

**TMDA/DMC/CIE/G/015**  
**Rev. #:00**



**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**

**FIRST EDITION**

**APRIL, 2023**

TMDA Headquarters, Plot No. 56/1, Block E, Kisasa B Centre, Hombolo Road, P. O. Box 1253,  
Dodoma - Tanzania, Tel: +255 (26) 2961989/2061990/ +255(22) 2450512/2450751/2452108, Email:  
info@tmda.go.tz, Website: [www.tmda.go.tz](http://www.tmda.go.tz), Toll free: 08001100834

## TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS.....	ii
ACKNOWLEDGEMENTS .....	iii
FOREWORD .....	iv
DEFINITION OF TERMS .....	v
1.0 INTRODUCTION.....	1
2.0 GMP INSPECTION PROCESS.....	2
3.0 CLASSIFICATION OF OBSERVATIONS AND DECISION ON COMPLIANCE .....	6
4.0 PROCEDURE FOR HANDLING CAPA RESPONSE AND TIMELINES .....	9
5.0 REQUIREMENTS .....	10
6.0 BIBLIOGRAPHY .....	16
7.0 ANNEXES.....	17
Annex I: GMP main principles and descriptions.....	17
Annex II: Recommended regulatory actions against observed non-compliances.....	21
Annex III: CAPA Report Format .....	22
8.0 Revision History .....	23

## **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

## ACKNOWLEDGEMENTS

I wish to thank all staff who assisted in the preparation of these guidelines. I am especially indebted to the following TMDA staff whose technical experience and valuable contributions enabled the preparation and finalization of this document;

Mr. Emmanuel Alphonse	-	Manager of Medicines and Complementary Products Inspection and Enforcement
Ms. Grace Shimwela	-	Manager Quality and Risk Management
Ms. Chimpaye Julius	-	Drug Inspector
Ms. Marcia Awe	-	Drug Inspector
Mr. Maganga Bundala	-	Drug Inspector
Mr. Paul Sonda	-	Drug Inspector
Dr. Misambwa Yongolo	-	Drug Inspector
Ms. Aziza Sengo	-	Drug Inspector

The secretarial task offered by Ms. Joyce Komba is likewise notable and again would like to acknowledge her service towards the completion of this document.

The World Health Organization (WHO) is also acknowledged for making their guidelines and information available for reference.

Last but not least the TMDA Management is acknowledged for positive comments and guidance during deliberations and final approval of these Guidelines.



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 the 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 the manufacturing of pharmaceutical products.

In accordance with this Section of the Act, TMDA crafted the 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 a 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 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.

We expect that adherence to these Guidelines will facilitate in Manufacturing of human medicinal products that meet quality standards



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 medicinal products.

**Manufacturing site means;**

An area with a specified physical address where a facility is located.

**Production block means;**

Part of the facility consists 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 sequences of operations.

## 1.0 INTRODUCTION

TMDA is responsible for regulating the quality, safety and effectiveness of medicinal products circulating on the market. It is therefore obliged to inspect 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 several operations such as the purchase of materials, production, quality control, release, storage, shipment of finished products and related controls. Such operations need to be carried out according to GMP which forms an important part of a comprehensive system of quality assurance. Adherence with cGMP requirements ensures medicinal products are consistently manufactured to meet the 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 medicinal products for human use. It targets both domestic and foreign manufacturers who intend to obtain marketing authorization for their products in Tanzania in line with the requirements of the Tanzania Medicines and Medical Devices Act, Cap 219.

These Guidelines have described the types of inspection, application of inspection, fees for inspection, inspection frequencies, preparation for inspection, execution and conclusion of the inspection, inspection duration, communication of inspection findings, classification of observations, the 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 to manufacturing facilities. They should be considered as a 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 conducted under the following circumstances: -

- (i) To a newly established manufacturing facility or a manufacturer who has expressed interest in expanding manufacturing activities e.g., the introduction of new products;
- (ii) When there is a modification to manufacturing methods or processes, or changes in premises and/or equipment; and
- (iii) When the 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 the 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 labelling. 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 the application, Site Master File (SMF) filled-in in the GMP application form should be uploaded.

2.2.2 Applicant shall indicate in the SMF and application form the 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 the Fees and Charges Regulations in force.

2.3.2 The Authority shall charge additional fees of twenty-five per cent (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, an additional fee of twenty-five per cent (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 at any time when necessary.
- 2.4.2 A domestic manufacturing facility shall be inspected once a year for the issuance of an annual business permit.

## **2.5 Preparation for inspection**

- 2.5.1 The Authority shall inform the facility of the proposed inspection date before the inspection takes place. The inspector shall be responsible for communicating with the facility regarding the inspection 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 on the TMDA website. Nevertheless, 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 the strength, identity, purity, and safety of the product and may have an adverse psychological response to the consumer. When critical non-compliance occurs, there is a high probability of 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 <ul style="list-style-type: none"> <li>• No qualification records,</li> <li>• No maintenance and monitoring records,</li> <li>• Absence of HVAC</li> <li>• The material flow is not logical and there are no effective control measures to address the matter</li> </ul>	8.	Poor cleaning procedures of the manufacturing equipment and premises <ul style="list-style-type: none"> <li>• No or poor cleaning validation,</li> <li>• Lack of cleaning procedures</li> <li>• Lack of cleaning monitoring records</li> </ul>
3.	There are no dedicated areas for weighing, storing, holding, processing and packaging highly toxic products (penicillin, cytotoxic materials, hormones, steroids)	9.	Poor quality control methods such as: <ul style="list-style-type: none"> <li>• Analytical methods used in the analysis of starting and finished products are not validated</li> <li>• Major equipment for analysis has no installation and/or operation qualification records</li> <li>• Major equipment not calibrated</li> </ul>
4.	Key personnel not meeting qualifications	10.	Unethical practices such as: <ul style="list-style-type: none"> <li>• Use of unqualified personnel in key areas</li> </ul>

SN	Observation	SN	Observation
			<ul style="list-style-type: none"> <li>• Release of products without proper authorization</li> <li>• Cheating</li> </ul>
5.	Lack of proper controls in handling starting materials, in-process bulk materials and materials in quarantine or rejected areas.	11.	The majority of workers are employed on a casual basis
6.	Wrong reconciliation of starting (raw) materials	12.	Storing of reference standards is not correct

### b. Major non-compliances

These are non-compliances that have no impact on the strength, identity, purity or safety of the product. There is a 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 <ul style="list-style-type: none"> <li>• No training programs</li> <li>• No training SOP</li> <li>• No training records</li> </ul>	4.	Building materials not fit for pharmaceutical industries e.g., Asbestos roofing or ceiling.

### c. Minor non-compliances

These are non-compliances with a 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 a correction pen, overwriting without signatures, some signatures missing in the batch record, and delay in the change of SOP's.

## 3.2 DECISION ON COMPLIANCE

3.2.1 When the facility is found with no non-compliance observation or with only minor non-compliance observation, the facility shall be considered to be operating at an acceptable level of compliance with these guidelines.

- 3.2.2 In case of minor non-compliance observation, the facility will be required to prepare and implement Corrective Action and Preventive Action (CAPA) that will be followed up during the next inspection.
- 3.2.3 When there are minor and less than six (<6) major non-compliance observations from different six quality systems namely, pharmaceutical quality; production; facilities and equipment; laboratory control; materials; and packaging and labelling systems, the facility shall be considered to be operating at an acceptable level of compliance with these guidelines after submission, assessment and deemed to have successfully implemented the CAPA.
- 3.2.4 When there are six or more ( $\geq 6$ ) major non-compliance observations from different quality systems, the facility shall be considered to be operating at an unacceptable level of compliance with these guidelines.
- 3.2.5 When there are one or more critical non-compliance observations, the facility is considered to be operating at an unacceptable level of compliance with these guidelines GMP.
- 3.2.6 When the facility is deemed to be operating at an unacceptable level of compliance with these GMP guidelines, another inspection will be required. Therefore, the applicant will be required to reapply for re-inspection.
- 3.2.7 When non-compliances are observed in the manufacturing facility, the inspector has to recommend to the Authority appropriate regulatory action to be taken as stipulated in Annex II of these guidelines.

#### **4.0 PROCEDURE FOR HANDLING CAPA RESPONSE AND TIMELINES**

- 4.1** The facility shall prepare and implement a CAPA plan where applicable upon receiving the final inspection report.
- 4.2** The CAPA plan and evidence for its implementation shall be prepared based on quality risk management principles and submitted to the Authority within 90 calendar days from the date of the inspection report cover letter.
- 4.3** If the company fails to submit a CAPA report within the prescribed period without any request for an extension, the facility shall be considered to be non-compliant.
- 4.4** The CAPA report shall indicate root cause analysis, corrections, corrective actions and preventive actions, timelines and evidence for implementation for each non-compliance observation as per the format provided in **Annex III** of these guidelines.

## **5.0 REQUIREMENTS**

GMP requirements stipulated in these Guidelines are based on WHO Technical Report Series (TRS) documents. Only the current version of the WHO TRS will be applicable for adherence by both domestic and foreign medicinal product 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/](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, World 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/](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/](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](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. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6. Short name: WHO TRS No. 961, Annex 6

[http://whqlibdoc.who.int/trs/WHO TRS 961\\_eng.pdf?ua=1](http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1)

## **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](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](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/](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](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](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](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](http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1)

### **5.19 Sampling**

WHO guidelines for a 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](http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1)

### **5.20 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

<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](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](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](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>

## **6.0 BIBLIOGRAPHY**

EAC (2014), Compendium of GMP Technical Document for Harmonization of Medicines Regulation in the East African Community, Arusha, Tanzania.

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

### Annexe 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 the extension of investigation to other batches, the 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, the existence of comprehensive contracts and clarity of responsibilities and limits
8.	Self-inspection, quality audits and suppliers' audits and approval	<p>a) Self-inspection: describe the procedures and items for self-inspection and quality audits; constitution of self-inspection team(s); frequency of self-inspection; the existence of self-inspection schedules and reports; system for monitoring follow-up actions.</p> <p>b) Suppliers' audits and approval: describe procedures for evaluation and approval of suppliers including</p>

S/N	PRINCIPLE	DESCRIPTION
		applications of risk management principles, especially determining the need and frequency for on-site audits
9.	Personnel	Describe the 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 the production, head(s) of the quality unit(s), authorized person) and procedures for delegation of their responsibilities
10.	Training	Describe the 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 the system in place for initial and regular health examination of staff appropriate to their responsibilities. Measures and facilities to impart, maintain and monitor the 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.	<p>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.</p> <p>Describe the procedures, facilities, organization and documentation in place which ensure that the necessary and relevant tests are 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.</p> <p>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 for initial and ongoing stability studies; policy,</p>

<b>S/N</b>	<b>PRINCIPLE</b>	<b>DESCRIPTION</b>
		procedures, facilities and records for retention samples.

**Annex II: Recommended regulatory actions against observed non-compliances**

<b>S/N</b>	<b>CATEGORY OF NON-COMPLIANCES</b>	<b>REGULATORY ACTION(S)</b>
1.	Minor	<ul style="list-style-type: none"><li>• Instruct the facility to prepare and implement CAPA within a given timeframe</li></ul>
2.	Major	<ul style="list-style-type: none"><li>• Instruct the facility to prepare, implement and submit the CAPA report within a given timeframe</li><li>• Institute temporary withdrawal or suspension of GMP certificate and/or marketing authorization of the products</li><li>• Conduct follow-up inspection to verify implementation if necessary</li></ul>
3.	Critical	<ul style="list-style-type: none"><li>• Institute permanent withdrawal of marketing authorization in case of registered products</li><li>• Recommend not to grant marketing authorization for new applications.</li></ul>

**Annex III: CAPA Report Format**

Facility Name:

Physical Address:

Inspection Dates:

Report Number:

Report Received Date:

<b>Observation No</b>	<b>Category</b>	<b>Observation</b>	<b>Root Cause</b>	<b>Correction</b>	<b>Corrective Action</b>	<b>Preventative Action</b>	<b>Implementation Status</b>	<b>Evidence (e.g., appendix/ annex /attachment)</b>

## 8.0 Revision History

Revision No:	Date	Author	Description of change	Section(s) Modified	Approvals