Botswana Medicines Regulatory Authority

Approved By:

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Date of Approval (DD/MM//YY)

Revision status sheet

Page	Changes made	Issue No	Process owner's name	Date
5	Under 3 Definitions and Abbreviations changed to Abbreviations and Definitions	2.0	Team Leader – Post Registration	05 July 2023
7 & 8	Reworded the Apendices	2.0	Team Leader – Post Registration	31 March 2023
7	Included Appendix – Product quality review requirements for all products as explained in the BOMRA Registration Quality Guideline BOMRA/ER/MD/P02/G01	2.0	Team Leader – Post Registration	31 March 2023
8	Renamed Renewal Application Form BOMRA/ER/MD/P11/F01 to Renewal Application Addendum BOMRA/ER/MD/P11/F01	2.0	Team Leader – Post Registration	31 March 2023
6	Under 1 "conventional medicines"included	2.0	Team Leader – Post Registration	31 March 2023
6	Under Scope, "innovator products, generic medicines and biosimilar"replaced with "all products registered in Botswana and appearing on the register'	2.0	Team Leader – Post Registration	31 March 2023
7	Under 4.4 "API and FPP"changed to product	2.0	Team Leader – Post Registration	31 March 2023
7	Under 5.1 c and d included	2.0	Team Leader – Post Registration	31 March 2023
8	Under 6 "form"replaced with addendum	2.0	Team Leader – Post Registration	31 March 2023
8	Under 6b "variations should be captured in appendix 2"replaced with Pending and approved variations should be highlighted as in the addendum below.	2.0	Team Leader – Post Registration	31 March 2023
9	In the renewal application addendum item "pack size"and remarks "state all the different pack size"included separately	2.0	Team Leader – Post Registration	31 March 2023

	and item "API Specifications"and "Stability"included			
8	Deleted appendix 2 and renumbered	2	Team Leader – Post Registration	06 March 2023
4	Under 3.2.2, Replaced Applicant with Market Authorisation holder	1.0	Manager - Human Medicines	13 July 2022
5	Under 4.5 replaced "the BOMRA Registration Quality Guidelines Ref No. BOMRA/ER/MD/P02/G01"with all current BOMRA registration guidelines.	1.0	Manager – Human Medicines	13 July 2022
6	Under 5.1, Included "and hard copy" for point b and deleted points c, d e.	1.0	Manager – Human Medicines	13 July 2022
6	Deleted 5.2	1.0	Manager – Human Medicines	13 July 2022
	Under Appendix 1, deleted point a	1.0	Manager – Human Medicines	13 July 2022
6	Under Appendix 1, included points a and b	1.0	Manager – Human Medicines	13 July 2022
7	Included appendix 2	1.0	Manager – Human Medicines	13 July 2022

Table of Contents

1 Purpose

The guideline provides guidance on the format and content of the applications for renewal of registration of conventional human medicines. It is intended to assist the applicant in the preparation of the submission documentation for renewal of registration of medicinal products.

2 Scope

This guideline applies only to applications for renewal of registration of conventional Human Medicines, that is; it covers all products registered in Botswana.

3 Abbreviations and Definitions

3.1 Abbreviations

The following abbreviations shall apply.

3.1.1 **API:** Active Pharmaceutical Ingredient

3.1.2 **APIMF:** Active Pharmaceutical Ingredient Master File

3.1.3 **BOMRA:** Botswana Medicines Regulatory Authority

3.1.4 **CEP:** Certification of suitability of European Pharmacopoeia monographs

3.1.5 **CPP / CoPP:** Certificate of Pharmaceutical Product

3.1.6 **CTD:** Common Technical Document

3.1.7 **EMA:** European Medicines Agency

3.1.8 **FPP:** Finished Pharmaceutical Product

3.1.9 **GMP:** Good Manufacturing Practice

3.1.10 **ICH:** International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

3.1.11 **MAH:** Marketing Authorisation Holder

3.1.12 **SmPC:** Summary of Product Characteristics

3.2 Definitions

The following definitions shall apply.

3.2.1 **Renewal** - The process of extending the period of validity of the Marketing Authorisation at the end of the stipulated 5 years from initial registration, or previous extension.

3.2.2 **Applicant** - means a company or entity registered in terms of the Companies Act and operating in Botswana

3.2.3 **Benefit Risk balance** - A concept used to make regulatory decisions which focus on minimising risks and optimising benefits throughout the lifecycle of a medicinal product. It will promote and protect public health and enhance patient safety by avoiding unnecessary risks

to patients. Benefit-Risk balance of a medicinal product can change and there is a need for re-assessment.

4 General Principles

4.1 As Per the provisions set out in the Medicines and Related Substances Act (MRSA) of 2013, Market Authorization holders should submit renewal applications for all their products registered with Botswana Medicines Regulatory Authority (BOMRA), before the lapse of five (5) years from the date of registration of the product.

4.2 An application for the renewal of registration shall be submitted at least six (6) months before the expiry of the validity period of registration.

4.3 The renewal process includes verification of the product compliance with conditions of registration and current regulatory standards, assessment of the consistency of the quality of the registered FPPs, and its manufacturing process(es) over the identified period, and acceptability of the product's benefit-risk-balance.

4.4 The content of this guideline should be read in conjunction with relevant information described in other existing ICH, WHO, or EMA reference documents and guidelines, as well as, all current BOMRA registration guidelines.

5 Documents to be submitted

Applications should contain the documents listed below:

5.1 Full electronic dossier (CD) in CTD format including the following, either as annexures or in the dossier:

a) Cover letter

b) Duly signed and dated application form *BOMRA/ER/MD/P04/F05* (e-copy and hard copy).

c) Appendix – Product quality review requirements for established generic products

For an established multisource product a product quality review may satisfy the requirements of Sections 3.2.P.2.2.1 (a), 3.2.P.2.3 (a) and 3.2.P.3.5 of the PD and QOS.

A product quality review should be submitted with the objective of verifying the consistency of the quality of the FPP and its manufacturing process.

Rejected batches should not be included in the analysis but must be reported separately together with the reports of failure investigations, as indicated below.

Reviews should be conducted with not less than 10 consecutive batches manufactured over the period of the last 12 months, or, where 10 batches were not manufactured in the last 12 months, not less than 25 consecutive batches manufactured over the period of the last 36 months and should include at least:

1. A review of starting and primary packaging materials used in the FPP, especially those from new sources.

2. A tabulated review and statistical analysis of quality control and in-process control results.
3. A review of all batches that failed to meet established specification(s).
4. A review of all critical deviations or non-conformances and related investigations.
5. A review of all changes carried out to the processes or analytical methods.
6. A review of the results of the stability-monitoring programme.
7. A review of all quality-related returns, complaints and recalls, including export- only medicinal products.
8. A review of the adequacy of previous corrective actions.

A list of validated analytical and manufacturing procedures and their revalidation dates.

Notes

Reviews must include data from all batches manufactured during the review period.

Data should be presented in tabular or graphical form (i.e. charts or graphs), when applicable.

The above is specific to the dossier assessment process requirements and does not relieve the applicant of related GMP requirements.

d) Duly completed renewal application addendum *BOMRA/ER/MD/P11/F01*

6 Guidance on completion of Renewal Application Addendum *BOMRA/ER/MD/P11/F01*

6.1 This section provides guidance on completion of the renewal application addendum *BOMRA/ER/MD/P11/F01* which should be submitted with the renewal application.

To complete the Remarks section:

a) This form is solely for renewal only.

b) **Pending and approved variations should be highlighted as in the addendum below.**

c) Provide any clarity on submitted information in this section. Each new version of documents should allow traceability to the registered dossier and approved variations.

Item	Registered dossier	Renewal Submission[1]	Remarks[2,3] *Guidance Notes for completion of form*
Product Registration number			*State all the BOT numbers*
Pack size (s)			*State all the different pack sizes*
INN Name, strength and pharmaceutical form			
Applicant (Company name, physical address and contact numbers)			
Manufacturer(s) of API(s), with physical address			*Including unit and/or block numbers and contact numbers.* *List each API separately.* *List separately if different steps are performed by different sites e.g. packaging, quality control.*
Number/version of each APIMF or CEP associated with the FPP			*List separately for each API.*
API Specifications			*List separately for each API.* *FPP manufacturer's API specifications should be provided in this section.* *Updated specifications should be provided in the updated dossier*
Retest period/shelf life and storage conditions of API(s) Stability			*Updated stability data should be provided if proposed retest period/shelf life and storage conditions are different from approved shelf life.* *Provide outcome(s) on any commitments made at registration or variation.*
Product description (visual appearance)			

Manufacturing site(s) of FPP, with physical address			*Including unit and/or block numbers and contact numbers.* *List separately if different steps are performed by different sites e.g. packaging, quality control*
Batch size(s) of FPP			
Primary and secondary packaging material(s) and pack size(s)			
Shelf-life of FPP and storage conditions			*Updated stability data should be provided if proposed shelf life and storage conditions are different from approved shelf life.* *Provide outcome(s) on any commitments made at registration or variation* *Shelf life and storage conditions should be in line with current regulatory requirements e.g. long-term stability data at 30 °C for products stored at room temperature*

[1] If there has been no update of the dossier then indicate "N/A" (not applicable).
[2] provide evidence as attachment or refer to the section in the updated dossier with the requested information.
[3]Provide any clarity on submitted information in this section. Each new version of documents should allow traceability to the registered dossier and approved variations.

7 Guidance on completion of the variation table

Fill in the below for variations (both approved and pending) that have been submitted to the authority since the product was registered.

Variation description	Date of submission	Status	Evidence(Annexure) *State in the submission where the evidence is located*
…etc.	*…etc.*	*…etc.*	*…etc.*