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RWANDA FDA Rwanda Food and Drugs Authority	Title: **SOP FOR GMP REPORTING FOR PHARMACEUTICAL MANUFACTURING FACILITY**	

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1.0 Purpose

This Standard Operating Procedure is to ensure that:

1.1 All GMP inspection reports are prepared and peer-reviewed in a consistent and uniform manner as to provide a factual and objective record of the inspection.

1.2 Follow-up action is handled systematically up to close-out the inspection.

2.0 Scope

This Standard Operating Procedure:

2.1 Applies to both local and foreign GMP reports for inspected manufacturing facilities for finished pharmaceutical products (FFPs) and of active pharmaceutical ingredients (APIs)

2.2 Does not apply to desk review of documents for GMP conformity assessment

3.0 Policy

Article 8 (2) ...” regulate compliance with quality standards relating to the manufacture”; and
Article 9 (1) …” formulate regulations and guidelines for regulating the manufacture” regulated products 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.

3.3 GMP Guide – PE 009-13 (Part I), Pharmaceutical Inspection Cooperation Scheme, 1 January 2017, PIC/S Secretariat, Geneva.

4.0 Definitions and Abbreviations

4.1 “Critical” non-compliance

A non-compliance which has produced, or leads to a significant risk of producing either product which is harmful to the human or veterinary patient or a product which could result in a harmful residue in a food producing animal

4.2 “Major” non-compliance

A non-critical deficiency which has produced or may produce a product, which does not comply with its marketing authorization.

Or

Which indicates a major deviation from PIC/s Good Manufacturing Practice;

Or

(within PIC/S) which indicates a major deviation from the terms of manufacturing authorization;

Or

Which indicates a failure to carry out satisfactory procedures for release batches or (within PIC/S) a failure of the authorized person to fulfil his/her required duties

Or

A combination of several “other” deficiencies, none of which on their own may be major, but which may together represent a major deficiency and should be explained and reported as such.

4.3 “Other” non-compliance

A deficiency which cannot be classified as either critical or major, but which indicates a departure from good manufacturing practice

(A deficiency may be “other” either because it is judged as minor, or because there is insufficient information to classify it as major or critical)

Note: “Adopted from PIC/S SOP for inspection format, PI 013-3-1 Annex 25 Sep 2007

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

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

4.6 "**Checked by/ Authorized by**" Endorsement signifying that the internal document is ready for approval

4.7 "**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.

4.8 "**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.

4.9 "**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.

4.10 "**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.

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

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

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

4.14 "**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.

4.15 "**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.

4.16 "**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.

4.17 "**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.

4.18 "**Review**"

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

4.19 "**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.

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

4.21 "**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.

4.22 "**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.

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

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

4.25 "**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 "GMP"**

Good manufacturing practice (GMP) is a system for ensuring that products are consistently produced and controlled according to quality standards.

5.0 Responsibility

5.1 The Head of Food and Drugs Inspection and Safety Monitoring Department is responsible for the implementation of decisions on all manufacturing facilities in a timely manner and in accordance with the legislation to protect public health

5.2 The Division Manager, Food and Drugs Inspection & Compliance ensures that administrative or enforcement actions are undertaken as appropriate and update databases and prepare communication by letter or email.

5.3 Quality assurance analyst ensures the use of update version of the SOP, recalls obsolete documents and keeps document master list.

5.4 The GMP inspectors are responsible for ensuring that corrective actions and preventative actions for non-compliances after GMP inspections reports are assessed by the respective GMP inspection teams in a timely manner and appropriate conclusion made

5.5 The GMP inspection team is responsible for preparing the inspection report and reviewing and assessing the corrective action and preventative measures from the inspected facility and make final conclusion on the GMP rating of the facility.

5.6 The Good Manufacturing Practice Peer Review Committee of Rwanda FDA is responsible for peer-review of the inspection report and recommending final conclusion of the report.

5.7 The GMP analysts are responsible for:

a) Updating and maintaining hard and electronic records arising from GMP inspections
b) Preparing covering letters and email communication to the inspected company. And
c) Preparing GMP certificates for facilities that are rated compliant to GMP.

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 Precautions

Not applicable to this SOP

8.0 Materials and Equipment

8.1 Laptop computers
8.2 Current Rwanda FDA GMP guidelines
8.3 Inspection reports
8.4 Site Master File

8.5 Inspection checklist used
8.6 Product dossier, if necessary
8.7 Compliance report following CAPA

9.0 Procedure

9.1 Writing a GMP Inspection Report

9.1.1 The GMP inspection report shall be written in third person passive style using Arial 12 single spacing and following the approved format. (See Appendix 12.1 for GMP inspection report Format)
9.1.2 The inspection team shall collectively write and agree upon the final GMP inspection report. Any differences of opinion should be resolved by discussion of the facts from the evidence available against the inspection criteria used. However, where this is not possible, the Lead GMP inspector makes the final decision.

9.1.3 The GMP inspection report should be objective, unbiased and factual. It should be detailed enough to enable GMP Peer Review Committee (GPRC) make an informed opinion of the recommendation made by the inspectors.

9.1.4 Each non-compliance listed in the report should be:

a) Clear, concise, accurate, factual, objective, complete, not subject to misinterpretation;
b) Written in the past tense
c) Classified as “Critical”, “Major” or “Other”, (See Appendix 12.2 for guide to risk classification of GMP non-compliance).
d) Referenced to a specific section of the Rwanda FDA guideline on Good Manufacturing Practice for pharmaceutical products Doc. No.: DIS/GDL/003 Revision No. 0 and
e) Cover only one issue per observation. Multiple non-compliances dealing with the same issue should be combined.

9.1.5 A non-compliance that was corrected during the inspection should also be included in the inspection report but include a statement that it was corrected. Corrective action and preventative action done shall still be required from the company for such non-compliances.

9.1.6 The inspection team should prepare, finalize, sign and the GMP Lead inspector submit the final draft GMP inspection report within 6 working days to the Division Manager of Food and Drugs Inspection and Compliance.

9.1.7 The Division Manager of Food and Drugs Inspection and Compliance shall circulate copies

of the draft report.

9.2 Peer Review and Approval of the GMP Inspection Report

9.2.1 The Lead GMP Inspector, accompanied by the team inspector (s), shall present the draft GMP Inspection Report to the GMP Peer Review Committee (GPRC) meeting

9.2.2 The GMP Peer Review Committee members, serving as per the GPRC Terms of References, shall; read the reports, assess their text, context and facts and agree or disagree with the recommendations of the GMP audit team during committee meetings

9.2.3 A site shall be rated compliant to GMP if it has:

a) No "non-compliance"
b) No "critical" or "major" non-compliances but has only "other" non-compliances
c) Major non-compliances that are rectified and corrective action and preventative action (CAPA) submitted by the manufacturer not more than three months from the date of the report has been evaluated found satisfactory within **six months** from the date of inspection.

9.2.4 A site shall be rated non-compliant to GMP if it has:

a) One or more "critical" non-compliances
b) One or more "major" non-compliances for which the CAPA submitted has been found unsatisfactory or the CAPA has not been submitted to Rwanda FDA **three months** from date of the GMP inspection report.

9.2.5 The GMP Inspection team shall make conclusion of their assessment of the acceptability of the GMP status of the facility for the range of products manufactured, using one of the examples below that is appropriate for the rating.

9.2.5.1 *"Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, the facility was considered to be operating at an acceptable level of compliance with Rwanda FDA GMP guidelines and Rwanda FDA GMP requirements*

However, the observations (non-compliances with guidelines) listed below must be addressed in a timely manner. The manufacturer is expected to respond to all observations and for each include a description of the corrective action implemented or planned to be implemented, and the date of completion or target date for completion. The acceptability of corrective actions will be assessed through evaluation of the response to each observation and will be followed up during the next inspection."

Or

9.2.5.2 "Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the in the Inspection Report, the facility was considered to be operating at an unacceptable level of compliance with Rwanda FDA GMP requirements.

Another inspection will be required to verify the implementation of corrective actions before the manufacturer's level of GMP compliance can be reconsidered."

9.2.6 The inspection team shall sign the final inspection report and forward it to the GMP Analyst within 1 working day after the meeting

9.2.7 GMP certificate of compliance shall be issued only after a site has been rated compliant as per section 9.2.2 above. Both a GMP certificate and manufacturing license in case of local facilities in Rwanda, shall be issued if a site is rated compliant, however, a manufacturing license shall only be issued if a site's compliance status is to be made after approval of the corrective action and preventative action report. (see Appendix 12.3 for standard format for GMP certificate of compliance,

9.2.8 Rwanda FDA shall demand for corrective actions and preventative actions to be done and a compliance report with evidence of implementation of corrective actions and supporting documentation submitted for review and approval before the GMP certificate of compliance is issued.

9.2.9 where necessary, and depending on the risk category, a follow-up inspection may be undertaken for a site that has major non-compliances prior to close-out of the inspection and issuance of a GMP certificate of compliance

9.2.10 The GMP analyst shall forward the signed report, covering letter (see Appendix 12.4 for standard format for covering letter together with the GMP certificate of compliance (only for facilities rated as GMP compliant) for review and verification by Division Manager of Food and Drugs Inspection and Compliance.

9.2.11 The GMP analyst shall then forward the signed report, covering letter together with the GMP certificate for endorsement by the Director General.

9.2.12 The GMP analyst shall then scan and email the signed report, covering letter giving the time frame for the plan for corrective measures together with the GMP certificate (the latter applies only if a facility is rated compliant to GMP) to the applicant and/ or contact person in

the manufacturing facility within 45 working days from the date GMP inspectors return to office.

9.2.13 The hard copy of the report shall be sent to the site of manufacture by courier and a copy sent to the local technical representative in Rwanda.

9.2.14 The timeframe for corrective measures may be dependent on the risk category of the non-compliance and the inspection rating but generally, the company is given one month from the date of the report to respond to the inspection report and provide a plan for corrective measures and preventative actions.

10.0 Records

10.1 The quality manuals, master distribution list file, obsolete documents file and general list of documents shall be kept and maintained by QMS for a period specified in the respective document

10.2 Department list of documents shall be kept and maintained by the Head of Food and Drugs Inspection and Safety Monitoring Department

11.0 References

11.1 EAC SOP for preparation and reviewing a GMP Inspection report, 2014

11.2 EMA Compilation of Community Procedures on Inspection and exchange of information, 16 July 2012, EMA/INS/GMP/321252/2012 Rev 15, Compliance and Inspection

11.3 Rwanda FDA guidelines on Good Manufacturing Practices on Pharmaceutical Products

11.4 PIC/S Inspection Report Format, PI 013

11.5 PIC/S SOP on Team Inspections, PI 031-1, 29 July 2009

12.0 Appendices

12.1 Standard Format for GMP Report

12.2 Guide to Risk Classification of GMP non-compliances

12.3 Standard format for GMP certificate of compliance

12.4Standard format for covering letter for GMP Inspection Reports

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

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