HPT/PER/GUD/039

Rev. No. 0

REPUBLIC OF KENYA

MINISTRY OF HEALTH

PHARMACY AND POISONS BOARD

GUIDELINES ON MEDICINES RE-REGISTRATION AND RENEWALS

JANUARY 2022

Citation:

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For clarifications, comments, or suggestions, please contact:

The Chief Executive Officer

Pharmacy and Poisons Board

P.O. Box 27663 – 00506, Nairobi

Telephone: 0709770100

Email: info@pharmacyboardkenya.org

HPT/PER/GUD/039	Guidelines On Medicines Re-Registration And Renewals	Revision No. 0	**Effective Date:** 01/02/2022 **Review Date:** 21/10/2027

Prepared by Deputy Director, Product Evaluation and Registration

Sign.....

Date.....07/02/2022.....

Reviewed by Director, Health Products and Technologies

Sign.....

Date.....07/02/2022.....

Checked by Head, Quality Management

Sign.....

Date.....07/02/2022.....

Authorized by CEO

Sign.....

Date.....07-02-2022.....

ACKNOWLEDGEMENTS

The Registrar, Pharmacy and Poisons Board would like to thank the following persons for their comments and contributions to the development of this guideline.

Contributor:

Dr. Peter Mbwiiri Ikamati Chief Principal Regulatory officer, Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies

Dr. Paulyne Wairimu, Senior Principal Regulatory Officer Product Evaluation and Registration (PER) (MD&IVDs) Department, Directorate of Health Products and Technologies

REVIEWERS

Dr. Ronald Inyangala, Deputy-Director, Senior Principal Regulatory Officer, Drug Product Evaluation and Registration (DPER) Department, HPT

Dr. Jonathan Meriakol, Senior Principal Regulatory officer, Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies

Dr. Ali Arale, Principal Regulatory Officer, Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies

Dr. James Owuor, Assistant Principal Regulatory Officer, Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies

Dr. Edwin Burugu, Assistant Principal Regulatory Officer, Drug Product Evaluation and Registration (DPER) Department Directorate of Health Products and Technologies

Dr. Eugene Odame, Senior Regulatory officer, Product Evaluation and Registration (PER) (MD&IVDs), Department, Directorate of Health Products and Technologies

Dr. Serah Chebet Chesaro, Principal Regulatory officer, Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies

Mr. Alex Mutai, Assistant Principal Regulatory Officer, Blood and Blood Products Department, Directorate of Health Products and Technologies

Ms. Jacqueline Yahuma , Assistant Principal Regulatory Officer, Cosmetics Department, Directorate of Health Products and Technologies

Mr. Henry Chweya, Assistant Principal Regulatory Officer, Border line Products Department, Directorate of Health Products and Technologies

Mr. Peter Mugala, Senior Information and Communication Technology Officer; Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies

Mr. Anthony Kemboi, Information and Communication Technology Officer; Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies

Mr. Victor Kipchumba, Information and Communication Technology Officer Medical Devices Department Directorate of Health Products and Technologies

TABLE OF CONTENTS

Glossary of terms

Re-registration:	Marketing Authorization renewal every five years.
Retention:	Maintenance of a Marketing Authorization upon payment of the prescribed annual fee.
Product Quality Review (PQR):	A mechanism (regular periodic or rolling quality reviews of all licensed medicinal products) to ensure that data captured by the Pharmaceutical Quality System (PQS) is reviewed for trends in order to verify the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished products, highlight any adverse quality trends and to identify product and process improvements. The Product Quality review (PQR) is an effective quality improvement tool to enhance the consistency of the process and the overall quality of the product.
Pharmacovigilance:	the practice of monitoring the effects of medical drugs after they have been licensed for use, especially in order to identify and evaluate previously unreported adverse reactions.
Product complaints:	A complaint is a statement from a customer expressing dissatisfaction with the manufactured product, whether with the manufacturer's service, the product's packaging, the product's usability, or damage to the product.
Market Surveillance:	Activities carried out and measures taken by public authorities to ensure that products comply with the applicable legislations and do not endanger health, safety or any other aspect of public interest protection. It may include product traceability activities.
Risk management plan:	A risk management plan (RMP) provides information on a medicine's safety profile, describes the activities of the marketing authorisation holder to further characterise the safety profile during post-marketing (pharmacovigilance activities), and explains the measures that are taken in order to prevent or minimise the risks.

Product retention:	Means maintenance of a product in the register of licensed products.
Marketing Authorization (MA):	Also means product registration
MA withdrawal:	Means voluntary withdrawal of a marketing authorization by the marketing authorization holder.
PRIMS:	Pharmaceutical Regulatory Information Management System

INTRODUCTION

1.1 Background

Pharmacy and Poisons Board, hereafter referred to as "The Board" is mandated under the Pharmacy and Poisons Act to regulate Health products and Health Technologies.

This guideline provides guidance for applicants preparing an application for submission to the Pharmacy and Poisons Board for re-registration & Renewal of Marketing Authorisation of a medicinal product.

1.2 Legal Framework

The Board is empowered under Section 3A of the Pharmacy and Poisons Act, Cap 244 Laws of Kenya ("The Act"), to formulate guidelines for regulating the manufacture, distribution, sale and use of medical products. Further, the Board is empowered under the same section to grant or withdraw marketing authorization for medical products subject to appropriate conditions and revise such conditions for marketing as necessary. Section 3B of the Act, further mandates the Board to maintain a register of all authorized/registered medical products and health technologies.

Medical products and health technologies registered under the Act are issued with a certificate of registration, valid for a period of five (5) years as specified under Rule 7 of the Pharmacy and Poisons (Registration of Drugs) Rules. Such registered products, under Rule 9A, are to be retained in the register of medical products annually upon payment of a specified retention fee. It is therefore a requirement, under Rule 9, that certificates of registration are renewed every five (5) years upon satisfactory compliance with specified conditions.

These guidelines seek to provide for the framework for re-registration and renewal of marketing authorizations/ certificates of registration issued under the Pharmacy and Poisons Act, Cap 244

1.3 Scope

These guidelines will assist applicants to prepare applications to re-register medicinal products for all Health Products and Technologies(HTPs).

1.4 Application Process

The format for applications for re-registration will include a cover letter, Common technical document (please note that a requirement for Module 3, 4 and 5 shall only apply for manually registered products only), Appendix 1 (List of Variations), Appendix 2 (Quality information Summary), Appendix 3 (Product Quality Review) and Appendix 4 (vigilance and safety reports).

Please note that for CTD structure and content refer to "Guidelines on medicines evaluation and Registration, July 2021) and Guidelines for Biotherapeutics that describe how to organize applications based on the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines on the CTD.

According to the CTD format, each application is a collection of documents, grouped into 5 modules. Module 1 prescribes Administrative Information and Prescribing Information requirements which is region specific. The Summaries, Quality, Non-clinical, and Clinical modules have been described in Modules 2 to 5, respectively. Applicants should not modify the overall organization 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.
Information in these Modules should be present in relevant sections.
Product re-registration shall be every five years.

Annex I – Cover Letter

<Applicant>
<Address>
<Address>
<Post code><Town>
<Country

<Applicant's reference> <Date>

<Pharmacy and Poisons Board>
<Address>
<Address>
<Post code><Town>
<Kenya>

Dear Sir/Madam,

Subject: Submission of Application Dossier(s) for Re-Registration & Renewal <Product Name(s), [strength(s) of active pharmaceutical ingredient(s) and dosage form(s)

We are pleased to submit our Application Dossier(s) for re-registration of human medicines which details are as follows:

Name of the medicinal product(s):
……
Pharmaceutical form(s) and strength(s):
……
INN/active Pharmaceutical ingredient(s):
……
ATC Code(s):
……

You will find enclosed the submission dossier as specified hereafter:

☐ CTD format; PRIMS portal

☐ The electronic submission contains the following:

- Cover letter
- **Module 1**: Administrative information and product information
- **Module 2:** Overview and summaries

- **Module 3:** Quality (for manually Registered products only)
- **Module 4:** Non clinical study reports (for manually Registered products only)
- **Module 5:** Clinical study reports (for manually Registered products only)
- **Appendix 1:** List of variations (All manually approved variations must have been submitted to the PRIMS system)
- **Appendix 2:** QIS
- **Appendix 3:** Product Quality Review (for the last three years)
- **Appendix 4** (vigilance and Product safety reports, including product complaints and market surveilance).

<The relevant fees have been paid and samples submitted.>

I declare that the information provided is true and correct.

Yours sincerely,

……
<Signature>
<Name>
<Title>
<Phone number(s)>
<Email address>

Annex II: Application Form

Application Number		
Date of submission of the dossier		
Name of the 1st Evaluator		Signature
Name of the 2nd Evaluator		Signature
Date of 1st evaluation		
Date of 2nd Evaluation		
Number of files received		
CONCLUSION OF THE ASSESSMENT **RECOMMENDED** *(no outstanding issues)* **QUERY RAISED** *(Indicate the sections where query is raised)* **REJECTED** *(indicate the module(s) that led to the rejection)* ***(Please delete which does not apply)***		

TYPE OF APPLICATION – HUMAN PRODUCT (Re-Registration)	
MODULE 1: ADMINISTRATIVE INFORMATION	
SECTION 1: PARTICULARS OF THE PRODUCT	
1.0 Name and address of Applicant	
Company name: **Address:** **Country:** **Telephone:** **E-Mail:**	
For PPB use only	
1.1	**Type of the Medicinal product licence application**
	Type of the medicinal product application New/innovator MA Generic MA Conditional Authorization Emergency Use Authorization Extension application Duplicate license Renewal/Re-registration* *** If variation has been made, information supporting the changes should be submitted. See variation guidelines for registered medicinal products.**
1.2	Trade/Proprietary name (proprietary Product name):

For PPB use only	
1.3	**Approved / INN / generic name/Active Pharmaceutical Ingredient (API):**
For PPB use only	
1.4	**Strength of the Active Pharmaceutical Ingredient (API) per unit dosage of the product and specifications of the API::**
For PPB use only	
1.5	**Dosage form**
1.5.1	*Pharmaceutical Dosage form of the product:*
1.5.2	*Therapeutic Indication(s)::*
1.5.2	*Route(s) of administration (use current list of standard terms - European Pharmacopoeia):*
For PPB use only	
1.6	**Packing/Pack size of the product:**
1.6.1	**Pack size:**
1.6.2	**Primary packing materials:**
1.6.3	**Secondary packing materials:**
For PPB use only	
1.7	**Visual Description of the product**
For PPB use only	

1.8	**1.8 Approved Shelf life of the product (in months):**
1.8.1	*Approved shelf life (after reconstitution or dilution):*
1.8.2	*Approved shelf life (after first opening container):*
1.8.3	*Approved storage conditions:*
1.8.4	*Approved storage conditions after first opening:*
For PPB use only	
1.9	**Pharmacotherapeutic group and ATC Code**
1.9.1	*Pharmacotherapeutic group:*
1.9.2	*ATC Code:*
1.9.3	*If no ATC code has been assigned, please indicate if an application for ATC code has been made:*
1.9.4	*Approved indication(s) for the product:*
For PPB use only	
1.10	**Legal category**
1.10.1	*Approved dispensing category/ classification:*
1.10.2	*For products subject to medical prescription:*
For PPB use only	
1.11	**Country of origin or country of release:**
For PPB use only	
1.12	**Product Marketing Authorisation in the country of origin. (Attach certificate of pharmaceutical product from competent regulatory authority)**

☐ **Authorised** Countr**y:** Date of authorisation**:** Proprietary name**:** Authorisation number**:** ☐ Refused Country: **Not applicable** Date of refusal (dd-mm-yyyy): Reason for Refusal:	☐ Withdrawn (by applicant after authorisation) Country: Date of withdrawal (dd-mm-yyyy): Proprietary name: Reason for withdrawal: ☐ Suspended/revoked (by competent authority) Country: **Not applicable** date of suspension/revocation (dd-mm-yyyy): Reason for suspension/revocation:

For PPB use only	
1.12.1	**Registration status from countries with Stringent Regulatory Authorities (SRAs) where applicable**
For PPB use only	
1.12.2	**List of countries in which a similar application has been submitted**
For PPB use only	

1.12.3	**Statement on whether an application for the Marketing Authorisation has been previously rejected, withdrawn or repeatedly deferred in the EAC Partner States**
For PPB use only	
1.12.4	**Certificates of approval of DMF (Drug Master File) by Stringent Regulatory Authority**
1.12.5	**Manufacturing Licence and Product Licence**
For PPB use only	
1.13	**Name(s) and complete address (es) of the manufacturer(s)**
1.13.1	**Name and complete address(es)of the manufacturer(s) of the FPP, including the finished pharmaceutical product release if different from the manufacturer.**

Marketing Authorisation Holder:
Company name:
Address:
Country:
Telephone:
E-Mail:

Manufactured By:
Company) Name :
Address :

Country :.
Telephone :
Telefax :

If the manufacturer is different to 1.1 above, explain the relationship

1.13.2	*Name(s) and complete address (es) of the manufacturer(s) of the active pharmaceutical ingredient*

ACTIVE INGREDIENT:
Company) Name :
Office Address :
Country :
Telephone :
Fax :
Contact Person :

E-mail :	
For PPB use only	
1.14	**Compliance to Good Manufacturing Practice (GMP) and Good Clinical Practice**
1.14.1	**Good Manufacturing Practice (GMP) from PPB**
1.14.2	**1.15.2 Good Clinical Practice (GCP) or Good Laboratory Practice (GLP)**
For PPB use only	
1.15	Name and complete address of the Local Technical Representative of Manufacture (for finished pharmcautical Product) Company name: Address: Country: Telephone: E-Mail: If the Local Technical Representative is different to 1.1 above, explain and provide evidence for the relationship:
For PPB use only	
1.16	Product Information
1.16.1	Summary of Product Characteristics (SPC):
1.16.2	Prescribers/Patient information leaflet:
1.16.3	Mock-ups and Photo scan of the product:
1.17	State the reference/monograph standard such as British Pharmacopeia United States Pharmacopeia, Ph. Eur, Japanese Pharmacopeia, In-hous monograph e.t.c. used for Finished Medicinal Product.
1.18.1	Specification of active ingredient(s) from API manufacturer (Specificatio number and Version):
1.18.2	Specification of active ingredient(s) from FPP manufacturer (Specificatio number and Version):
1.18.3	Specification of Finished Pharmaceutical Product (Specification numbe and Version):

1.19	Name and address (physical and postal) of the Contract Researc Organisation(s) where the clinical studies of the product were conducte *(If applicable)*
Name: Company name: Address: Country: Telephone: Telefax: E-Mail:	

1.20 DECLARATION BY AN APPLICANT	
	I, the undersigned certify that all the information in this form an accompanying documentation is correct, complete and true to the best o my knowledge. I further confirm that the information referred to in my application dossie is available for verification during GMP inspection. I also agree that I shall carry out pharmacovigelance to monitor the safet of the product in the market and provide safety update reports to th National Medicines Regulatory Authority. I further agree that I am obliged to follow the requirements of Kenya, and Legislations and Regulations which are applicable to medicinal products. Name: Position in the company: Signature: Date: For PPB use only OVERALL QUERIES AND RECOMMENDATIONS FOR THIS MODULE Official stamp:…… ** Note: If fees have been paid, attach proof of payment*

PPB use only

Appendix 1 (List of variations)

No.	Variation Number	Variation description	Status i.e. Accepted, under review or rejected

Appendix 2: QUALITY INFORMATION SUMMARY (QIS)

< Add Dossier Application number>

Background:

The EAC Quality Information Summary model is adopted from the WHO QIS template of 12th July 2017.

Template revision date:

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	
Country (Within EAC)	
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	*(EAC use only)*

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

Application number ( )	EAC jointly registered (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:	
□	Certificate of suitability to the European Pharmacopoeia (CEP) Option 1.
□	Confirmation of API prequalification document: Option 2
□	EAC API registration Number_____. Option 3a.
□	EAC Active pharmaceutical ingredient master file (EAC APIMF) procedure: APIMF number assigned by EAC (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.
□	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/ EAC registration No./EAC APIMF/ if applicable)	Letter of access provided?

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

(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:	
□	Full details
□	WHO collaborative procedure
□	SRA Abridged procedure
□	EAC Mutual Recognition
□	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 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	%
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	
	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 PPB 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 EAC 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 EAC. 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 EAC in the event that the CEP is revised or withdrawn, and that revisions to the CEP will be handled as per variation EAC 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 EAC in the event that the WHOAPI-CPQ is revised or withdrawn, and that revisions to the WHOAPI-CPQ will be handled as per variation EAC 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 EAC. The possible impact on batches on the market will be considered in consultation with EAC-EWG 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 to EAC 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 EAC. 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 EAC.

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 EAC. The possible impact on batches on the market will be considered in consultation with EAC-EWG 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 EAC-EWG GMP inspection.

Change History

Date of preparation of original QIS:

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

Appendix 3 (Product Quality Review).

The PQR should be submitted in line with the accepted PQR as per GMP requirements. The section on Complaints should include a section dedicated to complaints received from the Kenyan and East African Market.

Appendix 4 (Vigilance and Product Safety reports including Risk management plan)

a) Pharmacovigilance reports
b) Market Surveillance reports
c) Product complaints
d) Risk management plans

Product Retention

For a product to be re-registered, it has to meet requirements for product retention. Product retention is mandatory annually. The applicant is required to fill in information in the PRIMS system as per the format prescribed. Product retention maybe suspended upon application for marketing Authorization withdrawal or upon a notification for discontinued marketing of a medicinal product or interrupted (including a possible shortage) of a medical product or health technology.

If the applicant wishes to reinstate the marketing Authorization (in case of withdrawal), the applicant shall provide product details aligned to the current requirements through variations and in case of extended periods of 5 years or more, a re-registration application is to be submitted upon payment of a prescribed fee and full payment of Retention fees for all the years. **In case of**

Product retention suspension upon a notification for discontinued marketing of a medicinal product or interrupted supply (including a possible shortage) of a medical product or health technology, the applicant shall meet the requirements of the product retention, including full payment of retention fees for missed years and in case of prolonged periods of 3 years but not exceeding five years, provide the current requirements of the product dossier through applicable variations and payment of requisite fees.

Notification for discontinuation of supply of Medical product of health technology

The marketing of a medicinal product is being discontinued or interrupted (including a possible shortage) due to justification such as:-

- The marketing of a medicinal product is being discontinued or interrupted (including a possible shortage)
- A possible shortage because a medicinal product is being placed on the market in smaller quantities or to an insufficient degree
- A quality defect in relation to a medicinal product.
- A medicinal product is placed on the market for the first time, or again following an interruption

The MAH can revoke a previously made notification of a (possible) shortage because it will not occur through notification to the Board.

P. O. Box 27663 00506 Lenana Road Opposite Russian Embassy Nairobi,
Tel:
+2540212345/6789,Fax:+2540212345,Website:www.Pharmacyboardkenya.
org.ke,Email: info@pharmacyboardkenya.org.ke