Zambia Medicines Regulatory Authority

GUIDELINES ON GOOD MANUFACTURING PRACTICES

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1. INTRODUCTION

The Zambia Medicines Regulatory Authority (ZAMRA) regulates medicines for human and animal use in accordance with the provisions of the Medicines and Allied Substances Act No. 3 of 2013 of the laws of Zambia and the relevant Regulations made thereunder. (Hereafter referred to as "the Act").

Good Manufacturing Practice (GMP) is that part of quality management which ensures that products are consistently produced and controlled according to the quality standards appropriate to their intended use and as required by the marketing authorisation, clinical trial authorisation or product specification. Therefore, it is important that manufacturers comply with requirements of current Good Manufacturing Practices (cGMP) to ensure that products manufactured meet the required standards of safety, quality and efficacy.

ZAMRA subscribes to the World Health Organisation (WHO) current Good Manufacturing Practice (cGMP) guidelines for inspections for pharmaceutical products. ZAMRA GMP inspections are conducted in line with current World Health Organisation (WHO) GMP guidelines for both local and foreign manufacturers intending to place their products on the Zambian market and those whose products are already on the market.

These guidelines were therefore developed and formatted based on the WHO requirements. Any other supplementary guidance documents referenced address issues not explicitly covered in aforementioned WHO GMP guidelines and serves to clarify the ZAMRA expectations.

2. OBJECTIVE

These Guidelines are intended to provide guidance to manufacturers of medicines and allied substances on how to comply with Good Manufacturing Practice (GMP).

3. SCOPE

These guidelines are intended to serve as guidance for both local and foreign manufacturers of medicines and allied substances on the requirements for Good Manufacturing Practice (GMP) in Zambia. They shall be used for GMP inspection of manufacturers within and outside Zambia whose products are registered or subjected to registration in Zambia. They are not intended as an exclusive approach. ZAMRA reserves the right to request any additional information to establish the safety, quality and efficacy of medicines and allied substances.

Disclaimer

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;

"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;

"Regulatory Reliance" Means the act whereby the regulatory Authority in one jurisdiction may take into account and give significant weight to regulatory work performed by another regulatory or trusted institution for purposes of reaching its own regulatory decisions.

"Recognition" Means an act of acceptance of the regulatory decision of another regulator or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of a recognised Authority is sufficient to meet the regulatory requirements of ZAMRA. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement.

"Standard Operating Procedure" Means an authorised 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.

"**Work-sharing"** Means a process by which the regulatory Authority of two or more jurisdictions shares activities to accomplish a specific regulatory task.

5. ABBREVIATIONS

cGMP: current Good Manufacturing Practice

GL: Guidelines

GMP: Good Manufacturing Practice

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

SMF: Site Master File

TRS: Technical Report Series

ZAMRA: Zambia Medicines Regulatory Authority

6. STANDARDS OF PHARMACEUTICAL MANUFACTURING

Good Manufacturing Practices – Main Principles
The following sections are intended as summary introductions to the main principles of GMP set out in the WHO main GMP guidelines. The sections are not to be taken as the only requirement with regards to the particular principle but should be read together with the full current WHO main guideline on GMP including other specific guidelines outlined in the Annexure I of these guidelines.

6.1. Pharmaceutical quality system
The manufacturer shall be responsible for the quality of products to ensure that they are fit for their intended use, comply with the requirements of the marketing authorisation and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of this quality objective is the responsibility of senior management and requires the participation and commitment of staff in many different departments and at all levels within the company, the company's suppliers and the distributors. To achieve this quality objective reliably there must be a comprehensively designed and correctly implemented pharmaceutical quality system (PQS) incorporating GMP and Quality Risk Management (QRM).

6.2. Sanitation and hygiene
A high level of sanitation and hygiene should be practiced in every aspect of the manufacture of products. The scope of sanitation and hygiene covers personnel, premises, equipment and apparatus, production materials and containers, products for cleaning and disinfection, and anything that could become a source of contamination to the product. Potential sources of contamination should be eliminated through an integrated comprehensive programme of sanitation and hygiene.

6.3. Qualification and validation
In accordance with GMP, the manufacturer should identify what qualification and validation work is required to prove that the critical aspects of their particular operations are controlled.

6.4. Complaints
All complaints and other information concerning potentially defective products should be carefully reviewed according to written procedures and the corrective actions should be taken.

6.5. Contract production, analysis and other activities
Contract production, analysis and any other activities covered by GMP must be correctly defined, agreed and controlled in order to avoid misunderstandings that could result in a product, work or analysis, of unsatisfactory quality.

6.6. Product recalls

There should be a system to recall from the market, promptly and effectively, products known or suspected to be defective.

6.7. Self-inspection, quality audits and suppliers' audits and approval

The purpose of self-inspection is to evaluate the manufacturer's compliance with GMP in all aspects of production and Quality Control. The self-inspection programme should be designed to detect any shortcomings in the implementation of GMP and to recommend the necessary corrective actions. Self-inspections should be performed routinely, and may be, in addition, performed on special occasions, e.g., in the case of product recalls or repeated rejections, or when an inspection by the health authorities is announced. The team responsible for self-inspection should consist of personnel who can evaluate the implementation of GMP objectively. All recommendations for corrective action should be implemented. The procedure for self-inspection should be documented, and there should be an effective follow-up programme.

6.8. Personnel

The establishment and maintenance of a satisfactory system of Quality Assurance (QA) and the correct manufacture and control of medicine and allied substances rely upon people. For this reason, there must be sufficient qualified personnel to carry out all the tasks for which the manufacturer is responsible. Individual responsibilities should be clearly defined and understood by the persons concerned and recorded as written descriptions.

6.9. Training

The manufacturer should provide training in accordance with a written programme for all personnel whose duties take them into manufacturing areas or into control laboratories (including the technical, maintenance and cleaning personnel) and for other personnel as required.

6.10. Premises

Premises must be located, designed, constructed, adapted and maintained to suit the operations to be carried out.

6.11. Equipment

Equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. The layout and design of equipment must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt, and, in general, any adverse effect on the quality of products.

6.12. Documentation

Good documentation is an essential part of the quality assurance system and, as such, should exist for all aspects of GMP. Its aims are to define the specifications and

procedures for all materials and methods of manufacture and control; to ensure that all personnel concerned with manufacture know what to do and when to do it; to ensure that authorised persons have all the information necessary to decide whether or not to release a batch for sale; to ensure the existence of documented evidence, traceability, and to provide records and an audit trail that will permit investigation. It ensures the availability of the data needed for validation, review and statistical analysis. The design and use of documents depend upon the manufacturer.

6.13. Good practices in production

Production operations must follow clearly defined procedures in accordance with manufacturing and marketing authorisations, with the objective of obtaining products of the requisite quality.

6.14. Good practices in quality control

Quality Control (QC) is the part of GMP concerned with sampling, specifications and testing, and with the organisation and documentation which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be compliant with the requirements. QC is not confined to laboratory operations but may be involved in many decisions concerning the quality of the product. The independence of QC from production is considered fundamental.

7. GMP GUIDELINES REFERENCES

NB: The reference guideline documents listed below are the current WHO guidelines and may be updated from time to time by the WHO. The latest published WHO guidelines must be used for each area/ system, even before the review period of this guideline.

GMP TOPIC/AREA	REFERENCE GUIDANCE DOCUMENT
GMP main principles	WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2*** https://www.who.int/publications/m/item/trs986-annex2
Water for Pharmaceutical Use	WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3. ***Short name: WHO TRS No. 1033, Annex*** 3 https://www.who.int/publications/m/item/annex-3-trs-1033
Heating Ventilation and Air-conditioning, HVAC	Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. ***Short name: WHO TRS No. 1010, Annex 8*** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/ Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Second Report Geneva, World Health Organization, 2018, Part 2: Interpretation of *Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products* Annex 2, WHO Technical Report Series, 1019, 2019. ***Short name: WHO TRS No. 1019 Annex 2*** TRS 1019 - Annex 2: WHO good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products (part 2): interpretation of guidelines
Good practice in Quality Control	WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052 Annex 4) ***Short name: WHOT TRS 1052, Annex 4*** TRS 1052 - Annex 4: WHO good practices for pharmaceutical quality control laboratories

Pharmaceutical Microbiology	WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2. ***Short name: WHO TRS No. 961, Annex 2*** TRS 961 - Annex 2: WHO good practices for pharmaceutical microbiology laboratories
Sterile pharmaceutical products	WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 2. ***Short name: WHO TRS No. 1044, Annex 2*** https://www.who.int/publications/m/item/trs1044-annex2
Finished goods transportation validation	Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. ***Short name: WHO TRS No. 961, Annex 9*** http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1 WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5*** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf
Quality risk management	WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. ***Short name: WHO TRS No. 981, Annex 2*** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/ International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human use, ICH Harmonisation Guideline, ICH, **Quality Risk Management Q9(R1), January 2023** ICH_Q9(R1)_Guideline_Step4_2022_1219.pdf
Non-sterile process validation	WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. ***Short name: WHO TRS No. 992, Annex 3*** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf
Data integrity	Guideline on data integrity . WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS No. 1033, Annex 4*** TRS 1033 - Annex 4: WHO Guideline on data integrity
Hold time studies	WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations.

	Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4*** TRS 992 - Annex 4: General guidance on hold-time studies
Site Master File	WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. ***Short name: WHO TRS No. 961, Annex 14*** TRS 961 - Annex 14: WHO guidelines for drafting a site master file
Sampling	WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4. ***Short name: WHO TRS No. 929, Annex 4*** http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1
Validation -HVAC -Water system -Analytical methods -Computerised systems -cleaning - Guideline on qualification of equipment and systems - Non-sterile process validation	WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-third report (WHO Technical Report Series, No. 1019). ***Short name: WHO TRS No. 1019, Annex 3*** TRS 1019 - Annex 3: Good manufacturing practices: guidelines on validation https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-eng.pdf?ua=1
Hazardous substances	WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 3*** TRS 957 - Annex 3: WHO good manufacturing practices for pharmaceutical products containing hazardous substances
Chemical reference standards	General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3*** http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1
Technology transfer	WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4. ***Short name: WHO TRS No. 1044, Annex 4*** https://www.who.int/publications/m/item/trs1044-annex4

Biological products	WHO Expert Committee on Biological Standardization Sixty-sixth report WHO Technical Report Series, No. 999, 2016 Annex 2. ***Short name: TRS No. 999 Annex 2*** WHO good manufacturing practices for biological products, Annex 2, TRS No 999
Blood products	WHO Good Practices for Blood Establishments. WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-eighth report. Geneva, World Health Organisation, 2025. WHO Technical Report Series, 1060 Annex 4 (2025) TRS 1044 - Annex 2: ***Short name: WHO TRS No. 1060 Annex 4*** TRS 1060 - Annex 4: Good practices for blood establishments
Stability studies	WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-second report WHO Technical Report Series, No. 1010, Annex 10. ***Short name: WHO TRS No. 1010 Annex 10*** TRS 1010 - Annex 10: WHO guidelines on stability testing of active pharmaceutical ingredients and finished pharmaceutical products
Herbal medicines	WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-second report. WHO Guidelines on good herbal processing practices for herbal medicines, ***WHO TRS No. 1010, Annex 1*** https://www.who.int/publications/m/item/trs1010-annex1 WHO good manufacturing practices for the manufacture of herbal medicines. ***WHO TRS, No. 1010, Annex 2*** https://www.who.int/publications/m/item/trs1010-annex2
Biosimilars	WHO Expert Committee on Biological Standardization Sixtieth report; WHO Technical Report Series, No. 977, 2013 Annex 2. ***Short name: WHO TRS No. 977 Annex 2*** https://www.who.int/biologicals/publications/trs/areas/biological_therapeutics/TRS_977_Annex_2.pdf?ua=1
Pharmacovigilance	Zambia Medicines Regulatory Authority, 2020. Handbook for Reporting Adverse Drug Reactions, Medication Errors and Product Quality Problems. https://www.zamra.co.zm/wp-content/uploads/2023/06/ZAMBIA-PHARMACOVIGILANCE-Handbook-March-2020-Edited-June-23.pdf
New premises	ZAMRA Guidelines on Establishment of a Pharmaceutical Manufacturing Facility in Zambia. Manufacturers are also free to use any reference engineering texts that help them attain the WHO cGMP Compliance. The following organization can be used as an example; *International Society of Pharmaceutical Engineering* https://ispe.org/
Medical devices	Medical devices — Quality management systems — Requirements for regulatory purposes **ISO 13485** and other related standards
Reliance and recognition	ZAMRA Reliance Guidelines and Policies