nhra BAHRAIN

الهيئة الوطنية لتنظيم المهن والخدمات الصحية
NATIONAL HEALTH REGULATORY AUTHORITY

Medicine Licensing Guideline

National Health Regulatory Authority (NHRA)

Kingdom of Bahrain

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Version 2.0

Chief of Pharmaceutical Product Regulation:

Dr / Roaya Al Abbasi Date:

NHRA CEO Approval:

Dr / Mariam Al Jalahma Date:

Document Control

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Table of contents

Definitions

NHRA

National Health Regulatory Authority.

PPR

Pharmaceutical Product regulation is the responsible department for medicine licensing at NHRA.

Manufacturer

Manufacturing site of batch release, the final manufacturing site from which the medicine is dispatched to Bahrain.

Marketing Authorization Holder (MAH)

The pharmaceutical company that legally holds the right and responsibility of marketing the medicine in Bahrain.

Local Agent

The pharmacy in Bahrain; designated by the MAH to act on its behalf in communication with NHRA.

Country of Origin (COO)

It is the country where the pharmaceutical product has been released with certificate of analysis signed by the responsible qualified person.

ICH

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH).

Certificate of Pharmaceutical Product (CPP)

A certificate issued in the format recommended by the World Health Organization (WHO), which establishes the status of the pharmaceutical product and the applicant for the certificate in the exporting country.

Package Leaflet (PL)

The package leaflet is the medicine information provided in the pack .It should be drawn up in accordance with the summary of the product characteristics.

Summary of Product Characteristics (SmPC)

The definitive description of the product. The SmPC is an integral part of the marketing authorization and should take the form as outlined in Annexes.

1. Introduction

Guideline documents are meant to provide assistance to industry and professionals on how to comply with governing statutes and regulations. Guideline documents also provide assistance to staff on how NHRA mandates and objectives should be implemented in a manner that is fair, consistent and effective. Medicine licensing is done through PPR department in NHRA.

This guideline has been developed to assist license holders in the preparation and submission of applications for licensing medicines in the Kingdom of Bahrain.

It should be noted that the NHRA has the right to request any information and data within the context of this guideline.

This document should be read in conjunction with other applicable guideline documents.

2. Scope

This guidance document describes the procedures and requirements for submitting an application to obtain a new medicine License in the Kingdom of Bahrain.

Applicants are expected to comply with the procedures and requirements laid out in this guidance.

3. Medicine Licensing

Any medicine must be licensed before marketing in Bahrain as per law no. (18) of 1997, medicine Importation and distribution must be done through authorized pharmacy only (Local agent), this agent can be the applicant on behalf of the pharmaceutical company as long as the agreement is prone to NHRA and acknowledged.

The local agent must inform NHRA with any agreements made with new pharmaceutical companies for review and approval before starting the licensing process.

Pharmaceutical companies (MAH) should note that they are responsible for the medicines quality, efficacy and safety throughout its life cycle. Responsibilities start with the licensing of the medicine and end when the medicine license is cancelled. Since the medicine quality, efficacy and safety can change at any time during the course of its life cycle, it is the MAH responsibility to inform NHRA when these changes occur as per the current guidelines.

These responsibilities include:

1. To ensure that all of the information given in the application form and supporting documents are true and valid.
2. To notify NHRA if the application submitted to NHRA has been rejected, withdrawn or deferred by any drug regulatory agency, with reasons in each case if applicable, throughout the medicine life cycle in the Bahraini market.
3. To notify NHRA of any change in the information submitted in the application and of any new significant safety information during the course of evaluation and throughout the product's life cycle

in the Bahraini market

4. To respond to NHRA queries or requests for more data for review, within the timelines.
5. To ensure that the medicine will be sold, supplied and recommended for use in accordance with the approved PI/PIL and in compliance with all license conditions, applicable legislation and guidelines.

Failure to comply with the above shall render the product registration license cancelled. NHRA, thus reserves the right to, suspended or cancel the registration license of the product anytime during the life cycle of the product, if found non-compliant.

4. Licensing procedure

4.1. Before Submission

Before submission of medicine licensing application the manufacturer license must be valid. The applicant must prepare the file according to requirements laid out in this guideline and assure all the requested documents are available.

Please note that for each application the most up to date version of forms should be downloaded directly from NHRA website.

4.2. Application fees

As per resolution 17 of 2016, application fees and service fees is chargeable for each new medicine application submitted to NHRA. The applicant must refer to the latest fee structure from NHRA website.

4.3. Data requirement

The data requirement for each application will differ, depending on the drug submission type. However all required data should be in accordance with ICH Common Technical Document (CTD) in eCTD format.

The Common Technical Document is organized into five modules. Module 1 is region specific. Modules 2, 3, 4, and 5 are intended to be common for all regions and must be submitted in soft copy according to ICH guideline. Specific details to eCTD submission are mentioned in Annex I.

In case of New Chemical Entity (NEC) & Biological all CTD modules are required.

In case of generic products the comparative bioavailability/bioequivalence study report should be present under module 5. This should be in accordance with GCC bioequivalence guideline. It is mandatory that the center conducting bioavailability/bioequivalence study should be approved with GCC-DR. However centers approved from either of the listed authorities shall be considered viz. European Medicine agency (EMA), United stated Food and Drug Administration(USFDA), World Health Organization (WHO) & Ministry of Health, Labour & Welfare Japan (MHLW).

The applicant must refer to GCC approved bioavailability/bioequivalence center list on NHRA website

Module 1 requirements:

1. **Cover letter: Original company paper signed and dated.**

2. **Comprehensive CTD table of contents.**

3. **Forms:** Completed forms must be included in this section. The latest version of the below forms must be filled, signed and stamped with date by the MAH Company.

   i. Application Form.
   ii. Check list.
   iii. Pricing form.

4. **Product Information**

   i. Summary of product characteristics (SmPC): the template for this document is part of the application form however in Module 1 a declaration from the MAH that the SmPC submitted is correct and similar to the one approved in COO is included in this section (If there is any differences the company shall declare it).
   ii. Label text (immediate and secondary packaging).
   iii. Package leaflet (bilingual English/Arabic).
   iv. Artwork (outer pack, inner pack and package leaflet).
   v. One finished product sample.

5. **Contact details for the Marketing Authorization Holder responsible person for communication with the NHRA on quality issues.**

6. **Patency Information:**

   New medicine (Innovator): Declaration about the patency status worldwide, in the Gulf region & Bahrain is required.
   Generics: Proof that the innovator patency is expired form Bahrain patency office and GCC patency office is required.

7. **Certificates**

   i. Certificate of Pharmaceutical Product (CPP) according to WHO format; legalized and issued from the COO (batch releaser country).
   ii. Good manufacturing practice (GMP) certificates or proof of inspection by a recognized health authority for all finished product manufacturer(s) including bulk manufacturer, primary packager, and secondary packager.
   iii. Certificate of suitability for the active substance, if available. If not, **legalized** good manufacturing practice (GMP) certificates or proof of inspection by a recognized health authority for API manufacturer(s).
   iv. Certificate of suitability for TSE.
   v. Certificate of analysis for the drug substance from the API supplier.
   vi. Certificate of analysis for the finished product.
   vii. Price Certificate showing, ex-factory price, whole sale and public retail price in the country of origin (legalized by the Ministry of Foreign Affairs & Embassy and issued within the last six

months from the submission date). The price certificate must be issued from the Health Authority in the COO of the finished product (i.e. from which it is batch released). If the Health Authority doesn't issue price certificate the company can use NHRA price form (annex V) and it must be filled for all the countries where the product is registered and attested/endorsed by the Health Authority.

viii. Manufacturer registration certificate in Bahrain (batch releaser).

8. Other Documents

i. Alcohol content declaration.
ii. Pork content declaration.
iii. Worldwide registration status (registered, marketed (date), under registration and rejected).
iv. Proof of Payment for submission.
v. Proof of prior registration under SFDA, GCC-DR, FDA(US), TGA(Australia), Health Canada, Japan, Medsafe , Swissmedic or EMA (EU)*.

*Includes medicines licensed by the European Medicines Agency (EMA) under the Centralized Procedure and medicines licensed by one of the following countries Denmark, France, Germany, Italy, Ireland, Netherland, Portugal, Spain, Sweden or UK.

9. Laboratory Analysis:

It is mandatory to analyze the product samples for new registration applications prior to issuance of license. Thus a request to submission of the laboratory analysis documents with sample will be sent upon assessment.

Documents to be submitted are as follows:

i. Samples of the product.
ii. Certificate of analysis for the sample submitted.
iii. Reference standard for the active ingredients and related substances along with their certificate of analysis.
iv. Product composition certificate.
v. Complete method of analysis.
vi. Product Specification.
vii. Material safety data.
viii. Documents in CD.

Minimum quantity of sample required for analysis:

	Dosage form	Quantity
1.	Capsules & Tablets	100 nos
2.	Oral liquids	10 bottles
3.	Parenteral (ampoule)	50 nos
4.	Parenteral (vials)	20 nos
5.	Parental solution up to 500ml	5 nos
6.	Parental solution above 500ml	1 no
7.	Suppositories	50 nos

8.	Creams and ointments	10 nos
9.	Inhalers	10 nos
10.	Powders	20 nos
11.	Ophthalmic preparations	20 nos
12.	Nasal drops	10 nos
13.	Ear drops	10 nos

4.4. GCC-DR Registered Products

Since the Kingdom of Bahrain is an active member state in the Co-operation Council for the Arab States of the Gulf (GCC). NHRA recognizes and pledges to fast track the assessment of new drug registration applications already approved in GCC-DR.

Documents required for submission:

1. Covering letter from the MAH and agent
2. Medicine license application form
3. Medicine license checklist
4. Valid registration certificated by GCC-DR for the product
5. Patent status in Bahrain
6. Legalized price certificate form
7. Modules 2-5 shall be requested on a CD containing all queries and responses.
8. A signed and stamped declaration letter to be submitted for no change or update in the information submitted, from that approved in GCC-DR by the MAH.

NHRA, reserves the rights to request for more information if required.

4.5. Submission & Validation

In order to submit new medicine licensing application the applicant must request an appointment by duly filing an appointment request form (Annex III) and sending to the PPR department by email. Appointments are assigned on a first-come basis.

On the appointment day NHRA staff will check the file to make sure all the requested documents are available only valid applications will be accepted as per the checklist (Annex IV). If the application is accepted, the applicant has to pay the required fees. A stamped and signed copy of the medicine licensing checklist is returned to the applicant and the file will be added to the new medicines files record.

4.6. Assessment & Queries

Each application is assessed in accordance with NHRA standard operating procedures and where queries arise, a request for further information will be sent to the applicant. The applicant is requested to respond to such requests in a timely manner and in accordance with any decided timeline.

NHRA will not be held responsible for the delay of registration process if the applicant fails to respond to NHRA request in a timely manner.

Failure to respond to NHRA request for information will result in rejection of the application.

4.7. Approval

After completion of assessment and pricing of medicine a decision to approve or disapprove a product for licensing is done by the licensing committee. Upon approval from the committee the applicant has to pay the required fees prior to collection of the license.

Medicine license is valid for 5 years.

4.8. General notes

1. Medicine License is specific to a particular name, formulation, dosage form, strength, pack size with a particular set of approved indications and directions for use.
2. The medicine must be licensed and marketed in the country of origin for at least one year before submission of the medicine licensing application.
3. When required Bioequivalence study must be according to GCC guidelines.
4. When required Stability study must be according to GCC guidelines.
5. Two API sources will be accepted upon the first registration addition or deletion of source can be submitted later through variations.
6. Two Bulk manufacturers will be accepted at the time of registration, after that any addition or deletion will be through variation application and will be studied case by case.
7. Medicines can be classified into one of the following categories at the time of licensing (method of sale):
   i. **Prescription Only Medicines (POM)** – available only on a prescription.
   ii. **Over-the –counter but Pharmacy only (P)** – available under the supervision of a pharmacist.
   iii. **General Sale (GS)** – available in general retail outlets.

5. Importation & Invoice Clearance

Importation of medicine is governed by Bahrain Pharmacy law no. (18) Of 1997/2015 which states that "the importation of medicines must be through authorized legal entity".

The following details must be included in the invoice and will be checked against the PPR Medicine database:

1. Medicine name - strength.
2. Pack size - dosage form.
3. Importer name and address (local agent)
4. Manufacturer name and country.
5. MAH name.

6. CIF (Cost, Insurance & Freight) price.
7. Batch number.
8. Manufacturing date - expiry date.

When all the invoice particulates are complying with the approved medicine information the invoice will be approved.

Annex I

Electronic Common Technical Document (eCTD)

I. Introduction

According to NHRA's eCTD implementation plan, the eCTD is mandatory from the 1st of November 2016. This applies only to human medicine applications.

The ICH M4 Expert Working Group (EWG) has defined the Common Technical Document (CTD). The ICH M2 EWG has defined, in the current document, the specification for the Electronic Common Technical Document (eCTD). The eCTD is defined as an interface for industry to agency transfer of regulatory information while at the same time taking into consideration the facilitation of the creation, review, life cycle management and archiving of the electronic submission.

The CTD as defined by the M4 EWG does not cover the full submission that is to be made in a region. It describes only modules 2 to 5, which are common across all regions. The regional Administrative Information and Prescribing Information is described in Module 1. The CTD does not describe the content of module 1 because it is regional specific, nor does it describe documents that can be submitted as amendments or variations to the initial application. Module 1 Specifications of the electronic Common Technical Document (eCTD) for Gulf Cooperation Council (GCC) are described in "GCC module 1 specifications."

This document should be read together with ICH eCTD specifications and with GCC module 1 specifications to prepare a valid eCTD submission to NHRA. The latest version of the ICH eCTD Specification can be found at: http://estri.ich.org and of GCC module 1 specification can be found at: http://www.sfda.gov.sa

Documents to be submitted as hard copy for new registration application are listed in Appendix I.

NHRA will show all the cases and scenarios of eCTD submissions especially the baseline eCTD submissions.

II. 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 NHRA but in another format. Where an eCTD application is being used for the first time as variation or renewal application, applicants are obliged to 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 NHRA to assess baseline submissions and hyperlinks between documents are not necessary. The submission unit 'reformat' should be used in the envelope for the baseline sequence and submission type should be "none".

III. Baseline eCTD Submission

One of the principles of eCTD is that with the use of the operation attributes, it is possible to manage the lifecycle of a product and generate a view of the "current dossier".

To convert from CTD format to eCTD, a baseline needs to be submitted. A baseline submission is the resubmission of currently valid documents to start the eCTD life cycle.

An eCTD baseline should not contain any new information as it will not be subject to review by NHRA.

Submission of a baseline shall be after the end of a regulatory activity, i.e. the company will follow the same original submission for products under assessment until the end of the regulatory activity.

IV. Baseline Starting as Sequence 0000

For product files that are submitted as CTD, the baseline submission should be submitted as sequence (0000). However, in some cases e.g. renewal and variation submitted as eCTD, the submission could continue to the next sequence of the submission life cycle. The baseline should always be a separate submission and should never include new applications.

V. Baseline Cases

1. For products submitted as CTD:

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. See table below:

Sequence No.	Submission description	Submission type	Submission Unit	Related sequence
0005	Response to Question	CTD	-	-
0000	Baseline submission	None	Reformat	-
0001	Variation	Var-Type2		- -
0002	Response to Questions	Var-Type2	Response	0001

Table 1: Example for starting an eCTD with a baseline sequence.

2. For products submitted as eCTD for renewal or variation

Products submitted as eCTD submission, and are approved by NHRA with no ongoing regulatory activity, the baseline sequence may continue from the last one. Table 2 demonstrates more on this case.

Sequence No.	Submission description	Submission type	Submission Unit	Related sequence
0000	Renewal	Renewal	-	-
0001	Response to Questions	Renewal	-	0000
0002	Response to Questions	Renewal	-	0000
0003	Variation	Var	-	-
0004	Response to Questions	Var	-	0003
0005	Baseline Submission	None	Reformat	-

Table 2: Example for starting a baseline with a regulatory activity.

VI. Components of an eCTD Baseline Submission:

It is composed of the currently valid documents in an eCTD format. Refer to Appendix I for more details.

The cover letter should include declaration that indicates there is no new information, only the format dossier has changed.

Notes:

1. NHRA encourage applicants to move to a full eCTD (m1 to m5).
2. The applicant can submit the eCTD dossier for currently registered product in which it requires the submission of a baseline. However, once eCTD is submitted going back to other format will not be accepted.

Appendix I: Components of an eCTD Baseline Submission

Section	Requirements
Module 1	**Regional Administrative Information**
1.0	Cover letter
1.2	Application Form
1.3	Product Information
1.3.1	Summary of Product Characteristics (SPC)
1.3.2	Labeling
1.3.3	Patient information leaflet (PIL)
1.3.3.1	Arabic leaflet
1.3.3.2	English leaflet
1.3.4	Artwork
1.4	Certificates and Documents
1.4.1	CPP
Module 3	**Quality**
3.2.S	Drug Substance
3.2.P	Drug Product
3.2.A	Appendices

Annex II

New Medicine Application form

Part 1 – Administrative Data					
Applicant's full name and address					
Contact information					
Name:					
Tel:		Fax:		e-mail	
Commercial Registration (CR) number of applicant					
Address of storage premises					
Business name to be shown in the license if different from the above					
Marketing Authorization Holder's (MAH) name and address in Bahrain					
Contact information of responsible person					

Part 2 – Product Particulars				
1.	Name of the product:			
2.	Strength:			
3.	Pharmaceutical form:			
4.	Pack size:			
5.	Product description:			
6.	Pharmacotherapuetic group:		ATC code:	
7.	Proposed shelf-life (in months)			

8.	Active substance(s) - including relevant quality standard i.e. Ph.Eur., USP etc.):	Unit*		Unit*

9.	Excipient(s) – including relevant quality standard i.e. Ph.Eur., USP etc.):	Unit*		Unit*

**Quantity/dose unit or % quantity*

10.	Release specification reference number and approval date
11.	Is the finished product composition as that registered and marketed in country of origin.

Yes No

If no, please clarify.

12.	Country of origin (batch releaser country)
13.	Name of the product in the country of origin
14.	Reference number of the marketing authorization for the product in the country of origin and the date of authorization
15.	State if the product is licensed by any of the following authorities with the grant date: SFDA, GCC-DR, US FDA, HEALTH CANADA, TGA, EMA or regulatory authorities of Denmark, France, Germany, Italy, Ireland, Netherland, Portugal, Spain, Sweden, UK, or Swissmedic.
16.	Has the product license withdrawn, cancelled or rejected in any of the above mentioned authorities?

Yes No

If yes, please clarify.

17. Name and address of the manufacturer(s) involved in all stages of manufacture and activities carried out by each:

Manufacturer Name	Country	Manufacturer Address
API manufacturer name		
Bulk Manufacturer		
Primary Packaging		
Secondary Packaging		
Batch release of finished product		

18.	Method of sale & supply in country of origin
19.	Package leaflet revision date and number
20.	Invoicing company name and address must be declared
21.	Bioequivalence center name and address (FOR GENERICS)

PHARMACEUTICAL PRODUCT INFORMATION TEMPLATE

1. Name of the pharmaceutical product
2. Qualitative and quantitative composition
3. Pharmaceutical form
4. Clinical particulars
   - 4.1. Indications
   - 4.2. Posology and method of administration
   - 4.3. Contraindications
   - 4.4. Special warnings and precautions for use
   - 4.5. Interaction with other medicinal products and other forms of interaction
   - 4.6. Fertility, pregnancy and lactation
   - 4.7. Effects on ability to drive and use machines
   - 4.8. Undesirable effects
   - 4.9. Overdose
5. Pharmacological properties (medicines only)
   - 5.1. Pharmacodynamics properties
   - 5.2. Pharmacokinetic properties
   - 5.3. Preclinical safety data
6. Pharmaceutical particulars
   - 6.1. List of excipients
   - 6.2. Incompatibilities
   - 6.3. Shelf life
   - 6.4. Special precautions for storage
   - 6.5. Nature and contents of container
   - 6.6. Special precautions for disposal
7. Marketing authorisation holder
8. Agent
9. Marketing authorisation number(s)
10. Date of first authorisation/ renewal of the authorisation
11. Date of revision of the text
12. Instructions for preparation of radiopharmaceuticals (relevant medicines only)

I/we apply for a medicine license in respect of the product for which details are provided above.
It is hereby confirmed that all information relevant to the product have been supplied in the file as appropriate and they are all correct (must be filled by the MAH).

Name of signatory		Signature	
State capacity in which signed		Date	

Annex III

New Medicine Registration Appointment Request

Local Agent Name:			
Product Name:			
API(S) Name(S) & Concentration(S)			
API Manufacturing Site (1)	**Country**	**GMP Certificate**	**GMP Validity**
		☐Legalized ☐Not Legalized	
API Manufacturing Site (2)	**Country**	**GMP Certificate**	**GMP Validity**
		☐Legalized ☐Not Legalized	
FP Bulk Manufacturing Site	**Country**	**GMP Certificate**	**GMP Validity**
		☐Yes ☐No	
FP 1ry Packaging Site	**Country**	**GMP Certificate**	**GMP Validity**
		☐Yes ☐No	
FP 2ry Packaging Site	**Country**	**GMP Certificate**	**GMP Validity**
		☐Yes ☐No	
FP Batch Releasing Site	**Country**	**GMP Certificate**	**GMP Validity**
		☐Yes ☐No	

NHRA Manufacturing Site Registration Certificate for The FP Batch Releaser		
Registration Number:	**Registration Date:**	
CPP Issuing Country & Authority	**Legalization**	**Product Registration Number & Date**
	☐Yes ☐No	
MAH in Country of Origin		
Bioequivalence Center Details (FOR GENERIC ONLY)		
Center Name:	**Country:**	
MAH for Bahrain		
Current Registration Status		
☐GCC-DR ☐SFDA ☐Oman ☐UAE ☐Kuwait ☐Qatar ☐USFDA ☐EMA ☐Other (specify): Click here to enter text.		
***Name of Agent's Authorized Person:**	***Signature:**	***Date:**
Click here to enter text.		Click here to enter text.

Annex IV

New medicine checklist

Application Number		Application Date		
Product Name		Strength	Form	Pack Size
Active Substances				
Applicant Name				

Module 1	Administration Information Hard File (eCTD)	
1	Dossier CD with validation report	☐
2	Cover letter *(original company paper, signed and dated)*	☐
3	Application form *(signed and dated)*	☐
4	One finished product sample	☐
5	Certificate of Pharmaceutical Product (CPP) according to WHO format (legalized) from the COO (batch releaser country)	☐
6	Good manufacturing practice (GMP) certificates or proof of inspection by a recognised CA for all finished product manufacturer(s).	☐
7	Certificate of suitability for the active substance, if available. If not, legalised good manufacturing practice (GMP) certificates or proof of inspection by a recognised CA for API manufacturer(s)	☐
8	Price Certificate showing, ex: factory price, whole sale and public retail price in the country of origin (legalized and issued within the last six months from the submission date)	☐
9	Proof of Payment	☐

I declare that all the documents for the application for a medicine licence for as referred to in this check list are attached.

Name & Signature of responsible person: **Date:**

For internal use only

I declare that I have received the documents as outlined in the above checklist.

Name : **Date :**

Signature :

Comments :

Annex V

Pricing Form

General information					
Product Name		Strength		Pack Size	
Active Substance		Form			
Company Name & Nationality					

Country of Origin				
Ex-Factory Price (In USD)	**Wholesale Price** (In USD)	**Public Price** (In USD)	**Proposed CIF to Bahrain** (In USD)	Notes

Prices in other countries where the product is marketed

No	Country	Pack Size	Ex-Factory Price	currency	CIF Price	currency	Public Price	currency	Notes
GCC Countries									
1	Kuwait								
2	Oman								
3	Qatar								
4	Saudi Arabia								
5	U.A.E								
Other countries									
6	Algeria								
7	Australia								
8	Argentina								
9	Belgium								
10	Canada								
11	Cyprus								
12	Denmark								
13	Egypt								
14	France								

No	Country	Pack Size	Ex-Factory Price	currency	CIF Price	currency	Public Price	currency	Notes
15	Germany								
16	Greece								
17	Holland								
18	Hungary								
19	Ireland								
20	Italy								
21	Japan								
22	Jordan								
23	Lebanon								
24	New Zealand								
25	Portugal								
26	South Korea								
27	Spain								
28	Sweden								
29	Switzerland								
30	Turkey								
31	U.K.								

Declaration	
We :	
Certify that all prices in this form are correct and accurate	
Name of the person authorized to sign on behalf of the company	
Signature	
Stamp	

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

GCC Module 1 Specifications

Version 1.5

قطاع الدواء
Drug Sector

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

GCC Module 1 Specifications

Version 1.5

Drug Sector
Saudi Food & Drug Authority

Please visit SFDA's website at
http://www.sfda.gov.sa/En/Drug for the latest update

For Inquiries: SDR.Drug@sfda.gov.sa

For Comments or Suggestions: Drug.Comments@sfda.gov.sa

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Drug Sector

Vision & Mission

Vision

To be the leading regional Drug Regulatory Authority for pharmaceuticals and cosmetic products, with professional excellence and services that contribute to the protection and advancement of public health in the Kingdom of Saudi Arabia.

الرؤية

أن يكون قطاع الدواء رائداً إقليميا في الرقابة على الأدوية ومستحضرات التجميل، ويقدم خدماته بمهنية متميزة تسهم في حماية وتعزيز الصحة في المملكة العربية السعودية.

Mission

Protecting public health by ensuring safety, quality, efficacy and accessibility of human, veterinary drugs and biological products, and safety of cosmetics, through administration of a national regulatory system which is consistent with international best practice. Through our mission, we also provide accurate and scientific-based information to the public and healthcare professionals.

الرسالة

حماية الصحة العامة من خلال ضمان أمان وجودة وفعالية وتوفر الأدوية البشرية والبيطرية والمنتجات الحيوية وسلامة مواد التجميل عبر تطبيق نظام وطني للرقابة متوافق مع أفضل الممارسات الدولية وتقديم المعلومات الدوائية المبنية على أسس علمية للعامة والمهنيين الصحيين.

DOCUMENT CONTROL

Version	Date	Authors	Comments
0.1	07/12/2010	Regulatory Affairs	First draft
0.2	08/03/2011	Regulatory Affairs	Revised draft
0.3	12/06/2011	Regulatory Affairs	External consultation
0.4	03/12/2011	Regulatory Affairs	Final revision
1.0	17/12/2011	Regulatory Affairs	Published
1.1	08/05/2012	Regulatory Affairs	Revised document
1.2	10/11/2012	Regulatory Affairs	Minor changes, checksum update
1.3	17/08/2015	Regulatory Affairs	Add of submission unit concept, Add values in submission type, some minor changes
1.4	17/09/2015	Regulatory Affairs	Update
1.5	4/11/2015	Regulatory Affairs	Final version. Remove of Health/Herbal/Vet submission type

Note: For most recent update please refer to annex1

TABLE OF CONTENTS

1 Introduction

This document specifies Module 1 of the electronic Common Technical Document (eCTD) for Gulf Cooperation Council (GCC).

This document should be read together with the ICH eCTD Specification to prepare a valid eCTD submission for GCC. The latest version of the ICH eCTD Specification can be found at: http://estri.ich.org

The ICH M4 Expert Working Group (EWG) has defined the Common Technical Document (CTD). The ICH M2 EWG has defined, in the current document, the specification for the Electronic Common Technical Document (eCTD). The eCTD is defined as an interface for industry to agency transfer of regulatory information while at the same time taking into consideration the facilitation of the creation, review, life cycle management and archiving of the electronic submission.

The eCTD specification lists the criteria that will make an electronic submission technically valid. The focus of the specification is to provide the ability to transfer the registration application electronically from industry to a regulatory authority. Industry to industry and agency to agency transfer is not addressed.

1.1. Background

The specification for the eCTD is based upon content defined within the CTD issued by the ICH M4 EWG. The CTD describes the organization of modules, sections and documents. The structure and level of detail specified in the CTD have been used as the basis for defining the eCTD structure and content but, where appropriate, additional details have been developed within the eCTD specification. The philosophy of the eCTD is to use open standards. Open standards, including proprietary standards which through their widespread use can be considered de facto standards, are deemed to be appropriate in general.

1.2. Scope

The CTD as defined by the M4 EWG does not cover the full submission that is to be made in a region. It describes only modules 2 to 5, which are common across all regions. The regional Administrative Information and Prescribing Information is

described in Module 1. The CTD does not describe the content of module 1 because it is regional specific, nor does it describe documents that can be submitted as amendments or variations to the initial application. The value of producing a specification for the creation of an electronic submission based only upon the modules described in the CTD would be limited. Therefore, the M2 EWG has produced a specification for the eCTD that is applicable to all modules of initial registration applications and for other submissions of information throughout the life cycle of the product, such as variations and amendments.

1.3. Technical Requirements

The specification is designed to support high-level functional requirements such as the following:

- Copying and pasting
- Viewing and printing of documents
- Annotation of documentation
- Facilitating the exporting of information to databases
- Searching within and across applications
- Navigating throughout the eCTD and its subsequent amendments/variations

1.4. Change Control

The specification for the eCTD is likely to change with time. Factors that could affect the content of the specification include, but are not limited to:

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

1.5. Glossary

A brief glossary of terms (for the purpose of this document only) is indicated below:

Applicant	A pharmaceutical company or its agent that is submitting information in support of an ***application***.
Application	A collection of documents compiled by a pharmaceutical company or its agent in compliance with guidelines in order to seek a marketing authorization or any amendments thereof.
CTD	**C**ommon **T**echnical **D**ocument
DTD	**D**ocument **T**ype **D**efinition
eCTD	**e**lectronic **C**ommon **T**echnical **D**ocument An *eCTD application* may comprise a number of *sequences.*
EWG	**E**xpert **W**orking **G**roup; charged with developing a harmonised guideline that meets the objectives in the Concept Paper and Business Plan.
GCC	**G**ulf **C**ooperation **C**ouncil
ICH	**I**nternational **C**onference on **H**armonisation of technical requirements for registration of pharmaceuticals for human use
JPEG	**J**oint **P**hotographic **E**xperts **G**roup
PDF	**P**ortable **D**ocument **F**ormat
PNG	**P**ortable **N**etwork **G**raphics
Procedure	A registration procedure for the authorization of medicinal products
Regulatory activity	A collection of sequences covering the start to the end of a specific business process, e.g. an initial MA application or Type II variation. It is a concept used in some review tools to group together several business related sequences.
RTF	**R**ich **T**ext **F**ormat
Submission	A single set of information and/or documents supplied by the applicant as a part of, or the complete, Application. In the context of eCTD, this is equivalent to '*sequence*'
SVG	**S**calable **V**ector **G**raphics
ToC	**T**able **o**f **C**ontents
XML	e**X**tensible **M**arkup **L**anguage
XSL	e**X**tensible **S**tyle**S**heet **L**anguage
Reformat	Intended to support the reformatting of an existing submission application from any format to eCTD
Extension	change to a marketing authorization of a medicine such as changes to the active substance, available strengths, pharmaceutical forms or the route of administration.
ASMF	**A**ctive **S**ubstance **M**aster **F**ile
PMF	**P**lasma **M**aster **F**ile
PSUSA	**PSUR S**ingle **A**ssessment procedure

USR	**U**rgent **S**afety **R**estriction
RMP	**R**isk **M**anagement **P**lan
Submission type	The **submission type** describes the regulatory activity to which the content will be submitted.
Submission unit	The **submission unit** element of the envelope metadata set describes the content at a lower level (a "sub-activity") which is submitted in relation to a defined regulatory activity such as the applicant response to validation issues or list of questions or any other additional information

2 GCC Module 1: Regional Information

The ICH Common Technical Document (CTD) specifies that Module 1 should contain region specific administrative and product information. The content and numbering of Module 1 for GCC is specified in the latest version of the *Guidance for Submission* that can be found at http://www.sfda.gov.sa

It should be noted that for subsequent submissions in the lifecycle of a medicinal product, e.g. for a variation, not all of the above mentioned kind of documents need be included in Module 1. In addition, other items such as the rationale for variations and renewal documentation could also be included in Module 1.

This document describes only the region-specific information that is common to all eCTD submissions in the Gulf Cooperation countries.

2.1. General Considerations

Typically, an eCTD application will cover all dosage forms and strengths of a product with any one invented name.

2.1.1 Document granularity

Submissions are a collection of documents and each document should be provided as a separate file. The detailed structure of the eCTD should conform to the ICH Granularity Document and GCC M1 specifications.

2.1.2 Correspondence

In addition to the eCTD application information may need to be exchanged to assist the processing or handling of the application. Not all that correspondence should be included in the eCTD. This is because the eCTD exchange is currently one way only, from applicant to Agency, and not all correspondence is directly relevant to the application dossier.

2.1.3 Sequence Numbers

Sequence numbers are used to differentiate between different submissions of the same application over the life cycle of the product.

2.1.4 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 (see the eCTD specification for details). Documents without TOCs should have bookmarks included where it aids in the navigation around the document content. For example, a 4 page document summarizing findings could require bookmarks to aid navigation. However, a 300 page file containing a single data listing might not require bookmarks as there is no further internal structure. Please consult national guidance documents for further details."

In general terms, bookmarks and hyperlinks should be used to aid navigation. The overuse of hyperlinks may confuse rather than help assessors and may cause problems later in life cycle management.

Additional details on creating bookmarks and hypertext links in PDF documents can be found in the ICH eCTD Specification, Appendix 7.

2.2. Regional File Formats

2.2.1. Module 1

The file formats that can be included in Module 1 are given in Table 1. In addition to the common format PDF as defined by the ICH eCTD Specification Document, for other formats see regional guidance for narrative documents to be included in Module 1.

XML is also an acceptable format for the delivery of structured data in Module 1, specifically the application form and product information, as long as the XML is produced to the standard defined in the electronic Application Forms.

Although the use of the file formats defined in Table 1 is strongly recommended, the GCC and applicants could agree on the use of other formats in Module 1, for example, the proprietary format MS Word is for Product Information documents in Module 1.3 (see specific national guidance).

These documents, if requested, should not be referenced in the eCTD backbone, and should always be provided in addition to the PDF versions.

Table 1: Acceptable file formats for GCC Module 1

Document	File Format	Remark
Administrative forms: • Application form and its annexes • Variation application form incl. background for the variation • Renewal form and its annexes	XML, PDF, RTF PDF, RTF PDF, RTF	Documents should be generated from electronic source documents, any signature may be embedded as graphic file in the PDF text if desired, although this is not necessary as the hard paper copy contains the legally binding signature.
Product Information: • Labeling text • Packaging mock-ups • Reference to Specimens • Readability Testing • Information relating to Orphan Applications	XML, PDF, RTF XML, PDF, RTF PDF PDF PDF	If a higher resolution is necessary for the mock-ups, use JPEG, GIF, PNG or SVG on a case-by-case basis. Labeling texts can be submitted in XML format according to the PIM Data Exchange Standard. In that context, images can be transmitted in JPEG, GIF, PNG, TIF, SVG, or MathML.
Other	PDF, RTF	PDF preferably generated from electronic source
Document Type Definitions and Stylesheets	DTD, XSL	These are XML specific file formats and must only be the specified versions of the specific files required for the submission of electronic Application Forms

2.2.2. Modules 2 to 5

No additional file formats are defined for Modules 2 to 5 other than those mentioned in the ICH eCTD Specification Document. The GCC and pharmaceutical companies could agree on a case-by-case basis to use formats other than the common formats (e.g. RTF). However, the use of formats other than those specified by the ICH eCTD Specification Document is discouraged.

2.3. Handling of Empty or Missing eCTD Sections

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

Note that placeholder documents highlighting 'no relevant content' should not be placed in the eCTD structure, as these would create a document lifecycle for non-existent documents, and unnecessary complication and maintenance of the eCTD.

Note: for a generic application, there is no need to provide a justification for content that is typically absent.

2.4. Technical information

2.4.1. Use of Electronic Signatures

The use of advanced electronic signatures (digital signatures) will be crucial in achieving pure electronic communication between the pharmaceutical industry and regulatory agencies, particularly for authentication of electronic submissions and documents contained therein. Currently however, the use of digital signatures for electronic submissions within GCC is not fully supported and digital signatures should therefore not be used (Please refer to each national competent authority for detailed guidance on this matter).

2.4.2. Security issues

The physical security of the submission during transportation is the responsibility of the applicant. Once received by national competent authority, security and submission integrity is the sole responsibility of the national competent authority.

2.4.3. Virus protection

The applicant is responsible for checking the submission for viruses. Checking should be performed with an up-to-date virus checker and be confirmed in the cover letter.

2.4.4. Password protection

Submission or file level security is not permitted. If one-time security settings or password protection of electronic submissions are used this could constitute grounds for the rejection of the submission.

2.5. General Architecture of Module 1

The GCC Module 1 architecture is similar to that of modules 2 to 5 of the eCTD, comprising a directory structure and a backbone with leaves. The backbone must be a

valid XML document according to the GCC Regional Document Type Definition (DTD). The backbone instance (the `gc-regional.xml` file) contains meta-data for the leaves, including pointers to the files in the directory structure. In addition, the GCC Regional DTD defines meta-data at the submission level in the form of an envelope. The root element is "`gc-backbone`" and contains two elements: "`gc-envelope`" and "`m1-gc`".

The GCC Regional DTD is modularized i.e. the envelope and leaves are referenced from the main part of the DTD as external entities called respectively "`gc-envelope.mod`" and "`gc-leaf.mod`". The "`gc-leaf`" is identical to the leaf element described in the ICH eCTD DTD; reference is made to Table 6-8 of the ICH eCTD Specification. A full description of the GCC Regional DTD can be found in Appendix 4 of this specification.

2.5.1. Checksum

- ✓ GCC Module 1 v1.4 checksum for "gc-regional.dtd" is: 0e089da2bc79ddec16c8496e1644d558
- ✓ GCC Module 1 v1.4 checksum for "gc-envelope.mod" is: d2a8ea399fccf6af13b529f009c6f739
- ✓ GCC Module 1 v1.4 checksum for "gc-leaf.mod" is: f131823f73b74c4c8d16291d02643bec
- ✓ GCC Module 1 v1.4 checksum for "gc-regional.xsl" is: 96aef6e591f7a8337954faddb06f735d

Note: See "checksum.pdf" for complete hash values

2.5.2. Envelope

The "`gc-envelope`" element is designed to be used for all types of submissions (initial, variations, renewals, etc.) for a given medicinal product and will mainly be used for the first simple processing at the agency level. The envelope provides meta-data at the submission level. A description of each "envelope" element is provided in Appendix 1 of this specification.

2.5.3. XML Catalogue

The "m1-gc" element of the GCC regional DTD is based on the same conceptual approach as the common part of the ICH eCTD DTD. It provides an XML catalogue with meta-data at the leaf level including pointers to the location of files in a directory structure. As for the ICH eCTD DTD, the "m1-gc" element maps to the directory structure. (There may at times be what is seen to be a 'redundant' directory structure, but this is necessary in order to be able to use the same file/directory structure for all procedures.)

2.5.4. Directory / File Structure

The GCC Module 1 Specification provides the directory and file structure (see Appendix 2).

2.5.5. File Naming Convention

The eCTD file naming conventions described in the ICH M2 eCTD Specification and this document are highly recommended. If an applicant wishes to submit multiple files in one section, where only one highly recommended name is available, this can be achieved using a suffix to the filename,

File names have fixed and variable components. Components are separated by a hyphen. No hyphens or spaces should be used within each component.

Fixed components are mandatory. The variable component is optional and should be used as appropriate to further define these files. The variable component if used should be a meaningful concatenation of words without separation and should be kept as brief and descriptive as possible. File extensions in line with this specification should be applied as applicable.

The first component in a file name must be the country code as per Appendix 5 except when the document is valid for all countries within the particular procedure. The second component must be the document type code. The third component if necessary should be the variable component.

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

Examples are:

sa-cover.pdf (Saudi Arabia)
ae-cover.pdf (UAE)
bh-cover.pdf (Bahrain)
kw-cover.pdf (Kuwait)
qa-cover.pdf (Qatar)
ye-cover.pdf (Yemen)
sa-form.pdf (Saudi Arabia)
om-form.pdf (Oman)

2.6. Business protocol

The detailed business process between industry and the GCC will form part of the Industry Guidance for eCTDs. For some period of time the exchange of regulatory information will take place through exchange of physical media such as CD/DVD-Rs:

1. The actual submission of the physical media on which the application is contained should be accompanied by at least a signed, paper copy of the cover letter (the content of this cover letter is defined in the ICH eCTD Specification Document Appendix 5, as is the packaging of the media units)

2. The GCC will acknowledge the proper receipt and result of the validation process (technical [e.g. virus check, XML check, etc.] and content based) to the Sponsor or Agent that submitted the eCTD.

2.7. Change control

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

- Change in the content of the Module 1 for the CTD, either through the amendment of information, at the same level of detail, or by provision of more detailed definition of content and structure
- Change to the regional requirements for applications that are outside the scope of the CTD
- Update of standards that are already in use within the eCTD

- Identification of new standards that provide additional value for the creation and/or usage of the eCTD
- Identification of new functional requirements
- Experience of use of the eCTD by all parties, in particular Module 1.

2.8. Instructions for Extension Submissions

Several dosage forms, routes of administration or different strengths can be managed within a single eCTD application, and this helps avoid submission of data multiple times (e.g. active substance changes). Submissions for an extension can either be submitted within an existing eCTD application, as a new sequence (continuous sequence numbering), or as a new eCTD application (sequence 0000), depending on the procedure.

For Extension submission, only new data must be submitted as a new sequence in the already submitted eCTD. The submission type has to be "extension".

If single eCTDs are used for each strength or form of a product, full data concerning the extension applied for has to be included in the submitted eCTD and therefore clear information should be given to the assessor on what is new compared to earlier submitted data for the product to avoid unnecessary assessment.

2.9. Reformatting

To support the reformatting of an existing submission application from any format to eCTD, i.e. a baseline eCTD submission containing no content change and which will not be subject to review, the submission unit type 'reformat' should be used in the envelope. This type will always be used together with the submission type 'none'.

APPENDIX

Appendix 1: Envelope Element Description

The "gc-envelope" element is the root element that defines meta-data of the submission. This element may contain several envelope entries.

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
gc-envelope		Root element that provides meta-data for the submission. This element may contain several envelopes, which are country specific.		Mandatory	Unique
envelope	country	This element must be country specific (See appendix 5)	sa	Mandatory	Unique
application		This is the number issued for the sponsor and the product by the GCC and remains for the full lifecycle of the product from the first data submission		Mandatory	Unique
applicant		The name of the company submitting the eCTD	SAFarma	Mandatory	Unique
Agency	code	Parent element for the identification of the receiving agency (See appendix 5)	SA-SFDA		
ATC		Pick list ATC code			Repeatable
submission		Provides administrative information associated with the submission.		Mandatory	Unique
	type	See appendix 5	new-nce	Mandatory	Unique
submission-unit		Describes actions within the regulatory activity like initial submission, update, responses to questions, any additional information or consolidation submissions respectively when closing a regulatory activity.		Mandatory	Unique
	type	See appendix 5	reformat	Mandatory	Unique
procedure		See appendix 5	national	Mandatory	Unique
invented-name		The name of the medicinal product	Dawa	Mandatory	Repeatable
inn		International Non-proprietary Name, used to identify pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name.	Allopurinol	Optional	Repeatable

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
sequence		This is the sequence number of the submission – this should start at 0000 for the initial submission, and then increase incrementally with each subsequent submission related to the same product e.g. 0000, 0001, 0002, 0003 etc.	0000	Mandatory	Unique
related-sequence		This is the sequence number of a previous submission to which this submission relates e.g. the responses to questions to a particular variation.	0001	Optional	Repeatable
submission-description		This element is used to briefly describe the submission		Mandatory	Unique
number		This is any number, used by an agency or the applicant to track the submission, in any procedure, in relation to a particular product.		Optional	Repeatable

Example of the use of the Related Sequence:

The related sequence number describes the relationship of additional information to the original submission or subsequent submissions.

An illustration of how the related sequence number is used to describe the relationship of additional information to the original and subsequent submissions follows.

Example of how the Related Sequence should be used:

Sequence	Submission Description	Related Sequence	Comment
0000	Application for New Generic application	<none>	This is a new regulatory submission and so no related sequence is included
0001	Responses to Section 31 for New Generic application	0000	This is continued activity for the regulatory submission initiated in 0000 and so the related sequence points to the beginning of that submission
0002	Updated information for New Generic application	0000	This is the completion of the regulatory activity for this submission initiated in 0000 and so the related sequence points to the beginning of that submission
0003	Application for EXTENSION OF INDICATION (EOI) for the approved product	<none>	This is the beginning of a new regulatory submission and so no related sequence is included
0004	Responses Section 31 for the change in manufacturing site for the approved product	0003	This is continued activity for the regulatory submission initiated in 0003 and so the related sequence points to the beginning of that submission
0005	Responses to CLIN Section 31 EOI for the approved product	0003	This is continued activity for the regulatory submission initiated in 0003 and so the related sequence points to the beginning of that submission

Appendix 2: Directory/File Structure for GCC Module 1

The directory / file structure is defined in this appendix as a table containing the following information:

Sequential number		Each item in the table has a unique sequentially assigned reference number. These reference numbers can change with each version of this appendix.
	Number	CTD section number
	Title	CTD title
	Element	Element name in the GCC Backbone
	File/Directory	File/Directory name from m1-gc should be relative path from *gc-m1* e.g. `12-form/gc/sa-form.pdf` This is consistent with ICH standards. The file extension corresponds to the file type; i.e., the "pdf" extension is only illustrative.
	Comment	Comments

The names of the actual files and directories used should be presented in lower case in accordance with the eCTD specification. The codes "VAR" and "EXT" represent a variable component of the file name and a representation of a file extension respectively. The use of upper case for those codes is for illustrative purposes only to show differentiation between the variable parts and the fixed part of the name.

Please note that "*CC*" represents the country code and "*LL*" the language code. It is added to a directory if a file is specific to a country. If the file applied to all GCC countries, "*CC*" will be "*common*".

1	Number	
	Title	GCC Module 1
	Element	m1-gc
	Directory	m1/gc
	Comment	Top level directory for the GCC Module 1 as per ICH eCTD Specification
2	Number	
	Title	GCC Module 1 – DTD version 1.0
	Element	
	File	m1/gc/gc-regional.xml
	Comment	The GCC Regional XML instance including the envelope information. Note that the operation attribute for the `gc-regional.xml` should always be set to 'new'
3	Number	1.0

	Title	Cover letter
	Element	m1-0-cover
	Directory	m1\gc\10-cover
	Comment	General place holder for cover letter information If there is a special cover letter from specific agency, please add the country and language to the directory m1\gc\10-cover*CC**LL*.
4	Number	
	Title	Cover letter for SFDA
	Element	m1-0-cover
	Directory	m1\gc\10-cover
	File	*CC*-cover-*VAR.EXT*
	Comment	Example for the cover letter is specific for (SFDA) in Saudi Arabia, the placeholder will be m1\gc\10-cover\sa\sa-cover.pdf
5	Number	1.1
	Title	Module 1 table of contents
	Element	m1-1-table-of-contents
	Directory	0000
	Comment	The table of contents should include a list of all documents provided in the data submission by module. In eCTD, the xml backbone replaces the table of contents 0000\index.xml
6	Number	1.2
	Title	Application form
	Element	m1-2-application-form
	Directory	m1\gc\12-form
	File	*CC*-form-*VAR.EXT*
	Comment	General place holder for application form information.
7	Number	1.3
	Title	Product Information
	Element	m1-3-product-information
	Directory	m1\gc\13-pi
	Comment	General placeholder for Product Information
8	Number	1.3.1
	Title	Summary of Product Characteristics (SPC)
	Element	m1-3-1-spc
	Directory	m1\gc\13-pi\131-spc
	File	*CC*-spc-*VAR.EXT*
	Comment	General placeholder for SPC. English SPC the directory is m1\gc\13-pi\131-spc*CC*\en
9	Number	1.3.2
	Title	Labeling
	Element	m1-3-2-label

	Directory	m1\gc\13-pi\132-labeling
	File	*CC*-label-*VAR.EXT*
	Comment	General placeholder for labeling The directory is m1\gc\13-pi\132-labeling*CC**LL*
10	Number	1.3.3
	Title	Patient information leaflet
	Element	m1-3-3-pil
	Directory	m1\gc\13-pi\133-leaflet
	Comment	General placeholder for Patient information leaflet
11	Number	1.3.3.1
	Title	Arabic Patient information leaflet
	Element	m1-3-3-pil
	Directory	m1\gc\13-pi\133-leaflet*CC*\ar
	File	*CC*-leaflet-*VAR.EXT*
	Comment	Document in Arabic
12	Number	1.3.3.2
	Title	English Patient information leaflet
	Element	m1-3-3-pil
	Directory	m1\gc\13-pi\133-leaflet*CC*\en
	Comment	Document in English
13	Number	1.3.4
	Title	Artwork (mock-ups)
	Element	m1-3-4-mockup
	Directory	m1\gc\13-pi\134-artwork*CC**LL*
	File	*CC*-artwork-*VAR.EXT*
	Comment	Artwork or Mock-ups
14	Number	1.3.5
	Title	Samples
	Element	m1-3-5-samples
	Directory	m1\gc\13-pi\135-samples*CC**LL*
	File	CC-samples-*VAR.EXT*
	Comment	Samples
15	Number	1.4
	Title	Information on the Experts
	Element	m1-4-expert
	Directory	m1\gc\14-expert
	Comment	
16	Number	1.4.1
	Title	Quality
	Element	m1-4-1-quality
	Directory	m1\gc\14-expert\141-quality
	File	quality-*VAR.EXT*

	Comment	
17	Number	1.4.2
	Title	Non clinical
	Element	m1-4-2-non-clinical
	Directory	m1\gc\14-expert\142-nonclinical
	File	nonclinical-*VAR.EXT*
	Comment	
18	Number	1.4.3
	Title	Clinical
	Element	m1-4-3-clinical
	Directory	m1\gc\14-expert\143-clinical
	File	clinical-*VAR.EXT*
	Comment	
19	Number	1.5
	Title	Environmental Risk Assessment
	Element	m1-5-environrisk
	Directory	m1\gc\15-environrisk
	Comment	
20	Number	1.5.1
	Title	Non-GMO
	Element	m1-5-1-non-gmo
	Directory	m1\gc\15-environrisk\151-nongmo
	File	nongmo-*VAR.EXT*
	Comment	
21	Number	1.5.2
	Title	GMO
	Element	m1-5-2-gmo
	Directory	m1\gc\15-environrisk\152-gmo
	File	gmo-*VAR.EXT*
	Comment	
22	Number	1.6
	Title	Pharmacovigilance
	Element	m1-6-pharmacovigilance
	Directory	m1\gc\16-pharmacovigilance
	Comment	
23	Number	1.6.1
	Title	Pharmacovigilance System
	Element	m1-6-pharmacovigilance-system
	Directory	m1\gc\16-pharmacovigilance\161-phvig-system
	File	phvigsystem-*VAR.EXT*
	Comment	
24	Number	1.6.2
	Title	Risk Management Plan

	Element	m1-6-2-risk-management-system
	Directory	m1\gc\16-pharmacovigilance\162-riskmgt-system
	File	riskmgtsystem-*VAR.EXT*
	Comment	
25	Number	1.7
	Title	Certificates and Documents
	Element	m1-7-certificates
	Directory	m1\gc\17-certificates
	Comment	
26	Number	1.7.1
	Title	GMP Certificate
	Element	m1-7-1-gmp
	Directory	m1\gc\17-certificates\171-gmp
	File	*CC*-gmp-*VAR.EXT*
	Comment	
27	Number	1.7.2
	Title	CPP or Free-sales
	Element	m1-7-2-cpp
	Directory	m1\gc\17-certificates\172-cpp
	File	*CC*-cpp-*VAR.EXT*
	Comment	
28	Number	1.7.3
	Title	Certificate of analysis – Drug Substance / Finished Product
	Element	m1-7-3-analysis-substance
	Directory	m1\gc\17-certificates\173-analysis-substance
	File	*CC*-drugsubstance-*VAR.EXT*
	Comment	
29	Number	1.7.4
	Title	Certificate of analysis – Excipients
	Element	m1-7-4-analysis-excipients
	Directory	m1\gc\17-certificates\174-analysis-excipients
	File	*CC*-excipients-*VAR.EXT*
	Comment	
30	Number	1.7.5
	Title	Alcohol-content declaration
	Element	m1-7-5-alcohol-content
	Directory	m1\gc\17-certificates\175-alcohol-content
	File	*CC*-alcoholcontent-*VAR.EXT*
	Comment	
31	Number	1.7.6
	Title	Pork-content declaration
	Element	m1-7-6-pork-content
	File	*CC*-porkcontent-*VAR.EXT*

	Directory	m1\gc\17-certificates\176-pork-content
	Comment	
32	Number	1.7.7
	Title	Certificate of suitability for TSE
	Element	m1-7-7-certificate-tse
	Directory	m1\gc\17-certificates\177-certificate-tse
	File	*CC*-tse-*VAR.EXT*
	Comment	
33	Number	1.7.8
	Title	The diluents and coloring agents in the product formula
	Element	m1-7-8-diluent-coloring-agents
	Directory	m1\gc\17-certificates\178-diluent-coloring-agents
	File	*CC*-diluent-*VAR.EXT*
	Comment	
34	Number	1.7.9
	Title	Patent Information
	Element	m1-7-9-patent-information
	Directory	m1\gc\17-certificates\179-patent-information
	File	*CC*-patent-*VAR.EXT*
	Comment	
35	Number	1.7.10
	Title	Letter of access or acknowledgements to DMF
	Element	m1-7-10-letter-access-dmf
	Directory	m1\gc\17-certificates\1710-letter-access-dmf
	File	*CC*-accessdmf-*VAR.EXT*
	Comment	
36	Number	1.8
	Title	Pricing
	Element	m1-8-pricing
	Directory	m1\gc\18-pricing
	Comment	
37	Number	1.8.1
	Title	Price list
	Element	m1-8-1-price-list
	Directory	m1\gc\18-pricing\181-price-list
	File	*CC*-price-*VAR.EXT*
	Comment	
38	Number	1.8.2
	Title	Other documents related
	Element	m1-8-2-other-document
	Directory	m1\gc\18-pricing\182-other-doc
	File	*CC*-others-*VAR.EXT*
	Comment	

39	Number	1.9
	Title	Responses to questions
	Element	m1-9-responses
	Directory	m1\gc\19-responses*CC*
	File	*CC*-responses-*VAR.EXT*
	Comment	
40	Number	m1-additional-data
	Title	Additional data
	Element	m1-additional-data
	Directory	m1\gc\additional-data*CC*
	File	*CC*-additionaldata-*VAR.EXT*
	Comment	Any additional data requested should be put on this place such as documents that don't really fit in any other sections (transfer agreement, declaration of conformity of translation, etc.)

Appendix 3: Country Specific Elements

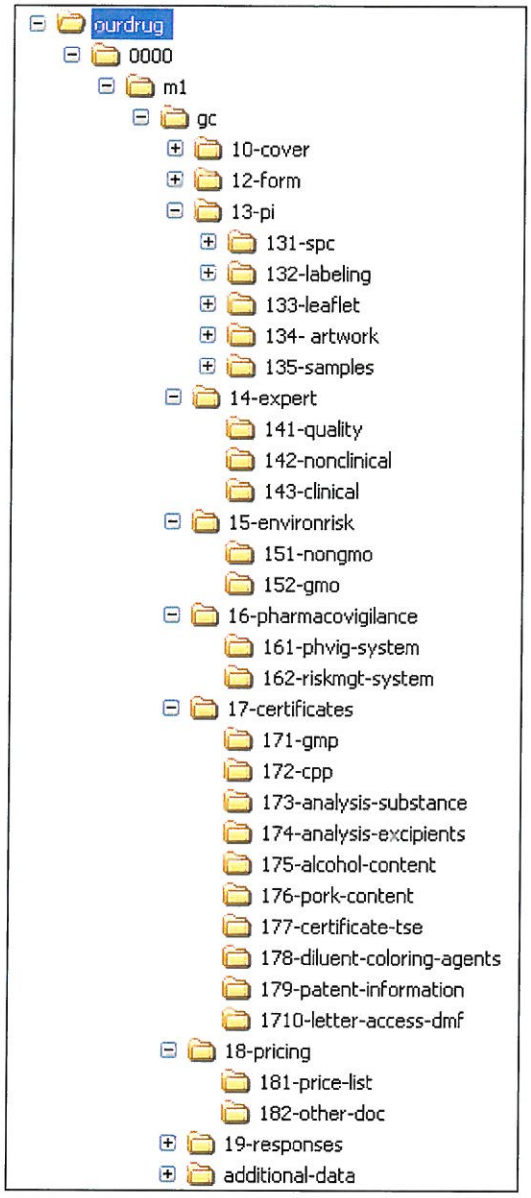
A number of the elements that represent Module 1 *TOC* headings possess the child element "`specific`", which allows country specificity of content to be explicitly indicated.

Module 1 elements that have "`specific`" child elements can therefore contain multiple documents, each with content for review by a different country in the Gulf Cooperation countries. These elements are listed below:

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
Specific		Parent element for identifying the receiving country for a document or documents.		Mandatory	Repeatable
	country	The receiving country for the document (see appendix 5)	sa	Mandatory	Unique

Appendix 4: Example Screenshot

This appendix is included only to demonstrate how the directory structure may appear for Module 1 for Gulf Cooperation Council (GCC).



Appendix 5: List of codes

GCC Agencies (in alphabetic order)

Country	Code agency	Description
Bahrain	BH-MOH	Ministry of Health
Kuwait	KW-MOH	Ministry of Health
Oman	OM-MOH	Ministry of Health
Qatar	QA-NHA	National Health Authority
Republic of Yemen	YE-MOPHP	Ministry of Public Health and Population
Saudi Arabia	SA-SFDA	Saudi Food and Drug Authority
UAE	AE-MOH	Ministry of Health

Procedure

Type	Description
gcc	GCC procedure
national	National procedure

Submission

Type	Description
asmf	Active Substance Master File
extension	Extension Submission*
new-bio	MAA - Biological
new-gen	MAA - Generic (Multisource)
new-nce	MAA - New chemical Entity
new-rad	MAA - Radiopharmaceuticals
none	In the exceptional case of reformatting the application no regulatory activity is allowed. Therefore, '*none*' must be stated. The submission unit will identify the sub-activity related to the product.
pmf	Plasma Master File
psur	Periodic Safety Update Report
psusa	PSUR single assessment procedure
renewal	Renewal of Marketing Authorization
rmp	Risk Management Plan
transfer-ma	Transfer of Marketing Authorization
usr	Urgent Safety Restriction
var-type1	Variation Type 1
var-type2	Variation Type 2
withdrawal	Withdrawal

*consult your local regulatory authority before submission

Submission unit

Type	Description
additional-info	Other additional Information (could include, for example, missing files) and should only be used, if response is not suitable
closing	Submission unit that provides the final documents in the GCC procedure following the decision of the GCC committee
correction	Correction to the published annexes in the GCC procedure (usually shortly after approval)
initial	Initial submission to start any regulatory activity
reformat	Intended to support the reformatting of an existing submission application from any format to eCTD, i.e. a baseline eCTD submission containing no content change and which will not be subject to review. This type will always be used together with the submission type '*none*'
response	Submission unit that contains the response to any kind of question, validation issues out-standing information requested by the agency

DESTINATION

In most cases the destination code is an ISO-3166-1 code usually called "country code".

Country code	Destination
AE	State of United Arab Emirates
BH	Kingdom of Bahrain
KW	State of Kuwait
OM	Sultanate of Oman
QA	State of Qatar
SA	Saudi Arabia
YE	Republic of Yemen

Note: Use "common" as country code when the submission applies to all countries.

LANGUAGE

Language	Description
ar	Arabic (when required)
en	English

Appendix 6: Modularized DTD for GCC Module 1

GCC Regional DTD

```
<!--
PUBLIC "-//GC//DTD eCTD GCBackbone 1.1//EN"
In the eCTD File Organisation: "util/dtd/gc-regional.dtd"

Created : August 2009

minor changes on elements (Oct 2012)
change "m1-7-5-alcohol-free" in "m1-7-5-alcohol-content"
change "m1-7-6-pork-free" in "m1-7-6-pork-content"
samples from "leaf-node" in "specific"

Modified: August 2015
Modification done in the envelope
Add submission unit concept
Add new values in submission
Minor changes : formatting the DTD

Meaning or value of the  suffixes:
   ?  : element must appear 0 or 1 time
   *  : element must appear 0 or more time
   +  : element must appear 1 or more times
   <none>: element must appear once and only once
-->

<!-- General declarations, external modules
references..................... -->
<!ENTITY % countries "(ae|common|bh|kw|om|qa|sa|ye)">
<!ENTITY % languages "(en|ar)">
<!ENTITY % leaf-node "(( leaf | node-extension )*)">
<!ENTITY % envelope-module SYSTEM "gc-envelope.mod" >
%envelope-module;

<!ENTITY % leaf-module SYSTEM "gc-leaf.mod" >
%leaf-module;

<!ELEMENT specific (
   %leaf-node;
)>
<!ATTLIST specific
   country %countries; #REQUIRED
>

<!-- Root element
.................................................... -->
<!ELEMENT gc:gc-backbone (
   gc-envelope,
   m1-gc
)>

<!ATTLIST gc:gc-backbone
   xmlns:gc       CDATA #FIXED   "http://sfda.gov.sa"
```

```
   xmlns:xlink     CDATA #FIXED
"http://www.w3c.org/1999/xlink"
   xml:lang        CDATA #IMPLIED
   dtd-version     CDATA #FIXED   "1.1"
>
<!--
.....................................................................
..... -->
<!ELEMENT m1-gc (
   m1-0-cover,
   m1-2-form?,
   m1-3-pi?,
   m1-4-expert?,
   m1-5-environrisk?,
   m1-6-pharmacovigilance?,
   m1-7-certificates?,
   m1-8-pricing?,
   m1-9-responses?,
   m1-additional-data?
)>

<!--
.....................................................................
..... -->
<!ELEMENT m1-0-cover (
   specific+
)>

<!--
.....................................................................
..... -->
<!ELEMENT m1-2-form (
   specific+
)>

<!--
.....................................................................
..... -->
<!ELEMENT m1-3-pi (
   m1-3-1-spc?,
   m1-3-2-label?,
   m1-3-3-pil?,
   m1-3-4-mockup?,
   m1-3-5-samples?
)>
<!ELEMENT m1-3-1-spc (
   pi-doc+
)>
<!ELEMENT m1-3-2-label (
   pi-doc+
)>
<!ELEMENT m1-3-3-pil (
   pi-doc+
)>
<!ELEMENT m1-3-4-mockup (
   specific+
```

```
)>
<!ELEMENT m1-3-5-samples (
   specific+
)>

<!ELEMENT pi-doc (
   %leaf-node;
)>
<!ATTLIST pi-doc
   xml:lang %languages; #REQUIRED
   type     (spc|label|pil) #REQUIRED
   country  %countries;    #REQUIRED
>

<!--
.....................................................................
..... -->
<!ELEMENT m1-4-expert (
   m1-4-1-quality?,
   m1-4-2-non-clinical?,
   m1-4-3-clinical?
)>

<!ELEMENT   m1-4-1-quality            %leaf-node;>
<!ELEMENT   m1-4-2-non-clinical       %leaf-node;>
<!ELEMENT   m1-4-3-clinical           %leaf-node;>

<!--
.....................................................................
..... -->
<!ELEMENT m1-5-environrisk (
   (m1-5-1-non-gmo | m1-5-2-gmo)?
)>
<!ELEMENT   m1-5-1-non-gmo            %leaf-node;>
<!ELEMENT   m1-5-2-gmo                %leaf-node;>

<!--
.....................................................................
..... -->
<!ELEMENT m1-6-pharmacovigilance (
   m1-6-1-pharmacovigilance-system?,
   m1-6-2-risk-management-system?
)>
<!ELEMENT   m1-6-1-pharmacovigilance-system  %leaf-node;>
<!ELEMENT   m1-6-2-risk-management-system    %leaf-node;>

<!--
.....................................................................
..... -->
<!ELEMENT m1-7-certificates (
   m1-7-1-gmp?,
   m1-7-2-cpp?,
   m1-7-3-analysis-substance?,
   m1-7-4-analysis-excipients?,
   m1-7-5-alcohol-content?,
   m1-7-6-pork-content?,
```

```
    m1-7-7-certificate-tse?,
    m1-7-8-diluent-coloring-agents?,
    m1-7-9-patent-information?,
    m1-7-10-letter-access-dmf?
)>
<!ELEMENT m1-7-1-gmp                          %leaf-node;>
<!ELEMENT m1-7-2-cpp                          %leaf-node;>
<!ELEMENT m1-7-3-analysis-substance           %leaf-node;>
<!ELEMENT m1-7-4-analysis-excipients          %leaf-node;>
<!ELEMENT m1-7-5-alcohol-content              %leaf-node;>
<!ELEMENT m1-7-6-pork-content                 %leaf-node;>
<!ELEMENT m1-7-7-certificate-tse              %leaf-node;>
<!ELEMENT m1-7-8-diluent-coloring-agents      %leaf-node;>
<!ELEMENT m1-7-9-patent-information           %leaf-node;>
<!ELEMENT m1-7-10-letter-access-dmf           %leaf-node;>

<!--
.....................................................................
..... -->
<!ELEMENT m1-8-pricing (
   m1-8-1-price-list?,
   m1-8-2-other-document?
)>
<!ELEMENT m1-8-1-price-list                   %leaf-node;>
<!ELEMENT m1-8-2-other-document               %leaf-node;>


<!--
.....................................................................
..... -->
<!ELEMENT m1-9-responses (
   specific+
)>

<!--
.....................................................................
..... -->
<!ELEMENT m1-additional-data (
   specific+
)>
<!-- +++ -->
```

GCC Envelope

```
<!--
In the eCTD File Organisation: "util/dtd/gc-envelope.mod"

Version 1.2
Oct 2015

-->

<!--
.....................................................................
..... -->
<!ELEMENT gc-envelope (
      envelope+
)>

<!ELEMENT envelope (
      application,
      applicant,
      agency,
      atc*,
      submission,
      submission-unit,
      procedure,
      invented-name+,
      inn*,
      sequence,
      related-sequence*,
      submission-description
)>

<!--
.....................................................................
..... -->
<!ELEMENT application                ( number* )>
<!ELEMENT applicant                  ( #PCDATA )>
<!ELEMENT agency                     EMPTY>
<!ELEMENT atc                        ( #PCDATA )>
<!ELEMENT submission                 EMPTY>
<!ELEMENT submission-unit            EMPTY>
<!ELEMENT procedure                  EMPTY>
<!ELEMENT invented-name              ( #PCDATA )>
<!ELEMENT inn                        ( #PCDATA )>
<!ELEMENT sequence                   ( #PCDATA )>
<!ELEMENT related-sequence           ( #PCDATA )>
<!ELEMENT submission-description     ( #PCDATA )>
<!ELEMENT number                     ( #PCDATA )>

<!--
.....................................................................
..... -->
<!ATTLIST agency code (
  AE-MOH
| BH-MOH
| KW-MOH
```

```
  | OM-MOH
  | QA-NHA
  | SA-SFDA
  | YE-MOPHP
  ) #REQUIRED>

  <!--
  ..............................................................
  ..... -->
  <!ATTLIST procedure type (
     gcc
   | national
   ) #REQUIRED>

  <!--
  ..............................................................
  ..... -->
  <!ATTLIST submission type (
    asmf
  | extension
  | new-gen
  | new-nce
  | new-bio
  | new-rad
  | none
  | pmf
  | psur
  | psusa
  | renewal
  | rmp
  | transfer-ma
  | usr
  | var-type1
  | var-type2
  | withdrawal
  ) #REQUIRED>

 <!--
 ..............................................................
 ..... -->
 <!ATTLIST submission-unit type (
   initial
 | response
 | additional-info
 | closing
 | correction
 | reformat
 ) #REQUIRED>

<!--
..............................................................
..... -->
<!ENTITY % env-countries "(ae|common|bh|kw|om|qa|sa|ye)">
```

```
<!--
.....
..... -->
<!ATTLIST envelope country %env-countries; #REQUIRED >

<!-- +++ -->
```

GCC Leaf

```
<!--
In the eCTD File Organisation: "util/dtd/gc-leaf.mod"
Version 1.0
May 2009
This is based on ich-ectd-3-2.dtd;
If the ich-ectd.dtd is modularized, this one could be
replaced.
Hence, one is certain that the common and GCC leaf are the
same.
-->

<!--
============================================================
-->
<!ELEMENT node-extension (title, (leaf | node-extension)+)>
<!ATTLIST node-extension
      ID ID #IMPLIED
      xml:lang CDATA #IMPLIED
>

<!--
============================================================
-->
<!ENTITY % show-list " (new | replace | embed | other | none)
">
<!ENTITY % actuate-list " (onLoad | onRequest | other | none)
">
<!ENTITY % operation-list " (new | append | replace | delete)
">
<!ENTITY % leaf-element " (title, link-text?) ">
<!ENTITY % leaf-att '
 ID                   ID                  #REQUIRED
 application-version  CDATA               #IMPLIED
 version              CDATA               #IMPLIED
 font-library         CDATA               #IMPLIED
 operation            %operation-list;    #REQUIRED
 modified-file        CDATA               #IMPLIED
 checksum             CDATA               #REQUIRED
 checksum-type        CDATA               #REQUIRED
 keywords             CDATA               #IMPLIED
```

```
  xmlns:xlink          CDATA                #FIXED
 "http://www.w3c.org/1999/xlink"
  xlink:type           CDATA                #FIXED    "simple"
  xlink:role           CDATA                #IMPLIED
  xlink:href           CDATA                #IMPLIED
  xlink:show           %show-list;          #IMPLIED
  xlink:actuate        %actuate-list;       #IMPLIED
  xml:lang             CDATA                #IMPLIED
  '>

<!ELEMENT leaf %leaf-element;>
<!ATTLIST leaf
      %leaf-att;
>
<!ELEMENT title (#PCDATA)>
<!ELEMENT link-text (#PCDATA | xref)*>

<!ELEMENT xref EMPTY>
<!ATTLIST xref
      ID ID #REQUIRED
      xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
      xlink:type CDATA #FIXED "simple"
      xlink:role CDATA #IMPLIED
      xlink:title CDATA #REQUIRED
      xlink:href CDATA #REQUIRED
      xlink:show %show-list; #IMPLIED
      xlink:actuate %actuate-list; #IMPLIED
>
<!-- +++ -->
```

Annex 1:

What's New in the GCC Module 1 Specifications (Version 1.5)?

New Capabilities

The concept of "**submission unit**" is introduced as currently implemented by the FDA. The existing attribute of the "**submission type**" will then solely describe a regulatory activity.
The "**submission unit**" will describe actions within that regulatory activity like an initial submission of an application, responses to questions from agencies or any additional information.
In the same way "**reformat**" will be used as a submission unit together with submission type "**none**" as it is not a regulatory activity, but just a reformatting of the dossier.

Corrected Issues

- Change of some PDF criteria Pass/Fail to Best Practices
- Remove the term 'EOI' from Glossary

Changes in this new release

Elements	Description
Hyperlink and bookmark	
http://estri.ich.org	Point to the new link of ICH website
ICH eCTD Specification	Point to the new link of ICH website
Appendix 2	Modification of the bookmark
Glossary	
EOI	Remove the term from Glossary
Terms	Add new terms
Controlled Vocabularies	
Submission type CVs	Remove 'responses' from the controlled vocabularies list
Submission unit CVs	Add the concept of submission unit type.
Checksum values	
checksum	Modified the checksum values following the modification of the Module 1 DTD, envelope, stylesheet
Sections	
2.8. Instructions for Extension Submissions	Corrected the text
2.9. Reformatting	Add this new section for *'reformat'*
Appendix 1	Add of submission unit type Add example for the element *'procedure'* Modified the constraint of Element *'number'* in *optional*
Appendix 5: List of codes	Add submission type codes Add submission unit type codes Removal of herbal/health/vet submission type
Envelope, DTD, Stylesheet	Minor modifications due to new controlled vocabularies
Validation criteria	
submission unit type for "*additional-info*" and "*correction*"	Added to Best practices (BP)

All PDF bookmarks are relative	Added to BP
All Bookmarks are set in "*inherit zoom*"	Added to BP
Fast Web View active	Added to BP
Hyperlinks and Bookmarks have a valid target	Added to BP
Submission unit type '*reformat*' should be used with submission type *'none'*	Added to Pass/Fail