

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY



**GUIDELINES ON SUBMISSION OF DOCUMENTATION FOR RENEWAL OF
MARKETING AUTHORIZATION OF HUMAN AND VETERINARY
MEDICINAL PRODUCTS**

*(Made under section 17 of the Tanzania Medicines and Medical Devices (Registration of
Medicinal Products) Regulations, 2015)*

January, 2021

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Akida M. Khea
Acting Director, Medical Products Control

FOREWORD


Tanzania Medicines and Medical Devices Authority (TMDA) was established under the Tanzania Medicines and Medical Devices Act, Cap. 219 with the mission of protecting and promoting public health by ensuring quality, safety and effectiveness of medicines, medical devices and in-vitro diagnostics. The primary step towards achieving this goal is to conduct pre-market evaluation of products so as to ensure that they meet standards of quality, safety and effectiveness before being allowed to circulate on the market. This is a fundamental requirement for authorization of medicinal products in Tanzania. In order to have consistent and uniform submissions, TMDA on regular basis issues application guidelines to provide guidance to applicants on content and format of minimum information required for new and renewal of registration of medicinal products.

Recognizing that during the life cycle of a medicinal product, there are current and emerging technical requirements which need to be met at all times. Therefore, it had been considered necessary to review these guidelines to address the existing gaps in terms of technical requirements during approval of applications for re-registration.

This is the second revision of the *Guidelines on Submission of Documentation for Renewal of Marketing Authorization of Human and Veterinary Medicinal Products*, which incorporates changes in processing applications due to the implementation of the online electronic application system. The revision has been done to align the guidelines with the CTD format requirements and also introduces the requirement of submitting the Quality Information Summary (QIS) document. The requirements specified in the guidelines have been developed taking into consideration the best practices gathered from other countries.

All applicants are encouraged to familiarize with the guidelines and follow them while preparing and submitting applications for renewal of registration of human and veterinary medicinal products. However, the guidelines are not intended to restrict innovation and they only provide for the minimum requirements thereby providing opportunity for applicants to submit additional data.

Adherence to these guidelines will ensure that all relevant information is provided in registration dossiers submitted for renewal of registration and hence facilitate efficient and effective evaluation. It will also assist to avoid queries which results in unnecessary delays in authorizing re-registration, thereby improving access to medicines of proven quality, safety and efficacy in the shortest time possible.



Adam M. Fimbo
Director General

ABBREVIATIONS

API	-	Active Pharmaceutical Ingredient
CEP	-	Certificate of Suitability to the European Pharmacopeia
DMF	-	Drug Master File
FPP	-	Finished Pharmaceutical Product
GMP	-	Good Manufacturing Practices
ICH	-	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
INN	-	International Non-proprietary Name
OoS	-	Out of Specification
PIL	-	Patient Information Leaflet
POM	-	Prescription Only Medicine
SmPC	-	Summary of Product Characteristics
TMDA	-	Tanzania Medicines and Medical Devices Authority

1. INTRODUCTION

Section 51 of the Tanzania Medicines and Medical Devices Act Cap. 219 prescribes that a medicinal product shall be registered only if:

- (a) The availability of the medicine is in the public interest;
- (b) The medicine is proved to be safe, efficacious and of acceptable quality;
- (c) The premises and manufacturing operations comply with the current Good Manufacturing Practice (GMP) requirements; and
- (d) The medicine complies with any other requirements as may be prescribed by the Authority.

Furthermore, Section 22 (1) of the Act prohibits the sell, supply or importation of any drug unless it is registered in accordance with the provisions of the Act. According to section 13 of the Tanzania Medicines and Medical Devices (Registration of Medicinal Products) Regulations, 2015, certificate of registration of a medicinal product shall unless earlier suspended or revoked, and subject to payment of prescribed annual retention fees is valid for a period of five (5) years from the date of issuance.

It is acknowledged that in the course of five (5) years, several aspects of the registered medicinal product may change significantly as a result of notified variations and other un-notified changes in manufacturing and control of the products. These may have significant impact on the respective product and therefore, the objective of renewal of registration is to ensure that the product continues to conform to the above-mentioned requirements.

Section 17 of the regulations further provides for requirements for application for renewal of registration of a medicinal product.

The guidelines therefore accommodate the steps that are followed from the submission of a dossier to the final outcome, the timeframe and procedure for the Authority to amend, where necessary the conditions of renewal of registration of a particular product.

The guidelines are divided into three major parts stipulating the general requirements and application procedures for human and veterinary medicinal products; processing of applications; and technical requirements for application for renewal of medicinal products.

Applicants are requested to carefully read these guidelines, fill in application forms, and upload the relevant sections of the dossier in the TMDA online application portal.

The guidelines present current thinking on technical requirements necessary to facilitate renewal of registration of medicinal products. Evaluation of the applications will as far as possible be based on the principles laid down in these guidelines. It is worth noting that TMDA will not accept outdated methods and techniques in the interest of patient safety and well-being. Furthermore, the Authority will evaluate products based on up-to-date scientific knowledge and standards known or existing at the time of evaluation. Applicants are therefore encouraged to keep abreast with

scientific developments and apply the most current scientific information and technology to develop and test their products.

Applicants are also requested to read these guidelines together with the Tanzania Medicines and Medical Devices Act, Cap. 219 and other relevant Regulations made there under.

2. GLOSSARY

In the context of these guidelines, the following words/phrases are defined as follows:-

Active Pharmaceutical Ingredient (API)

Means a substance or compound that is intended to be used in the manufacture of a medicinal product as a therapeutically active compound (ingredient).

Authority

Means the Tanzania Medicines and Medical Devices Authority, or its acronym - TMDA established under Section 4 of the Tanzania Medicines and Medical Devices Act, Cap. 219.

Drug Master File

A drug master file (DMF) is a master file that provides a full set of data on an API.

Finished Pharmaceutical Product (FPP)

Means a product that has undergone all stages of production, including packaging in its final container and labeling.

Manufacturer

Means a person or firm that is engaged in the manufacture of pharmaceutical product(s).

Medicinal product, Drug, medicine or pharmaceutical product

Means any substance or mixture of substances manufactured, sold or represented for use in:

- (a) The diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical or mental state, or the symptoms thereof, in man;
- (b) Restoring, correcting or beneficial modification of organic or mental functions in man;
- (c) Disinfection in premises in which drugs are manufactured, prepared or kept, hospitals and equipment;
- (d) Articles intended for use as a component of any articles specified in clause(a), (b) or (c); but does not include medical devices or their components, parts or accessories.

Pharmacopoeia

Means a current edition of the British Pharmacopoeia, European Pharmacopoeia, United States Pharmacopoeia, International Pharmacopoeia and Japanese Pharmacopoeia.

Registration of a medicine or Marketing authorization

Means an official authorization or registration of a product by TMDA for the purpose of marketing or free distribution in Tanzania after evaluation for safety, efficacy and quality.

Variation

Means a change to any aspect of a medicinal product, including but not limited to a change to formulation, method and site of manufacture, specifications for the finished product and ingredients, container and container labeling and product information.

3. SCOPE

These guidelines are relevant for application for renewal of marketing authorization of both human and veterinary medicinal products.

4. POST RENEWAL VARIATION TO MEDICINAL PRODUCTS

All variations to a registered pharmaceutical product shall be made according to requirements stipulated in the *Application Guidelines for Variation of Registered Medicinal Products*. No variation will be accepted during submission of renewal of registration.

5. REQUIREMENTS FOR RENEWAL APPLICATIONS

5.1 GENERAL REQUIREMENTS AND APPLICATION PROCEDURES

Applications should be made to the Authority at least ninety (90) days before expiry of validity of registration of a particular medicinal product. Please make note of the following:

- 5.1.1 All applications and supporting documents shall be in English. The submitted documents which are in any language other than English must be accompanied by a certified or notarized English translation.
- 5.1.2 The responsibility of applying for renewal of product registration remains with the company responsible for the introduction of the product into the Tanzanian market, i.e., the Marketing Authorization Holder (MAH).
- 5.1.3 Applications must be duly completed and supported by all of the required documents as stipulated in these guidelines and where appropriate in line with the current edition of the *Compendium of Guidelines for Marketing Authorization of Human Medicinal Products* and *Guidelines on Submission of Documentation for Registration of Veterinary Medicinal Products*.
- 5.1.4 The application should be submitted online along with a non-refundable product renewal fees as stipulated in the Tanzania Medicines and Medical Devices (Fees and Charges) Regulations in force. The evidence of payment of the fees must be presented at the time of submission of the product samples.
- 5.1.5 Two samples of the smallest commercial pack(s) from a single batch along with its certificates of analysis should be submitted. Kindly note that a complete application includes submission of physical samples. Therefore, the date of submission of the samples will be considered as the date of receiving the renewal application.
- 5.1.6 The evidence of conformance of the finished product manufacturing facility with the current good manufacturing practice (GMP) requirements as prescribed in the GMP guidelines of TMDA, should be provided.
- 5.1.7 List of all countries should be provided, where the product has been reviewed and approved over the registration period of the product along with their registration numbers. If available, copies of registration certificates should be submitted.

5.2 PROCESSING OF APPLICATIONS (MANAGEMENT OF APPLICATIONS)

The following stages are involved for renewal applications from the time of application submission to the final outcome:

- 5.2.1 Upon receipt of an application, a tracking number will be auto-generated.
- 5.2.2 Pre-checking will be done by the Authority and if satisfactory an invoice will be issued. After payment, a reference number will be auto-generated which

should be quoted during any communications made to the Authority regarding the product.

- 5.2.3 Evaluation of the application shall be carried out within the timelines stipulated in the Clients Service Charter implemented by the Authority and the respective outcomes will be communicated to the applicant(s);
- 5.2.4 In the course of evaluation, the Authority may request for further information and additional supporting documents from the applicant. Required information should be made available within sixty (60) days from the date of the request so as to facilitate timely renewal of the applied product;
- 5.2.5 Notification for renewal of registration of the product shall be communicated followed by an issuance of new registration certificate. Applicants should carefully read the conditions under which the medicine is registered overleaf the certificate and adhere to them throughout the product lifecycle.

5.3 TECHNICAL REQUIREMENTS FOR APPLICATION FOR RENEWAL OF MEDICINAL PRODUCTS

All applications for renewal of registration of human and veterinary medicinal products shall be accompanied by the following documentation/requirements:

5.3.1 ACTIVE PHARMACEUTICAL INGREDIENT(S) [API(S)]

- 5.3.1.1 Names and complete addresses of all current suppliers of active pharmaceutical ingredient(s) along with manufacturing and GMP certificates of the active pharmaceutical ingredient(s) manufacturing facilities issued by competent regulatory authorities;
- 5.3.1.2 Copy of current signed, dated and numbered specifications and analytical procedures used for testing of the active pharmaceutical ingredient(s) by the finished product manufacturer;
- 5.3.1.3 Information on container-closure system used for storage of the API in FPP manufacturer's storage facilities, storage conditions specified for the API and re-test period/shelf life implemented for the respective API;

5.3.2 FINISHED PHARMACEUTICAL PRODUCT (FPP)

- 5.3.2.1 Detailed description of qualitative and quantitative composition of the unit dosage form and of the commercial batch size(s) approved including colourants, coating agents in a manner provided for in section 3.2.P.1 of the main registration guidelines for human and veterinary medicinal products;
- 5.3.2.2 A copy of batch manufacturing record (BMR) for the largest production batch manufactured within six months before the date of submission of the renewal application;
- 5.3.2.3 Report on annual product quality review for all batches of the finished product manufactured in the past 36 months before the date of application

of the renewal. At minimum the report should include the following:

- a) A review of starting and primary packaging materials used in the FPP, especially those from new sources;
- b) A tabulated review of quality control and in-process control results;
- c) A review of all batches that failed to meet established specification(s);
- d) A review of all changes carried out to the processes or analytical methods;
- e) A review of the results of the stability monitoring programme; and
- f) A list of validated analytical and manufacturing procedures and their revalidation dates.

5.3.2.4 A copy of current signed, dated and version numbered release and shelf life specifications of the finished products along with standard testing procedures;

5.3.2.5 Information on container closure system(s). Data should be submitted according to the requirements stipulated under section 3.2.P.7 of the main registration guidelines for human and veterinary medicinal products;

5.3.2.6 Data on stability study. For pharmaceutical products previously registered with long term stability data which do not support stability of the product under zone IVB conditions, data should be provided to demonstrate stability of the product under storage conditions of 30°C ± 2°C/75% ± 5% relative humidity. Studies should be conducted according to requirements stipulated under section 3.2.P.8 of the main Guidelines on Submission of Documentation for Registration of Veterinary Medicinal Products and specific guidelines on Stability Testing Requirements for Active Pharmaceutical Ingredients (APIs) and Finished Pharmaceutical Products (FPPs) as part of the *Compendium of Guidelines for Marketing Authorization of Human Medicinal Products*.

5.3.2.7 List of all variations (any minor and/or major changes) submitted to and accepted by TMDA over the registration period of the product.

Reference number	Description of the change	Date submitted	Approval/Rejection date and reference number of the letter	Implementation status

5.3.3 PRODUCT INFORMATION

5.3.3.1 Specimen of current package insert and copies of colored mock-up labels of the product as per current requirements prescribed in part V and VI of the current *Compendium of Guidelines for Marketing Authorization of Human Medicinal Products*.

5.3.3.2 All prescription medicines should be accompanied by SmPC presented in

both pdf and Microsoft word formats; Refer *Compendium of Guidelines for Marketing Authorization of Human Medicinal Products, Part IV*.

- 5.3.3.3 All pharmaceutical preparations with potential for long-term use and self-administered injections and general sales medicines must contain a patient information leaflet (PIL). Languages used for PIL and labelling should be clearly expressed in English and/or Kiswahili. Refer *Compendium of Guidelines for Marketing Authorization of Human Medicinal Products, Part IV*.
- 5.3.3.4 Submission of periodic post-marketing surveillance and safety studies for evaluation and determination of risk benefit profile of the registered product. The periodic safety update reports (PSURs) should include the information on the adverse effects observed for the product on the market.

6. REVISION HISTORY

Revision No.	Date	Description of Change
1	16 March, 2020	<ul style="list-style-type: none">- Change in the name of the Authority from <i>Tanzania Food and Drugs Authority</i> to <i>Tanzania Medicines and Medical Devices Authority</i>- Change of the Act from <i>Tanzania Food, Drugs and Cosmetics Act</i> to <i>Tanzania Medicines and Medical Devices Act</i>- Change of the control number of the guidelines from <i>TFDA/DMC/HVR/G/003</i> to <i>TMDA/DMC/MRE/G/003</i>
2	18 January, 2021	<ul style="list-style-type: none">- Inclusion of QIS document- Change in name of the guidelines from <i>Pharmaceuticals</i> to <i>Medicinal</i> to accommodate for all medicines- Other minor amendments including grammar improvements

ANNEX1: APPLICATION FORM FOR RENEWAL OF REGISTRATION OF HUMAN AND VETERINARY MEDICINAL PRODUCTS

General Instructions:

Please read all the instructions carefully prior to completing this Application form.

Provide as much details, accurate and complete information as possible. Note that all areas are to be filled out by the applicant EXCEPT where indicated by GREY COLOURS which are for TMDA Official Use Only.

Please state the exact location (Annex number) of any appended documents in the relevant sections of the form.

Before submitting the completed form, please countercheck to confirm whether you have provided all requested information.

This application form should be accompanied by a Batch Manufacturing Record (BMR) of all commercial batches manufactured within the last six months from the date of submission of this application.

Should you have any questions regarding this form, please contact the Tanzania Medicines and Medical Devices Authority (TMDA).

A properly filled out and signed original copy of the form with all its annexes must be submitted together with the medicinal quality part of the dossier electronically.

1. For official use only

1.1 Application Number		
1.2 Date of submission of the dossier		
1.3 Evaluator	Name	Signature
1.4 Auditor	Name	Signature
1.5 Date of evaluation		
1.6 Date of auditing		
1.7 Number of files		
Conclusion of the assessment <i>If the dossier is RECOMMENDED specify:</i>	RECOMMENDED (no outstanding issues) QUERY RAISED REJECTED <i>(Please delete which does not apply)</i>	
<p>2. To be filled in by the applicant</p>		
Type of the medicinal product Human Veterinary		
2.1 Registration number		

2.2 Date of expiry of current registration	
2.3 Proprietary Name of the Product	
2.4 International Non-proprietary Name (INN) of the Active Pharmaceutical Ingredient (API), strength,	
2.5 Medicinal Dosage form	
2.6 Route of administration	
2.7 Anatomic Therapeutic Classification (ATC) Code	
2.8 Name and address (physical and postal) of Applicant	
2.9 Name and address(es) of the manufacturer(s) of the active pharmaceutical ingredient(s). <i>(Add as many rows as necessary)</i>	
2.10 Site/location of manufacture of API (s)	
2.11 Name(s) and complete address (es) of the manufacturer(s) of the finished product(s), including the final product release if different from the manufacturer. <i>(Add as many rows as necessary)</i>	
2.12. Site/location of manufacture of FPP	
2.13 Name and complete address of the Local Technical Representative (LTR) and Local Responsible Person (who must be resident in Tanzania and in case of company be incorporated in Tanzania)	
2.14 Visual physical description of the FPP	
2.15 Packing/pack size	
2.16 Proposed shelf life (in months)	
2.17 Proposed shelf life (after reconstitution or dilution)	
2.18 Proposed shelf life (after first opening container)	

2.19 Proposed storage conditions	
2.20 Proposed storage conditions after first opening	
2.21 Distribution category: eg Controlled Drug <input type="checkbox"/> POM <input type="checkbox"/> Pharmacy Only <input type="checkbox"/> OTC <input type="checkbox"/> General sale <input type="checkbox"/> (Applicants are invited to indicate which categories they are requesting, however, the NMRA reserves the right to change and/or apply only those categories provided for in their national legislation)	
2.22 Country of origin	
2.23 Current registration status in other countries including East African community (EAC) and the Southern African Development Community (SADC) countries	

3. FINISHED PHARMACEUTICAL PRODUCT(s) [FPP(s)]						
3.1 Manufacturing and Marketing authorization						
3.3 Formulation						
Strength (label claim)						
Master Production Document Reference Number and/or Version						
Batch Size (number of dosage units)						
Ingredients (APIs and excipients) starting with APIs	Quality standard	Specification	Dosage per unit composition		Batch quantities	
			m g	%	kg	%

Film coating/Hard capsule

Composition of all *components that are mixtures* (e.g., colourants, coatings, capsule shells, imprinting inks):

Description of accompanying reconstitution diluents (s), if applicable:

3.4 Control of the FPP

3.4.1 Specifications for the FPP

Standard Claimed (e.g., In-house, BP, Ph. Eur., Ph. Int., USP)			
Specification Reference Number and/or Version			
Test	Analytical Procedure (Type/Source/Version)	Acceptance Criteria	
		Batch release	Shelf life

3.5 Container/closure system(s) and other packaging				
(a) Description of the container closure systems, including unit count or fill size, container size or volume:				
(b) Materials of construction of each primary packaging component:				
(c) Summary of specifications of each primary and functional secondary (e.g., foil pouches) packaging components:				
3.6 Completed Real time stability testing:				
Applicable only if registration was based on accelerated and partial real time stability data				
Stability protocol for continuing (i.e., ongoing) batches:				
Protocol Parameter		Description		
Storage conditions (including tolerances)				
Testing frequency				
Number of batches per strength and batch sizes				
Container closure system(s)				
Stability-indicating quality parameters				
Photostability testing				
Tests and acceptance criteria				
Other				
FPPs packaged in impermeable containers				
FPPs packaged in semi-permeable containers				
Evaluation				
(a) Summary of stress testing and results (e.g., photostability studies, cyclic studies for				

semi-solids, freeze-thaw studies):

(b) Summary of real time testing (e.g., studies conducted, protocols used, results obtained):

(i) Description of stability study details:

Storage Conditions (□C,%RH)	BatchNumber	BatchSize	Container ClosureSystem	Completed (andProposed) TestIntervals (inmonths)

(ii) Summary and discussion of stability study results:

(c) Proposed storage conditions and shelf life (and in-use storage conditions and in-use period, if applicable):

Extrapolation of data

Core storage statements

3.7. Container labelling

3.7.1 Packaging or, where there is no outer packaging, on the immediate packaging

3.7.2 Blisters and strips

3.8 Current package insert and if available patient information leaflet

4.0 DECLARATION BY AN APPLICANT

I, the undersigned certify that all the information in this form and accompanying documentation is correct, complete and true to the best of my knowledge.

I further confirm that the information referred to in my application dossier is available for verification during GMP inspection.

I also agree that I shall carry out pharmacovigilance to monitor the safety of the product in the market and provide safety update reports to the National Medicines Regulatory Authority of the EAC Partners States.

I further agree that I am obliged to follow the requirements of the Partner States Legislations and Regulations, which are applicable to medicinal products.

I also consent to the processing of information provided by the EAC Partner States.

It is hereby confirmed that fees will be paid/have been paid according to the National/Community rules*

Name:

Position in the company

Signature:

Date:.....

Official stamp:.....

* Note: If fees have been paid, attach proof of payment

ANNEX 2: QUALITY INFORMATION SUMMARY (QIS)

INTRODUCTION

(a) Summary of product information:

Non-proprietary name(s) of the finished pharmaceutical product(s) (FPP)	
Proprietary name(s) of the finished pharmaceutical product(s) (FPP)	
International non-proprietary name(s) of the active pharmaceutical ingredient(s) (API(s)), including form (salt, hydrate, polymorph)	
Applicant name and address	
Dosage form	
Application Number	
Strength	
Route of administration	
Proposed indication(s)	
Local Technical Representative (Agency)	
LTR Contact person details	
Local Technical Representative (LTR) contact person	Surname: First Name:
Physical address details	
Town/City	
Postal code	
Contact person's email address	
Contact person's phone number	
FPP manufacturer Qualified Person	Surname: First Name:
FPP manufacturer Qualified person's contact details (including Physical address)	
Unit/block	
Road/Street	
Plant	
Village/suburb	
Town/City	
Postal code	
Country	
Contact person's email address	
Contact person's phone number	

(b) Administrative Summary:

Applicant's date of preparation or revision of the QIS	
Version and/or date of acceptance	<i>(official use only)</i>

Related dossiers (e.g. FPP(s) with the same API(s) submitted to TMDA by the applicant):

Application number ()	Registration status (Y/N)	API, strength, dosage form (eg. Irinotecan (as chloride) 20mg per ml Solution)	API manufacturer (including address if same manufacturer as current dossier)

2.3.S DRUG SUBSTANCE (or ACTIVE PHARMACEUTICAL INGREDIENT (API)) (NAME, MANUFACTURER)

Indicate which option applies for the submission of API information: <check one only>

Name of API:		
Name of API manufacturer:		
<input type="checkbox"/>	Certificate of suitability to the European Pharmacopoeia (CEP) Option 1.	
<input type="checkbox"/>	Confirmation of API prequalification document: Option 2	
<input type="checkbox"/>	API approval number _____. Option 3a.	
<input type="checkbox"/>	Active pharmaceutical ingredient master file (EAC APIMF) procedure: APIMF number assigned by TMDA (if known): _____ ; version number(s) including amendments (and/or date(s)) of the open part: _____ ; version number(s) including amendments (and/or date(s)) of the restricted part: : _____. Option 3b.	
<input type="checkbox"/>	Full details in the PD Open part DMF version number _____ Restricted part DMF version number _____ Identifier of current module 3.2.S: _____ Option 4.	

2.3.S.2 Manufacture (name, manufacturer)

2.3.S.2.1 Manufacturer(s) (name, manufacturer)

(a) Name, address and responsibility (e.g. fabrication, packaging, labelling, testing, storage) of each manufacturer, including contractors and each proposed production site or facility involved in these activities:

Name and address (including block(s)/unit(s))	Responsibility	CEP number/ WHOAPI-PQ number /WHO APIMF/ TMDA registration No./Approved APIMF/ if applicable)	Letter of access provided?

2.3.S.2.3 Control of Materials (name, manufacturer) – for API option 4 only

(a) Name of starting material:

(b) Name and manufacturing site address of starting material manufacturer(s):

2.3.S.4 Control of the API (name, manufacturer)

2.3.S.4.1 Specification (name, manufacturer)

(a) API specifications of the FPP manufacturer:

Standard (e.g.Ph.Int., Ph.Eur., BP, USP, in-house)		
Specification reference number & version effective date		
Test	Acceptance criteria	Analytical procedure (Type/Source/Version)
Description		
Identification		
Impurities		
Assay		
etc.		

2.3.S.6 Container Closure System (name, manufacturer)

(a) Description of the container closure system(s) for the storage and shipment of the API:

2.3.S.7 Stability (name, manufacturer)

2.3.S.7.1 Stability Summary and Conclusions (name, manufacturer)

(c) Proposed storage conditions and re-test period (or shelf-life, as appropriate):

Container closure system	Storage statement	Re-test period*

* indicate if a shelf-life is proposed in lieu of a re-test period (e.g. in the case of labile APIs)

2.3.P DRUG PRODUCT (or FINISHED PHARMACEUTICAL PRODUCT (FPP))

Indicate which option applies for the submission of FPP information: <check one only>

Name of API:	
Name of API manufacturer:	
<input type="checkbox"/>	Full details
<input type="checkbox"/>	WHO collaborative procedure
<input type="checkbox"/>	SRA Abridged procedure
<input type="checkbox"/>	EAC Mutual Recognition
<input type="checkbox"/>	EU Article 58 procedure

2.3.P.1 Description and Composition of the FPP

(a) Description of the FPP (in signed specifications):

(b) Composition of the FPP:

(i) Composition, i.e. list of all components of the FPP and their amounts on a per unit basis and percentage basis (including individual components of mixtures prepared in-house (e.g. coatings) and overages, if any):

Component and quality standard (and grade, if applicable)	Function	Strength (label claim)					
		Quant. per unit or per mL	%	Quant. per unit or per mL	%	Quantity per unit or per mL	%
<complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection>							
Subtotal 1							
<complete with appropriate title e.g. Film-coating>							
Subtotal 2							
Total							

(ii) Composition of all components purchased as mixtures (e.g. colourants, coatings, capsule shells, imprinting inks):

(c) Description of accompanying reconstitution diluent(s), if applicable:

2.3.P.2.2.1 Formulation Development

(b) Information on primary (submission, registration, exhibit) batches including comparative bioavailability or biowaiver, stability, commercial:

(i) Summary of batch numbers:

Batch number(s) of the FPPs used in

Bioequivalence	<e.g. bioequivalence batch A12345>.		
Biowaiver	<e.g. biowaiver batch X12345>		
For proportional strength biowaiver: the bioequivalence batch of the reference strength			
Dissolution profile studies			
Stability studies (primary batches)			
<packaging configuration I>			
< packaging configuration II>			
<Add/delete as many rows as necessary>			
Stability studies (production batches)			
< packaging configuration I>			
< packaging configuration II>			
(Add/delete as many rows as necessary)			
Validation studies (primary batches)			
< packaging configuration I>			
< packaging configuration II>			
(Add/delete as many rows as necessary)			
Validation studies (at least the first three consecutive production batches) version(s) for process validation protocol(s)			

Summary of formulations and discussion of any differences:

Component and quality standard (e.g. NF, BP, Ph.Eur, in-house)	Relevant batches							
	Comparative bioavailability or biowaiver		Stability		Process validation		Commercial (2.3.P.1)	
	<Batch nos. and sizes>		<Batch nos. and sizes>		<Batch nos. and sizes>		<Batch nos. and sizes>	
	Theor. quantity per batch	%	Theor. quantity per batch	%	Theor. quantity per batch	%	Theor. quantity per batch	%
<complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection>								
Subtotal 1								
<complete with appropriate title e.g. Film-coating>								

Component and quality standard (e.g. NF, BP, Ph.Eur, in-house)	Relevant batches							
	Comparative bioavailability or bio waiver		Stability		Process validation		Commercial (2.3.P.1)	
	<Batch nos. and sizes>		<Batch nos. and sizes>		<Batch nos. and sizes>		<Batch nos. and sizes>	
	Theor. quantity per batch	%	Theor. quantity per batch	%	Theor. quantity per batch	%	Theor. quantity per batch	%
Subtotal 2								
Total								

2.3.P.3 Manufacture

2.3.P.3.1 Manufacturer(s)

(a) Name, address and responsibility (e.g. fabrication, packaging, labelling, testing) of each manufacturer, including contractors and each proposed production site or facility involved in manufacturing and testing:

Name and address (include block(s)/unit(s))	Responsibility

2.3.P.3.2 Batch Formula

Largest intended commercial batch size:

Other intended commercial batch sizes:

<information on all intended commercial batch sizes should be in the QIS>

(a) List of all components of the FPP to be used in the manufacturing process and their amounts on a per batch basis (including components of mixtures prepared in-house (e.g. coatings) and overages, if any):

Strength (label claim)			

Master production document reference number and/or version			
Proposed commercial batch size(s) (e.g. number of dosage units)			
Component and quality standard (and grade, if applicable)	Quantity per batch (e.g. kg/batch)	Quantity per batch (e.g. kg/batch)	Quantity per batch (e.g. kg/batch)
<complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection>			
Subtotal 1			
<complete with appropriate title e.g. Film-coating >			
Subtotal 2			
Total			

2.3.P.3.3 Description of Manufacturing Process and Process Controls

- (a) Flow diagram of the manufacturing process:
- (b) Narrative description of the manufacturing process, including equipment type and working capacity, process parameters:

2.3.P.3.4 Controls of Critical Steps and Intermediates

- (a) Summary of controls performed at the critical steps of the manufacturing process and on isolated intermediates:

Step (e.g. granulation, compression, coating)	Controls (parameters/limits/frequency of testing)

Proposed/validated holding periods for intermediates (including bulk product):

2.3.P.3.5 Process Validation and/or Evaluation

- (a) Summary of the process validation and/or evaluation studies conducted and/or a summary of the proposed validation protocol for the critical steps or critical assays used in the manufacturing process (e.g. protocol number, parameters, results):

Document code(s) for the process validation protocol(s) and/or report(s) (including reference number/version/date):

2.3.P.5 Control of FPP

2.3.P.5.1 Specification(s)

(a) Specification(s) for the FPP:

Standard (e.g.Ph.Int., BP, USP, in-house)			
Specification reference number and version			
Test	Acceptance criteria (release)	Acceptance criteria (shelf-life)	Analytical procedure (type/source/version)
Description			
Identification			
Impurities			
Assay			
etc.			

2.3.P.7 Container Closure System

(a) Description of the container closure systems, including unit count or fill size, container size or volume:

Description (including materials of construction)	Strength	Unit count or fill size (e.g. 60s, 100s etc.)	Container size (e.g. 5 ml, 100 ml etc.)

2.3.P.8 Stability

2.3.P.8.1 Stability Summary and Conclusions

(c) Proposed storage statement and shelf-life (and in-use storage conditions and in-use period, if applicable):

Container closure system	Storage statement	Shelf-life

2.3.P.8.2 Post-approval Stability Protocol and Stability Commitment

- (a) **Stability protocol for Primary stability batches (e.g. storage conditions (including tolerances), batch numbers and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):**

Parameter	Details	
Storage condition(s) (°C, % RH)		
Batch number(s) / batch size(s)	<primary batches>	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing frequency		
Container closure system(s)		

- (b) **Stability protocol for Commitment batches (e.g. storage conditions (including tolerances), batch numbers (if known) and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):**

Parameter	Details	
Storage condition(s) (°C, % RH)		
Batch number(s) / batch size(s)	<not less than three production batches in each container closure system>	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing frequency		
Container closure system(s)		

- (c) **Stability protocol for Ongoing Batches (e.g. storage conditions (including tolerances), number of batches per strength and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):**

Parameter	Details	
Storage condition(s) (°C, % RH)		
Batch size(s), annual allocation	<at least one production batch per year (unless none is produced that year) in each container closure system >	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	

Parameter	Details	
	etc.	
Testing frequency		
Container closure system(s)		

2.3.P.8.3 Stability Data

- (c) Bracketing and matrixing design for commitment and/or continuing (i.e. ongoing) batches, if applicable:

WRITTEN COMMITMENTS OF THE MANUFACTURER - for TMDA use

API

If applicable (primary stability study commitment):

The Applicant (or API manufacturer) undertook in writing (date of letter of commitment) to continue long-term testing of <INN of API> for a period of time sufficient to cover the whole provisional re-test period (period ending month/year) and to report any significant changes or out-of-specification results immediately to TMDA for the following batches :

<Batch numbers, manufacturing dates, batch size, primary packing materials>

If applicable (commitment stability studies):

Since stability data on three production scale batches were not provided with the application, the remaining number of production scale batches should be put on long-term stability testing. Any significant changes or out-of-specification results should be reported immediately to TMDA. The approved stability protocol should be used for commitment batches.

API option 1 - CEP

The Applicant provided a commitment in writing (date of letter of commitment) to inform TMDA in the event that the CEP is revised or withdrawn, and that revisions to the CEP will be handled as per variation guidelines. Note that revisions or withdrawal will require additional consideration of the API data requirements to support the dossier.

API option 2 - WHOAPI-CPQ

The Applicant provided a commitment in writing (date of letter of commitment) to inform TMDA in the event that the WHOAPI-CPQ is revised or withdrawn, and that revisions to the WHOAPI-CPQ will be handled as per variation TMDA Variation guidelines. Note that revisions or withdrawal will require additional consideration of the API data requirements to support the dossier.

API option 4 - full details in the PD (ongoing stability study commitment)

The Applicant undertook in writing (date of letter of commitment) a commitment regarding ongoing stability studies. Unless otherwise justified, at least one batch per year of the product will be included in the stability programme (unless none is produced during that year). The stability protocol will be

that which was approved for primary batches (or the protocol was submitted for assessment). Out-of-specification results or significant atypical trends will be investigated. Any confirmed significant change or out-of-specification result will be reported immediately to TMDA. The possible impact on batches on the market will be considered in consultation with GMP inspection.

FPP

If applicable (primary stability study commitment):

The Applicant undertook in writing (date of letter of commitment) to continue long-term testing of < FPP reference number, trade name (INN of API), strength, pharmaceutical form> for a period of time sufficient to cover the whole provisional shelf-life (period ending month/year) and to report any out-of-specification results or significant changes immediately for the following batches :

<Batch numbers, manufacturing dates, batch size, primary packing materials >

If applicable (commitment stability studies):

Since stability data on three production scale batches was not provided with the application, the Applicant undertook in writing, (date of letter of commitment) to put the remaining number <e.g. additional two (2)> production scale batches of < FPP reference number, trade name (INN of API), strength, pharmaceutical form, primary packing material> on long-term stability testing. Any out-of-specification results or significant changes during the study will immediately be reported to TMDA. The approved stability protocol will be used for commitment batches.

If applicable (when the proposed largest commercial batch size is 200 000 units (x units) or less)

The Applicant undertook in writing (date of letter of commitment) to place the first three batches of any production size larger than x units on stability. The stability protocol will be that which was approved for primary batches (or the protocol was submitted for assessment). Out-of-specification results or significant atypical trends will be investigated. Any confirmed significant change or out-of-specification result will be reported immediately to TMDA.

Ongoing stability study commitment

The Applicant undertook in writing (date of letter of commitment) a commitment regarding ongoing stability studies. Unless otherwise justified, at least one batch per year of the product manufactured in every primary packaging type will be included in the stability programme (unless none is produced during that year). The stability protocol will be that which was approved for primary batches (or the protocol was submitted and found acceptable). Out-of-specification results or significant atypical trends will be investigated. Any confirmed significant change or out-of-specification result will be reported immediately to TMDA. The possible impact on batches on the market will be considered in consultation with GMP inspection.

If applicable (validation of production batches)

Validation data on production scale batches of not less than three (3) consecutive batches of <FPP reference number, trade name (INN of API), strength, pharmaceutical form, primary packing material> was not provided with the application. Therefore, the Applicant submitted a written commitment (date of letter of commitment) that three consecutive production batches would be prospectively validated and a validation report –in accordance with the details of the validation protocol provided in the dossier– would be made available as soon as possible for evaluation by assessors or for verification by the GMP inspection.

Change History

Date of preparation of original QIS:

Date of revised version	Section (e.g. S.2.1)	Revision

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