Zambia Medicines Regulatory Authority

GUIDELINES FOR ESTABLISHMENT OF PHARMACEUTICAL MANUFACTURING FACILITIES IN ZAMBIA

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1. INTRODUCTION

The Zambia Medicines Regulatory Authority (ZAMRA) was established under an Act of Parliament, the Medicines and Allied Substances Act No. 3 of 2013 of the Laws of Zambia to regulate and control the manufacture, importation, storage, distribution, supply, sale and use of medicines and allied substances. Its main objective is to ensure that all medicines and allied substances being made available to the Zambian people consistently meet the set standards of quality, safety and efficacy.

Section 34 of the Medicines and Allied Substances Act No. 3 of 2013 of the Laws of Zambia requires that a person who intends to manufacture, distribute or deal in any medicine or allied substance shall apply to the Authority for a Pharmaceutical Licence in the prescribed manner and form upon payment of the prescribed fee.

The manufacturing activities shall be carried out under the full supervision of a pharmacist or a person approved by the Authority as having specialised knowledge in medicines and allied substances to be manufactured.

In addition to these guidelines, prospective manufacturers shall be expected to comply with current WHO guidelines on GMP and other relevant guidelines as applicable.

2. OBJECTIVE

To guide prospective manufacturers on the requirements for the establishment of manufacturing facilities for medicines and allied substances in Zambia.

3. SCOPE

These guidelines apply to any person, institution, business or company engaging in the manufacturing of medicines and allied substances in Zambia. They are intended for sites for full manufacturing, primary packaging and secondary packaging and local manufacturing of natural remedies for both human and veterinary medicines.

4. DEFINITION

In these guidelines, unless the context otherwise requires -

"Act" Means the Medicines and Allied Substances Act (No. 3) of 2013;
"Allied Substances" Include acaricides, cosmetics, disinfectants, food supplements, feed additives and supplements, medical and surgical sundries, medical devices and condoms;
"Authority" Means the Zambia Medicines Regulatory Authority;
"Good Manufacturing Practice" Means the part of quality management that ensures that a product is consistently produced and controlled according to the quality standards appropriate to its intended use and as required by the marketing authorisation, clinical trial authorisation or product specification.
"Manufacture" in relation to a medicine or allied substance, includes any process carried out in the course of making that medicine or allied substance, but does not include the process of dissolving or dispensing a product in, or diluting or mixing it with, some other substance for purposes of administering it; or the incorporation of a medicine in any animal feed;
"Medicine" means human medicine, veterinary medicine, medicinal product, herbal medicine or any substance or mixture of substances for human or veterinary use intended to be used or manufactured for use for its therapeutic efficacy or for its pharmacological purpose in the diagnosis, treatment, alleviation, modification or prevention of disease or abnormal physical or mental state or the symptoms of disease in a person or animal;
"Pharmaceutical Licence" means the licence issued, under section *thirty-four* of the Act, to a person, to manufacture, distribute or deal in a medicine or allied substance;
"Quality Management System" Means a documented system with a collection of business processes focused on consistently meeting customer requirement and enhancing their satisfaction. It is aligned with an organization's purpose and strategic direction. It provides a proactive approach to identifying, evaluating and controlling potential risk to quality. It facilitates continual improvement process performance and maintenance of product quality.
"Quality Manual" Means a document stating the company management's intentions for operating the quality system. It includes policies for all areas of the manufacture, storage, distribution, procedures and facility, affecting or that which affect quality of product during manufacturing;
"Responsible Person" Means pharmacist or a suitably qualified individual with the authority and accountability to ensure that medicines and allied substances are

manufactured, tested, stored, and released in compliance with WHO Good Manufacturing Practices, approved procedures, and applicable regulatory requirements;

"Standard Operating Procedures" Means an authorized written procedure giving instructions for performing operations not necessarily specific to a given product or material (e.g. equipment operation, maintenance and cleaning; cleaning of premises and environmental control; sampling and inspection).

"Site Master File" Means a document prepared by the manufacturer containing specific and factual GMP information about the production and/or control of pharmaceutical manufacturing operations carried out at the named site and any closely integrated operations at adjacent and nearby buildings.

5. ABBREVIATIONS

CAPA: Corrective and Preventive Action

cGMP: current Good Manufacturing Practice

GMP: Good Manufacturing Practice

HPCZ: Health Professions Council of Zambia

MASA: Medicines and Allied Substances Act No. 3 of 2013

PL: Pharmaceutical Licence

SMF: Site Master File

ZAMRA: Zambia Medicines Regulatory Authority

ZEMA: Zambia Environmental Management Agency

6. APPLICATION PROCESS

6.1. An application for a new Pharmaceutical Licence for a facility for manufacture of medicines and / or allied substances shall be made in writing via the ZAMRA online portal.

6.2. An applicant intending to carry out manufacturing of medicines or allied substances in Zambia is required to submit an application containing all necessary documents to the Authority. The information should be sufficient to enable the Authority assess and determine that the processes will result in good quality, safe and efficacious products or meet the required standards.

6.3. Applicants must ensure that all relevant information is accurately entered in the applicable fields on the ZAMRA online application portal.

7. CONTENTS OF AN APPLICATION

7.1. To ensure a comprehensive and efficient review process, applicants must provide all necessary documents and information as part of their application.

7.2. An application for a Pharmaceutical Licence should be accompanied by applicable documents as per **Annex I** of these guidelines.

7.3. All documentation submitted shall be in English and must be legible. Applicants must ensure that all required documents are correctly uploaded to the relevant sections of the online application portal.

8. SCREENING AND EVALUATION OF APPLICATION

8.1. Upon receipt of an application, the Authority shall conduct screening of the submitted application for completeness.

8.2. The fees shall be as prescribed in the ZAMRA fees structure which can be accessed from the ZAMRA website.

8.3. If there are significant omissions or inadequacies that prevent a review of the application, the Authority may issue a request for additional information via the online portal.

8.4. Where a request for additional information is issued, timelines for submission of the additional information shall be stipulated by the Authority. Further processing of the application shall cease until the applicant provides sufficient responses to any queries raised.

8.5. The response to the request for additional information must be provided by the timeline indicated; however, where the applicant anticipates difficulty in responding in full or within the specified timeframe, the applicant should notify the Authority and may request an extension to this date in writing, providing sound justification for the failure to provide the solicited information within the stipulated timelines.

8.6. Where the applicant fails to provide all requested information by the stipulated date without any proper written justification to the Authority or the submitted information is false, incomplete or deficient, a Notice of Rejection of Application may be issued via the online portal.

8.7. Following receipt of a Notice of Rejection of Application, the applicant may re-file/ resubmit a new application. This will be processed as a new application.

9. INSPECTIONS

9.1. Where the application meets the screening requirements, the Authority shall conduct an initial onsite inspection of the facility within the timelines as set out in the current ZAMRA Service Delivery Charter available on the ZAMRA website.

9.2. The inspection shall be conducted to assess the facility's compliance to current guidelines on Good Manufacturing Practices set out by the World Health Organization and other applicable guidelines based on the medicines or allied substances to be manufactured at the facility and the scope of manufacturing.

9.3. The Authority shall inform the premises of the proposed inspection date(s) in writing before the inspection takes place. The respective premise shall make the necessary preparations for inspection on the agreed date(s).

9.4. Under exceptional circumstances and with proper justification, an applicant wishing to change the agreed inspection dates shall do so in writing proposing the most convenient date for both parties.

9.5. During the inspection, inspectors shall observe, verify and review documentation or data related to the quality management system and validation documentation and observe processes where applicable to establish compliance with GMP requirements and applicable licensing requirements.

9.6. Documentation required for review during an inspection include but is not limited to the following;

a. Site Master File;
b. Validation Master Plan and related validation documents
c. Standard operating procedures;
d. Work instructions;
e. Forms and records;

10. INSPECTION REPORT AND COMMUNICATION OF CAPA

10.1. Following completion of the onsite inspection, the Authority shall prepare a final inspection report detailing all inspection findings.

10.2. The final inspection report shall be submitted to an Internal Licensing Committee for review.

10.3. The inspection report shall be communicated with the facility along with a Corrective Action and Preventive Action (CAPA) report format via the online portal within a stipulated timeline as per the ZAMRA Service Delivery Charter.

10.4. The premises shall prepare and implement a CAPA plan where applicable upon receiving inspection findings. The CAPA plan and evidence for its implementation shall be prepared based on quality risk management principles and submitted to the Authority within the stipulated timelines form the date of receipt of the final inspection report.

10.5. The CAPA report shall indicate corrective actions and preventive actions, timelines and evidence for implementation for each deficiency observation and timelines

10.6. Upon receipt of the CAPA report, the inspectors review the CAPA plan and evidence of implementation and provide a CAPA assessment report as per the Service Delivery Charter timelines.

10.7. Upon successful implementation of the CAPA, a follow-up inspection may be conducted to verify the effectiveness of the implemented CAPA. Where such verification is required, the inspection shall be conducted subject to payment of the prescribed inspection fees.

10.8. If the company fails to submit a CAPA report within the prescribed period without any request for an extension, the premise shall be considered to be non-compliant and the application may be rejected by the Authority.

10.9. Upon satisfactory closure of all inspection observations and confirmation of compliance with applicable regulatory requirements, the Authority shall issue the Pharmaceutical Licence.

10.10. The overall duration for processing and issuance of a Pharmaceutical Licence shall be within ninety (90) calendar days, subject to timely submission of required documentation, satisfactory implementation of CAPA by the applicant, and compliance with all applicable regulatory requirements.

11. POST LICENSING INSPECTIONS

11.1. A licensed facility shall be subjected to periodic post licensing inspections on a risk-based approach to assess continued adherence to licensing terms.

11.2. Non-compliance to set standards of quality, safety and efficacy of medicines and allied substances manufactured by the facility may attract a post-licensing inspection of the facility at any given time.

12. RENEWAL OF PHARMACEUTICAL LICENCE

12.1. An application for renewal of the pharmaceutical licence shall be made to the Authority ninety (90) days before expiry of the current licence.

12.2. The application shall capture details of any changes as stated in part 12 of these guidelines, applied for within the period.

12.3. The prescribed fee shall be paid in respect of an application for renewal of a Pharmaceutical Licence.

13. NOTIFICATION OF AMMENDMENTS OR CHANGES RELATING TO LICENSED PREMISES

All licensed manufacturers are required to seek prior authorisation from the Authority for administrative amendments/ changes or structural changes post licensing.

The licensed manufacturer is required to inform the Authority for the purpose of acknowledgment or approval.

13.1. **Administrative Changes/Amendments:**

13.1.1. An administrative change means an amendment to a Pharmaceutical Licence which involves a change in trading name, composition of company directors, change in the responsible person etc.

13.1.2. These changes do not require an inspection of the premises to be undertaken.

13.1.3. The manufacturer will be required to make an application for amendment of Pharmaceutical Licence for the applicable change, via the online portal and paying the prescribed fee as per the fee schedule available on the ZAMRA website.

13.1.4. Examples of administrative amendments include;

13.2. Changes in the responsible person

13.3. **Structural Change:**

13.3.1. Means any changes that are made to a licensed or approved premises post licensing.

13.3.2. Structural amendments/ changes include to but are not limited to changes in the floor layout, flow of personnel and materials in the plant, heating ventilation and air conditioning (HVAC) system changes, water system changes etc.

13.3.3. Structural amendments also include addition (structural) of a production line or block or medication of an existing line (structural) or block.

13.3.4. The manufacturer will be required to make an application for the applicable change, via the online portal and paying the prescribed fee as per the fee schedule available on the ZAMRA website.

13.3.5. Examples of structural changes include;

13.3.5.1.1. Changes to the floor layout:

13.3.5.1.1.1. A manufacturer shall be required to submit a copy of the proposed floor layout of the premises;

13.3.5.1.1.2. The premises shall be inspected by the authority to ensure that they are compliant to set requirements .

13.3.5.1.1.3. The proposed floor layout shall only be adopted once approval is received from the Authority

13.3.5.1.2. Change to the HVAC system

13.3.5.1.3. Changes to the water system

13.4. **Manufacturing Changes:**

13.4.1. A manufacturing change means any changes made by a licensed manufacturer that involves addition of a manufacturing activity other than that which was licensed or a cessation of a manufacturing activity which had been licensed.

13.4.2. Manufacturing changs might require a premises to be inspected prior to amendment of the licence, depending on the nature of the manufacturing activity.

13.4.3. Examples of manufacturing changes include;

a. Addition of a manufacturing activity
    i. An applicant shall made an application via the online portal and by paying the applicable fee
    ii. If the additional manufacturing activity requires structural changes, the applicant shall submit schematics and documentation of the proposed activities. This shall be accompanied by a letter stating the proposed activities.

iii. The premises shall be inspected by the Authority to ensure compliance to set requirements.

iv. A manufacturing change may include addition of a new dosage form which was not part of the scope of the initial/ existing licence.

b. Cessation of a manufacturing activity

i. An intention to cease or discontinue a manufacturing activity which was in the scope of the licensed and approved activities shall be notified to the Authority.

ii. The premises shall not ordinarily be inspected by the Authority unless circumstances warrant an inspection prior to official ceasing of the manufacturing activity.

13.5. **Other Changes**

Relocation

13.5.1. If the location of the facility has been physically transferred, an application shall be made for Relocation to via the online portal and paying the prescribed fee. T

13.5.2. The applicant shall undergo the licensing process as for a new Pharmaceutical Licence.

Change of ownership

13.5.3. If there is change of ownership of the pharmaceutical manufacturing facility licensed, the following documents are required to be submitted in the prescribed manner and form:

i. Proof of business name registration reflecting the name of new owner

ii. Deed of sale or transfer of the facility

iii. Proof of payment

APPENDIX 1: LIST OF DOCUMENTS REQUIRED FOR LICENSING OF A PHARMACEUTICAL MANUFACTURING FACILITY

In order to apply for a Pharmaceutical Licence - manufacturing, the following documents are required to be submitted in the prescribed manner and form**:**

Initial Application

i. Copy of a valid practicing certificate for the responsible person
ii. Contract of employment of the responsible person with applicant
iii. Copy of a valid business registration certificate showing proof of the business name.
iv. Relevant certificate(s) from the local authority
v. Proof of payment of the prescribed fee for licensing of the facility.
vi. A Site Master File (SMF) of the facility in accordance with WHO TRS 961 Annex 14
vii. A permit from the agency responsible for environmental management where applicable.
viii. A Permit from the Zambia Environmental Management Agency (ZEMA).
ix. Architectural engineering permit issued by the local authority where the facility is located.
x. Copy of initial certificate issued (Applicable to renewals)

Reissuance of Lost Certificate or Destroyed Certificate

i. Letter of request
ii. Affidavit of loss or destruction
iii. Proof of payment

Voluntary cancellation of license

i. Letter of notification
ii. Original licence

APPENDIX 2: SERVICE DELIVERY CHARTER TIMEFRAMES

Service Type 5.2.7 Pharmaceutical Licence – Manufacture

Clients	Vital Steps	Standard of Service	Duration
Manufacturers of Medicines and allied substances.	Receive application and prescribed fees payment verification	Within 2 working days	Within 90 days
	Conduct Inspection	Within 18 working days	
	Draft Inspection report and communicate corrective and preventive actions	Within 17 working days	
	Receive and review corrective and preventive actions	Within 4 working days	
	Submit response to corrective and preventive actions	Within 5 working days	
	Conduct verification inspection	Within 7 working days	
	Write verification inspection report	Within 5 working days	
	Issue Pharmaceutical License	Within 4 working days	
Requirements - Duly completed application form - Site Master File - Practicing Certificate for the responsible person - Contract of employment of the responsible person with applicant			