Format: QMS/FMT/001 Revision No: 0 Effective Date: 13 Jan 2020		Department/Division	Food and Drugs Inspection and Safety Monitoring Department	
Document Type: **Standard Operating Procedure**			Doc. Number	: DIS/SOP/137
RWANDA FDA Rwanda Food and Drugs Authority		Title: **SOP FOR PREPARATION OF GMP INSPECTION OF PHARMACEUTICAL MANUFACTURING FACILITY**	Revision Number Revision Date Effective Date Review Due Date	: 0 : 09 Jul 2021 : 16 Jul 2021 : 16 Jul 2024

	Author	Checked by		Approved by
Title	GML&GLP Analyst	Quality Assurance Analyst	DM/FDIC	HoD/FDISM
Names	Fiona MURENZI PADUA	Dr. Vedaste HABYALIMANA	Dr. MURINDAHABI M. Marilyn	Alex GISAGARA
Date	16/07/2021	16/07/2021	16/07/2021	16/07/2021
Signature				

1.0 Purpose

This Standard Operating Procedure is to ensure that:

1.1 A standardized procedure is followed by all inspectors when preparing for routine inspections in order to ensure a consistent approach in conducting inspections.

2.0 Scope

This Standard Operating Procedure:

2.1 Applies for preparation of GMP inspections of manufacturers of Finished Pharmaceutical Products (FFPs) and of Active Pharmaceutical Ingredients (APIs) applied within the Rwanda FDA.

2.2 This SOP does not apply to GMP document review and non-routine inspections

3.0 Policy

3.1 Law No. 003/2018 of 09/02/2018 establishing Rwanda FDA, determining its mission, organization, and functioning states in:
Article 3 (12) ...” compliance with quality standards for the manufacture, export, storage, sale, distribution, use and export of products regulated by this Law”
Article 8 (2) ...” regulate compliance with quality standards relating to the manufacture, storage, sale, distribution, use, import and export, labels, packages and raw materials used in the manufacture of products regulated under this Law”

3.2 Regulations No DIS/TRG/001 Rev. No 0 governing authorization to operate as a manufacturer or wholesaler or small scale manufacturing / compounding or retail seller of pharmaceutical products, 2019, Rwanda Food and Drugs Authority, Kigali, Rwanda.

4.0 Definitions and Abbreviations

4.1 **“Author”** The Author shall be the person(s) who created a document or any subsequent revision of the controlled document.

4.2 “**Approved by**” Endorsement providing authority for a document to become officially valid and to be put into formal use.

4.3 “**Checked by/ Authorized by**” Endorsement signifying that the internal document is ready for approval

4.4 “**Controlled Copy**” A document which is distributed to pre-determined persons or staff and if any change or revision is made on the document, the Quality Management Systems Specialist shall submit the revised document and make sure that the previous (superseded) document is retrieved,

4.5 “**Document**”

a) “Document” means readable information and its supporting medium.
b) A “document” describes any policy, procedure, work instruction or form that is to be controlled.
c) A “document” can be a Law, Regulation, standard, policy statement, manual, guideline, protocol, process flow outlines, standard operating procedure, work instruction, drawing, specification, form, record, chart, report, certificate, checklist, aide memoir, register, worksheet, textbook, poster, notice, memorandum, software, photograph, drawing, or plan.

RWANDA FDA
Rwanda Food and Drugs Authority

d) A "document" may be on various media e.g. paper, magnetic, electronic or optical computer disc, and may be digital, analog, photographic or written.

4.6 "**Effective Date**" A date after the concerned staff or persons have been formally trained or notified or oriented on the use of the document and records maintained, but shall not be later than 15 working days from the revision date.

4.7 "**External Document**"

a) A legal, regulatory or technical document which is not written or created (not internally generated), issued or revised by Rwanda FDA.

b) "External document" can be used as reference in writing internal documents or as a manual for operating equipment.

4.8 "**Internal Document**": A document which is issued and revised by Rwanda FDA.

4.9 "**Master Document**" Original of a controlled internal document that contains original signatures of the authorities that checked/authorized and approved the document.

4.10 "**Objective**" A brief statement(s) describing the purpose of the document.

4.11 "**Policy**" A short statements derived from the applicable law(s), regulation(s), standard(s), resolutions(s), decision(s) or concept(s) that govern the document or provide a mandate or basis for the document.

4.12 "**Procedure**"

When used as a title, e.g. in a Standard Operating Procedure (SOP), or Work instruction, a procedure shall be written as follows:

1) Write clear, concise, step-by-step instructions on how to perform the procedure.
2) Write the instructions chronologically for the user to follow, without a lot of theoretical background.
3) Indicate the preliminary steps that must be done before beginning the actual procedure.
4) Number each step so that repeat steps can be referred to rather than making the SOP very long.
5) Number each sentence so as to make reference to it easy under document revision history when it is revised.
6) Include explanations and an example of how to do any required calculations.
7) Create and indicate the Form(s) where the results, observations or data should be recorded.

4.13 "**Responsibility**" indicates the designations or titles of the Rwanda FDA staff or member and briefly describe their specific responsibilities in performing the procedure

RWANDA FDA
Rwanda Food and Drugs Authority

in a document and in ensuring that the document is implemented and performed correctly and consistently.

4.14 "**Review Due Date**"

A date three years from the effective date, to ensure continued adequacy and suitability of a document. A document may remain valid beyond its review due date if no major change had happened in the process, until the revised document is authorized.

4.15 "**Review**" Assessment of the correctness, suitability and adequacy of a document including technical, legal, regulatory, health, safety, and environment compliance issues.

4.16 "**Reviewer**" The Reviewer shall be the person(s) who assesses a document for technical, legal, regulatory, health, safety, and environment compliance issues as per Section 9.3 of the Document Control SOP number QMS/SOP/001.

4.17 "**Revision Date**" The date when the document is approved and thereby becoming officially valid.

4.18 "**Revision Number**" A numerical figure that changes serially; the first document shall have revision number "0" and its first revision number "1", second revision number "2" and so on.

4.19 "**Safety Precautions**" When used in a procedure e.g. SOP, indicate all safety precautions that must be taken before the procedure is performed. Includes special precautions and protective garments (containment facility clothing, masks, hoods, goggles, gloves, cleanup of spills, etc.) for working with physical, chemical, radioactive, biological or microbiological hazards.

4.20 "**Scope**" A brief statement of where the document applies, when it need to be applied and any limitations of the document.

4.21 "**Title**" A title shall be a short, precise statement representing the contents of the procedures

4.22 "**Uncontrolled Copy**"

A document which is issued to persons or staff who are not part of the distribution list for that document for information purposes only and if any change or revision is made on the document, the Quality Management Systems Specialist is not in control of retrieval of the previous (superseded) document.

4.23 **"Routine GMP inspection"**

This is a full inspection of all applicable components of GMP and licensing provisions.

It may be indicated when the manufacturer:

a) Newly established
b) Requests for renewal of a manufacturing license
c) Has a history on non-compliance with GMP;

RWANDA FDA
Rwanda Food and Drugs Authority

d) Has introduced new product lines or new products, or has made significant modifications to manufacturing methods or processes, or has made changes in key personnel, premises, equipment, e.t.c.
e) Has not been inspected during the last 3 to 5 years.

4.24 **"Concise GMP inspection"**

The manufacturers with a consistent record of compliance with GMP through previous routine inspections are eligible for concise inspections. The focus of a concise inspection is on a limited number of GMP requirements selected as indicators of overall GMP performance, plus the identification of any significant changes that could have been introduced since the last inspection. Collectively, the information obtained will indicate the overall attitude of the firm towards GMP. Evidence of unsatisfactory GMP performance observed during a concise inspection should trigger a more comprehensive inspection

4.25 **"Follow-up GMP inspection"**

(reassessment or re-inspection): Follow-up visits are made to monitor the result of corrective measures. They are normally carried out from 6 weeks to 6 months after the initial inspection, depending on the nature of the defects and the work to be undertaken. They are limited to specific GMP requirements that have not been observed or that have been inadequately implemented.

4.4 "Special GMP inspection"

Special visits may be necessary to undertake spot checks following complaints, recalls related to suspected quality defects in products or reports of adverse drug reactions. Such inspections may be focused on one product, a group of related products, or specific operations such as mixing, sterilization, or labeling. Special visits may be also be made to establish how a specific product is manufactured as a prerequisite for marketing approval or issuance of an export certificate.

5.0 Responsibility

5.1 Head of Food and Drugs Inspection and Safety Monitoring Department is responsible for ensuring that this SOP is implemented and followed.
5.2 GMP inspectors are responsible for adhering to and following this SOP each time they are to prepare for GMP inspection.
5.3 Lead GMP inspectors are responsible for coordinating with:
5.4 The GMP administrator to ensure that all the relevant documentation for the inspection are availed, and
5.5 The auditee company drawn up a tentative inspection plan.
5.6 GMP inspection team members are responsible for assisting the lead GMP inspector in preparing for the inspection.

RWANDA FDA
Rwanda Food and Drugs Authority

5.7 GMP analyst is responsible for co-ordination with the Lead inspector and GMP inspector team members to ensure that all the relevant documentation and logistics for the inspection is provided in a timely manner.

6.0 Distribution

6.1 Director General
6.2 The Head of Food and Drugs Inspection and Safety Monitoring Department
6.3 Division Manager of Food and Drugs Inspection and Compliance
6.4 Quality assurance analyst
6.5 GMP Inspectors.

7.0 Safety Preparations

Not applicable to this SOP

8.0 Materials and Equipment

8.1 GMP guidelines on the manufacture of pharmaceutical products
8.2 Product dossier assessment report (where applicable)
8.3 Product dossier (where necessary)
8.4 Up-to-date site master file
8.5 Completed application form for GMP inspection (for routine inspection)
8.6 Invitation/confirmation letter from the company expressing readiness for the inspection (for routine inspection)
8.7 Previous inspection report (where applicable)
8.8 Corrective Action and Preventative Action (CAPA) report (where applicable)
8.9 Marketing authorization variation report (where applicable)
8.10 Market complaints reports (if any)
8.11 List of minimum documents for review during GMP inspection
8.12 Inspection schedule
8.13 Aide memoir

9.0 Procedures

RWANDA FDA
Rwanda Food and Drugs Authority

Inspectors should properly prepare for inspections, including familiarization with products, sites, types of technologies.

9.1 Once the inspection is allocated to the inspection team, the Lead Inspector is responsible for planning for the performance of the inspection as follows:

9.1.1 Obtain the relevant documents for the inspection as listed under materials in 8.0 above from the GMP analyst and/or from the relevant departments.

9.1.2 Verify the objective, scope and depth of the inspection that is to be carried out.

9.1.3 Familiarize with the products, site, types of manufacturing technologies e.t.c

9.1.4 Inform the relevant people meant to prepare the relevant documents at least 14 days before inspection.

9.1.5 Scrutinize and review the product dossiers for the products manufactured in the respective manufacturing site.

9.1.6 Decide what products will be covered during the inspection.

9.1.7 Review assessment reports from the dossier for individual products including assessment remarks.

9.2 Liaise with relevant departments/officers for any specific information related to the selected;

a) products
b) Pharmacovigilance and post market surveillance reports
c) Product dossiers and any notification/ Amendments
d) Previous inspection reports/CAPAs, if available
e) Confirm the amount of time that will be required to carry out the inspection and plan the date when the inspection will take place. A routine inspection for one site can be performed over a period of at least two to five working days. The length of an inspection is determined by a number of factors, including the type of inspection to be performed, the number of inspectors, the size of the company and the purpose of the inspection or visit. **Annex: criteria for deciding the duration**

9.3 Study the Site Master File and make notes to be followed up during the inspection. This should include:

a) Quality management system, available equipment, SOPs, records
b) Production and quality control processes used
c) Layout and design of the facility and the flow of materials, personnel and processes in the facility
d) Utilities available e.g. environmental control systems (heating, ventilation and air conditioning) water, compressed air, steam etc

9.4 If a current SMF does not exist, request for an updated copy from the company.

9.5 Prepare a checklist of points to be verified during the inspection. Prepare notes for verification in the aide memoire specific to site to be verified during the inspection

9.6 Prepare a Tentative Inspection Plan (Annex I) which can be used as a template that can be modified. Indicate in the programme which sections or departments will be inspected, and when.

9.7 Distribute the Plan to the team members for comments and after finalization, to the company approximately 2 weeks before the inspection.

9.8 The Lead GMP inspector, jointly with the responsible Rwanda FDA officers, the Local Technical Representatives for the facilities to be inspected and the travel agent selected by the procurement unit, shall review and optimize the travel routes and itinerary covering the facilities on the inspection schedule, before the air tickets are confirmed.

9.9 The Lead GMP inspector, jointly with the GMP analyst, shall prepare the necessary documentation to obtain the authorization to travel abroad, visas, international travel insurance, per diem and funds for internal (domestic) travel, and vaccination, where required.

9.10 Liaise with the facility to be inspected to ensure that hotel bookings, pickup from airport to hotel and hotel to manufacturing site; and transfer from site (hotel) to the site (hotel) in collaboration with involved sites in case inspection campaign are planned and confirmed.

10.0 Reference

10.1 WHO PQP SOP 402.1for preparing for an inspection

10.2 9.2 EAC SOP for conducting GMP Inspection,2014

10.3 9.3 PIC/S Standard Operating Procedure on Team Inspections PI 031-1, 29 July 2009

11.0 Appendices

12.1 GMP Inspection Plan format

12.0 Re-Inspection

12.1 During preparation for GMP inspection, the CAPA and/or previous GMP inspection reports should be reviewed

13.0 Records

13.1 The meeting attendance record, notes made during the GMP inspection preparation meetings, any checklists used, record of documents requested (if used), copies of any documents analysed during this planning, should be filed on the company file

14.0 Document Revision History

RWANDA FDA
Rwanda Food and Drugs Authority

Date of revision	Revision number	Author(s)	Changes made and/or reasons for revision
16 July 2021	0	Rwanda FDA Staff	First Issue

End of Document

Annex I: TENTATIVE INSPECTION PLAN

Manufacturer:	
Address:	
Date:	
Reference:	
Inspector(s):	

TIMES FOR GUIDANCE ONLY

Day 1 – AM	
OPENING MEETING 8.30 AM	Introductions
	Objectives and scope of the inspection
	Confirmation of the proposed programme
	Brief presentation of the factory
	Recent changes
DOCUMENT REVIEW	Quality system
	QM and quality policy
	Validation Master Plan
	Change control and deviation management: SOP's + summary list of changes and deviations (2010-2011)
	Annual product review for above mentioned products
	Risk management
	Complaints: SOP + summary list of complaints of (2010-2011)
	Recalls: SOP + summary list of recalls of (2010-2011)
	Site plan, production block layout, indicating the HVAC system and AHU's, material and personnel flow
	HVAC system schematic drawing and summary of specifications for

RWANDA FDA Rwanda Food and Drug Authority

	HVAC
	Purified water system plan and summary of specifications for PW
	Compressed air system schematic drawing and summary of specifications for compressed air
Day 1 – PM	
SITE INSPECTION	Receiving area and stores
	Starting materials, packaging materials and components
	Finished products
	Sampling, dispensing and issuing
DAY 2 – AM	
CONTINUATION OF SITE INSPECTION	Production of tablets - following material flow
Day 2 – PM	
INSPECTION OF PRODUCTION ACTIVITIES	Production of tablets - continuation Utilities • HVAC system • PW system • Compressed air system

Day 3 – AM	
LABORATORY INSPECTION	Wet chemistry laboratory
	Instrumental laboratory
	Laboratory materials management
	Microbiological laboratory
	Retention samples storage
Day 3 – PM	
DOCUMENTS REVIEW	Review of remaining documents
CLOSING MEETING	Approximately 4.30 pm

Notes:

- Tea and lunch breaks will be taken at suitable times
- The inspection will start at approximately 8.30 am and finish at approximately 5 pm each day

At the end of each day if need be a brief meeting will be held to review the findings and discuss the plan for the next.

RWANDA FDA
Rwanda Food and Drugs Authority