Medicines Control Authority of Zimbabwe

MCAZ/EVR /GL-06

GUIDELINE ON RENEWAL OF PRODUCT REGISTRATIONS

EFFECTIVE DATE: APRIL 2023

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Reviewed by:	..... Signature	30/03/2023 Date
Checked by HoD/HoU:	..... Signature	30/3/23 Date
Approved by QM:	..... Signature	03/04/2023 Date
Authorised for use by: Director-General	..... Signature	6/4/2023 Date

Contents

ABBREVIATIONS

API	Active Pharmaceutical Ingredient
CRO	Clinical Research Organisation
CTD	Common Technical Document
FPP	Finished Pharmaceutical Product
GMP	Good Manufacturing Practices
MCAZ	Medicines Control Authority of Zimbabwe
PIL	Patient Information Leaflet
QIS	Quality Information Summary
QOS	Quality Overall Summary
SmPC	Summary of Product Characteristics

1.0 APPLICATION

This guideline applies to holders of product registrations hereinafter referred to as applicants.

2.0 PURPOSE

These guidelines are intended to assist applicants to prepare applications for renewal of product registrations. The applicants are required to demonstrate the conformity of the product to the current standards and norms, and consistency of product quality over the registration validity period.

3.0 BACKGROUND / INTRODUCTION

Registration of a medicinal product is valid for a period of five years unless the product is cancelled or suspended. The registration should therefore be renewed before the expiry of the validity period.

4.0 DEFINITIONS

In these guidelines, unless the context requires otherwise;

4.1 "**Active ingredient**" means a biologically or chemically active substance or compound that is used or intended to be used in the manufacture of a product as an active compound (ingredient).

4.2 "**Applicant**" means a person who submits an application for renewal of registration, who may be a manufacturer, patent holder, or a person responsible for placing the product on the market with Power of Attorney from, or in contract with, the manufacturer or patent holder.

4.3 "**Authority**" means the Medicines Control Authority of Zimbabwe

4.4 "**Product registration**" means the authorisation granted under Section 38 of the Medical Products and Allied Substances Control Bill, for the placement of a medicine or allied substance on the market.

5.0 GUIDELINES

5.1 GENERAL REQUIREMENTS

5.1.1 Product registration will expire after 5 years. In the case where the applicant does not submit the renewal application and the registration expires, the product will be deregistered.

5.1.2 An application for re-registration of a medicine may be made by the applicant or nominee of the applicant.

5.1.3 No update of Module 3 quality data should be made at renewal. The product registration holder is obligated to keep this module updated on an ongoing basis throughout the product's life using variation applications. Attestation notifying the Authority that no further variations have occurred to information provided in the initial application, other than those already submitted to MCAZ as applications for variations, should be provided. A consolidated report of all variations made to the product should also be submitted, in PDF format (as per Annex 1).

5.1.4 The applicant shall submit an application to the Authority between 6 to 9 months before the expiry of registration.

5.1.5 The applicant shall submit a hard copy cover letter and an electronic copy of the application (i.e., in PDF or WinWord format, on CD-ROM or Flash Drive).

5.1.6 The application should be submitted to the following address:
The Director General
Medicines Control Authority of Zimbabwe
106 Baines Avenue
Harare
Zimbabwe

5.2 DOCUMENTATION TO BE SUBMITTED AT RENEWAL OF REGISTRATION

Applications for re-registration should be accompanied by the following documents:

5.2.1 ADMINISTRATIVE INFORMATION

i. A list of all countries where the product has been reviewed and approved along with the registration numbers should be provided. If available, copies of registration certificates should also be submitted.
ii. A cover letter, which includes a clear statement by the responsible person submitting the application, indicating that the information submitted is true and correct.
iii. A duly completed application form for re-registration.
iv. A consolidated report of all variations made to the product should be submitted, in PDF format (as per Annex 1).
v. A completed Quality Information Summary (QIS).
vi. One (1) sample of smallest commercial pack of the product.

5.2.2 TECHNICAL INFORMATION

1 ACTIVE PHARMACEUTICAL INGREDIENT (API)

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

2 FINISHED PHARMACEUTICAL PRODUCT (FPP)

i. Evidence of conformity of the finished product manufacturing facility with the current Good Manufacturing Practice (cGMP) requirements.
ii. 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 medicinal products.
iii. 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.
iv. 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 review of starting and primary packaging materials used in the FPP, especially those from new sources;
   - A tabulated review of quality control and in-process control results;
   - A review of all batches that failed to meet established specification(s);
   - A review of all changes carried out to the processes or analytical methods;
   - A review of the results of the stability monitoring programme; and
   - A list of validated analytical and manufacturing procedures and their revalidation dates.
v. A copy of current signed, dated and version-controlled release and shelf-life specifications of the finished products along with standard testing procedures;
vi. 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 medicinal products.
vii. Information on the shelf life of the products and the storage conditions should be submitted.

5.2.3 PRODUCT INFORMATION

Product information i.e., Summary of Product Characteristics (SmPC) and/or Patient Information Leaflet (PIL), in PDF and WinWord format. If a revised Summary of Product Characteristics (SmPC), labelling and/or Package Leaflet (PL) is proposed within the renewal application, the precise current and proposed wording should be specified. Such listing may be provided as a separate document attached to the application form under a tabular format (indicating the current and proposed texts). Any change(s) not listed, will not be considered as part of the renewal application.

5.2.4 CLINICAL DATA

i. A pharmacovigilance plan and a consolidated report on adverse drug reaction reports, as well as other safety updates, in PDF format. For medicinal products which have a Risk Management Plan (RMP), the applicant is requested to submit an update of the RMP within the renewal application in view of re-assessing the overall benefit-risk balance of the medicinal product concerned.
ii. For applications submitted before the Common Technical Document (CTD) format was implemented, a copy of the complete dossier in CTD format should also be submitted.

5.3 PROCESSING OF APPLICATIONS

5.3.1 The Authority may, during the assessment of applications, request for additional samples, documents, information, or clarifications. The application may be rejected, resulting in a lapse of registration if the applicant fails to satisfactorily address the issues within sixty (60) days from the date of request.

5.3.2 The Authority may reject an application for renewal if:

i. It is found that a product and/or specified manufacturing site no longer complies with the recommended standards.
ii. Any fraud or omissions by the applicant, manufacturer(s) of a FPP or API or CROs in the initial application, becomes evident; and
iii. The Authority considers that a batch (or batches) of the supplied approved product is (are) not in compliance with the approved specifications.
iv. The benefit-risk balance of the product has changed from positive to negative in the light of new scientific evidence from post-marketing experience, studies and publications.
v. The product registration is deemed to have failed to adhere to the conditions of approval of the product such as approved indications, labelling, production information for users.

5.3.2 Where the Authority refuses to renew the product registration, it shall notify the applicant in writing of such a decision and the reason(s) thereof.

6.0 KEY RELEVANT DOCUMENTS

N/A

7.0 HISTORY

DOCUMENT HISTORY		
Revision Number	Date Approved	**Reason(s) for change:** 1. The changes were necessitated by further clarification of medicines registration conditions requirements in line with MASCA chapter 15:03 including additional compliance with critical international good regulatory best practices to ensure that effective, quality, and safe medicines are available to the public. 2. To address IDPs identified and comply with the requirements of the World Health Organisation Global Benchmarking Tool (WHO GBT). **Changes made** **Abbreviations** **Added:** GMP- Good Manufacturing Practices **Section 1: General requirements** **5.2** An application for re-registration of a medicine may be made by: i. The applicant ii. A nominee of the applicant who must submit evidence of the power of attorney **Changed to** **5.1.2** An application for re-registration of a medicine may be made by the applicant or nominee of the applicant **5.3**. No update of Module 3 quality data should be made at renewal. The product registration holder is obligated to keep this module updated on an ongoing basis throughout the product's life using variation applications.
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		Changed to **5.1.3** No update of Module 3 quality data should be made at renewal. The product registration holder is obligated to keep this module updated on an ongoing basis throughout the product's life using variation applications. Attestation notifying the Authority that no further variations have occurred to information provided in the initial application, other than those already submitted to MCAZ as applications for variations, should be provided. A consolidated report of all variations made to the product should also be submitted, in PDF format (as per Annex 1). **5.4.** The applicant shall submit an application to the Authority 3 months before the expiry of registration. **Changed to** **5.1.4** The applicant shall submit an application to the Authority between 6 to 9 months before the expiry of registration. **Added** **5.1.5** The applicant shall submit a hard copy cover letter and an electronic copy of the application (i.e., in PDF or WinWord format, on CD-ROM or Flash Drive). **Section 2: Technical requirements for renewal of registration** **Changed to** **5.2.1 Administrative Information** **Deleted the following from Section 2** **V.** Product information i.e. Summary of Product Characteristics (SmPC) and/or Patient Information Leaflet (PIL), in PDF and WinWord format. If a revised Summary of Product Characteristics (SmPC), labelling and/or Package Leaflet (PL) is proposed within the renewal application, the precise current and proposed wording should be specified on the form. Alternatively, such listing may be provided as a separate document attached to the application form under a tabular format (indicating the current and proposed texts). Any change(s) not listed, will not be

		considered as part of the renewal application; **VI.** Attestation notifying the Authority that no further amendments have occurred to information provided in the initial application, other than those already submitted to MCAZ as applications for amendments. A consolidated report of all amendments made to the product should be submitted, in PDF format (as per Annex 3); and **VII.** A pharmacovigilance plan and a consolidated report on adverse drug reaction reports, as well as other safety updates, in PDF format. For medicinal products which have a Risk Management Plan (RMP), the applicant is requested to submit an update of the RMP within the renewal application in view of re-assessing the overall benefit-risk balance of the medicinal product concerned. **VIII.** For applications submitted before the CTD format was implemented, a copy of the complete dossier in CTD format should also be submitted. **Added the following sections** **5.2. Documentation to be submitted at renewal of registration** **5.2.1 Administrative information** **5.2.2 Technical information** **5.2.3 Product information** **5.2.4 Clinical data** **Section 3: Processing of applications** **Changed to** **5.3. Processing of applications** **5.8** The Authority may during the assessment of applications request additional samples, documents, information, or clarifications. The application may be rejected, resulting in a lapse of registration if the applicant fails to satisfactorily address the issues within thirty (30) days from the date of request. **Changed to**

		5.3.1 The Authority may, during the assessment of applications, request for additional samples, documents, information, or clarifications. The application may be rejected, resulting in a lapse of registration if the applicant fails to satisfactorily address the issues within sixty (60) days from the date of request. **Added** **Annex 1; Table for Summary of Variations submitted**

Annex 1: Summary of Variations Submitted

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

Add or delete rows as necessary