RWANDA FOOD AND DRUGS AUTHORITY	Department/Division/ Directorate	Drugs, Food Inspections and Compliance/PV-SM division
Document Type: **Standard Operating Procedure**		Doc. Number :DIS/SOP/005
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Standard Operating Procedure for conducting Good Pharmacovigilance Practice (GVP) Inspections and processing CAPA**	Revision Number :001 Revision Date: :12/06/2020 Effective Date :15/06/2020 Review Due Date :15/06/2021

1.0 Purpose

1.1 To provide a procedure for conducting Good Pharmacovigilance Practice inspections of pharmaceutical companies that have been granted marketing authorization by Rwanda FDA.

2.0 Scope

2.1 This SOP describes procedures for planning, coordinating and conducting PV Inspections.

3.0 Responsibility

3.1 The Director General of Rwanda FDA is responsible for all authorization of Pharmacovigilance Inspections

3.2 The Division Manager for pharmacovigilance and safety monitoring shall ensure that all GPV inspections are conducted according to this SOP.

3.3 The Division Manager for pharmacovigilance and safety monitoring is responsible for coordinating Inspections and facilitating joint inspections

3.4 The Division Manager for pharmacovigilance and safety monitoring is responsible for coordinating review of submitted RMPs and CAPAs and licensing facilities for compliance with GVP practices.

3.5 The PV analyst and specialist ensures that PV inspection is planned as per this SOP

3.6 The Pharmacovigilance specialists are responsible for conducting trainings for QPPVs, performing the inspections and compiling inspection reports and recommendations.

4.0 Distribution list

4.1 Director General

4.2 Heads of Department of Food and Drugs Inspection and Safety Monitoring

4.3 Division Manager of Pharmacovigilance & Safety Monitoring,

4.4 Pharmacovigilance and Post marketing Analyst

4.5 Pharmacovigilance and post market surveillance specialist

4.6 Quality assurance Analyst

5.0 Definition of terms

5.1 **"Local Technical Representative":** The company or legal entity who represents the MAH in EAC and performs functions delegated by the MAH.

5.2 **"Marketing Authorization Holder (MAH)":** The company or legal entity in whose name the marketing authorization for a product has been granted and is responsible for all aspects of the product and compliance with the conditions of marketing authorization.

5.3 **"NMRA"** means National Medicine Regulatory Authorities

5.4 **"Pharmacovigilance System Master File":** A document that describes the pharmacovigilance system for one or more products of the marketing authorization holder.

5.5 **"Qualified Person for Pharmacovigilance (QPPV):"** An individual named by a Marketing Authorization Holder (MAH) as the main person responsible for ensuring that the company (the MAH) meets its legal obligations as specified in the EAC Pharmacovigilance compendium and respective partner state regulations.

5.6 **"Risk Management Plan":** A systematic approach and set of pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimize risks relating to products, and the assessment of effectiveness of those interventions and how these risks will be communicated to the NMRAs and the general population.

6.0 Procedures

6.1 Preparing for a GVP Inspection

Preparatory work for a pharmacovigilance inspection should involve collaboration of the inspectors commissioned for conducting the inspection and shall include the following steps:

6.1.1 Identify the MAH to be inspected.

6.1.2 Allocate resources to conduct the inspection including making the necessary logistical arrangements. The resources include:

6.1.2.1 Selection of inspectors (reporting inspector, lead inspector) with the necessary training and experience in performing PV inspections

6.1.2.2 Sufficient inspection days

6.1.2.3 Financial resources

6.1.3 Announce the inspection to the inspected entity unless it is 'for cause' inspection to investigate an immediate public health or compliance concern;

6.1.3.1 an advance notice of a period of six to eight weeks for a routine inspection and notice is sent to the QPPV

6.1.4 The lead inspector shall prepare the inspection plan which may include: the objectives and scope of the inspection, identification of the inspection team members and their respective roles, the date and place, where the inspection is to be conducted, units to be inspected and duration of inspection

6.1.5 Inspector(s) shall familiarize themselves with the pharmacovigilance system and any relevant product specific issues, prior to the inspection. The information submitted by the inspected entity, may be considered including Pharmacovigilance inspection history

6.1.6 Inspectors may gather information on number of products from the MAH, therapeutic area, specific concerns that need to be addressed, clinical trials and Pharmaco-epidemiological studies :

6.2 Coordinating the PV inspection

6.2.1 The inspectors shall verify that the site(s) identified for inspection, and included in the inspection announcement, are appropriate with respect to ensuring the objectives of the inspection can be achieved.

6.2.2 If teleconference(s) are planned during the inspection with experts, assessors, MAH personnel located off site etc. This should be identified in advance.

6.2.3 If upon agreement from Rwanda FDA, it is decided to conduct a remote inspection, the inspected entity should be contacted to make the necessary

arrangements. Any communication between Rwanda FDA and MAH shall be documented

6.3 Conducting a GVP Inspection

The inspection activities shall be carried out in accordance to the inspection plan. The inspection plan can be amended during the inspection, to ensure that the objectives are achieved. Any amendment to the plan shall be documented.

6.3.1 Opening Meeting

Before the start of the inspection, an opening meeting must take place between the inspector(s) and in particular the key personnel of the inspectee (s), for the purpose of providing an overview of the inspection plan. The chair of the meeting shall be the lead inspector. In particular, the following points should be addressed during the opening meeting:

6.3.1.1 The lead inspector should describe the purpose and the scope of the inspection. ,

6.3.1.2 The item headings in the Pharmacovigilance Inspection Plan should be mutually agreed, and inspection logistics should be discussed.

6.3.1.3 The lead inspector should re-confirm that the resources, documents and means required by the inspectors are available.

6.3.1.4 The time and date for the closing meeting and any interim meetings should be confirmed.

6.3.2 Conduct of the Inspection/Collecting information and recording observations

6.3.2.1 Sufficient information to fulfill the inspection objective(s) should be collected through examination of relevant documents and computer systems, as well as through the conduct of interviews with relevant

personnel and review of internal and external communication e.g. logbooks, registries, communication with authorities etc

6.3.2.2 The following items should be reviewed as part of the pharmacovigilance inspection:

6.3.2.2.1 Legal and Administrative Aspects

i. Documentation of the responsible parties for pharmacovigilance/drug safety activities, QPPV, Contracts, reports and others

6.3.2.2.2 Organizational Structure

i. Quality System and Standard Operating Procedures (SOP) for Pharmacovigilance Activities

ii. Qualified Person for Pharmacovigilance (QPPV)
   a. Documentation identifying the QPPV, along with qualification and training documentation.
   b. Documentation of the QPPV and contact details in the quality

iii. Resources and Training of Personnel
   a. Interview of personnel involved in any pharmacovigilance activity.
   b. Documentation of job description, qualifications and training of individuals involved in any stage of pharmacovigilance/safety evaluation process.
   c. Documentation on policies and procedures for training of personnel.
   d. Allocation of deputies to key personnel.

6.3.2.2.3 Equipment and Computer Systems

i. Computer systems in use (administration, use and hardware/software specifications and validation approvals).
ii. Migration of data and legacy system, where relevant.

iii. System for the archiving and retrieval of documents.
iv. Procedure for collecting, archiving, filing and recovering documents.
v. Controlled access to the archives.

6.3.2.2.4 Safety Information from Clinical Trials

i. Safety information in connection with clinical trials undertaken by the MAH and matters relating to the harmonization of pharmacovigilance databases may be inspected in accordance with the applicable guidelines.
ii. Links between the post-marketing pharmacovigilance activities and clinical trial activities (people, procedures, departments, computer systems, organizations)
iii. Reconciliation of information in clinical trial and pharmacovigilance databases

6.3.2.2.5 Safety Information from Other Departments: quality defects, medical information, legal information

i. Quality defects and complaints should be examined to determine whether there are quality defects that could lead to adverse reactions or whether there may be a quality defect reported that could be the cause of actual or potential adverse reactions and vice versa. Reconciliation of these data should be arranged.
ii. Handling of medical information and legal information should also consider detection of potential adverse reactions.
iii. Information collected by marketing and regulatory affairs departments.

6.3.2.2.6 Data/Documentation Review

The strategies used during inspection will depend on the objective(s) of the inspection, and the minimum elements that must be considered during review of data/documents are provided below:

i. Confirmation that potential adverse reactions from any source have been processed appropriately.
ii. Determination of seriousness.
iii. Determination of expectedness.
iv. Causality assessment.
v. Consistency and correctness of coding with terminologies used/internal procedures.
vi. Quality and completeness of the medical review.

6.3.2.2.7 Recording Inspection Observations.

i. All inspection observations should be documented. If possible, copies should be made of records containing inconsistencies or illustrating non-compliance.
ii. At the end of the inspection, the inspectors should list and review the non-compliances or system deficiencies. The inspector(s) should ensure that these are documented in a clear and concise manner and are supported by objective evidence.
iii. All reported observations (findings) should be indicated, taking into account the specific requirements of the regulations or other related documents based on which the inspection has been conducted.
iv. The names and titles of persons interviewed or present during the inspection meetings and the details of the inspected organization should be documented.

6.3.3 Closing Meeting

At the end of the inspection, the inspector(s) should conduct a closing meeting with the inspectee. The QPPV, his deputy or other responsible persons for pharmacovigilance activities should attend the meeting. The purpose of the closing meeting is:

i. To summarize inspection findings and observations to ensure that the results of the inspection are clearly understood and that there is no misunderstanding by either the inspectors or the inspectees;

ii. To provide the inspectee with an opportunity to correct any misconceptions made by the inspector or to supply additional information in response to the findings;
iii. To clarify the procedures for the distribution of the inspection report, for the production of responses to the inspection report and for inspection follow-up (as appropriate);
iv. To request copies of any documents that may be required by the inspector (e.g. to assist with the preparation for other activities associated with the inspection). An inspection may consist of visits to more than one location. If possible, a closing meeting may be held at each location inspected

6.4 Preparation of Inspection Report

6.4.1 An inspection report (IR) shall be prepared in English by the members of the inspection team, coordinated by the lead inspector or, reporting inspector in accordance with the template provided in the *Rwanda FDA safety and vigilance guidelines ANNEX ….*

6.5 Follow-up of Inspection Findings and CAPA

6.5.1 Where an inspection reveals non-compliances, the MAH will be required to provide responses to the inspection report in form of a CAPA plan within 30 working days following receipt of the same. The CAPA plan shall contain solution proposals to correct the non-compliances and to avoid their recurrence.

6.5.2 There may be a follow-up inspection at an appropriate time to verify the progress and success of the action plan containing the solution proposals**.**

6.5.3 The MAH may also take the opportunity to correct misconceptions or misunderstandings in response to the findings. If findings are disputed, the inspector(s) should request relevant documentary evidence supporting the responses.

6.6 Regulatory Action and Sanctions

In the event of non-compliances revealed during an inspection, the regulatory action that may be taken include:

i. **Education and facilitations**: The MAH is informed of the non-compliance and advised on how this can be remedied.
ii. **Re-inspection**: Non-compliant MAH may be re-inspected to determine whether the non-compliance has been remedied.
iii. **Warning**: Rwanda FDA may issue a formal warning to MAH, reminding them of their pharmacovigilance regulatory obligations.
iv. **Publication of MAHs**: Rwanda FDA may publish a list of persistently non-complying MAHs.
v. **Urgent safety restriction**: Rwanda FDA may act in accordance with the applicable respective partner state NMRA regulations.
vi. **Suspension of Registration**: Rwanda FDA may act in accordance with regulations governing registration of medical products.
vii. **Revocation of Registration:** Where necessary Rwanda FDA may revoke the registration of the medicines

7.0 Record keeping

7.1 Responsibilities

7.1.1 Rwanda FDA shall record all pharmacovigilance information and ensure that it is handled and stored so as to allow for accurate reporting, interpretation and verification of that information.

7.1.2 They shall put in place a record management system for all documents used for pharmacovigilance activities that ensures the retrievability of those documents as well as the traceability of the measures taken to investigate safety concerns, of the timelines for those investigations and of decisions on safety concerns, including their date and the decision-making process.

7.2 Storage

7.2.1 The records/files of all pharmacovigilance inspections conducted must be stored safely, protected from unauthorized access, protected from

unauthorized alteration and in accordance to the Rwanda FDA QMS requirements.

7.2.2 The inspection files should be stored safely in a suitable archive for the whole retention period and access to the archives granted to authorized personnel only.

7.2.3 All soft copies of records shall be maintained in Management Information System (MIS) database or any other system in place.

7.2.4 If documents are to be stored and archived using electronic or optical media, the methods for transferring the data to these media should be validated.

7.2.5 A suitable back up-strategy must be implemented to prevent loss or destruction of data.

7.2.6 There must be a possibility to generate hard copies throughout the period of retention.

7.2.7 either electronically or as hard copy, in the archives for unlimited time.

8.0 References

8.1 EAC Harmonized Compendium on Safety and Vigilance of Medical Products and Health Technologies

8.2 The National Drug Authority and Policy Regulations (Pharmacovigilance) 2014, Regulation 3

8.3 The EAC QMS Requirements for the regulation of medicines, cosmetics, medical devices and diagnostics.

8.4 Procedure for conducting Pharmacovigilance Inspections requested by the CHMP-EMA EMEA/INS/GCP/218148/2007 Procedure no: INS/PhV/2

9.0 Annexes

ANNEX I: PHARMACOVIGILANCE INSPECTION REPORT FORMAT

Company Name:

PSMF:

Inspection number: [Enter inspection reference number as applicable] Date of issuance

SECTION A: ADMNISTRATIVE INFORMATION.

Inspection type:	
Name and address(es) of site(s) inspected:	
Contact person:	
Date(s) of inspection:	

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		Revision Date:	:12/06/2020
		Effective Date	:15/06/2020
		Review Due Date	:15/06/2021

Lead inspector:	
Reporting inspector	
Accompanying inspector(s) and experts:	
Previous PV inspections: (Date and inspecting authority)	
Purpose of inspection:	
Products selected to provide system examples:	As part of the general systems review, there are products chosen for close evaluation of ADR reports, PSURs, etc.
Name and location of the qualified person for pharmacovigilance (QPPV):	Name: Contact details:
Date of first issue of report to MAH:	Date of submission
Deadline for submission of responses by MAH:	
Date(s) of receipt of responses from MAH:	
Date of final version of report:	
Report author:	Name Job title

SECTION B: GENERAL INFORMATION

1. Scope and reason for the inspection
2. Reference texts and documents for the inspection
3. Conduct of the inspection with summary of the organization and any significant Changes and action taken since the last inspection

SECTION C: INSPECTED ITEMS

SECTION D: FINDINGS

Definitions of inspection finding grading

1. Critical (CR):

Finding CR1 Use the categories (and subcategories) listed in Annex II followed by a short title for the finding

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<<Inspector to add text>> References: Directive 2001/82/EC as amended, Article xxx Volume 9B, section xxx (as appropriate) Add any local requirement (if appropriate)	
Root cause analysis	
<<MAH to add text>>	
Further assessment	
<<MAH to add text>>	
Corrective action(s)	
<<MAH to add text>>	
Deliverable(s) <<MAH to add text>>	Due date(s) <<MAH to add text>>
Preventative action(s)	
<<MAH to add text>>	
Deliverable(s) <<MAH to add text>>	Due date(s) <<MAH to add text>>
Recommendation / Observation (amend as necessary)	

MAJOR FINDINGS

Present the major findings as corresponding to the definition

Finding MA1 Use the categories (and subcategories) listed in Annex II followed by a short title for the finding

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<<Inspector to add text>> References: Directive 2001/82/EC as amended, Article xxx Volume 9B, section xxx (as appropriate) Add any local requirement (if appropriate)	
Root cause analysis	
<<MAH to add text>>	
Further assessment	
<<MAH to add text>>	
Corrective action(s)	
<<MAH to add text>>	
Deliverable(s) <<MAH to add text>>	Due date(s) <<MAH to add text>>
Preventative action(s)	
<<MAH to add text>>	
Deliverable(s) <<MAH to add text>>	Due date(s) <<MAH to add text>>
Recommendation / Observation (amend as necessary)	

MINOR FINDINGS

Present the minor findings as corresponding to the definition

Finding MI1 Use the categories (and subcategories) listed in Annex II followed by a short title for the finding	
<<Inspector to add text>> References: Directive 2001/82/EC as amended, Article xxx Volume 9B, section xxx (as appropriate) Add any local requirement (if appropriate)	
Root cause analysis	
<<MAH to add text>>	
Further assessment	
<<MAH to add text>>	
Corrective action(s)	
<<MAH to add text>>	
Deliverable(s) <<MAH to add text>>	Due date(s) <<MAH to add text>>
Preventative action(s)	
<<MAH to add text>>	
Deliverable(s) <<MAH to add text>>	Due date(s) <<MAH to add text>>
Recommendation / Observation (amend as necessary)	

Comment:

SECTION E:

1. Conclusions recommendations
2. Evaluation by the inspectors of the response from the inspectee
3. Final conclusions and recommendations

SECTION F:
Date and signatures of lead and other inspectors, experts if applicable

ANNEX II: CLASSIFICATION OF INSPECTION FINDINGS

Critical: a situation in pharmacovigilance systems, practices or processes that adversely affects the rights, safety or well-being of patients or that poses a potential risk to public health or that represents a serious violation of applicable legislation.

Major: a situation in pharmacovigilance systems, practices or processes that adversely affects the rights, safety or well-being of patients or that poses a potential risk to public health or that represents a violation of applicable legislation.

Minor: a situation in pharmacovigilance systems, practices or processes that would not be expected to adversely affect the rights, safety or well-being of patients.

Annex III: GVP certificate / license-not developed yet

10.0 Revision History

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

End of Document