Guidance for eCTD Submission

Version 1.0 - July 2019

Pharmacy & Drug Control Department,

Ministry of Public Health, Qatar

T: +974 44070000
P.O. Box: 42, Doha - Qatar

ت: ٤٤٠٧٠٠٠٠ ٩٧٤+
ص.ب: ٤٢، الدوحة – قطر

www.moph.gov.qa

This page is kept blank intentionally

Contents

Introduction

Ministry of Public Health (MOPH), represented in Pharmacy & Drug Control Department (PDCD), is considered the highest drug authority in the State of Qatar. Its main responsibility is to ensure quality, safety and efficacy of any health product that is proposed to be marketed in Qatar until it reaches the hands of the end-users, and after that, to ensure the optimum use of these products.

This document is intended to guide the pharmaceutical industry and professionals through the process of preparing and submitting regulatory information in electronic Common Technical Document format (eCTD) to Pharmacy & Drug Control Department (PDCD). It also aids on how to comply with MOPH regulations and standards.

This document has been developed based on International Conference of Harmonization (ICH) guidelines, GCC guideline for submission and Qatari MOPH regulatory framework for human drug approval. This guidance is intended for registration, re-registration & variation applications for human drug products.

Its worthy to mention that this document reflects the current status and will be regularly updated in light of changes. It should be read in conjugation with other relevant guidelines.

It should be noted that MOPH has the right to request any further information or documents, with a commitment that such requests are justifiable, and will be for the purpose of ensuring quality, safety and efficacy of the submitted product.

Scope

This document applies for all registration, re-registration & variation applications for human drug products in eCTD format.

Objective

This guidance aims to provide detailed information on how to submit regulatory information in eCTD format for all human drug products within the MOPH human drug registration framework.

Registration Process

It is the responsibility of the product license holder to ensure the quality, safety and efficacy of the product before the submission, as well as the preparation of the dossier in the right eCTD format. This responsibility lasts even after the approval and as long as the product is licensed to be placed in the Qatari market. The local agent is the one responsible for the product in Qatar and he is the only authorized body to deal with MOPH as per Qatari law. However, PDCD has the right to communicate directly with the product license holder in certain cases. The product license holder should inform PDCD through his local agent with any variation on the product, as well as any emerged safety signal, as soon as possible.

Any local Qatari organization has the right to register itself as an agent for pharmaceutical companies after fulfilling MOPH requirements. The local agent should ensure the registration of the product license holder; known as marketing authorization holder in most cases (MAH), as well as the manufacturing sites before submission of any product application as per MOPH requirements.

It is worthy to mention that the most up-to-date information should be always submitted. As a general rule, any application related to any type of request should be submitted through PDCD E-system (https://eservices.moph.gov.qa/dps/).

New product registration - Submission and validation

1. Online filling of application

The applicant should fill the appropriate application through PDCD E-system. The application will be subjected to primitive administrative review, after which an appointment will be scheduled in order to submit the file. The agent has the right to request a change in the appointment through sending email to the administrative office of human drugs registration section. In case the applicant did not appear on the scheduled date (no show), a new appointment request has to be made.

2. Acceptance of submission

Upon appointment, the applicant should bring the submission requirements (appendix 1). The file will be subjected to initial review by PDCD staff to ensure that the submission requirements have

been fulfilled as per the PDCD eCTD submission checklist (appendix 3). The file will be subjected to virus scan as well as technical validation as per latest *GCC validation specifications*

2.a Application without deficiencies:

The applicant will be notified at the same appointment that the submission is accepted via a hard receipt, and the file will be transferred to the next stage in the process directly.

2.b Application with deficiencies:

If deficiencies are identified, the applicant will be notified by the deficiencies in the same appointment.

It should be noticed that another appointment can be scheduled on applicant request to re-submit the file, and that after at least 1 month from the first appointment.

3. Assessment/review:

All application will be assessed depending on the type of the application as well as the type of the product itself.

If any comments or issues were identified in this stage, the applicant will be notified via email and he will be given a period of 4 months to reply to these comments as per registration committee circular issued in 6/2015. It is the responsibility of the applicant to ensure that the MAH has received the comments. In case the applicant failed to fulfil the PDCD requirements within the period of 4 months, the application will be considered rejected and the applicant will be informed to collect the file back. Otherwise, the file will be passed to the next stage automatically.

4. Acceptance of application:

After passing the validation and the assessment phases, as well as fulfilling the full MOPH requirements, the file will be passed to the registration committee to review the application and decide whether to accept or reject it.

The committee may ask for extra documents or raise certain issues. The applicant will be notified with the committee decision. In case the committee asks for further requirements, the applicant will be given a period of 4 months (or equivalent time to perform a study requested by the committee) to

response to these comments. If the company failed to response in this period, the application will be deleted automatically, and the file should be submitted again as a new application.

GCC-centrally registered products

As a member in the Co-operation Council for the Arab States of the Gulf (GCC), PDCD allows fast-track assessment of the new-registration applications for products that already registered centrally by GCC, and exempts it from full assessment. However, full data requirements should be submitted as ordinary new-registration submission. PDCD has the right to treat the file as ordinary submission and do not consider its GCC-central registration whenever it deemed to be necessary.

The application form should state clearly that the product is GCC-centrally registered, and the following conditions should be fulfilled in this type of submission:

1. Copy of valid GCC registration certificate with all its attachment should be submitted within the file. The copy should be stamped from GCC executive office as a copy the same as original. Any variation(s) approval(s) gained after registering the product should be submitted as well.
2. Company should declare in the covering letter that the submitted product information and studies included in the file is the same as approved by GCC without any modification or alteration.

Re-Registration / Renewal

Applicants must submit a renewal request every five years for drug products that have already received marketing authorization. The applicant can process with submission once the registration certificate is expired and up to 6 months after the end of the 5-year registration period. If applicant fails to submit the renewal request with the above-mentioned period, the registration of the product will be cancelled automatically, and the applicant should submit full eCTD file for evaluation; in other words, it will be treated as a new product application.

The renewal process is the same as the registration process except for the data requirements for renewal file (refer to Qatari data requirements for renewal).

Variation(s)

Applicants have the right to submit variation(s) application on the registered products. Submission should be made in eCTD format. Data requirements for each type of variation can be found in Qatari data requirements for variation.

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.

Fast Track Review

The applicant has the right to submit a request to treat the file as a fast track file with priority review. The request should be submitted by hand to the registration administration office, and it should be justified and the reasons for such consideration should be mentioned in the request along with any supportive documents and the proposed submission date. Written approval from PDCD should be guaranteed before the submission of the file itself, and it should be attached to the file upon submission.

Technical Baseline Application

A baseline submission is a compiled submission of the current status of the dossier, i.e. resubmission of currently valid documents that have already been provided to PDCD but in another format, in other words it is the conversion from CTD to eCTD. Where an eCTD application is being used for the first time as variation or renewal application, applicants should submit a technical baseline for the product as this will greatly facilitate the review process.

It should be clearly stated in the cover letter of the "baseline eCTD sequence" that the content of the previously submitted dossier has not been changed, only the format. There is no need for the PDCD registration section to assess baseline submissions. The submission unit 'reformat' should be used in the envelope for the baseline sequence and submission type should be "none".

Baseline Starting as Sequence 0000

The baseline submission should be submitted as sequence (0000). The baseline should always be a separate submission and should never include new applications

If the product was submitted as CTD and has no regulatory activity or complete regulatory activity, a baseline shall be submitted as sequence 0000. The first regulatory activity after baseline (for example a variation request) shall be submitted as sequence 0001. For the next submissions, the sequence number will advance, 0002, 0003, etc.

Components of an eCTD Baseline Submission

It is composed of the currently valid documents in an eCTD format. The cover letter should include declaration that indicates there is no new information, only the format dossier has changed.

Data Requirements

This section includes 3 important subsections as follows:

I. Content & structure of eCTD submission

II. Hard Copies for Module I

III. Qualifications of the Product File

Content & structure of eCTD submission

In terms of dossier content, the compiled scientific information enclosed in an eCTD is identical to that of CTD submissions. The difference between CTDs and eCTDs lies in the type of media used, and the method of structuring documents. An eCTD submission is an electronic dossier built using an XML backbone with a unified pattern of arranging documents into branches and leaves. It allows better accessibility and therefore improving the overall review process. We do recommend reading GCC Data Requirements for Human Drugs Submission (Content of the Dossier) guideline.

If the product was submitted as CTD and has no regulatory activity or complete regulatory activity, a baseline shall be submitted as discussed earlier in this document.

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

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

Hard Copies for Module I

eCTD dossiers are submitted electronically. Nonetheless, for legal reasons, specific documents of Module 1 that are listed in Appendix I must be available in hard and soft copies. Both copies must be identical. Hard copies should be bound to one volume (one flat file) with the following criteria and specifications

1. Legibility, Size & labelling

All documents including tables should be legible and the page size should be A4 Norm. Color codes for the files are as follows:

Table 1. Color codes for hard files

Application type	Folder color
New registration	Black hard folder
New registration – fast track	Red hard folder
Variation	Grey
Variation – fast track	Yellow
Renewal	Green hard file

Labelling of the file should include the following:

- Application number generated from the PDCD E-system
- Application type (new registration/ variation/ renewal)
- Product trade name
- Active ingredients and strengths
- Marketing authorization holder name
- Applicant name
- Date of submission (as a title only and the actual date will be added manually by PDCD staff upon submission)

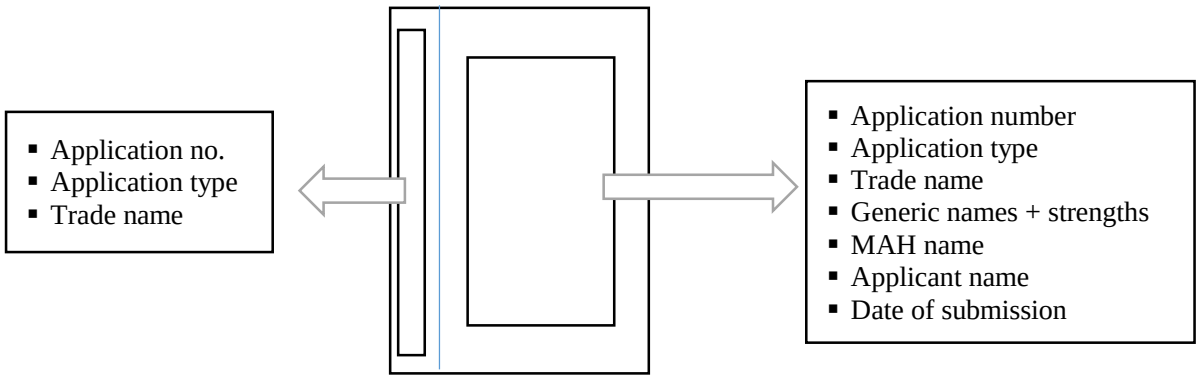

Figure 1. Labelling of hard files

2. <u>Page divider / tab</u>

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

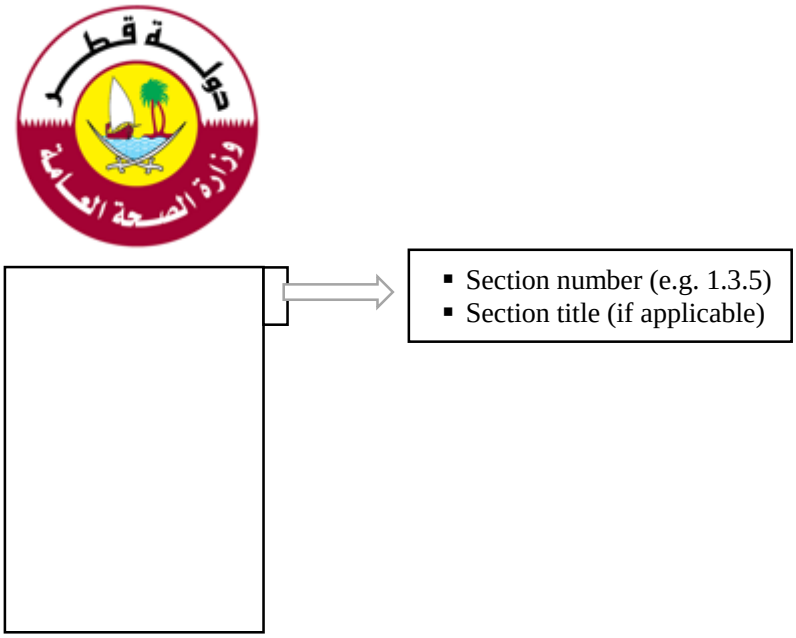

Figure 2. Section divider

3. Language

Information and documents supporting a drug application such as certificates and approval letters must be in English (except for the product labels that should be in both Arabic & English languages). If documents are not in English, a translation to English (from an authorized translation office) are required.

4. Authentication

Authentication, also known as legalization, refers to the process whereby the origins of the document are attested. Authentications of documents are made to MOPH - Qatar by the Health authority and/or the Ministry of Foreign affairs in the country of origin, in addition to Qatar Embassy or Consulate where the document was issued.

Qualifications of the Product File

The following qualifications and specifications should be considered:

1. Softcopy requirements

For the softcopy, 2 DVDs should be submitted for each submission, each in a hard-plastic cover for protection. They should include the following labeling information, clearly presented and printed on the media with eligible font size.

- The company name (MAH)
- The product trade name
- The submission type

- The sequence number of the submissions contained on the DVD (e.g. 0002)

2. Media

The electronic submission may only be submitted in DVD (single or dual layer). The disc must not be bootable or have auto-start programs.

3. System Compatibility

The electronic submission (as provided) must be directly readable and usable on MOPH hardware and software.

4. Validation Confirmation

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

5. Security

There are various aspects related to security. The physical security of the submission during transportation/transmission is the responsibility of the applicant.

6. Password Protection

One-time security settings or password protection of electronic submissions for security purposes is not acceptable during transportation/transmission from the applicant to PDCD. 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.

Appendix 1. Hard Copies Requirements for Module I

Section	Requirements	Hard copy	HC conditions
Module 1	**Regional Administrative Information**		
1.0	**Cover letter**	√	**1,2,3**
1.1	**Comprehensive Table of content**		
1.2	**Application Form**	√	**1,2,3**
1.3	**Product Information**		
1.3.1	Summary of Product Characteristics (SPC)		
1.3.2	Labeling		
1.3.3	Patient information leaflet (PIL)		
1.3.3.1	Arabic leaflet		
1.3.3.2	English leaflet		
1.3.4	Artwork (Mock-ups)		
1.3.5	Samples & reference standards (with their certificates of analysis)	√	**2,3,5**
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	√	**1,2,3,4**
1.7.2	CPP	√	**1,2,3,4**
1.7.3	Certificate of analysis – Drug Substance & finished products		
1.7.4	Certificate of analysis – Excipients		
1.7.5	Alcohol-free declaration	√	**1,2,3**
1.7.6	Pork-free declaration	√	**1,2,3**
1.7.7	Certificate of suitability for TSE		
1.7.8	The diluents and coloring agents in the product formula	√	**1,2,3**
1.7.9	**Patent Information**	√	**1,2,3**
1.7.10	Letter of access or acknowledgment to DMF	√	**1,2,3**
1.8	**Pricing**		
1.8.1	Price certificate (including ex-factory, whole sale and CIF price for Qatar in USD along with CIF for other GCC countries)	√	**1,2,3,4**
1.9	Other related documents	√	**1,2,3,4**
1.10	**Responses to questions**		

1: Company original paper (original hard copy)
2: Signature of authorized person
3: Company official stamp
4: Authentication
5: Physical Sample

Some general considerations

In case of local manufacturers:

1. Section 1.7.1. Only a copy of GMP certificate shall be submitted
2. Section 1.7.2. CPP is not required

Section 1.2 Application form:

Original application form should be submitted, along with 2 copies of the file DVDs, the validation report and virus scan report. The application form should be signed and stamped.

Section 1.7.1 GMP certificate(s):

Original, valid and legalized GMP certificate for any manufacturing site involved in any step of the finished product manufacturing process should be included in this section, as well as copy of valid GMP certificate(s) for all API suppliers.

Section 1.9 Other related documents:

This section should include the following:

1. Original, legalized authorization letter in which the MAH authorize the applicant to handle any regulatory activities in relation to the addressed product. This includes any activity and/or communication with PDCD and any related MOPH departments during the registration process, and beyond. Also, it should state clearly that the applicant will act as the product agent in the state of Qatar, following Qatari regulations and laws in this context.
2. Registration status worldwide with supporting documents including registration in other GCC states
3. Any other related documents
4. Copy of the original GCC central registration certificate with all its attachments (as discussed earlier in this document)

Appendix 2. Cover Letter

The ideal cover letter should include the following items. It should be printed on applicant's original letter headed paper.

1. Local Agent:
2. Company Name and Address:
3. Trade Name:
4. ATC code:
5. Dosage Form:
6. Dosage Strength:
7. International Non-proprietary Name (INN):
8. Number of CDs/DVDs provided:
9. Application Number:
10. Validation Tool used:
11. Validation Specification: GCC validation specifications 1.4
12. Sequence Tracking Table:

Date of submission (Filled by PDCD staff)	**Sequence number**	**Submission type**	**Related eCTD sequence**	**Regulatory activity/ Submission description**	**Submission status (approved / rejected)** (Filled by PDCD staff)

13. The following declarations:

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

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

14. Company authorized person name, title & signature
15. Company stamp

Appendix 3. eCTD Submission Checklist

(Note: Applicant should fill it by computer and bring with him at the submission appointment)

Name of Medicine, strength & pack size: ----------

Section	Requirements	Submitted	Remarks
1.0	**Cover letter**		
1.2	**Application Form (with validation report and virus scan report)**		
1.3	**Product Information**		
1.3.5	Samples & reference standards (with their certificates of analysis)		**Samples:** **Number:** **Pack size:** **Storage condition:** **Batch No:** **MFR:** **Exp:** **Reference standards** **Number:** **Standard name:** **Pack size:** **Storage condition:** **Batch No:** **MFR:** **Exp:**
1.7	**Certificates and documents**		
1.7.1	GMP Certificate		
1.7.2	CPP		
1.7.5	Alcohol-free declaration		
1.7.6	Pork-free declaration		
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 (including ex-factory, whole sale and CIF price for Qatar along with CIF for other GCC countries)		
1.9	**Other related documents**		
1.10	**Responses to questions**		
	2 DVDs of eCTD submission		

The applicant confirms that he/she has no objection to submit any other related documents whenever PDCD requests.

Applicant's name & signature:

Name & signature of receiving person from PDCD:

Submission date:

References

- GCC Module 1 Specifications
- Oman Guidance for eCTD Submission
- NHRA Medicine licensing guidelines
- SFDA Guidance for Submission
- Guidance for Industry Providing Regulatory Submissions in Electronic Format — Human Pharmaceutical Product Applications and Related Submissions using the eCTD Specifications - USFDA
- Harmonised Guidance for eCTD Submissions in the EU
- ICH electronic Common Technical Document (eCTD)
- ICH Specification 3.2 (Modules 2 - 5)