NAMIBIA COMMON TECHNICAL DOCUMENT

NAMIBIA MEDICINES REGULATORY COUNCIL

MINISTRY OF HEALTH AND SOCIAL SERVICES

APPLICATION FOR REGISTRATION OF A MEDICINE

GUIDANCE FOR THE PREPARATION AND SUBMISSION OF DOSSIERS IN COMMON TECHNICAL DOCUMENT FORMAT

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REGISTRAR OF MEDICINES

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ABBREVIATIONS AND ACRONYMS

API	Active Pharmaceutical Ingredient
CEP	Certificate of Suitability (Ph Eur monograph)
CHMP	Committee for Medicinal Products for Human Use (formally, Committee for Proprietary Medicinal Products) (EU)
CTD	Common Technical Document
EDQM	European Directorate for the Quality of Medicines
EU	European Union
GCP	Good Clinical Practice
GMO	Genetically Modified Organism
GMP	Good Manufacturing Practice
ICH	International Conference on Harmonisation (of Technical Requirements for Registration of Pharmaceuticals for Human Use)
IPD	Individual Patient Data
IPI	Inactive Pharmaceutical Ingredient
IT	Information technology
MHRA	UK Medicines and Health products Regulatory Authority
NMRC	Namibian Medicines Control Council
pdf	portable document format
PI	Package Insert
PIL	Patient Information Leaflet
PMF	Plasma Master File
SA	South Africa
SmPC	Summary of Product Characteristics (European)
TGA	Australian Therapeutic Goods Authority
UK	United Kingdom
US FDA	United States Food and Drug Administration
USA	United States of America

INTRODUCTION

This guideline provides recommendations for applicants preparing a Common Technical Document for the Registration of Medicines (CTD) for submission to the Namibian Medicines Control Council (NMRC). The document describes how to organise applications based on the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines on the CTD. These guidelines are largely based on the *South African Guidance for the submission of the South African CTD/eCTD – General & Module 1* [1] and the *WHO Guidelines on preparation of product dossiers in CTD format.* [2]

This document provides recommendations on the format and presentation for product dossiers (PDs).

Objectives

These guidelines are intended to:

- assist applicants in the preparation of PDs by providing clear general guidance on the format of these dossiers;
- fully adopt the modular format of the CTD as developed by ICH; and
- provide guidance on the location of regional information (Module 1) and other general data requirements. These measures are intended to promote effective and efficient processes for the development of these PDs and the subsequent assessment procedures.

Organisation of product dossier in common technical document format

According to the CTD format, each application is a collection of documents, grouped into 5 modules.

This guideline provides information on the contents of the *Namibian CTD Module 1: Administrative Information,* as Module 1 is region specific.

The European *Notice to Applicants: Medicinal products for human use. Volume 2B: Presentation and format of the dossier CTD* (July 2003) describes the format and organisation of the Summaries, Quality, Non-clinical, and Clinical modules (Modules 2 to 5, respectively).

The CTD guidelines, together with the *Namibian Registration Guidelines* provide detailed information about the contents of an application. These guidelines apply to applications to register medicines and all related variations. Applicants should not modify the overall organisation of the CTD. If not contained in the bulk of the documentation, any additional data should be included as addenda to the relevant part, together with additional expert comment that may be provided as a supplement to, or incorporated into, the relevant summary, overall summary or overview.

This guideline should be read together with the Registration guideline.

Module 1 - Administrative information and prescribing information

Relevant administrative documentation should be submitted in Module 1 of the CTD dossier. This module should be divided into the relevant sections, as described in Part B of this guideline.

Module 2 - Summary of the dossier

Module 2 of the CTD dossier contains the summaries and overviews for the quality, non-clinical and clinical sections of the dossier (refer to the European *Notice to Applicants: Medicinal products for human use. Volume 2B: Presentation and format of the dossier CTD* (July 2003).

The Clinical Overview should include a statement regarding Good Clinical Practice (GCP) compliance.

In cases concerning well-known active pharmaceutical ingredients, the Council may grant exemption from the submission of Non-clinical and Clinical Overviews and Summaries (2.4, 2.5, 2.6 and 2.7).

Module 3 – Quality

Module 3 of the dossier contains the chemical, pharmaceutical and biological data relevant to the application.

Refer to the Registration guideline for the current requirements for this module.

Full reports on biopharmaceutical studies, including methodology and validation data for bioavailability studies, should be included in Module 5.3.1.

Module 4 - Non-clinical study reports

Module 4 of the dossier contains the non-clinical (pharmaco-toxicological) data relevant to the application.
In cases concerning well-known active pharmaceutical ingredients, the Council may grant exemption from the submission of Non-clinical study reports in Module 4.

Module 5 - Clinical study reports

Module 5 of the dossier contains the clinical data relevant to the application. In most circumstances, the clinical studies included in Module 5 of the dossier will be international studies used to establish the pharmacodynamics, pharmacokinetics, safety and efficacy of the medicine across an international patient population. However, where there is evidence to suggest that the pharmacokinetics or pharmacodynamics of the product may vary across the populations that will use the medicine in Namibia; the sponsor should consider submitting studies relevant to those target populations.

In cases concerning well-known active pharmaceutical ingredients, the Council may grant exemption from the submission of Clinical study reports, other than bioequivalence study reports, in Module 5.

European Union guidelines on quality, safety and efficacy

The technical content of the documents in the CTD modules is outside the scope of this guidance. The CTD guidelines do not indicate the data or studies required; they merely indicate an appropriate format and organisation for the data that have been acquired. The main Registration Guideline and the relevant guidelines (SADC, WHO, ICH or EU) as indicated should be consulted.

PART A: GENERAL INFORMATION FOR APPLICATIONS

Please read together with the Registration guideline.

1 Preparing and organising the Common Technical Document

To facilitate the review of the basic data and to help an evaluator become oriented with the application contents, the display of information should be unambiguous and transparent throughout the CTD.

If additional or supplementary data are submitted, the module(s) should be identified and numbering should follow from the original documentation.

The applicant should not submit the modules that are not used i.e. it is unnecessary to include "not applicable" pages against unused CTD headings.

For new applications, detailed statements justifying the absence of data or specific CTD sections should be provided in the relevant Quality Overall Summary (QOS) and/or Non-Clinical/Clinical Overviews (Module 2.3, 2.4, 2.5). If relevant, justification for empty sections in Module 1 is to be provided in the cover letter.

Acronyms and abbreviations should be defined the first time they are used in each module.

2 Documentation

2.1 Electronic review documents

Electronic submission of documentation (CD or DVD) should be submitted in Microsoft Word (required for templates/summaries, e.g. QOS–PD, BTIF) or text-selectable PDF format (other documentation).

Guidance on eCTD submissions will be provided in future.

2.2 Paper submissions

Set 1 – Full dossier

One complete application for registration dossier and the following:

- Screening fee or proof of payment in terms of Fees payable to the Registrar (proof of payment must be included in section 1.2.2.1 of Module 1) (*please do not include the application fee with the screening fee*)
- Sample and copy of the sample's API and final product release certificates of analysis

  The copy of the sample's API and final product release certificates of analysis should be included in section 1.7.10.3)

On completion of administrative screening the following:

- Original letter of application for final submission must be included in section 1.0 of Module 1 (this date becomes the date of application and must be amended in Module 1.2.1)
- All administrative screening outcome correspondence (Module 1.8)
- Application fee or proof of payment in terms of Fees payable to the Registrar (proof of payment must be included in section 1.2.2.1 of Module 1)

3 Organising documents

Each section of the dossier is to be marked by use of clearly annotated tabs and the documentation should be filed in accessible files. Lever arch files are not acceptable. Documents can be combined in volumes as long as appropriately named tab identifiers separate them. For example, the Package insert

should be separated from the other documents by a tab identifier. In general, documents from different CTD modules should not be included in the same volume. Documents from different modules may be combined in the same volume for amendments consisting of a small number of short documents.

Administrative documents (e.g. Application letter, Statement on the availability of Individual Patient Data) are included in Module 1. The organisation of such documents should be consistent with the structure described in this guideline. Since these administrative documents are small, they should be placed in the same volume, separated by tab identifiers.

4 Volume identification

Volumes must be numbered by module, resulting in a separate set of numbers for each module.

The labelling of each volume should include:

- Name of applicant
- Name of medicine
- Module and Volume number. The volumes in each module should be numbered separately and sequentially using the format: *x of y volumes,* where x is the number for the specific volume and y is the total number of volumes submitted for the respective module, e.g. Module 3, Vol.1 of 6.
- Copy number: The copies of Modules 1, 2 and 3 should be numbered as copies *x of y.*
- Contents. Each volume must also be labelled according to the section(s) which it contains, e.g.:

Section 3.2.P.4 means:

3. – Module 3 - Quality
2. – Body of data
P. – Product
4. – Control of excipients

5 Pagination

A document is a set of pages, numbered sequentially and divided from other documents by a tab.

Page numbering should be at the document level and not at the volume or module level. (The entire submission should never be numbered consecutively by page.) In general, all documents should have page numbers. Since the page numbering is at the document level, there should only be one set of page numbers for each document.

Cross-referencing to documents should be made by referring to the CTD module, volume, tab identifier, and page number (for example: "*see Module 3, Vol. 6, P.4.3 Method validation, p 23"*).

Documents must be printed on both sides of a page, legibility must not be impaired and margin space must be sufficient on both the left and right side, so that information is not obscured when the page is placed in a binder. However, Module 1.3 Namibian labelling and packaging (1.3.1.1, 1.3.2, 1.3.3), and Module 1.5.5 Clinical Package Insert and Patient Information Leaflet amendments / updates must be copied single-sided. Copying of each document must start on a new page and must be separated from the next document by a tab.

6 Paper size

Standard A4 paper should be used for all submissions. Text and tables should be prepared using margins that allow the document to be printed on A4 paper. The left-hand margin should be sufficiently large that information is not obscured through binding.

7 Fonts

Font sizes for text and tables should be of a style and size that are large enough to be easily legible, even after photocopying or when provided electronically. Arial 12 point font is preferred for narrative text, but printing in a font size with a legibility equivalent to at least Arial 10 point black on white could be used. The copies, including figures, tables, photo's should be clearly legible. Shading and/or coloured filling/background and/or print, e.g. in tables and headers, or across pages, is unacceptable and should be avoided.

8 Granularity of Module 1

Module 1	1.0		
	1.1		
	1.2	1.2.1	
		1.2.2	1.2.2.1
			1.2.2.2
			1.2.2.3
			1.2.2.4
			1.2.2.5
			1.2.2.6
			1.2.2.7
			1.2.2.8
	1.3	1.3.1	1.3.1.1
			1.3.1.2
		1.3.2	
		1.3.3	
		1.3.4	
	1.4	1.4.1	
		1.4.2	
		1.4.3	
	1.5	1.5.1	
		1.5.2	1.5.2.1
			1.5.2.2
			1.5.2.3
		1.5.3	
		1.5.4	
		1.5.5	
	1.6	1.6.1	
		1.6.2	
	1.7	1.7.1	
		1.7.2	
		1.7.3	
		1.7.4	1.7.4.1
			1.7.4.2
			1.7.4.3
			1.7.4.4
		1.7.5	
		1.7.6	
		1.7.7	
		1.7.8	
		1.7.9	
		1.7.10	1.7.10.1
			1.7.10.2
			1.7.10.3
		1.7.11	
		1.7.12	

		1.7.13	
	1.8		
	1.9		
	1.10	1.10.1	
		1.10.2	
		1.10.3	
		1.10.4	
	1.11		
	1.12		
	1.13		
	1.14		

Documents rolled up to this level are not considered appropriate
One document may be submitted at this level

PART B: MODULE 1

Module 1 should contain all administrative documents (e.g. application forms and certifications), labelling, general correspondence and annexes as needed. Documents should be organised in the order listed below. Generally, all of the documents in Module 1, other than the annexes, can be provided in a single volume. The annexes to the module should be submitted in separate volumes.

Module 1.0 Letter of Application

Documentation		
1.	1.0	Letter of Application

Applicants should include a *Letter of Application* with all applications. A copy of the letter should be placed at the beginning of Module 1.

At least the following should be addressed in the letter of application:

- If the application is being submitted simultaneously with one or more additional applications for the identical product this should be stated and also confirmed that the submissions are identical except for the proprietary name.
- If the dossier has been licensed in from a third party and the third party's name or logo is included in documents in the dossier, an explanation should be provided in the cover letter to clarify the relationship between the third party and the applicant.
- Clarification if the proprietary name in the original dossier (e.g. where a product has been licensed in) differs from the proposed proprietary name included in the application for registration.
- If relevant, justification for empty sections in Module 1 is to be provided in the cover letter.

For further submissions during the registration process or post-registration amendments the covering letter must be included here.

If replying to a letter from the Registrar of Medicines, a copy of this letter must be included here.

Module 1.1 Comprehensive table of contents

Documentation		
1.	1.1	Comprehensive table of contents

Module 1 should include a comprehensive table of contents for the entire application. The comprehensive table of contents should include a complete list of all documents provided in the application by module.

In the table of contents, the location of each document should be identified by referring to the volume numbers that contain the relevant documents and any tab identifiers. In general, the name for the tab identifier should be the name of the document (section heading according to the CTD format e.g. 3.2.P.4.2). If the full name of the document is too long for the tab identifiers, an alternative name that adequately identifies the document should be substituted.

Page numbers only should not be used in the table of contents to refer to documents, rather; tab identifiers as described above should be used. Page numbers in addition to the tab identifier should be used to facilitate location within documents where relevant.

Module 1.2 Application

Documentation		
1.	1.2.1	Application Form
2.	1.2.2	Annexes to the application form

1.2.1 Application form

An application to register a prescription medicine for human use in Namibia must be accompanied by a completed application form[1]. The paper application form is available on the NMRC website [2]. The application form must also be submitted with every response to a Council recommendation and/or an application for amendment of the dossier.

In addition to the paper dossier, Module 1.2.1 should be submitted electronically on CD or DVD.

1.2.2 Annexes to the application form

1.2.2	1.2.2.1	Proof of payment
	1.2.2.2	Letter of authorisation for communication on behalf of the applicant/PHCR
	1.2.2.3	Dossier product batch information
	1.2.2.4	Electronic copy declaration
	1.2.2.5	Curriculum vitae of the qualified person for pharmacovigilance
	1.2.2.6	API change control
	1.2.2.7	Copy of EMA certificate for a Vaccine Antigen Master File (VAMF)
	1.2.2.8	Copy of EMA certificate for a Plasma Master File (PMF)

1.2.2.1 Proof of payment

Include a copy of the proof of payment. For the various fees, refer to Fees payable to the Registrar.[3]

1.2.2.2 Letter of authorisation for communication on behalf of the applicant/PHCR

The application must be signed by the pharmacist responsible for the compilation of the application. This should be an original signature (scanned signature not acceptable). Attach an individualised, person specific letter of authorisation for the signatory, issued by the Person responsible for the overall management and control of the business (CEO).

Note that such a letter is not required for the Responsible Pharmacist if the Responsible Pharmacist signs the application.

[1] Namibian Module 1.2.1

[2] www.nmrc.com.na

[3] www.nmrc.com.na

1.2.2.3 Dossier product batch information

The following are particulars which clarify the pharmaceutical development of the dosage form, from which data furnished in the undermentioned Modules were derived:

	3.2.P.3	3.2.P.5	3.2.P.8	3.2.R.1	
	Manufacture	Control of final pharmaceutical product	Stability	Bioequivalence	Dissolution
1. *Types of batches					
2. Lot number/s					
3. Lot size/s					
4. Date/s of manufacture					
5. Site/s of FPP manufacture					
6. Formulation and manufacturing process as applied for (Y/N) (clarify if not)					
7.** Site 1 of API 1					
8. Site 2 of API 1					
9.** Site 1 of API 2					
10. Site 2 of API 2					

* Experimental, pilot or production

** Add as many rows as necessary for APIs and API manufacturing sites

1.2.2.4 Electronic copy declaration

Both paper and electronic submissions must comply fully with the Common Technical Document as regards presentation and content of the dossier. Any documents submitted on CD-ROM/DVD have to be declared identical to that in the paper submission.

When electronic dossiers are supplied to replace approved paper dossiers, Applicants must submit an affidavit in which they confirm that the data on the CD-ROM/DVD supplied is identical to that in the written submission.

1.2.2.5 Curriculum vitae of the qualified person responsible for pharmacovigilance

Include curriculum vitae of the qualified person responsible for pharmacovigilance.

1.2.2.6 API change control

A formal agreement exists between the applicant of the medicine and each manufacturer of the active pharmaceutical ingredient (API), which ensures that information will be communicated between them and to the NMRC before any significant change is made to the site of manufacture, manufacturing procedure or quality control specifications of the API. Except when permitted by the NMRC's Amendments guideline relating to changes to medicines, such changes will not be made to the API(s) to be used in manufacture of medicines destined to be distributed in Namibia before written approval is granted by the NMRC. Both parties understand that the consequences of failure to obtain approval for changes where approval is necessary may include de-registration and recall of batches of medicines containing this material in Namibia.

1.2.2.7 Copy of EMA certificate for a Vaccine Antigen Master File (VAMF)

Insert a copy of the European Medicines Agency certificate for a Vaccine Antigen Master File (VAMF) if applicable.

1.2.2.8 Copy of EMA certificate for a Plasma Master File (PMF)

Insert a copy of the European Medicines Agency certificate for a Plasma Master File, if applicable.

Module 1.3 Namibian labelling and packaging

Documentation	
1.3.1	Namibian Package Insert
1.3.1.1	Package Insert
1.3.1.2	Standard References
1.3.2	Patient Information Leaflet
1.3.3	Labels
1.3.4	Braille

Applicants should include the proposed or approved texts of Package Insert (PI) (Module 1.3.1) and Patient Information (PIL) leaflet (Module 1.3.2). Namibian specific labels should be submitted in Module 1.3.3 (mock-ups, specimens or text).

1.3.1 Namibian Package Insert

1.3.1.1 Package Insert

Module 1.3.1.1 should include a copy of the Namibian PI - either the proposed PI in the case of a new application, or the currently approved PI in the case of amendments. The PI shall comply with Regulation 12 of the Medicines & Related Substances Control Act 13 of 2003, the requirements of the General Information Guideline, the Package Insert Guideline and any class labelling requirements that may be issued by the NMRC from time to time.

For package insert amendments, these should be submitted in accordance with the Package Insert Guideline. See also Module 1.5.5

1.3.1.2 Standard References

Refer to the Package Insert Guideline for requirements in terms of standard references.

1.3.2 Namibian Patient Information Leaflet

Module 1.3.2 should contain a copy of the proposed or approved Namibian consumer medicine information, also known as *Patient Information Leaflet (PIL)*.

For details of the format and content see Regulation 13 of the Medicines & Related Substances Control Act 13 of 2003.

1.3.3 Labels

Regulation 11 of the Medicines & Related Substances Control Act 13 of 2003 must be complied with unless otherwise exempted.

If the applicant has a specimen or mock-up of the sales presentation of the medicine available at the time of initial application, it should be included in Module 1.3.3.

A mock-up is a copy of the flat artwork design in full colour, providing a replica of both the outer and immediate packaging, providing a two-dimensional presentation of the packaging / labelling of the medicine. It is also referred to as a paper copy or computer generated version.

A specimen is a sample of the actual printed outer and inner packaging materials and package leaflet. If there are multiple strengths and/or pack sizes, one representative specimen or mock-up will be sufficient. If batch number and expiry date are to be printed on the label during packaging, a statement to this effect should accompany the labels. If mock-ups or specimens are not available at the time of initial application, a text version may be submitted.

1.3.4 Braille

For future use.

Module 1.4 Information about the experts

Documentation	
1.4.1	Declaration signed by the expert - Quality
	Information about the Expert - Quality
1.4.2	Declaration signed by the expert - Non-clinical
	Information about the Expert - Non-clinical
1.4.3	Declaration signed by the expert - Clinical
	Information about the Expert - Clinical

Experts must provide detailed reports of the documents and particulars, which constitute Modules 3, 4 and 5.

The requirement for these signed Expert Reports may be met by providing:

- The Quality Overall Summary, Non-clinical Overview / Summary and Clinical Overview / Summary in Module 2,

- A declaration signed by the experts in Module 1.4.
- Brief information on the educational background, training and occupational experience of the experts in Module 1.4.
- In cases concerning well-known active pharmaceutical ingredients, the Council may grant exemption from the submission of sections 1.4.2 and 1.4.3.

References must be provided for any additional claims not supported by the dossier.

Module 1.5 Specific requirements for different types of applications

Documentation		
1.	1.5.1	Literature based submissions
	1.5.2	Amendments / Variations
	1.5.2.1	Tabulated schedule of amendments
	1.5.2.2	Medicines Register Details
	1.5.2.3	Affidavit by Responsible Pharmacist
2.	1.5.3	Proprietary name applications and changes
3.	1.5.4	Genetically modified organisms (GMO)
4	1.5.5	Package Insert and Patient Information Leaflet amendments / updates

1.5.1 Literature based submissions

If clinical evidence in support of efficacy is not submitted, studies and data to demonstrate the pharmaceutical and/or biological availability of the product should be included. If in the opinion of the applicant no data are required to substantiate efficacy (e.g. parenteral solutions) the rationale for accepting safety and efficacy, including reference to standard Reference Books, should be clearly stated. Refer to Registration Guideline and SADC Bioavailability / Bioequivalence Guideline. [3]

For package insert amendments, refer to the Package Insert Guideline.

1.5.2 Amendments / Variations

1.5.2.1 Tabulated schedule of amendments (refer to Post Registration Amendment Guideline)

1.5.2.2 Medicines Register Details

1.5.2.2.1 Medicines Register Details (refer to Post Registration Amendment Guideline)

1.5.2.2.2 Registration certificate
Include original or certified copy of registration certificate.

1.5.2.3 Affidavit by Responsible Pharmacist (refer to Post Registration Amendment Guideline)

1.5.3 Proprietary name applications and changes

Submit a letter with details on the current and proposed names and the reason for the change in Module 1.0.

Include any information in support of a proposed name or alternative proposed names in this section 1.5.3

Changing of the proprietary name during the evaluation and registration phase will only be permitted if the Council has not accepted the name originally proposed by the HCR/applicant.

Proof of payment must be filed under 1.2.2.1

1.5.4 Genetically modified organisms

Genetically modified organism (GMO) means an organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination.

1.5.5 Package Insert and Patient Information Leaflet amendments / updates

Include annotated PI / PIL for any proposed amendments to an approved PI / PIL.
When updating or amending clinical aspects of the PI/PIL, the Storage Instructions should be updated to reflect the currently accepted wording. Refer to the Amendments guideline.

Module 1.6 Environmental risk assessment

For future use.

Module 1.7 Good manufacturing practice

Documents required by the Inspectorate		
1.	1.7.1	Date of last inspection of each site
2.	1.7.2	Inspection reports or equivalent document
3.	1.7.3	Latest GMP certificate or a copy of the appropriate licence
4.	1.7.4	Release
	1.7.4.1	API
	1.7.4.2	IPIs
	1.7.4.3	Finished Product Release Control (FPRC) tests
	1.7.4.4	Finished Product Release Responsibility (FPRR) criteria
5.	1.7.5	Confirmation of contract
6.	1.7.6	CPP (WHO certification scheme) if applicable
7.	1.7.7	Namibia Pharmacy Council registration
8.	1.7.8	Registration with the Registrar of Companies
9.	1.7.9	Proof of qualification as an applicant (in terms of Regulation 3 (1) of the Medicines & Related Substances Control Act 13 of 2003.
10.	1.7.10	Sample and Documents
	1.7.10.1	Confirmation of submission of the sample
	1.7.10.2	BMR of the sample (or refer to 3.2.R.8, or confirm available for inspection)
	1.7.10.3	CoA of sample (final product and API used)
11.	1.7.11	Certified copy of permit to manufacture S5, S6, S7 and S8 substances
12.	1.7.12	Inspection flow diagram
13.	1.7.13	Organogram

For all medicines, irrespective of the country of origin, it is expected that key manufacturing and/or processing steps in the production of active ingredients and finished pharmaceutical products are performed in plants of acceptable standards (see WHO GMP Guideline).[4]

1.7.1 Date of last inspection of each site

The applicant should provide a list of manufacturers', packers' and FPRCs' names and licence numbers, with a list of the dates of inspection by the Health Authorities of either SA, US FDA, MHRA, TGA, EU, Canada, Japan at each site. [Annexure II of the Regulations]

1.7.2 Inspection reports or equivalent document

The applicant should provide copies of inspection reports or equivalent document, not older than three years, from the Health Authorities of either SA, US FDA, MHRA, TGA, EU, Canada, Japan at each site.

1.7.3 Latest GMP certificate or a copy of the appropriate licence

Include the latest GMP certificate, not older than three years, for manufacturer/s, packer/s and FPRCs or a copy of the appropriate licence.

1.7.4 Release

1.7.4.1 API

The following minimum requirement should be confirmed and the name and physical address of the laboratory (ies) performing the tests stated:

a) Identification and assay of the API will be performed by the product manufacturer irrespective of the possession of a CoA from the API manufacturer.
b) Any tests included in the specifications and not included in a valid CoA will be performed.

1.7.4.2 IPIs

(1) The following minimum requirement should be confirmed and the name and physical address of the laboratory (ies) performing the tests stated:
   a) Identification of the IPI will be performed irrespective of the possession of a CoA from the supplier.
   b) Any tests included in the specifications and not included in a valid CoA will be performed.

(2) For IPIs for which a conclusive identification test is not described, all parameters that are specific to the identification of such ingredients should be listed and the tests performed irrespective of the possession of a CoA from the supplier.

1.7.4.3 Finished Product Release Control (FPRC) tests

For future use

1.7.4.4 Finished Product Release Responsibility (FPRR) criteria

For future use

1.7.5 Confirmation of contract

The applicant should include a signed declaration that contracts with all third party manufacturer/s and/or packer/s and FPRC/s are in place, and these should be available for inspection purposes.

[4] www.who.int

1.7.6 CPP (WHO certification scheme) (if applicable)

This is the information required by the Inspectorate.

1.7.7 Pharmacy Council of Namibia registration

1.7.7.1 Proof of current registration of the Responsible Pharmacist by the Pharmacy Council of Namibia

Submit a copy of the Namibia Pharmacy Council Registration certificate of the responsible pharmacist and also proof of current registration (annual registration card) OR

Proof of authorization of the technical person by the NMRC to act as representative responsible for communication with Council in terms of Regulation 3 (4) of the Medicines & Related Substances Control Act 13 of 2003

1.7.7.2 Proof of current registration by the Namibia Pharmacy Council or equivalent in the country of origin of the pharmacist signing the dossier or an authorised person

Submit a copy of the Namibian Pharmacy Council Registration certificate equivalent in the country of origin of the pharmacist signing the dossier and also proof of current registration (annual registration card), if different from the Responsible Pharmacist or copy of authorisation for the person signing dossier.

1.7.8 Registration with the Registrar of Companies in Namibia

Submit a copy of the certificate of registration of the company with the Registrar of Companies (if relevant).

1.7.9 Proof of qualification as an applicant (in terms of Regulation 3 (1) of the Medicines & Related Substances Control Act 13 of 2003.

If the applicant is a person residing in Namibia, submit proof of residence.

If the applicant is manufacturer or a subsidiary of a manufacturer in foreign country, submit copy of registration by the medicines regulatory authority in that country. In addition, a subsidiary should submit proof that the manufacturer partly or wholly owns the subsidiary.

If the applicant is a manufacturer in Namibia, submit proof of registration of the manufacturing premises by NMRC.

1.7.10 Sample and Documents

1.7.10.1 Confirmation of submission of a sample: All medicine applications for registration must include three samples of the medicine in the smallest pack (refer to Regulation 5 (a) of the Medicines & Related Substance Control Act).

1.7.10.2 Batch manufacturing record of the sample

a) included in Module 3.2.R.7 or

b) available for inspection

1.7.10.3 CoA of the sample

Include the CoA of the FPP and of the API used in the sample. Ensure that the batch number on the CoA corresponds with the batch number on the sample.

1.7.11 Certified copy of a permit to manufacture specified Schedule 3, 4 and 5 substances

Include a duly certified permit to manufacture Schedule 3, 4 and 5 (specified list) substances.

1.7.12 Inspection flow diagram

Submit the Inspection flow diagram, also of FPP intermediates, clearly indicating the sites and processes, including clear distinction between primary and secondary packers.
Ensure that all role players are filled in and that final release for distribution is an FPRR function.

1.7.13 Organogram

Include the current company organogram, reflecting the Responsible Pharmacist and other key responsibilities.

Module 1.8 Details of compliance with screening outcomes

Documentation:	
1.	Details of compliance with screening outcomes
2.	Details of any additional data submitted

Address the screening comments and where documentation is involved only provide an overview of the relevant documentation submitted. Applicants should not modify the overall organisation of the CTD; amended modules must be filed under the appropriate CTD section.

A copy of the completed screening template must be included in module 1.8, with the original completed form being submitted separately with the application.

If new document versions are submitted, an updated version of Module 1.2.1 must also be submitted.

Module 1.9 Individual patient data - statement of availability

Documentation:	
1.	Declaration concerning availability of individual patient data

Include a statement that raw clinical and pre-clinical data have been removed from the application and that individual patient data are available on request.

Data in respect of each individual patient from each clinical trial are not required to be included in the documentation at the time of application, except in the case of any bioavailability studies where individual patient data (IPD) for plasma concentrations and derived data are required.

The individual patient data, may be requested during the evaluation period and, if a request for these data is not met within 15 working days, the application will usually lapse. Individual patient data may be requested by the NMRC:

- to support a particular study if, during the evaluation, there is any reason to doubt the analysis or conclusions reached;
- if, after registration, the application is selected for auditing of the summary results and conclusions.

If a marketing application for the medicine has been rejected in the USA, UK, Sweden, Australia, Canada, EU, or Japan, before or during the Namibian evaluation process, for reasons related to the clinical data in any way, full individual patient data must always be available and may be required to be submitted in Namibia. In the event that the Namibian evaluation process has commenced, applicants should contact the Registrar of Medicines.

Module 1.10 Foreign regulatory status

Documentation:		
1.	1.10.1	List of countries in which an application for the same product as being applied for has been submitted

1.10.2	Registration certificates or marketing authorisation
1.10.3	Foreign prescribing and patient information
1.10.4	Data set similarities

Applicants are advised that this module should be completed for all applications (including those for multisource products).

1.10.1 List of countries in which an application for the same product as being applied for has been submitted

The applicant should provide, in Module 1.10.1 of the dossier, a list of countries in which an application for the same product as being applied for in Namibia has been submitted, dates of submission (if available). This should detail approvals (with indications).

Applicants must declare whether a marketing application for the medicine has been rejected in the countries listed under 1.10.1 prior to submission of the application in Namibia. If the medicine has been rejected, repeatedly deferred or withdrawn, then the NMRC must be informed and the reasons supplied.

If no application has been submitted for registration in the country of origin, include a statement to provide the reason for this decision.

1.10.2 Registration certificates or marketing authorisation

In the case of registration in the country of origin, or where a marketing authorisation has been granted by the health authority of a country with which Council aligns itself, copies of the registration certificates or marketing authorisation should be supplied in Module 1.10.2.

1.10.3 Foreign prescribing and patient information

In the case of marketing authorisations in country of origin, or where marketing authorisation has been granted by the health authority of a country with which Council aligns itself (see General Information guideline 3.1.4) copies of relevant prescribing and patient information should be supplied in Module 1.10.3, e.g. the Canadian Product Monograph, the Summary of Product Characteristics (SPC) in the EU, UK, and Sweden, Prescribing Information (PI) in USA. If the overseas SPC, monograph or PI has not been approved at the time the application is lodged in Namibia, a draft document may be included. The approved overseas SPC, monograph or PI should then be supplied to the NMRC as they become available.

1.10.4 Data set similarities

Module 1.10.4 should contain a summary of the similarities / differences in the data packages submitted in other countries.

Module 1.11 Bioequivalence trial information

Documentation		
1.	1.11.1	Study Title(s) (or brief description giving design, duration, dose and subject population of each study)
	1.11.2	Protocol and study numbers
	1.11.3	Investigational products (test and reference) details in tabulated format, including
		• active ingredient
		• strength
		• dosage form
		• manufacturer
		• batch no
		• expiry or retest date
		• country in which procured
	1.11.4	Confirmation that the test product formulation and manufacturing process is that being applied for
	1.11.5	Proof of procurement of the biostudy reference product (may include cross-reference to 3.2.R.1)
	1.11.6	Name and address of the Research Organisation(s) / Contract Research Organisation(s) where the bioequivalence studies were conducted
	1.11.7	Sponsor and responsible sponsor representative: name and address, contact details
	1.11.8	Duration of Clinical phase: dates of dosing and last clinical procedure
	1.11.9	Date of final report

Namibia's requirements for biopharmaceutic studies are described in the SADC Bioavailability/Bioequivalence Guideline. [3]
The BE guideline is based to a large extent on the FDA guidelines and the relevant WHO guidelines e.g. TSR Annexes 7, 8 and 9. It also takes into account relevant CHMP *Note for Guidance of Bioavailability and Bioequivalence* (CPMP/EWP/QWP/1401/98). [4]

In relation to the content of biopharmaceutic study reports, this guideline states that: The report of a bioavailability or bioequivalence study should give the complete documentation of its protocol, conduct and evaluation complying with GCP rules.

The NMRC considers it essential that the principal investigator(s) sign the study reports after their completion, either in an unqualified fashion or clearly taking responsibility for all aspects of the conduct of the study for which they might reasonably be held responsible. If the signature of the principal investigator is absent from the report of a bioavailability or bioequivalence study, it will be requested by the NMRC during the evaluation process.

Module 1.12 Paediatric development program

Documentation

1.	1.12	References to paediatric development program

There is a recognised global problem with the availability of paediatric-specific formulations and a lack of information from proper investigations of the use of medicines in children. This problem leads to medicines being used outside of their approved indications, and, at times, being reformulated by pharmacists to make them more suitable for use by children. However, the basic precept that children should not be discriminated against by being supplied poorly investigated medicines has been accepted internationally.

The CTD guidelines require that the safety and efficacy in the paediatric population should be routinely analysed in applications for a proposed indication that occurs in children.

Please state whether there is a paediatric development program for this medicine and if so, the relevant sections of the dossier.

Module 1.13 Risk management plan

For future use

NA CTD MODULE 1.7.12

INSPECTION FLOW DIAGRAM OF MANUFACTURED PRODUCTS

PRODUCT DETAILS

Product Name : _____

Reg. no. : _____

PHCR/Applicant : _____

Dosage form : _____

Strength(s) : _____

Pack sizes(s) : _____

LOCATION

A : _____

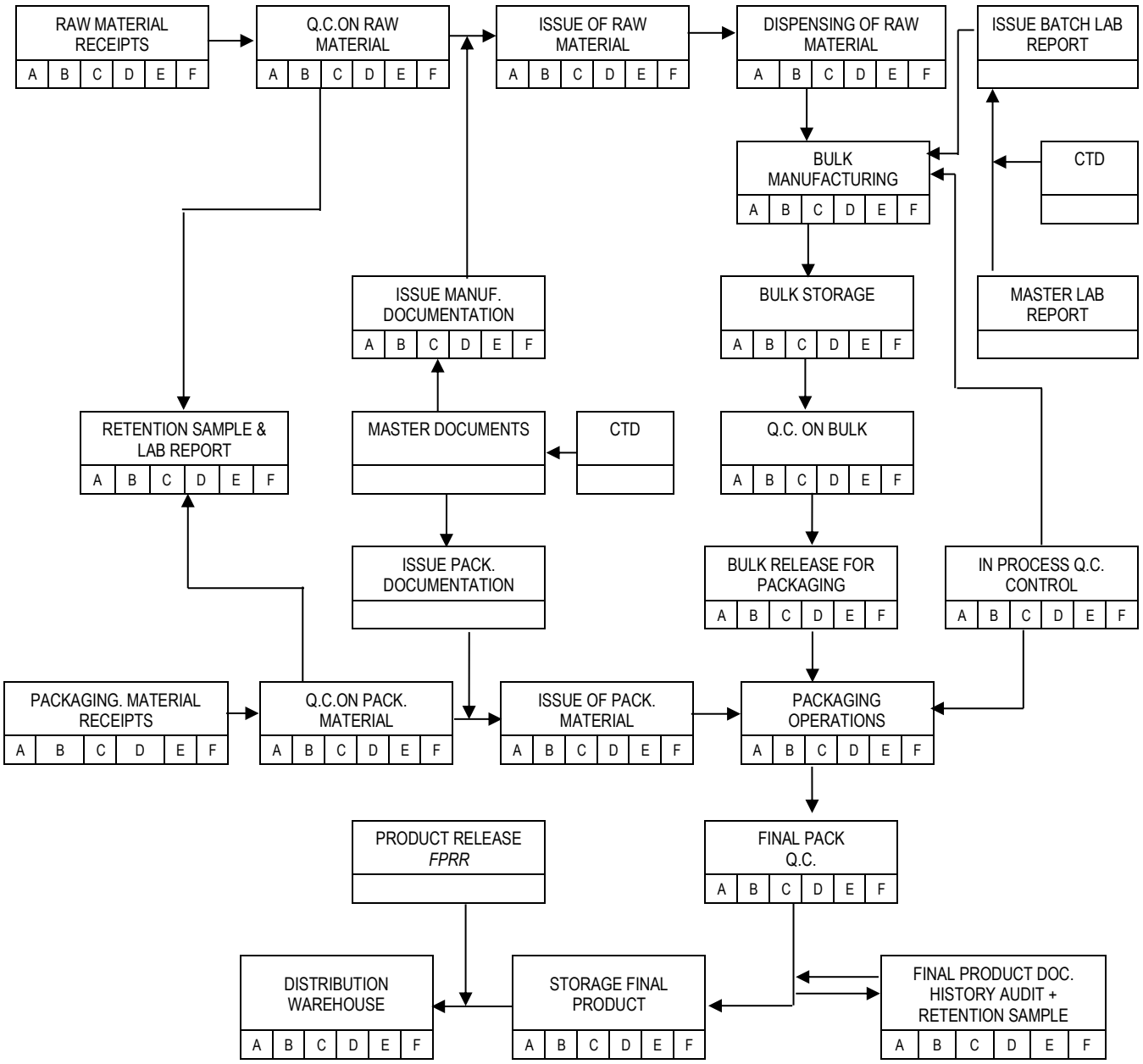
B : _____

C : _____

D : _____

E : _____

F : _____



References

1. Medicines Control Council. South African Guidance for the submission of the South African CTD/eCTD – General & Module 1, August 2012
2. Guidelines on submission of documentation for a multisource (generic) finished product. General format: preparation of product dossiers in common technical document format In: *WHO Expert Committee on Specifications for Pharmaceutical preparations. Forty-fifth report.* Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 15
3. SADC Bioavailability/Bioequivalence Guideline.
4. CHMP *Note for Guidance of Bioavailability and Bioequivalence* (CPMP/EWP/QWP/1401/98).

UPDATE HISTORY

Date	Reason for update	Version & publication