**Botswana Medicines Regulatory Authority**

**Approved By:**

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| **Dr. P. Gurumurthy**<br>**Director**<br>**Pharmacovigilance and Clinical Trials** | **Date of Approval (DD/MM//YY)** |

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## Revision status sheet

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## 1 Purpose

The purpose of this document is to provide guidance to Market Authorisation Holders (MAHs) and their contractors, on the conduct of good pharmacovigilance practices inspections.

## 2 Scope

The scope of this guideline includes all pharmacovigilance inspection activities for all MAHs or their contractors who have registered medicinal products in Botswana.

## 3 Definitions and abbreviations

### 3.1 Definition

The following definitions shall apply:

**3.1.1 Contractors-** Companies or individuals appointed by the MAHs to carry out Pharmacovigilance obligations on their behalf.

**3.1.2 Market Authorization Holder (MAH**)- is a company, firm or non-profit organization that has been granted a marketing authorization.

**3.1.3 Pharmacovigilance (PV)** - the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

**3.1.4 Pharmacovigilance inspections-** are activities conducted by BoMRA to ensure that requirements and /or obligations for monitoring the safety of medicines are met. The responsibility for carrying out the inspection's rests with the national competent authorities**.**

**3.1.5 The Authority**- refers to Botswana Medicines Regulatory Authority (BoMRA)

### 3.2 Abbreviations

The following abbreviations shall apply;

**3.2.1 ICSR**- Individual Case Safety Report
**3.2.2 GCP**- Good Clinical Practice
**3.2.3 GDP-** Good Distribution Practice
**3.2.4 GMP**- Good Manufacturing Practice
**3.2.5 GLP**- Good Laboratory Practice
**3.2.6 MAH**- Market Authorization Holder
**3.2.7 SmPC**- Summary of Product Characteristics
**3.2.8 CAPA**- Corrective Action and Preventative Action plan
**3.2.9 PSUR**- Periodic Safety Update Reports
**3.2.10 DSUR**- Development Safety Update Reports
**3.2.11 PASS**- Post-Authorization Safety Studies
**3.2.12 PAES-** Post-Authorization Efficacy Studies
**3.2.13 PSMF**- Pharmacovigilance System Master File
**3.2.14 PV**- Pharmacovigilance
**3.2.15 QPPV**- Qualified Person Responsible for Pharmacovigilance
**3.2.16 RMP**- Risk Management Plan

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**3.2.17 SUSAR**- Suspected Unexpected Serious Adverse Reactions

## 4. Method

### 4.1 Inspections Of Pharmacovigilance System At Market Authorization Holders

For the Authority to determine whether marketing authorization holders (MAHs) and/or their contactors comply with pharmacovigilance obligations established within Botswana, the Authority conducts pharmacovigilance inspections. The inspection shall include but not limited to inspecting the premises, records, documents, interview staff/personnel, assess procedures/processes, and pharmacovigilance system master file (PSMF) of the MAH or their contactors.

### 4.1.1 The structure and format of the Pharmacovigilance System Master File (PSMF)

The structure and format of the PSMF should be in-line with the recent European Union (EU) Guideline on good pharmacovigilance practices (GVP) Module II – Pharmacovigilance system master file and any other applicable guidelines.

### 4.2 Objectives

The objectives of PV inspections include but not limited:

a) To verify by examination and evidence, the appropriateness and effectiveness of the implementation and operation of the PV system
b) To find evidence and help evaluating the evidence objectively to determine the extent to which the inspection criteria are fulfilled and contributing to the improvement, control, and governance of the PV process.
c) To assess and establish that the MAH has qualified personnel, robust system, documented processes/procedures, and facilities to conduct PV activities
d) To identify, record and address non-compliance which may pose a risk to public health
e) To take regulatory action wherever considered necessary, based on the result of the inspection.

### 4.3 Inspection Types

The inspections shall include system and product-related inspections, routine inspections and "for cause" inspections, pre-and post-authorization inspections, announced and unannounced inspections as well as re-inspections. The inspection could be carried out 'On Site' or remotely as appropriate.

### 4.3.1 Routine inspection

These are scheduled in advance as part of inspection strategy/ programme devised by BoMRA. They are usually system inspections, but one or more specific products may be selected as examples to verify the implementation of the system and to provide practical evidence of its functioning and compliance. The focus of these inspections is to determine that the MAH personnel, systems, and facilities are in place to meet their regulatory PV obligations for the marketed medical products in Botswana. These inspections will be prioritized based on the potential risk to public health, the nature of the products, the extent of use, and number of products that the MAH has in the market.

Routine inspections could include but not limited to the following elements, as appropriate:

i. Individual Case Safety Reports (ICSRs)

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a) Collecting, receiving, and exchanging reports.
b) Assessment, including mechanisms for obtaining and recording reporter assessments, company application of event terms, seriousness, expectedness, and causality.
c) Follow-up and outcome recording, for example final outcome of cases of exposure in pregnancy and medical confirmation of consumer reported events.
d) Reporting according to the requirements for various types of reported ICSRs, including onward reporting to the relevant bodies and timeliness of such reporting.
e) Record keeping and archiving for ICSRs.

ii. Periodic Safety Update Reports (PSURs)
a) completeness and accuracy of the data included, appropriateness of decisions concerning data that are not included;
b) addressing safety topics, providing relevant analyses and actions;
c) formatting according to requirements
d) timelines of submissions

iii. Ongoing safety evaluation
a) Use of all relevant sources of information for signal detection;
b) Appropriately applied methodology concerning analysis;
c) Appropriateness of investigations and follow-up actions, e.g. The implementation of recommendations following data review;
d) Implementation of the Rmp, or other commitments, e.g. Conditions of marketing authorisation;
e) Timely identification and provision of complete and accurate data to the competent authority(ies), in particular in response to specific requests for data;
f) Implementation of approved changes to safety communications and product information such as labels, SmPCpcs, including internal distribution and external publication;

iv. Interventional and non-interventional clinical trails
a) reporting suspected unexpected serious adverse reactions (SUSARs) according to Directive 2001/20/EC and non-interventional study cases according to Directive 2001/83/EC;
b) receiving, recording and assessing cases from interventional and non-interventional trials (see ICSRs);
c) submission of study results and relevant safety information (e.g. development safety update reports (DSURs) and information included in PSURs), where applicable, PASS or post-authorization efficacy studies (PAES) submissions, particularly when associated with specific obligations or RMP commitments;
d) appropriate selection of reference safety information, maintenance of investigator brochures and patient information with respect to safety;
e) the inclusion of study data in ongoing safety evaluation

v. Pharmacovigilance system
a) QPPV roles and responsibilities, e.g., access to the quality system, the pharmacovigilance system master file, performance metrics, audit and inspection reports, and their ability to take action to improve compliance;

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b) the roles and responsibilities of the marketing authorization holder in relation to the pharmacovigilance system;
c) accuracy, completeness and maintenance of the pharmacovigilance system master file which shall be permanently and immediately available for inspection at the site where it is kept;
d) quality and adequacy of training, qualifications and experience of staff;
e) coverage and adherence to the quality system in relation to pharmacovigilance, including quality control and quality assurance processes;
f) fitness for purpose of computerized systems;
g) contracts and agreements with all relevant parties appropriately reflect responsibilities and activities in the fulfillment of pharmacovigilance and are adhered to.

vi. May include the system for the fulfillment of conditions of a marketing authorization and the implementation of risk-minimization activities, as they relate to any of the above safety topics.

### 4.3.2 For Cause Inspections

These types of inspections may be considered as and when there is a trigger and BoMRA determines that inspection is the appropriate way to examine the issues. Triggering factors that may lead to such inspections are listed below (but not limited to):

a) Continuous delays or omission or poor-quality reporting of ICSRs/PSURs/RMPs or inconsistencies between reports and other information sources.
b) risk-benefit balance of the product:
   i. Change in the risk-benefit balance where further examination through an inspection is considered appropriate.
   ii. Delays or failure to identify or communicate a risk or a change in the risk-benefit balance.
   iii. Communication of information on pharmacovigilance concerns to the general public without giving prior or simultaneous notification to the national competent authorities or Agency, as applicable.
   iv. Non-compliance or product safety issues identified during the monitoring of pharmacovigilance activities by the national competent authorities and/or the Agency;
   v. Suspension or product withdrawal with no advance notice to the competent authorities.
c) Failure to provide the requested information or data within the deadline specified by the regulatory authority.
d) Delays or failure to carry out specific obligations relating to the monitoring of pharmaceutical product safety, identified at the time of marketing authorization.
e) Delays in the implementation or inappropriate implementation of CAPAs.
f) Inspections received from other authorities, which may highlight issues of non-compliance.
g) Sudden product withdrawal.
h) others:
   i. concerns following review of the pharmacovigilance system master file;
   ii. non-inspection related information received from other authorities, which may highlight issues of non-compliance; – other sources of information or complaints.

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### 4.3.3 Pre-Authorization Inspections

Pre-authorization pharmacovigilance inspections are inspections performed before a marketing authorization is granted. These inspections are conducted with the intent of examining the existing or proposed pharmacovigilance system as it has been described by the applicant in support of the marketing authorization application. Pre-authorization inspections are not mandatory but may be requested in specific circumstances determined by BoMRA.

A risk assessment based on a combination of product-specific and system-related issues should be performed before a pre-authorization pharmacovigilance inspection is requested.

The following aspects shall be considered during the validation phase and/or early during the assessment phase:

a) The applicant has not previously operated a pharmacovigilance system or is in the process of establishing a new pharmacovigilance system;
b) Previous information (e.g. Inspection history and non-compliance notifications or information from other authorities) indicates that the applicant has a poor history or culture of compliance. If the marketing authorization holder has a history of serious and/or persistent pharmacovigilance non-compliance, a pre-authorization pharmacovigilance inspection may be one mechanism to confirm that improvements have been made to the system before a new authorization is granted;
c) Due to product-specific safety concerns, it may be considered appropriate to examine the applicant's ability:
    i. to implement product specific risk-minimization activities; or
    ii. to meet specific safety conditions which may be imposed; or
    iii. to manage routine pharmacovigilance for the product of concern (e.g. anticipated significant increase in adverse reaction reports when compared to previous products).

### 4.3.4 Post-Authorization Inspections

Post-authorization pharmacovigilance inspections are inspections performed after a marketing authorization is granted and are intended to examine whether the marketing authorization holder complies with its pharmacovigilance obligations. This may be one of the routines and/or For Cause Inspections.

### 4.3.5 Announced and unannounced inspections

It is anticipated that the majority of inspections will be announced i.e. notified in advance to the inspected party, to ensure the availability of relevant individuals for the inspection. However, on occasion, it may be appropriate to conduct unannounced inspections or to announce an inspection at short notice (e.g. when the announcement could compromise the objectives of the inspection or when the inspection is conducted in a short timeframe due to urgent safety reasons such as for Cause Inspections).

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### 4.3.6 Re-inspections

A re-inspection may be conducted on a routine basis as part of a routine inspection programme. Risk factors will be assessed in order to prioritize re-inspections. Early re-inspection may take place where significant non-compliance has been identified and where it is necessary to verify actions taken to address findings and to evaluate ongoing compliance with the obligations, including evaluation of changes in the pharmacovigilance system. Early re-inspection may also be appropriate when it is known from a previous inspection that the inspected party had failed to implement appropriate corrective and preventive actions in response to an earlier inspection.

### 4.3.7 Remote inspections

These are pharmacovigilance inspections performed by inspectors remotely, away from the premises of the marketing authorization holder or firms employed by the marketing authorization holder. In situations where the Authority wants to conduct a remote inspection, clear communication will be sent to the MAH. The logistical aspects of the remote inspection should be considered following liaison with the marketing authorization holder.

## 4.4 Inspection Procedure

### 4.4.1 Inspection planning

PV inspections will be based on a systematic and risk-based approach to make the best of surveillance and enforcement resources whilst maintaining a high level of public health protection. A risk-based approach to inspection planning will enable the frequency and scope of inspections to be determined accordingly. PV inspections will be done by the BoMRA officials responsible for PV inspections.

### 4.4.1.2 Factors to consider.

There are factors which may be taken into consideration, as appropriate, by BoMRA when establishing pharmacovigilance inspection programs. These include, but are not limited to:

**a) Inspection related:**

i. Compliance history identified during previous pharmacovigilance inspections or other types of inspections (GCP, GMP, GLP and GDP).
ii. Re-inspection date recommended by the inspectors or assessors/reviewers as a result of a previous inspection.

**b) Product related:**

i. Product with additional pharmacovigilance activities or risk-minimization activities.
ii. Authorization with conditions associated with safety, e.g. Requirement for post-authorization safety studies (PASS) or designation for additional monitoring.
iii. Product(s) with large sales volume, i.e. Products associated with large patient exposure in Botswana.
iv. Product(s) with limited alternative in the market.

**c) MAH related:**

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i. MAH that has never been subjected to a pharmacovigilance inspection.
ii. MAH with large volume products in Botswana market.
iii. Resources available to the MAH for the pharmacovigilance activities they undertake.
iv. MAH with no previous health products registered in Botswana.
v. Negative information and/or safety concerns raised by BoMRA, other bodies outside Botswana or other areas (i.e. GCP, GMP and GLP).
vi. Changes in the MAH organization, such as mergers and acquisitions.

**d) Pharmacovigilance system related:**

i. MAH with sub-contracted pharmacovigilance activities (function of the pharmacovigilance officer in Botswana, reporting of safety data etc.) And/or multiple manufacturers employed to perform pharmacovigilance activities.
ii. Change of the QPPV since the last inspection.
iii. Changes to the pharmacovigilance safety database(s), which could include a change in the database itself or associated databases, the validation status of the database as well as information about transferred or migrated data.
iv. Changes in contractual arrangements with pharmacovigilance service providers or the sites at which pharmacovigilance is conducted.
v. Delegation or transfer of pharmacovigilance system master file management.

### 4.4.2 Organizations to be Inspected

Any party carrying out PV activities in whole or in part, on behalf of, or in conjunction with the MAH may be inspected, in order to confirm their capabilities to support the MAH 's compliance with PV obligations.

### 4.4.3 Inspection procedures

The inspection procedures depend on the nature of the inspection and the conditions of inspection. Essentially Inspections comprises of following phases (as applicable):

i. Pre-Inspection Notification
ii. Inspection Plan
iii. Pre-Inspection Document request
iv. Finalizing Audit Agenda
v. Inspection conduct (on site or remote)
vi. Issuance of Inspection Report

a) The inspectee will be notified of the inspection 20 working days prior to the inspection wherein they will receive a notification letter, the Inspection Plan (**BOMRA/PCT/PV/P16/F03**) and the Pre-Inspection Document Request Form (**BOMRA/PCT/PV/P16/F03**).

b) The inspectee will be required to acknowledge receipt and respond to the notification no more than 3 working days after receiving the notification.

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c) Thereafter, the inspectee will also be mandated to fulfil all requests as listed out in the Pre-Inspection Document Request form within 10 days after receiving the inspection plan and request as outlined in Section 4.4.1 (a).

d) The method of document sharing, as outlined in the Pre-Inspection Document Request, shall be determined through mutual agreement between the Authority and the inspectee.

e) The Authority will share the Agenda of the inspection no less than 3 days before the inspection date.

All the requested PV documents (prior to inspection and/or during the inspection) should be submitted to the inspectors as instructed, including the PSMF which will be used to gather information during inspection conduct. When necessary, the inspectors may also request other documents containing related information. The MAH shall ensure that relevant staff, other than QPPVs, involved in pharmacovigilance activities or related activities are present and available during the inspection for interviews or clarification of issues identified.

### 4.4.4 Scope of inspection

The inspection scope will depend on the objectives of the inspection as well as the coverage of any previous inspections by BoMRA or other NRA or whether it is a system or product related inspection. The following elements should be considered when preparing the scope of the inspection, as applicable:

a) Information supplied in the Pharmacovigilance System Master File.
b) Information concerning the functioning of the pharmacovigilance system.
c) Specific safety related trigger, as applicable.

It may be appropriate for additional data to be requested during the inspection in order to select appropriate sites or clarify aspects of the pharmacovigilance system.

#### 4.4.4.1 Routine Pharmacovigilance Inspections

Routine pharmacovigilance inspections should examine compliance with BoMRA's legislation and guidance, and the scope of such inspections should include the following elements, as appropriate:

#### 4.4.4.2 Individual case safety reports (ICSRs):

i. Collecting, receiving and exchanging reports from all types of sources, sites and departments within the pharmacovigilance system, including from those companies employed to fulfil applicant pharmacovigilance obligations and departments other than drug safety.
ii. Assessment, including mechanisms for obtaining and recording reporter assessments, company application of event terms, seriousness, expectedness and causality.
iii. Follow-up and outcome recording, for example final outcome of cases of exposure in pregnancy and medical confirmation of consumer reported events.

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iv. Reporting according to the requirements for various types of reported icsrs, including onward reporting to the regulatory pharmacovigilance unit and timeliness of such reporting.
v. Record keeping and archiving for ICSRs.

**4.4.4.3 Periodic safety update reports (PSURs), (as applicable):**

i. Completeness and accuracy of the data included, appropriateness of decisions concerning data that are not included.
ii. Addressing safety topics, providing relevant analyses and actions.
iii. Formatting according to requirements.
iv. Timeliness of submissions and adherence thereto.

**4.4.4.4 Ongoing safety evaluation;**

i. Use of all relevant sources of information for signal detection.
ii. Appropriately applied methodology concerning analysis.
iii. Appropriateness of investigations and follow-up actions, e.g. The implementation of recommendations.
iv. Following data review.
v. Implementation of the risk management plan (RMP), or other commitments, e.g., conditions of marketing authorisation;

4.4.4.5 timely identification and provision of complete and accurate data to the Authority, in particular in response to specific requests for data.

4.4.4.6 implementation of approved changes to safety communications and product information, including internal distribution and external publication.

**4.4.4.7 Interventional (where appropriate) and non-interventional clinical trials:**

i. Reporting suspected unexpected serious adverse reactions (SUSARs) and non-interventional study cases.
ii. receiving, recording and assessing cases from interventional and non-interventional trials (see ICSRs).
iii. submission of study results and relevant safety information and information included in PSURs, where applicable, particularly when associated with specific obligations or RMP commitments.
iv. appropriate selection of reference safety information, maintenance of investigator brochures and patient information with respect to safety.
v. the inclusion of study data in ongoing safety evaluation.

**4.4.4.8 Pharmacovigilance system:**

i. Roles and responsibilities of the QPPV and other pharmacovigilance officers, e.g. Access to the quality system, the pharmacovigilance system master file, performance metrics, audit and inspection reports, and their ability to take action to improve compliance.
ii. The roles and responsibilities of the MAH in relation to the pharmacovigilance system.
iii. Accuracy, completeness and maintenance of the pharmacovigilance system master file.

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iv. Quality and adequacy of training, qualifications and experience of staff;
v. Coverage and adherence to the quality system in relation to pharmacovigilance, including quality control and quality assurance processes.
vi. Fitness for purpose of computerized systems;
vii. Contracts and agreements with all relevant parties appropriately reflect responsibilities and activities in the fulfilment of pharmacovigilance and are adhered to.

The inspection may include the system for the fulfilment of conditions of registration and the implementation of risk–minimization activities, as they relate to any of the above safety topics.

#### 4.4.4.9 For cause Inspections

The scope of the inspection will depend on the specific trigger(s). Some, but not all of the elements listed in 4.3.2 and below, may be relevant:

i. Pharmacovigilance officer involvement and awareness of product-specific issues.
ii. in-depth examination of processes, decision-making, communications, and actions relating to a specific trigger and/or product.

#### 4.4.4.10 Re-inspections

For the scope of a re-inspection, the following aspects should be considered:

i. Review of the status of the system and/or corrective and preventative action plan(s) resulting from previous pharmacovigilance inspection(s);
ii. Review of significant changes that have been made to the pharmacovigilance system since the last pharmacovigilance inspection (e.g. Change in the pharmacovigilance database, company mergers or acquisitions, significant changes in contracted activities, change in pharmacovigilance officer);
iii. Review of the process and/or product-specific issues identified from the assessment of information provided by the applicant, or not covered in a prior inspection. The scope of re-inspection will depend on inspection history. It may be appropriate to conduct a complete system review, for example if a long time has elapsed since the previous inspection, in which case the elements listed in **4.3.2** may be considered for the inspection scope, as appropriate.

### 4.4.5 Inspection findings

Each inspection will result in an inspection report and the findings shall be classified into critical, major, and minor. The results of an inspection shall be made available to the PV department of the inspected entity. The MAH will be given the opportunity to comment on any non-compliance identified within timelines prescribed by BoMRA. Any non-compliance shall be rectified in a timely manner through the implementation of a Corrective and Preventive Action Plan (CAPA).

### 4.5 Classification of inspection findings

**a) Critical**- Fundamental weakness in the PV System or practices that adversely deviate from the PV regulations of BoMRA and or affect the rights and safety of patients or pose a potential risk to the public.

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**b) Major** -It is an insignificant weakness in one or more PV processes or practice or a fundamental weakness in part of one or more PV process or practices that is detrimental to the whole process and could potentially adversely affect the rights, safety, or wellbeing of patients.

**c) Minor** - It's a weakness in the part of one or more PV processes or practices that is not expected to adversely affect the whole PV system or process and or rights, safety, or wellbeing of patients.

**d) Opportunity For Improvement /Recommendation** – A recommendation from the Inspection team through which an existing process and/or activity can be improved or made simpler/user friendly. No CAPAs are expected for OFIs

### 4.6 Inspection follow up

When non-compliance with pharmacovigilance obligations is identified during an inspection, follow-up will be required until a corrective and preventive action plan is completed. The following follow-up actions should be considered, as appropriate:

a) Review of the MAH's corrective and preventive action plan;,
b) Review of the periodic progress of CAPAs, when deemed necessary.
c) Re-inspection to assess appropriate implementation of the corrective and preventive action plan;
d) Requests for submission of previously un-submitted data, submission of variations, e.g. To amend product information, submission of impact analyses, e.g. Following review of data that were not previously considered during routine signal detection activities.
e) Requests for issuing safety communications, including amendments of marketing and/or advertising information.
f) Requests for a meeting with the marketing authorization holder to discuss the deficiencies, the impact of the deficiencies and action plans.
g) Communication of the inspection findings to other regulatory authorities.
h) Other product-related actions depending on the impact of the deficiencies and the outcome of follow-up actions (this may include recalls or actions relating to the marketing authorizations or clinical trial authorizations).

### 4.7 Responding to Findings

a) Inspection findings (in the inspection report) will be shared with the MAH within 30 working days post inspection. Please note that the MAH will be made aware of these findings during the inspection closing meeting. Therefore, the inspection report will be a comprehensive report of the whole inspection.
b) Following the issue of the inspection report, the MAH is requested to respond to any deficiencies identified and to provide the Authority with an appropriate corrective action and preventative action plan (CAPA) within 14 days or a deadline to be determined by the Authority based on the magnitude of non-compliance identified.

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c) The MAH may be required to provide reports and where necessary evidence of the progress and completion of the action plan. There may be re-inspection at an appropriate time to verify the progress and success of these remedial actions.
d) In certain circumstances, the MAH may be required to take immediate action to address critical or major findings, for the protection of public health and safety. Where required, evidence of completion of all CAPAs should be submitted to the Authority not later than 14 working days following their completion.

## 5.0 In the event of non-compliance

In the event of non-compliance, possible regulatory options include the following, in accordance with applicable legislations;

a) education and facilitation: BoMRA may communicate with marketing authorisation holder to summarise the identified non-compliances, to clarify the legal requirements and the expectations of the regulator, and to review the marketing authorisation holder's proposals for corrective and preventive actions;
b) provision of information to other competent authorities as provided by the regulations
c) inspection: non-compliant marketing authorisation holders may be inspected to determine the extent of non-compliance and then re-inspected to ensure compliance is achieved;
d) warning letter, non-compliance statement or infringement notice: these are non-statutory or statutory instruments in accordance with national legislation, stating the legislation and guideline that has been breached, reminding marketing authorisation holders of their pharmacovigilance obligations or specifying the steps that the marketing authorisation holder must take and in what timeframe in order to rectify the non-compliance and in order to prevent a further case of non-compliance;
e) actions against a marketing authorisation(s) or authorisation application(s) e.g.
    i. Urgent Safety Restriction;
    ii. variation of the marketing authorisation;
    iii. suspension or revocation of the marketing authorisation;
    iv. delays in approvals of new marketing authorisation applications until corrective and preventive;
f. actions have been implemented or the addition of safety conditions to new authorisations;
    i. requests for pre-authorisation inspections;
g. product recalls e.g. where important safety warnings have been omitted from product information;
h. action relating to marketing or advertising information;
i. amendments or suspension of clinical trials due to product-specific safety issues;
j. administrative penalties, usually fixed fines or based on company profits or levied on a daily basis;
k. Prosecution as per the MRS Act and the regulations.

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## 6 Roles and responsibilities of different stakeholders

### 6.1 Role and Responsibility of the Pharmacovigilance Advisory Committee (PVAC)

a) PVAC may make recommendations on the need and scope of "for cause" pharmacovigilance inspections related to medicinal products depending on safety findings following assessment by the PVCT department or other technical department within the Authority.
b) The PVAC is also responsible for providing input in the preparation of and agreeing on the risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders.

### 6.2 Role and responsibilities of the Authority

The role of the Authority is to ensure that the MAHs comply with pharmacovigilance obligations. The following are some of the roles:

a) coordination of the safety monitoring of medical products which have been authorized or registered with BoMRA, in particular by coordinating the evaluation and implementation of pharmacovigilance obligations and systems and the monitoring of such implementation.
b) coordinating the verification of compliance with pharmacovigilance obligations.

### 6.3 The Role and Responsibilities of the Applicant

All MAHs with registered medicinal products and those who have submitted new applications are subject to pharmacovigilance inspections. Therefore, both have responsibilities in relation to inspections, including but not limited to the following:

a) to be always inspection-ready as inspections may be unannounced;
b) to maintain and make available to the inspectors on request, no later than 7 calendar days after the receipt of a request, the pharmacovigilance system master file as required.
c) to ensure that the sites selected for inspection, which may include contractors employed by the MAH to perform pharmacovigilance activities, agree to be pre-inspected before the inspection is performed;
d) to make available to the inspectors any information and/or documentation required for the preparation of the inspection within the deadline given or during the conduct of the inspection;
e) to ensure that relevant staff involved in pharmacovigilance activities or related activities are present and
f) available during the inspection for interviews or clarification of issues identified;
g) to ensure that relevant pharmacovigilance data is accessible from at least one point;

to ensure that appropriate and timely corrective and preventive action plans are implemented to address findings observed during an inspection, with appropriate prioritization of critical and/or major findings.

## 7. References:

a) Medicines and Related Substances Act of 2013

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b) Medicines and Related Substances Regulations of 2019
c) Guideline on Good Pharmacovigilance Practices (GVP); Module II – Pharmacovigilance system master file (Rev 2)

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