable, all conditions as set for the variation(s) concerned are fulfilled

Company Director/CEO:

Signature:

Date:

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

Appendix-VII

Application form

- This Application Form to be filled by the applicant by typing **ONLY** (original & one photocopy).
- All the documents submitted with this application should either be in English and Arabic or English only.
- Arrangement of the documents in the folder should follow the same sequence as CTD format.
- A separate submission is required for each strength, dosage form, flavoring agent and presentation.
- In case of new drug and Biological products, all the CTD modules are required.
- In case of Generic, Health and Herbal products, it is acknowledged that certain sections the CTD would generally not be applicable and should be marked as such and not to be deleted.
- All the documents should be submitted as PDF format.

Type of Application:

☐ New

☐ Re-sourcing *: from …… to ……

☐ Re-registration *

☐ Baseline

This Application concerns:

☐ New Drug
  - Known Active Substance
  - New Chemical Entity (NCE)

☐ Generic

☐ Biological
- Biosimilar
- Blood product
- Vaccine
- Others (specify) ……...

☐ Health *
☐ Herbal *

* Not applicable at this stage

Part I: *(to be filled by the company for the agent)*

1. Cash receipt for R.O. …….

Receipt No. : ……

Date: …….

2. Name and Address of the Local Agent: …

Address	**Administration Office**
P.O. Box:	_____
P.C.	
Tel. No.	
Fax No.	
E-mail	

3. Full Description of the Product:

- Trade Name: … … … … … … … … … … … … … …
  - Strength: … … … … … … … … … … … … … … …
  - Dosage Form: … … … … … … … … … … … … ….
  - Pack Size(s): … … … … … … … … … … … … …..

4. Legal Category in the COO:

☐ OTC
☐ POM
☐ CD
☐ Other (specify)…….

5. Full Description of the Manufacturer:

Name:……
Reg. No. with MOH:……
Approved production lines: ……

- Reg. Date:…….
  Expiry Date:……

6. Full Description of the MAH:

Name:…… Reg. Date:……

Reg. No. with MOH:……..… Expiry Date:……

Name and Signature of the authorised Pharmacist in the pharmacy	Stamp of the Pharmacy

Part II: *(To be filled by the company)*

1. Product Information:

1.1 Trade Name of the Product in Oman: …

1.2 Trade Name of the product in Country of Origin (COO): … … … … … … … … … … … … … … … … …
Note: if the trade name is different from that of the COO, you are requested to submit a legalized certificate from the Health Authority to clarify the same.

1.3 International Non-Proprietary Name (INN): …

1.4 Dosage Form: …

1.5 Route of Administration: …

1.6 Strength/Unit: …

1.7 Pack Size (by weight, volume or number of doses): … … … … … … … … … … … … … … … … … …

1.8 Type of Packaging Material (in details):
1.8.1 Primary: …
1.8.2 Secondary: …
Note that if the pack contains additional device, it has to be clearly specified

1.9 Proposed Shelf Life: …
1.9.1 Proposed shelf life after first opening: …
1.9.2 Proposed shelf life after reconstitution / dilution: … … … … … … … … … … … … … … … …

1.10 Proposed Storage Conditions in figures: …
1.10.1 Proposed storage conditions after first opening in figures: … … … … … … … … … … …
1.10.2 Proposed storage conditions after reconstitution / dilution in figures: … … … … … … …

1.11 Composition in details:

Ingredient	**Quantity**	**Action**	**Pharmacopoeia Reference**
Active(s)			
Inactive(s)			

- *To include any diluents, solvents, etc, incorporated in the manufacturing formula.*
- *Please note that animal type or alcohol quantity, it has to be clearly specified. For product containing animal materials, a legalized certificate confirming that the product is free from BSE/TSE should be provided.*

2. Company Information:

2.1 Manufacturer:
- Reg. No. with MOH: …
- Name: …
- Address: … Country: ... … … … … … ….

2.2 Marketing Authorization Holder:
- Reg. No. with MOH: …
- Name: …
- Address: … Country: ... … … … … … …..

2.3 Primary Packager:
- Reg. No. with MOH: …
- Name: …
- Address: … Country: … … … … … … …

2.4 Secondary Packager:
- Reg. No. with MOH: …
- Name: …
- Address: … Country: … … … … … … …

2.5 Batch Releaser to Oman:
- Reg. No. with MOH: …
- Name: …
- Address: … Country: … … … … … … …

Note: To include manufacturing sites of any diluents/solvent/any device that is presented in the same or in a separate pack but forming part of the medicinal product

---

3. Certificate of Pharmaceutical Product (CPP):

Note that a legalized and recent CPP should be submitted

- The authority issues the CPP: …
- Date of issue: …
- Date of registration in COO: …
- Date of marketing in COO: …

Note: To provide a list of countries where the product is registered / marketed / rejected / withdrawn / pending / suspended supported by photocopies of registration certificates if available

---

4. Pricing:

Note that a Price Certificate should be submitted and should include the followings:

- Ex-factory Price in COO: …
- Wholesale Price in COO: …
- Retail Price in COO: …
- CIF Price to Oman: …
- CIF Price to other Countries (appendix II): …

---

5. Sources of Active Pharmaceutical Ingredients (API):

Manufacturer Name	Address	Is CoS certified?

Note: To provide last updated copy of the Certificate of Suitability (CoS) in the technical file.

If CoS is not available, a certified copy of GMP certificate for API manufacturer should be included in the file.

6. Labeling:

6.1 Summary of Product Characteristics (SmPC)

(Rev. Date:… … … … … … … … … … … … …)

- Recommended Clinical Use: …
- Recommended Dose for Adults: …
- Recommended Dose for Children and Infants by Age Group: … … … … … … … … … … … … … …
- Pharmacotherapeutic Group (ATC code): …

6.2 Submission of Two specimens of pack insert + CD containing the same

(Rev. No. … … … … … … … … … … … … … … Date: … … … … … … … … … … … … … …)

6.2.1 Language(s) used in the pack insert:

- ☐ Arabic
- ☐ English
- ☐ Others, specify… … … … … … … … … … …

6.2.2 Type of pack insert to be packed in the package:

- ☐ Professional Pack Leaflet

☐ Patient Pack Leaflet
☐ Both

6.2.3 The Pack Insert must contain the following:

- Trade & Generic names
- Pharmaceutical dosage form
- Dosage & Administrations
- Pharmacological effect / mode of action
- Side effects / Adverse reactions
- Indications
- Contraindications
- Storage Conditions in figures
- Drug interactions (Drug-Drug, Drug-Food)
- Over dosage & Antidote

- Precautions & Warnings (during pregnancy, lactation and the other special cases)
- Other available pharmaceutical dosage forms, pack sizes and concentration of the active ingredients.
- Name of the Manufacturer, COO and Address
- Number and Date of revision of the pack insert
- Legal category in the COO

Note: for generic drugs, provide a detailed comparison between the generic and the brand leaflets.

6.3 Submission of Two specimens of Outer / Inner Labels + CD containing the same:

The outer labels *must* include the following:

- Composition (The amount of the active ingredient/s should be specified)
  Brand Name
  - Generic Name
  - Strength
  - Dosage form
  - Route of administration
  - Pack size
  - Storage conditions in figures
  - Manufacturing & Expiry dates
  - Manufacturer and/or MAH
  - Batch No.

6.4 Submission of two sample of finished product

- Batch No.: … … … … … … … … … … …
- Mfr. Date: … … … … … … … … … … …
- Exp. Date: … … … … … … … … … … …

Note: To provide copies of BACs of finished product and API
further samples will be required upon QCL request

7. Stability Study:

Indicate the storage conditions for the following:

- Real time study: …
- Accelerated study: …

Batch Nos.	**Batch Sizes**	**Batch Type**	**Manufacturing Date**	**Expiry Date**	**Packaging Type & Material**

8. Bioequivalence Study:

If the Application for generic product, specify the following:

- Reference Drug: …
- Manufacturer Name & its Nationality: …
- Name & place of the Study: …… …
- Date of the Study: …

Declaration

I have certify that the submitted information is true and accurate and changes will not be made until they are approved by MOH, Oman

Name and Signature of the authorised Pharmacist in the pharmacy	Stamp of the Pharmacy

FOR OFFICIAL USE ONLY

☐ Received ☐ Not Received

Checked by: ……

Signature: ……

Date: ……

Record No.: ……

Application No.:……

Date: ……..

17.1.1.1.1

- ❖ Reasons of refusal if the product was not received:

1) ……

2) ……

3) ……

4) ……

5) ……

6) ……

7) ……...

APPENDIX-VIII

Price form 30

Product Name		Concentration		Pack size	
Pharmaceutical Form		Company Name & Nationality			
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 Price (in USD)	Notes	

Price in countries where the product is marketed

No.	Country Name	Pack Size	Ex-Factory or wholesale	Currency	CIF Price	Currency	Public Price	Currency	Notes
1	Algeria								
2	Australia								
3	Argentina								
4	Bahrain								
5	Belgium								
6	Canada								
7	Cyprus								
8	Denmark								
9	Egypt								
10	France								
11	Germany								
12	Greece								
13	Holland								
14	Hungary								
15	Ireland								
16	Italy								
17	Japan								
18	Jordan								
19	Kuwait								
20	New Zealand								
21	Portugal								
22	Lebanon								
23	Saudi Arabia								
24	South Korea								
25	Spain								
26	Sweden								
27	Switzerland								

28	Turkey								
29	U.A.E								
30	U.K.								

We rectify that all prices in this form are true.
Name of the person authorised to sign on behalf of the company.
Company Stamp:
Date:

تشهد شركة: ان جميع الاسعار الواردة في هذا النموذج صحيحة.
اسم الشخص المفوض بالتوقيع عن الشركة.

ختم الشركة:
التاريخ:

In case registering multiple package sizes, each pack must have a separate stamp.

في حالة وجود اكثر من عبوة مسوقة يذكر سعر كل عبوة والبلدان المسوق بها في نموذجمستقل مختوما بختم الشركة.

Appendix-IX
References

GCC Reference document

- GCC Module 1 Specifications

SFDA Reference document

- Guidance for Submission

Thailand FDA

- TH eCTD Specification Module 1 and Regional Information

Swiss medic

- 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 Granula