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RWANDA FDA Rwanda Food and Drugs Authority	Title: **SOP FOR PLANNING OF GMP INSPECTIONS OF PHARMACEUTICAL MANUFACTURING FACILITIES**	

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Title	GML&GLP Analyst	Quality Assurance Analyst	DM/FDIC	HoD/FDISM
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Signature				

1.0 Purpose

This Standard Operating Procedure is to ensure that:

1.1 GMP Inspectors follow a standardized procedure when planning for routine GMP inspections to ensure consistency and efficiency of the inspection.

2.0 Scope

This Standard Operating Procedure:

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

2.2 This SOP does not apply to Follow-up and Special GMP inspections because they cannot be predicted. It is not possible to prescribe their preparation. This SOP shall only be used as a guide for such non-routine inspections.

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/ Authorised 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document, the Quality Management Systems Specialist shall submit the revised document and make sure that the previous (superseded) document is retrieved,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.

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 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;
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.

5.0 Responsibility

5.1 Head of Food and Drugs Inspection and Safety Monitoring Department is responsible for providing oversight over the planning of inspection of all manufacturers of Finished Pharmaceutical Products (FPPs), and Active Pharmaceutical Ingredients (APIs).

5.2 Division Manager of Drug and Food Assessment and Registration is responsible for the preparation and submission of inspection requests for new facilities to the Division Manager of Food and Drug Inspection and Compliance in a timely manner

5.3 Division Manager of Drug and Food Assessment and Registration is responsible for review and approval of GMP inspections schedules for all manufacturers of Finished Pharmaceutical Products (FPPs) and Active Pharmaceutical Ingredients (APIs).

5.4 GMP analysts are responsible for the selection of manufacturers of Finished Pharmaceutical Products (FFPs) and Active Pharmaceutical Ingredients (APIs) and to prepare schedules and plans for GMP inspections

5.5 Lead GMP inspector is responsible for ensuring that all GMP Inspection team members acquire all the necessary travel documents including visas in time before the inspection dates.

5.6 Logistics officer is responsible for the booking and confirmation of air tickets for the GMP inspectors as per approved travel itinerary and in consultation with the Lead GMP Inspector

5.7 Human Resource and administration director is responsible for obtaining international travel insurance for the GMP inspectors whilst travelling on journeys during the period covered under the stipulated itinerary.

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 Procedures

7.1 Source of manufacturing sites for GMP inspection

7.1.1. The product dossiers shall be submitted by the applicant and accepted by the department of drug and Food assessment and registration before the facility is selected for GMP inspection.

7.1.2. The department of Drug and Food Assessment and Registration shall send notifications to the department of Food and Drugs Inspection and Monitoring about new manufacturing sites for finished pharmaceutical products to be inspected.

7.1.3. The department of Food and Drugs Inspection and Monitoring shall generate a list of sites that manufacture API's where applications have included in the dossier as sources of API's. This list will be used by the inspectorate department to plan and send inspection notifications to the applicants

7.1.4 The GMP Analyst shall retrieve sites that are due for re-inspection from the GMP database and draft letters reminding the manufacturers to re-apply for GMP inspection six months before expiry of their GMP status

7.1.5 Reminder letters shall be reviewed and endorsed by the Head of Department Food and Drugs Inspection and Safety Monitoring and thereafter dispatched by the central secretariat.

7.2 Receipt of application for GMP inspection

7.2.1 The GMP analyst shall receive the application for GMP inspection and check for the availability and completeness of the following;

7.2.1.1 Duly completed GMP inspection application form

7.2.1.2 Current Site Master File

7.2.1.3 Receipt of payment for inspection

7.2.1.4 Department of Drug and Food assessment and Registration request form (for new manufacturing sites)

7.3 Selection of companies to be inspected

7.3.1 The GMP analyst shall undertake the selection of sites to be inspected by verifying the accuracy and correctness for the following:

a) That the applicant has filled in the details in the application form; actual site to be inspected, lines and contact details of the responsible persons.

b) That the applicant has paid the prescribed fee for the blocks and production lines as applicable.

7.3.2 Manufacturing facilities for inspection shall be selected on the basis of:

7.3.2.1 First In First Inspected basis

7.3.2.2 Type of activities or products (sterile/non-sterile, biological or biotechnological product; packaging or API production.)
7.3.2.3 Need to expedite an ongoing regulatory decision process
7.3.2.4 Need to meet a health emergency in the country
7.3.2.5 Prevailing socio-political atmosphere
7.3.2.6 Economic/cost effectiveness of conducting the inspections
7.3.2.7 Weather/climatic conditions
7.3.2.8 Availability of Inspectors with specialized expertise in the team
7.3.2.9 Level of compliance in the previous inspection (Type/class of findings in the previous inspection, Criminal/illegal practices)
7.3.2.10 Expiry of GMP compliance certification
7.3.2.11 Type of inspection to be carried out (refer to types of GMP inspection in SOP for preparation for GMP Inspections.
7.3.2.12 Geographical location of the site to be inspected
7.3.2.13 Public health/interest

7.2 Scheduling of selected companies for inspection

The Division Manager shall allocate dates and durations of inspection based on:

7.2.1 Type of inspection to be performed and the purpose of the inspection or visit.
7.2.2 Anticipated duration of inspection based on plant size, number of blocks/production lines and activities. A combination of all, or some of the factors for selection as appropriate.
7.2.3 Scheduling to be carried out within a period of six months and allocate tentative dates and will be checked and reviewed regularly within the specified period.
7.2.4 The Division Manager of Food and Drugs Inspection and Compliance department shall appoint the inspection team and designate the lead inspector with the adequate competency as per the inspection to be undertaken. He/she will forward the tentative draft schedule of facilities to be inspected to the Head of Department Food and Drugs Inspection, Safety and Monitoring Department.
7.2.5 The Head of Department Food and Drugs Inspection and Safety Monitoring Department shall:
7.2.5.1 Review and approve the inspection schedules
7.2.5.2 Communicate the proposed inspection dates to the manufacturing site for confirmation
7.2.5.3 Receive the confirmation of the inspection dates whether by email or hard copy and forward them to the GMP analyst to liaise with team lead inspector to prepare for the inspection as per SOP for preparation for GMP inspection.

7.3 Out-of-site planning for the inspection

Once the inspection is allocated to a duly-constituted inspection team, the GMP analysts shall be responsible for planning for the performance of the inspection as follows:

7.3.1 Inform the manufacturer(s) through the respective local agents of the proposed date(s) for the inspection and organize letter for invitation to assist in the preparation for travel.

7.3.2 Ensure that the proposed dates for the inspections are suitable for members of the inspection team.

7.3.3 Appropriately Fill Annex 1 for the necessary information that will be used to organize the inspection and facilitate approval.

7.3.4 Verify the objective of the inspection that is to be carried out.

7.3.5 Determine what the scope and depth of the inspection will be to enable to prepare properly for the inspection.

7.3.6 Scrutinize the relevant documents as indicated in SOP for Preparing for inspection.

7.4 Dossier Submission

The dossiers have to be submitted before GMP application and inspection should be carried out before issuing the Marketing authorization. Marketing authorization will only be issued once GMP certificate has been granted.

7.5 Re-Inspection

The CAPA and/or previous GMP inspection reports should be reviewed before planning for the GMP inspection.

7.6 Administration

7.6.1 The GMP analyst shall identify the logistical requirements for the inspection team and submit the request to the Head of Food and Drugs Inspection and Safety Monitoring department through the Division Manager of Food and Drugs Inspection and Compliance

7.6.2 The Head of Food and Drugs Inspection and Safety Monitoring department shall request the Logistics officer to prepare logistical requirements for the inspection team including but not limited to:

7.6.2.1 Application form to travel abroad where applicable

7.6.2.2 Per diem and internal travel funds

7.6.2.3 Visa fees

7.6.2.4 Air-tickets

7.6.2.5 Medical Insurance

7.6.2.6 Transport (for local GMP inspections)

8.0 Re-Inspection

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

9.0 Reference

9.1 WHO PQP SOP; PLANNING FOR AN INSPECTION
9.2 EAC MRH Project SOP for planning for GMP Inspection 2014
9.3 PIC/S Standard Operating Procedure on Team Inspections PI 031-1, 29 July 2009

10.0 Safety Precautions

Not applicable to this SOP

11.0 Records

11.1 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 analyzed during this planning, should be filed on the company file

12.0 Appendices

12.1 Application Form for GMP inspection for pharmaceutical Manufacturing Facilities
12.2 Attachments for GMP Inspection Application for Finished Pharmaceutical Products &Active Pharmaceutical Ingredients Manufacturing Facilities

13.0 Document Revision History

Date of revision	Revision number	Author(s)	Changes made and/or reasons for revision
16 Jul 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 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 5pm 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 day.

Rue. KN 9 Avenue, Nyarutarama Plaza

P.O. Box 1948, Kigali, Rwanda.

email: info@rwandafda.gov.rw;

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Doc Nº: DIS/FDM/016

Rev. Nº: 0

Effective date: 01/03/2019

Ref: Doc: DIS/TRG/001

Application for Good Manufacturing Practice Inspection for Finished Pharmaceutical

Products and Active Pharmaceutical Ingredients Manufacturing Facilities

1. Particulars of the Applicant

Name_____

Physical Address_____

Country_____Telephone_____

E-mail_____

2. Particulars of Manufacturing Site to be Inspected

Name of site_____

Physical Address (if different from 1. above)_____

Country_____Tel_____

E-mail:_____

Note: Separate application to be filled in for each individual site

3**. Contact Person on Site**

Name of contact person_____

Tel: _____Fax:_____

E-mail:_____

4. **Authorized Representative/Agent in Rwanda**

Name of Local Technical Representative_____

Tel: _____ E-mail: _____

5. **Type of Medicines/ Active Pharmaceutical Ingredients**

Type of medicines manufactured (double click to check applicable box)

Human ☐ Veterinary ☐ Human & Veterinary ☐ Herbal ☐

6. **Registration of Products in Rwanda**

Have you registered any products in Rwanda YES ☐ NO ☐

Have you submitted product dossier for registration from the production line(s) applied for inspection? YES ☐ NO ☐ (If "YES", list of the products in the table below)

Trade Name (if any)	Generic Name	Dosage Form	Strength	Primary Packaging

7. **Inspection Applied for (Double click to check applicable box)**

☐ First Inspection

☐ Routine Inspection (state previous inspection dates ……DD/MM/YYYY)

☐ Re-inspection (after failure)

☐ Other (please specify) …….

8. **Major Site Changes Since Last Inspection**

Provide summary of changes to personnel, equipment, buildings, specifications, computer systems, products (type, range or category), suppliers and contractors since last inspection, below or as an Attachment to this form.

……
……

……
……

……
……..

……
…….

Production Lines to be Inspected (Please tick or fill in the applicable boxes)

		Yes	No	Building Block name/ number	Number of production lines	Non B-lactam	b-lactam					
							Penicillin	Cephalos	Cytotoxic	Hormone	Human	Veterinary
1.MANUFACTURING OPERATIONS												
1.1 Sterile Products												
	Aseptically prepared (list of dosage form)											
a)	Large Volume liquids											
b)	Luophilisates											
c)	Semi-solids											
d)	Small volume liquids											
e)	Solids and Implants											
f)	Other aseptically prepared products											

	(e.g. eye drops, prefilled syringes)											
g)	Terminally sterilized (list of dosage forms											
h)	Large volume liquids											
i)	Semi-solids											
j)	Small volume liquids											
k)	Solids and Implants											
l)	Other terminally sterilized prepared products											
1.2 Non-sterile products (list of dosage forms)												
A)	Capsules, hard shell											
b)	Capsules, soft shell											
c)	Impregnated matrices											
d)	Liquids for external use											
e)	Liquids for internal use											
f)	Dry powders for oral suspension											
g)	Medicated lozenges											
h)	Powders/granules in sachets											
i)	Medicinal gases											
j)	Other solid dosage forms (please specify)											
k)	Pressurized preparations											

l)	Radionuclide generators											
m)	Semi-solids											
n)	Suppositories											
o)	Tablets											
p)	Transdermal patches											
q)	Intraruminal devices											
r)	Veterinary premixes											
s)	Other non-sterile medicinal products											
1.3	Biological medicinal products											
a)	Blood products											
b)	Immunological products											
	i)vaccines											
	ii)sera											
	iii) other immunological products											
c)	Cell therapy products											
d)	Gene therapy products											
e)	Biotechnology products											
f)	Human or animal extracted products											
g)	Biosimilar products											
h)	Other											
1.4	Other products or manufacturing activity											
	Manufacture of:											
a)	Herbal products a											

b)	Homoeopathic products											
c)	Biological active starting materials											
d)	Active pharmaceutical ingredients (chemical)											
e)	Other											
2.0	**Sterilization of active substance/excipients/finished product:**											
a)	Filtration											
b)	Dry heat											
c)	Moist heat (steam, superheated water)											
d)	Chemical (ethylene oxide, ozone											
e)	Gamma irradiation											
f)	Electric beam											
g)	Other											
3.0	**Quality Control testing**											
a)	Microbiological: sterility											
b)	Microbiological: non-sterility											
c)	Chemical/Physical											
d)	Biological											
e)	Animal											
f)	Stability											

9. Declaration

I hereby certify that the above information is correct and apply for Good Manufacturing Practice inspection of the above-named site(s). I also commit to welcome the Rwanda FDA GMP inspectors for the inspection.

Signature of applicant……. Date……

Name…….. Designation.....

1. Please submit a copy of the current Site Master File together with this application (refer to Guideline on

preparation of a Site Master File)

2. Submit the completed application together with proof of payment of the appropriate fees, to the Director General

This box is to be completed by Rwanda FDA official only

Inspection Reference Number:		
Assigned to:	Lead GMP Inspector	Team GMP Inspector(s)
Name		
Assigned by:	Date Title:	signature:

Attachments for GMP Inspection Application for Finished Pharmaceutical Products &

Active Pharmaceutical Ingredients Manufacturing Facilities

a) Application letter addressed to DG of Rwanda FDA
b) Filled and signed application form
c) Proof of payment of prescribed fees
d) Site master file (Annex 14, WHO Technical Report Series, No. 961) that is not older than
e) One year from its approval date and any forecasted modifications, including legible colored
f) printouts of water treatment, air-handling systems, including pipeline and instrumentation drawings (P&IDs) in A3 or A2 format
g) Current manufacturing license
h) Current GMP Certificate (GLP, ISO/IEC 17025 accreditation Certificate or WHO prequalification for outsourced laboratory)
i) List of all the products (medicinal or other) manufactured on site and List of products intended for supply in Rwanda. The lists should include proprietary names and international non-proprietary names (INN).
j) Copy of the recent GMP inspection report done by Local medicine regulatory authority and
k) recent GMP inspection report from PIC/S SRA/WLAs or EAC NMRAs if available with
l) a certified translated copy where this is not in English or French or Kinyarwanda.
m) A copy of any warning letter or equivalent regulatory action issued by any authority to which the site provides or has applied to provide the product.

n) Corrective and preventive action (CAPA) and proof of CAPA implementation related to the inspection report observations/deficiencies.
o) The most recent product quality review(s) (PQR)(s) of the concerned product(s)
p) A confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product(s) has been performed and all matters dealt with
q) Quality Manual/Laboratory Manual or equivalent
r) The completed batch manufacturing/packaging record(s) including the analytical part for the most recent released batch of relevant product(s).
s) A list of any recalls or any Market complaints register in the last three years.
t) Aseptic validation report (Required for products applied for that are not terminally sterilized).
u) Contract or agreement between the FPP or API manufacturer and the outsourced testing
v) laboratory or sterilization institution (for Outsourced testing laboratory; and Outsourced sterilization).