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THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

GUIDELINES FOR GOOD MANUFACTURING PRACTICES INSPECTION OF HUMAN MEDICINAL PRODUCTS MANUFACTURING FACILITIES

THIRD EDITION

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ABBREVIATIONS AND ACRONYMS

CAPA	-	Corrective Action and Preventive Action
cGMP	-	current Good Manufacturing Practices
ICH	-	International Council for Harmonization
		Inspection Co-operation Scheme
PIC/S	-	Pharmaceutical Inspection Convention Pharmaceutical
TMDA	-	Tanzania Medicines and Medical Devices Authority
WHO	-	World Health Organization
WHO-TRS	-	World Health Organization-Technical Report Series

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Dr. Yonah H. Mwalwisi
Director, Human and Veterinary Medicines

FOREWORD

Tanzania Medicines and Medical Devices Authority (TMDA) was established under the Tanzania Medicines and Medical Devices Act, Cap 219 with the mission of protecting and promoting public health by ensuring quality, safety and effectiveness of medicines, medical devices, diagnostics and other health related products.

The Authority has a legal mandate of ensuring that all pharmaceutical products manufactured and used in the country meet the prescribed standards for the intended use. The Authority has also been given powers through section 51 of the Act to prescribe requirements for manufacturing of pharmaceutical products.

In accordance with this Section of the Act, TMDA crafted first edition of the Good Manufacturing Practices Guidelines in 2008. These Guidelines were later replaced by the Compendium of Good Manufacturing Practices (GMP), Technical Documents for Harmonization of Medicines Regulations in the East African Community, 2014 which was a result of cooperation of the EAC member states aimed at conducting joint GMP inspections.

However, Advancement in technology and scientific development in the pharmaceutical sector has necessitated the review of current guidance on GMP inspections, thus, these Guidelines has been developed by making direct link to the WHO Technical Report Series on GMP and other international guidelines such that whenever they are reviewed, these Guidelines remain up to date by recognizing the most current version.

These guidelines are intended to be used by manufacturers of the human pharmaceutical products and GMP Inspectors. They are also intended to be used as a training tool for pharmaceutical products industry personnel, GMP auditors and training institutions.

It is our expectation that adherence to these Guidelines will facilitate in Manufacturing of human medicinal products that meet quality standards.

Dr. Adam M. Fimbo
Director General

DEFINITION OF TERMS

For the purpose of these guidelines, the following terms are defined as follows: -

Facility means;
A building that may contain one or more blocks suitably constructed for manufacturing of medicinal products.

Manufacturing site means;
An area with a specified physical address where a facility is located.

Production block means;
Part of the facility consisting of one or more production lines.

Production line means;
An arrangement in the production block in which a medicinal product is being manufactured through a set of linear sequence of operations.

1.0 INTRODUCTION

TMDA is responsible for regulating quality, safety and effectiveness of medicinal products circulating on the market. It is therefore obliged to conduct inspection of medicinal products manufacturing facilities to verify adherence to the current Good Manufacturing Practices (cGMP) which is the requirement for obtaining marketing authorization.

Manufacturing of medicinal products involves a number of operations such as purchase of materials, production, quality control, release, storage, shipment of finished products and the related controls. Such operations need to be carried out according to GMP which form an important part of a comprehensive system of quality assurance. Adherence with cGMP requirement ensures medicinal products are consistently manufactured to meet quality standards required for their intended use.

These guidelines highlight in detail the principles of GMP that should be followed by all companies involved in any aspect of manufacturing of medicinal products for human use. It targets both domestic and foreign manufacturers who intend to obtain marketing authorization of their products in Tanzania in line with the requirements of the Tanzania Medicines and Medical Devices Act, Cap 219.

This Guidelines has described the types of inspection, application of inspection, fees for inspection, inspection frequencies, preparation for inspection, execution and conclusion of inspection, inspection duration, communication of inspection findings, classification of observations, decision on compliance, procedure and timelines for CAPA responses and GMP requirements.

Finally, the guidelines consist of links for the WHO TRS and other international guidelines which details GMP requirement for various aspects applicable for manufacturing facilities. They should be considered as minimum and they are not meant to replace other legal controls, but rather to complement or supplement them.

2.0 GMP INSPECTION PROCESS

2.1 Type of GMP Inspections

GMP inspection may be of four types as indicated below: -

a) **Routine inspection**

Routine inspection is a full review of all aspects and components of GMP within a facility. This type of inspection should be announced and is conducted under the following circumstances: -

(i) To a newly established manufacturing facility or a manufacturer who has expressed interest of expanding manufacturing activities e.g., introduction of new products;

(ii) When there is modification to manufacturing methods or processes, or changes in premises and/or equipment; and

(iii) When business permit or GMP certificate has expired.

b) Concise inspection

Concise inspection is the evaluation of limited aspects relating to GMP compliance within a facility. A limited number of GMP requirements are selected by the inspector to serve as indicators of the overall GMP compliance by the manufacturer. The inspector also has to identify and evaluate any significant changes that could have been introduced by the manufacturer since the last inspection.

Collectively, the selected indicators and the changes identified indicate the manufacturer's attitude toward GMP. A concise inspection is conducted under the following circumstances: -

(i) Where a manufacturer has a consistent record of compliance with GMP through routine inspections in the past; and

(ii) Where a sample of aspects can be taken as a good indication of the overall level of compliance with GMP.

However, if the concise inspection uncovers evidence that the level of GMP compliance has fallen, a more comprehensive or full GMP inspection should be performed soon after the concise inspection. These inspections can be announced or unannounced.

c) Follow-up inspection

A follow up inspection is also referred to as a re-inspection or a reassessment of the manufacturing facilities. It is performed specifically to monitor the result of corrective actions of the manufacturer following a previous inspection.

Depending on the nature of the defects and the work required, the follow-up inspection could be carried out within the agreed timeframe after the previous inspection. The follow-up inspection is limited to specified GMP non compliances that have been observed. A follow up inspection shall be unannounced.

d) Special inspection

A special inspection is undertaken to do spot checks which could focus on one product, a group of related products, or specific operations e.g., mixing, or labeling. The inspection shall be unannounced and is conducted under the following circumstances: -

(i) When there are complaints about a specific product that suggest there may be defects;

(ii) When there is a product recall due to events such as adverse drug reactions; and

(iii) To gather specific information, or to investigate specific operations of the manufacturing processes.

2.2 Application for GMP inspection

2.2.1 Submission of application for GMP inspection should be submitted through TMDA online trader portal. During submission of application, Site Master File (SMF) and filled in GMP application form should be uploaded.

2.2.2 Applicant shall clearly indicate in the SMF and application form number of production blocks and lines to be inspected which are related to products registered or applied for marketing authorization in Tanzania.

2.2.3 The Application should be accompanied by prescribed fees as provided in the Fees and Charges Regulations in force.

2.3 Fees for GMP inspection

2.3.1 The application fees paid for GMP inspections shall be determined and charged as per Fees and Charges Regulations in force.

2.3.2 The Authority shall charge additional fees of twenty five percent (25%) of GMP inspection fees for each additional production block.

2.3.3 In case of one production block with more than four (4) production lines, additional fee of twenty five percent (25%) shall be charged for each additional production line.

2.4 Inspection Frequency

2.4.1 Manufacturing facility shall be inspected once after every 3 years. However, a facility may be inspected any time when necessary.

2.4.2 A domestic manufacturing facility shall be inspected once a year for the purpose of issuance of annual business permit.

2.5 Preparation for inspection

2.5.1 The Authority shall inform the facility on the proposed inspection date before inspection takes place. The inspector shall be responsible for communicating with the facility regarding modality and plan of inspection.

2.5.2 The respective facility shall make the necessary preparations for inspection at the agreed time.

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

2.6 Execution and conclusion of an inspection

2.6.1 During the inspection, inspectors shall observe, verify and review manufacturing processes, procedures and records to establish compliance with the GMP requirements stipulated in these guidelines.

2.6.2 The inspector shall inspect elements of the main GMP principles stipulated under **Annex I** of these guidelines.

2.6.3 At the end of an inspection, observations shall be documented in the GMP inspection Memorandum Form which shall be signed by both parties and a copy given to the inspectee.

2.6.4 Inspection of one facility shall take two (2) days. However, this may vary depending on the number of production blocks or lines available at the facility.

2.7 Reporting and communication of inspection findings

2.7.1 Inspection report shall be prepared and communicated to the inspectee within 45 working days from the last date of inspection.

2.7.2 Summary inspection reports of the inspected facilities will be prepared for publishing in the TMDA website. Nevertheless, the consent from the respective manufacturing facilities shall be sought before publishing.

3.0 CLASSIFICATION OF OBSERVATIONS AND DECISION ON COMPLIANCE

3.1 CLASSIFICATION OF OBSERVATIONS

Non-compliance observations shall be classified as “critical”, “major” and “minor” as follows: -

a. Critical non-compliances

Non-compliance is termed critical if it may cause a significant effect on strength, identity, purity, and safety of the product and may have an adverse psychological response to the consumer. When a critical non-compliance occurs, there is a high probability in product recall. Examples of critical non-compliances are listed in **Table 1** below: -

Table 1: List of examples of critical non-compliances

SN	Observation	SN	Observation
1.	Cross contamination	7.	Improper documentation i.e., documentation is confusing
2.	There is no acceptable air supply system • No qualification records, • No maintenance and monitoring records, • Absence of HVAC • The material flow is not logical and there are no effective control measures to address the matter	8.	Poor cleaning procedures of the manufacturing equipment and premises • No or poor cleaning validation, • Lack cleaning procedures • Lack of cleaning monitoring records
3.	There are no dedicated areas for weighing, storing, holding, processing and packaging of highly toxic products (penicillin, cytotoxic materials, hormones, steroids)	9.	Poor quality control methods such as: • Analytical methods used in the analysis of starting and finished products are not validated • Major equipment for analysis has no installation and/or operation qualification records • Major equipment not calibrated
4.	Key personnel not meeting qualifications	10.	Unethical practices such as: • Use of unqualified personnel in key areas

SN	Observation	SN	Observation
			• Release of products without proper authorization • Cheating
5.	Lack of proper controls in handling of starting materials, in process bulks materials and materials in quarantine or rejected areas.	11.	Majority of workers employed on casual basis
6.	Wrong reconciliation of starting (raw) materials	12.	Storing of reference standard is not correct

b. Major non-compliances

These are non-compliances that have no impact in the strength, identity, purity or safety of the product. There is reduced probability of causing harm to the consumer. Observation of a major non-compliance puts a question mark on the reliability of the firm's quality assurance system. Examples of major non-compliances are listed in **Table 2** below: -

Table 2: List of examples of major non-compliances

SN	Observation	SN	Observation
1.	Lack of self-inspection	3.	Storing of reagents is not correct
2.	Poor training for the workers • No training programs • No training SOP • No training records	4.	Building material not fit for pharmaceutical industries e.g., Asbestos roofing or ceiling.

c. Minor non-compliances

These are non-compliances with low probability of affecting the quality or usability of the product. The inspector has to pinpoint these non-compliances and ask for immediate corrective action by the manufacturer.

Observations which may be classified as minor include using correction pen, overwriting without signatures, some signatures missing in the batch record, delay in the change of SOP’s.

3.2 DECISION ON COMPLIANCE

3.2.1 The status of GMP compliance should be determined by the nature and number of identified deficiencies;

3.2.2 When there are no deficiencies, the facility shall be deemed to be GMP compliant;

3.2.3 When there are minor deficiencies, the facility shall be considered to be operating at an acceptable level of compliance with GMP guidelines. However, the facility shall be required to prepare and implement a Corrective Action and Preventive Action (CAPA) plan, which will be followed up during the next inspection;

3.2.4 When there are minor deficiencies and less than six (6) major deficiencies, the facility will be considered to be operating at an unacceptable level of GMP compliance. The facility shall be required to prepare and submit CAPA plan within 30 calendar days, then submit evidence of implementation within 60 calendar days from the date of the report covering letter

3.2.5 When there is one or more critical deficiencies, or six (6) or more major deficiencies, the facility shall be considered to be operating at an unacceptable level of compliance with GMP guidelines. In this case, the applicant will be required to apply for re-inspection; and

3.2.6 When there is non-compliance, the inspector shall recommend the appropriate regulatory action to the Authority, as specified in Annex II of this Guideline.

4.0 PROCEDURE FOR HANDLING CAPA RESPONSE AND TIMELINES

4.1 The facility shall prepare and implement CAPA plan where applicable upon receiving the final inspection report. The CAPA plan and evidences for its implementation shall be prepared based on quality risk management principles and submitted to the Authority within the timelines stipulated under Annex II of this Guideline.

4.2 If the company fails to submit CAPA plan or implementation report within the prescribed period without any request for extension, the facility shall be considered to be non-compliant.

4.3 The CAPA plan and implementation report shall indicate root cause analysis, corrections, corrective actions and preventive actions, timelines and evidences for implementation as applicable for each non-compliance observation as per format provided in the **Annex III** of these guidelines.

4.4 Manufacturers shall be allowed a maximum of two rounds to submit CAPA responses within the timelines indicated under Annex II. If the assessment of the second CAPA response is still non-satisfactory, the facility will be required to be re-inspected.

5.0 REQUIREMENTS

GMP requirements stipulated in these Guidelines, are based on WHO Technical Report Series (TRS) documents. Only current version of the WHO TRS will be applicable for adherence by both domestic and foreign medicinal products manufacturing facilities.

Besides the WHO TRS, other guidelines such as ICH guidelines and PIC/S guidelines may be used as supplementary guidance documents while establishing compliance of facilities to GMP requirements. The reference guideline documents listed below are the current WHO Guidelines and may be updated from time to time: -

5.1 GMP main principles for finished pharmaceutical products

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

http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

5.2 WHO good manufacturing practices for active pharmaceutical ingredients (bulk drug substances)

WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-six reports. Geneva, Word Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2

https://www.who.int/publications/m/item/annex-2-trs-957

5.3 Antimicrobial resistance

Points to consider for manufacturers and inspectors: Environmental aspects of manufacturing for prevention of antimicrobial resistance

https://www.who.int/publications/m/item/trs-1025-annex-6

5.4 Water for pharmaceutical use

WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-six Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2. Short name: WHO TRS No. 970, Annex 2

http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

5.5 Water for Injection

TRS 1025 Annex 3; Production of water for injection by means other than Distillation

https://www.who.int/publications/m/item/trs-1025-annex-3-water-for-injection

5.6 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/

5.7 Good practice in Pharmaceutical Chemical Testing

WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1. Short name: WHO TRS No. 957, Annex 1

http://www.who.int/medicines/publications/44threport/en/

5.8 Good Chromatography Testing

Good chromatography practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025, Annex 4. Short name: WHO TRS No. 1025, Annex 4

https://www.who.int/publications-detail/978-92-4-000182-4

5.9 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

5.10 WHO good practices for pharmaceutical microbiology laboratories

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

https://www.who.int/publications/m/item/trs961-annex2

5.11 WHO good manufacturing practices for sterile pharmaceutical products

WHO good manufacturing practices for sterile pharmaceutical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-sixth report. WHO Technical Report Series No. 1044, Annex 2. Geneva: World Health Organization; 2011 (https://www.who.int/publications/m/item/trs1044-annex2).

5.12 Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products

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

5.13 WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products

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

5.14 WHO guidelines on 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/

5.15 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

5.16 Guidance on good data and record management practices.

Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5. Short name: WHO GDRMP guidance or WHO TRS No. 996, Annex 5

http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

5.17 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

http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

5.18 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

http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

5.19 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

5.20 Validation (HVAC, Water system, Analytical methods, Computerized 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

https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-eng.pdf?ua=1

5.21 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

http://www.who.int/medicines/publications/44threport/en/

5.22 Technology transfer

WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7. Short name: WHO TRS No. 961, Annex 7

http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

5.23 Biological products

WHO Expert Committee on Biological Standardization Sixty-sixth report WHO Technical Report Series, No. 999, 2016 Annex 2

https://www.who.int/biologicals/areas/vaccines/Annex_2_WHO_Good_manufacturing_practices_for_biological_products.pdf?ua=1

WHO Expert Committee on Biological Standardization Sixtieth report; WHO Technical Report Series, No. 977, 2013 Annex 2

https://www.who.int/biologicals/publications/trs/areas/biological_therapeutics/TRS_977_Annex_2.pdf?ua=1

5.24 Stability studies

WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-second report WHO Technical Report Series, No. 1010, Annex 10

http://apps.who.int/medicinedocs/documents/s23498en/s23498en.pdf

5.25 Herbal medicines

WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-second report WHO Technical Report Series, No. 1010, Annex 2

http://apps.who.int/medicinedocs/documents/s23498en/s23498en.pdf

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EFDA (2021), Good Manufacturing Practices (GMP) Inspection Procedure Directive, Addis Ababa, Ethiopia.

EMA (2022), Compilation of Union Procedures on Inspections and Exchange of Information, European Commission Health and Food Safety Directorate-General, The Netherlands.

FDA GHANA (2020), Guideline for GMP Inspection of Manufacturing Facilities, Accra, Ghana.

Health Canada (2022), Good Manufacturing Practices Inspection Policy for Drug Establishments, Ottawa, Canada.

PPB (2022), Guidelines for GMP Inspection of Manufacturers of Health Products and Technology, Nairobi, Kenya.

TMDA (2018), The Tanzania Food, Drugs and Cosmetics (Good Manufacturing Practice Enforcement) Regulations, 2018, Government Printer, Dar es Salaam, Tanzania.

7.0 ANNEXES

Annex I: GMP main principles and descriptions

S/N	PRINCIPLE	DESCRIPTION
1.	Pharmaceutical quality system	Describe the pharmaceutical quality system (PQS) in place and how well the elements are institutionalized and implemented, including the quality risk management (QRM) and product quality review (PQR)
2.	Good manufacturing practices for pharmaceutical products	Briefly describe how the elements of GMP are implemented
3.	Sanitation and hygiene	Describe procedures and records relating to sanitation and hygiene for personnel, premises, equipment, production materials, cleaning materials and others that could become a source of contamination
4.	Qualification and validation	Describe policies, procedures, records and any other evidence for qualification and validation and how the validation status is monitored and maintained
5.	Complaints	Describe procedures, responsibilities and records for handling complaints, including extension of investigation to other batches, possibility of counterfeits, trending and consideration for recall and notification of competent authorities
6.	Product recalls	Describe the existence of a recall procedure and evidence of its effectiveness; provisions for notification of customers and competent authorities and segregation of recalled product
7.	Contract production, analysis and other activities.	Describe how contractors are evaluated, how compliance with marketing authorization is ensured, existence of comprehensive contracts and clarity of responsibilities and limits
8.	Self-inspection, quality audits and suppliers' audits and approval	a) Self-inspection: describe the procedures and items for self-inspection and quality audits; constitution of self-inspection team(s); frequency of self-inspection; existence of self-inspection schedules and report; system for monitoring follow-up actions. b) Suppliers' audits and approval: describe procedures for evaluation and approval of suppliers including

S/N	PRINCIPLE	DESCRIPTION
		applications of risk management principles, especially determining the need and frequency for on-site audits
9.	Personnel	Describe availability of adequate numbers of sufficiently qualified and experienced personnel, clarity of their responsibilities, limits and reporting hierarchy. Qualifications, experience and responsibilities of key personnel (head of production, head(s) of the quality unit(s), authorized person) and procedures for delegation of their responsibilities
10.	Training	Describe comprehensiveness of procedures and records for induction, specialized and continuing training and evaluation of its effectiveness; coverage of GMP and concepts of quality assurance during training; training of visitors and evaluation consultants and contract staff
11.	Personal hygiene	Describe system in place for initial and regular health examination of staff appropriate to their responsibilities. Measures and facilities to impart, maintain and monitor knowledge of a high level of personal hygiene. Measures to ensure personnel do not become a source of contamination to the product, including hand-washing and gowning. Appropriate restriction of smoking, eating, drinking, chewing and related materials from production, laboratory and storage areas
12.	Premises	Description of the appropriateness of the location, design, construction and maintenance of premises to minimize errors, avoid cross-contamination, permit effective cleaning and maintenance; measures for dust control; specific measures for ancillary areas, storage areas, weighing areas, production areas and quality control areas; measures for appropriate segregation and restricted access; provisions for appropriate lighting, effective ventilation and air-control to prevent contamination and cross-contamination, as well as control of temperature and, where necessary, humidity
13.	Equipment	Describe the adequacy of the numbers, type, location, design and construction, and maintenance of equipment to minimize errors, avoid cross-contamination, permit effective cleaning and maintenance; use, cleaning and maintenance

S/N	PRINCIPLE	DESCRIPTION
		procedures, records and logs; calibration of balances and other measuring instruments; status labelling
14.	Materials	Describe measures in place to select, store, approve and use materials (including water) of appropriate quality and how these measures cover starting materials, packaging materials, intermediate and bulk products, finished products, reagents, culture media and reference standards. Describe also the measures for the handling and control of rejected, recovered, reprocessed and reworked materials; recalled products; returned goods; and waste materials
15.	Documentation	Describe the comprehensiveness and adequacy of the documentation system in place (labels; specifications and testing procedures, starting, packaging materials, intermediate, bulk products and finished products; master formulas; packaging instructions; batch processing and packaging records; standard operating procedures (SOPs) and records) and how principles of good documentation and data management (attributable, legible, contemporaneous, original, accurate (ALCOA)) are institutionalized, implemented and maintained
16.	Good practices in production.	Describe procedures, facilities and controls in place for production (processing and packaging); prevention of risk of mix-up, cross-contamination and bacterial contamination during production
17.	Good practices in quality control.	Good practices in quality control Describe the extent of the organizational and functional independence of the quality control function and the adequacy of its resourcing. Describe the procedures, facilities, organization and documentation in place 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. Describe the procedures for the control of starting materials and intermediate, bulk and finished products; test requirements; procedures and responsibilities for batch record review; procedures, records and facilities

S/N	PRINCIPLE	DESCRIPTION
		for initial and ongoing stability studies; policy, procedures, facilities and records for retention samples.

Annex II: Recommended regulatory actions against observed non-compliances

S/N	CATEGORY OF NON-COMPLIANCES	REGULATORY ACTION(S)
1.	Minor deficiencies only	• Instruct the facility to prepare and submit CAPA Plan within 30 calendar days. • The implementation of the identified CAPA will be verified in the next inspection.
2.	Minor and less than 6 Major deficiencies	The facility will be considered to be operating at an unacceptable level of GMP compliance: • Instruct the facility to prepare and submit CAPA plan within 30 calendar days, then submit evidence of implementation within 60 calendar days from the date of the report covering letter. • Failure to submit CAPA, issue a warning letter for intention to suspend GMP certificate for the respective lines and/or marketing authorization of the products. Issue a final 30 calendar days for addressing the non-conformances. • Failure to address non-conformance within an additional 30 calendar days, suspend GMP certificate and/or marketing authorization of the products. • For facilities declared as GMP compliant after CAPA, verify implementation of CAPA during the next onsite GMP inspection.
3.	One or more critical deficiencies or six (6) or more than six (6) major deficiencies	The facility will be considered to be operating at an unacceptable level of GMP compliance: In case of domestic facilities; • Instruct the facility to prepare a CAPA plan within 15 calendar days and then submit evidence of implementation within 30 calendar days from the date of the report covering letter. Conduct re-inspection within 30 calendar days. • Failure to submit CAPA on time, issue a regulatory action letter notifying-, i. Suspension of the affected manufacturing lines, and/or; ii. Suspension or withdraw GMP certificate and/or; iii. Suspension or withdraw marketing authorization in case of products and/or; iv. Recommend not to grant marketing authorization for the new products. v. Seize API and products upon identified risk and extension of actions to recall products.

		In case of overseas facilities; • Instruct the facility to prepare a CAPA plan within 15 calendar days. • CAPA implementation report should be submitted as part of application for re-inspection. • Suspend marketing authorization of products. • Recommend not to grant marketing authorization for the new products. • Seize API and products upon identified risk and extension of actions to recall products.

Annex III: CAPA Plan

The facility should use the format below to submit CAPA Plan.
Facility Name:
Physical Address:
Inspection Date:
GMP Application Reference No:
Report Received date:

Observation No.	**Category**	**Observation**	**Root cause**	**Correction**	**Corrective action**	**Preventive action**	**Planned completion Date**

Annex IV: CAPA Report Format

Facility Name:

Physical Address:

Inspection Dates:

GMP Application Reference No: Report Received Date:

Observation No.	Category	Observation	Root cause	Correction	Corrective action	Preventive action	Implementation status (refer to evidence in annexes,appendix, attachment	Auditors Comments (Co-inspector and Lead Inspector)	Response Accepted Y/N

8.0 Revision History

Revision No:	Date	Author	Description of change	Section(s) Modified	Approvals
2	10/6/2025	DMC	Change of timelines for CAPA submission based on the type/number of deficiencies observed	Section 4.2 & 4.4	DG
2	10/6/2025	DMC	Change of enforcement actions	Annexes	DG