NATIONAL AGENCY FOR FOOD AND DRUG ADMINISTRATION AND CONTROL (NAFDAC)

PHARMACOVIGILANCE INSPECTION GUIDELINES FOR NIGERIA-REGULATED DRUGS

TABLE OF CONTENT

1.0 ABBREVIATIONS AND ACRONYMS

CAPA	Corrective Action and Preventive Action
CIOMS	Council for International Organization of Medical Sciences
CRH	Certificate of Registration Holder
CV	Curriculum Vitae
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GVP	Good Pharmacovigilance Practice
ICSR(s)	Individual Case Safety Report(s)
MAH(s)	Marketing Authorization Holder(s)
PBRER(s)	Periodic Benefit-Risk Evaluation Report(s)
PIL	Patient Information Leaflet
PSMF	Pharmacovigilance System Master File
PSUR(s)	Periodic Safety Update Report(s)
PV	Pharmacovigilance
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
SOP(s)	Standard Operating Procedure(s)
SUSAR(s)	Suspected Unexpected Serious Adverse Reaction(s)

2.0 GLOSSARY

The definitions given below apply to the terms used in this guide. They may have different meanings in other contexts.

Term	Definitions
Agency	National Agency for Food and Drug Administration and Control
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 the effectiveness of those interventions and how these risks will be communicated to the Agency and the general population.
Local Representative	The company or legal entity that represents the MAH/CRH in Nigeria and performs functions delegated by the MAH/CRH.
Local Distributor or Local Agent	A company or legal entity appointed by the manufacturer or the Marketing Authorization Holder to import, receive as a donation, distribute, or sell a medicinal product in Nigeria.
Marketing Authorization Holder or Certificate of	A person authorized by the Agency to manufacture, import, receive as donation, distribute, or sell a medicinal product in the country.

Registration Holder	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.
Pharmacovigilance	The science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem.
Pharmacovigilance System Master File	A document that describes the pharmacovigilance system for one or more products of the marketing authorization holder. The pharmacovigilance system master file provides an overview of the pharmacovigilance system put in place by the MAH/CRH and contributes to the appropriate management of and improvement(s) of the pharmacovigilance system.
Qualified Person for Pharmacovigilance (QPPV)	An individual named by an MAH/CRH as the main person responsible for ensuring that the company (the MAH) meets its legal obligations under the Good Pharmacovigilance Practice Regulations, Section 3C for monitoring the safety of the product marketed in Nigeria.
Computerized System	A system includes the input of data, electronic processing, and the output of information to be used either for reporting or automatic control.
Individual Case Safety Report	A document in a specific format for the reporting of one or several suspected adverse reactions to a medicinal product that occurs in a single patient at a specific point in time.
Periodic Benefit-Risk Evaluation Report	An update of the worldwide marketing experience of a medicinal product at defined times with a focus on formal evaluation of benefits in special populations at defined times during the post-registration period.
Periodic Summary Update Report	A regular update of the worldwide safety experience of a medicinal product at defined times during the post-registration period.

3.0 INTRODUCTION

This Guideline provides instructions for the planning, conducting, reporting, and follow-up of Pharmacovigilance inspections conducted by the National Agency for Food and Drug Administration and Control (NAFDAC). All Local Representatives/ MAHs shall be subjected to pharmacovigilance inspection and shall be responsible for meeting requirements for pharmacovigilance reporting.

This guideline describes how to schedule pharmacovigilance inspections, the types of pharmacovigilance inspections, responsibilities of MAHs in facilitating the inspection to enable compliance by the Local Representatives / MAHs and to enhance consistency in the application of the regulatory requirements regarding Good Pharmacovigilance Practices.

NAFDAC shall conduct pharmacovigilance inspections of MAHs/CRHs at the designated location to ascertain compliance with regulatory pharmacovigilance obligations. Inspectors

appointed by NAFDAC are empowered to inspect the premises, procedures, records, and documents from the Pharmacovigilance system master file (PSMF) of the local Representative/MAH or any firm or contractor employed by the Local Representative/MAH to perform the pharmacovigilance activities on their behalf. Local representatives/MAHs are required to provide, on request, the PSMF to inform inspection conduct.

For this guideline, NAFDAC uses the terms "Certificate of Registration Holder" and Marketing Authorization Holder interchangeably.

4.0 INSPECTION PROCESS

4.1 Pharmacovigilance Inspections

Pharmacovigilance inspections are designed to review systems, personnel, procedures, and facilities put in place to comply with pharmacovigilance regulatory requirements and facilitate compliance. Inspections will be routine as well as targeted to Local Representatives and Marketing Authorization Holders suspected of being non-compliant. The results will be used to help Local Representatives and Manufacturers improve compliance and may also be used as a basis for enforcement of regulatory action. The scheduling and conduct of these inspections will be driven by routine programs and by risk analysis criteria. The inspection will be conducted where pharmacovigilance activities of the Local representatives or Marketing Authorization Holders are located.

4.2 Objectives of Pharmacovigilance Inspection

- To ascertain that the pharmacovigilance system established by Local Representatives and MAHs has personnel, systems, and facilities in place to meet their pharmacovigilance obligations
- To ensure compliance with the pharmacovigilance obligations of the local representative and MAH to protect public health and safety.
- To improve the pharmacovigilance system established by local representatives/MAHs
- To identify, record, and address non-compliance that may pose a public health risk.
- To use the inspection results as a basis for enforcement action, where considered necessary.

4. 3 Types of Pharmacovigilance Inspections

It is anticipated that the majority of inspections will be announced in advance to the inspected party, to ensure the availability of relevant individuals for the inspection. However, on certain occasions, 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).

Pharmacovigilance inspections can either be system or product-related. System-related inspections are designed to review the procedures, systems, personnel, and facilities in place

and determine their compliance with regulatory pharmacovigilance obligations. Product-specific examples may be used to demonstrate the operation of the pharmacovigilance system. Product-related inspections are primarily focused on product-related pharmacovigilance issues, including product-specific activities and documentation, rather than a general system review. Some aspects of the general system may still be examined as part of a product-related inspection.

4.3.1 Routine Pharmacovigilance Inspections

These are scheduled inspections that Local representatives or MAHs shall undergo at periods as part of the pharmacovigilance inspection program which the Agency would determine in advance. The frequency of routine inspection will be determined based on risk analysis criteria (risk-based approach). There is no specific trigger to initiate these inspections, although a risk-based approach to optimize oversight activities should be implemented. Local representatives or MAHs shall be given advanced notices of these inspections. These inspections shall be aimed at identifying whether the Local representatives or MAHs have the personnel, procedure, systems, and facilities in place to meet their regulatory obligations for registered products under the NAFDAC Mandate, Act Cap N1 LFN (Laws of the Federation of Nigeria) 2004 and Good Pharmacovigilance Practice Regulations. These inspections may be requested with one or more specific products selected as examples for which specific information can be traced and verified through the various processes, to provide practical evidence of the functioning of the pharmacovigilance system of the Local representatives or MAHs and their compliance with their regulatory obligations.

The scope of such inspections should include the following elements, as appropriate:

4.3.1.1 Individual Case Safety Reports (ICSRs):

i) Collecting, receiving, and exchanging reports from all sources, sites, and departments within the pharmacovigilance system, including those companies employed to fulfil applicant/HCR's 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, the outcome of cases of exposure in pregnancy and medical confirmation of consumer-reported events.

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.

4.3.1.2 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, and providing relevant analyses and actions.

iii) Formatting according to requirements.

iv) Timeliness of submissions.

4.3.1.3 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 following data review.

iv) Implementation of the risk management plan (RMP), or other commitments, e.g., conditions of marketing authorization.

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

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

4.3.1.6 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 concerning safety.

v) The inclusion of study data in ongoing safety evaluation.

4.3.1.7 Pharmacovigilance system:

i) Roles and responsibilities of pharmacovigilance officer, e.g. access to the pharmacovigilance quality management 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 Local Representatives/MAH regarding the pharmacovigilance system.

iii) Accuracy, completeness, and maintenance of the pharmacovigilance system master file.

iv) Quality and adequacy of training, qualifications, and experience of staff.

v) Coverage and adherence to the quality system concerning pharmacovigilance, including quality control and quality assurance processes.

vi) Fitness of purpose of computerized systems.

vii) Contracts and agreements with all relevant parties appropriately reflecting responsibilities and activities in the fulfillment of pharmacovigilance and ensuring adherence to all requirements.

4.3.1.8 The inspection may include a pharmacovigilance quality management system for the fulfillment of conditions of registration and the implementation of risk– minimization activities, as they relate to any of the above safety topics.

4.3.2 "For Cause" Pharmacovigilance Inspections

These inspections are undertaken when a trigger is recognized, and an inspection is considered an appropriate way to examine the issues. "For cause" inspection requires Pharmacovigilance officer involvement, awareness of the product-specific problems; and in-depth examination of processes, decision-making, communications, and actions relating to a specific trigger, and/or product.

"For cause" inspections are more likely to focus on specific pharmacovigilance processes or examine identified compliance issues and their impact on a specific product. However, full system inspections may also be performed if a trigger is present. "For cause" inspections may arise when, for example, one or more of the triggers listed below are identified:

4.3.2.1 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 NAFDAC.

4.3.2.2 Non-compliance or product safety issues identified during the monitoring of pharmacovigilance activities by NAFDAC:

i) Suspension or product withdrawal with no advance notice to NAFDAC.

4.3.2.3 Reporting obligations (expedited and periodic):

i) Delays or omissions in reporting.

ii) Poor quality or incomplete reports.

iii) Inconsistencies between reports and other information sources.

4.3.2.4 Requests from the Agency:

i) Failure to provide the requested information or data within the deadline specified by the Agency.

ii) Poor quality or inadequate provision of data to fulfill requests for information from the Agency.

4.3.2.5 Fulfilment of commitments:

i) Concerns about the status or fulfillment of risk management plan (RMP) commitments.

ii) Delays or failure to carry out specific obligations relating to the monitoring of product safety, identified at the time of product registration.

iii) Poor quality of reports requested as specific obligations.

4.3.2.6 Inspections:

i) Delays in the implementation or inappropriate implementation of corrective and preventive actions.

ii) Information such as non-compliance or product safety issues from other types of inspections (GCP, GMP, GLP, and GDP).

iii) Inspection information received from other authorities, which may highlight issues of non-compliance.

4.3.2.7 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.

iii) Other sources of information or complaints.

4.3.3 Pre-authorization Inspections

Pre-authorization pharmacovigilance inspections are inspections performed before a registration certificate is issued. These inspections are conducted with the intent of examining the existing or proposed pharmacovigilance system as it has been described by the local representative/MAH in support of the registration application. Pre-authorization inspections are not mandatory, however, the Agency may conduct it in specific circumstances where deemed necessary.

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

4.3.3.1 The Local Representative/MAH has not previously operated a pharmacovigilance system within the country or is in the process of establishing a new pharmacovigilance system.

4.3.3.2 Previous information (e.g. inspection history and non-compliance notifications or information from other authorities) indicates that the Local Representative/MAH has a poor

7history or culture of compliance. If the Local Representative/MAH has a history of serious and/or persistent pharmacovigilance non-compliance, a pre-authorization pharmacovigilance inspection may be conducted to confirm that improvements have been made to the system before a new authorization is granted.

4.3.3.3 Due to product-specific safety concerns, it may be considered appropriate to examine the local representative/MAH 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 other products)

4.3.3.4 In most cases, 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.

4.3.3.5 If the outcome of the pre-authorization inspection raises concerns about the local representative/MAH's ability to comply with the requirements laid down in the Regulations, the following recommendations may be considered.

i) Non-approval of registration application.

ii) A re-inspection before approval of the registration certificate to confirm that critical findings and recommendations have been addressed.

iii) Granting of the registration certificate with the recommendation to perform an early post-authorization pharmacovigilance inspection. In this case, the findings would influence the timing of an inspection conducted as part of the Agency's routine pharmacovigilance inspections.

iv) Imposing safety conditions on the registration certificate.

4.3.4. Post authorization Pharmacovigilance Inspections

Post-authorization pharmacovigilance inspections are inspections performed after a registration certificate is issued and are intended to examine whether the Local Representative/MAH complies with its pharmacovigilance obligations. They can be any of the above-mentioned types except pre-authorization pharmacovigilance inspection.

4.3.5. Pharmacovigilance Re-Inspection

A Pharmacovigilance Re-inspection may be conducted on a routine basis as part of a routine inspection program. Risk factors should be assessed 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.

The scope of re-inspection will depend on the inspection history. It may be appropriate to conduct a complete system review, for example, if a long time has elapsed since the previous inspection.

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 preventive 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. changes in the pharmacovigilance database, company mergers or acquisitions, significant changes in contracted activities, changes in pharmacovigilance officer).

iii) Review of process and/or product-specific issues identified from the assessment of information provided by the Local Representative/MAH, or not covered in a prior inspection.

iv) The results of an inspection should be provided to the inspected Local Representative/MAH, who should be allowed to comment on any non-compliance identified.

4.3.6 Remote Pharmacovigilance Inspection

These are pharmacovigilance inspections performed by inspectors remotely from the premises of the applicant/CRH or manufacturers employed by the Local Representative/MAH.

Communication mechanisms such as virtual meetings or telephones may be used in the conduct of the inspection. For example, in cases where key sites for pharmacovigilance activities are located outside the country or a third-party service provider is not available at the actual inspection site, but it is feasible to arrange interviews of relevant staff and review of documentation, including the safety database, source documents, and PSMF, via remote access.

This approach may also be taken where there are logistical challenges to an on-site inspection during exceptional circumstances (e.g., a pandemic outbreak or travel restrictions). Such approaches are taken at the discretion of the inspectors. The logistical aspects of the remote inspection should be considered following liaison with the Local Representative/MAH. Where feasible, a remote inspection may lead to a visit to the inspection site if it is considered that the remote inspection has revealed issues, that require on-site inspection, or if the objectives of the inspection could not be met by remote inspection.

4.3.7 Unannounced Pharmacovigilance Inspections

These are inspections that are triggered because of, for example, safety issues, or suspected violations of legislation relating to the monitoring of the safety of products. Under these circumstances, the Local Representatives/MAH will not be notified of these inspections in advance.

4.4 The Inspection Schedule

The Agency will carry out pharmacovigilance inspection for Local Representatives/MAHs based on risk analysis. This will help to focus resources to improve the protection of public health where there is a potentially higher risk. Factors that may affect inspection scheduling may include but are not limited to the following:

4.4.1. Number of products issued marketing authorization by the Agency.

4.4.2. Product portfolio.

4.4 3. Failure to provide details of the Qualified Person for Pharmacovigilance to the Agency.

4.4.4. Number of products with known safety risks.

4.4.5. Non-compliance with the Agency's reporting requirements.

4.5 Phases of the Inspection Process

There are three main phases of each pharmacovigilance inspection:

4.5.1. Inspection Planning

Pharmacovigilance inspection planning is based on a systematic and risk-based approach to make the best use of surveillance and enforcement resources while maintaining a high level of public health protection. A risk-based approach to inspection planning will enable inspections' frequency, scope, and extensiveness to be determined accordingly.

A preliminary notification shall be sent to the Local Representative/MAH about the scheduled inspection. The Agency will also request pertinent documents to facilitate the inspection at least 14 calendar days before the scheduled inspection date. The date for the inspection is agreed upon together with the Local representative/MAH for the announced inspection.

The Agency may request the following documents before the inspection. This may include but not limited to:

4.5.1.1. **Pharmacovigilance System Master File (PSMF)** should reflect the Nigerian Pharmacovigilance system including but not limited to human resources for pharmacovigilance, organizational chart for pharmacovigilance, the job description of the QPPV and other staff involved in pharmacovigilance, information relating to the QPPV, SOPs and other work instructions, changes in contractual arrangements with pharmacovigilance service providers, subcontracted pharmacovigilance activities for the

MAHs. For details on this, refer to **APPENDIX I** of this guideline. 4.5.1.2. Minutes of meetings specific to pharmacovigilance

4.5.1.3. Individual adverse reaction case files and CIOMS reports.

4.5.14. Recent PSURs / PBRERs for marketed products.

4.5.1.5. Nigeria-specific RMPs for selected products when applicable.

4.5.1.6. Line listings of adverse reaction reports.

4.5.2 Conduct of Inspection:

The inspection may be conducted at the Local representative or the MAH's location, and if a third party is involved in any pharmacovigilance activity, their site may also be inspected by the Agency. The inspection will normally start with an opening meeting and end with a closing meeting. The Local representative or the MAH has the right to choose which members of staff participate in these meetings but should always include the QPPV.

Reporting and Follow-Up: Deficiencies identified during the Agency's pharmacovigilance inspections are graded as follows.

i) Critical: A deficiency 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 NAFDAC Mandate, Act Cap N1 LFN (Laws of the Federation of Nigeria) 2004 and Good Pharmacovigilance Practice Regulations. Deficiencies classified as critical may include a pattern of deviations classified as major. A critical deficiency also occurs when a local representative/MAH is observed to have engaged in fraud, misrepresentation, or falsification of data.

ii) Major: A deficiency in pharmacovigilance systems, practices, or processes that could potentially adversely affect the rights, safety, or well-being of patients or that could potentially pose a risk to public health or that represents a violation of NAFDAC Mandate, Act Cap N1 LFN (Laws of the Federation of Nigeria) 2004 and Good Pharmacovigilance Practice Regulations. Deficiencies classified as major may include a pattern of deviations classified as minor.

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

In general, preliminary findings will be communicated at the closing meeting. An inspection report is then prepared and reviewed internally to ensure consistency in the classification of deficiencies before the issue of the final report. The report is sent to the Local representative or MAH, usually within 30 working days of the site visit or the date of the provision of the last document requested. It should be noted that the factual matter contained in the inspection report relates only to those things that the inspection team sees and hears during the inspection process.

4.5.3 Responding to Findings

The Local representative or MAH is asked to reply to any deficiencies found when the inspection report is released and to provide the Agency with an appropriate corrective action and preventative action (CAPA) plan within 21 working days or a deadline to be determined by the Agency based on the magnitude of non-compliance identified.

When its appropriate, there might be re-inspection to verify the effectiveness and progress of these corrective actions.

Keep in mind that, in certain situations, the local representative or MAH may be required to take immediate action to address a critical or major finding, to safeguard the public's health and safety.

The Local representative or 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.

Note that, in some circumstances, the Local representative or MAH may be required to take immediate action to address a critical or major finding, for the protection of public health and safety.

Where required, evidence of completion of all CAPAs should be submitted NAFDAC not later than 30 working days following their completion.

4.5.4 Record Management and Archiving

All pharmacovigilance data should be maintained in a secure area (dedicated for that purpose) and the data should be stored to ensure:

ii. Limited access to data
iii. Protection of confidentiality of patients
iiii. Protection of information
iiv. Easy retrieval
iv. Documents must be stored in secured cabinets that will protect them from hazards (rodents, flood, fire). Pharmacovigilance data should be stored throughout the life cycle of the product.

4.5.5 Inspection Follow-up

When non-compliance with pharmacovigilance obligations is identified during an inspection, follow-up should be done until a corrective and preventive action plan is completed.

The following follow-up actions should be considered, as appropriate:

i) Review of the Local Representative/MAH corrective and preventive action plan.

ii) Review of the periodic progress reports, when deemed necessary.

iii) Re-inspections, to assess appropriate implementation of the corrective and preventive action plan.

iv) 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.

v) Requests for issuing safety communications, including amendments of marketing and/or advertising information.

vi) Requests for a meeting with the Local Representative/MAH to discuss the deficiencies, the impact of the deficiencies and action plans.

vii) Communication of the inspection findings to other regulatory authorities outside Nigeria if necessary for safety reasons.

viii) 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 registration certificate).

5.0 ROLES AND RESPONSIBILITIES OF THE LOCAL REPRESENTATIVE/MAH

5.1 The Local Representative must have permanently and continuously at its disposal a Qualified Person Responsible for Pharmacovigilance (QPPV) for all products, sold or registered and marketed in Nigeria. The QPPV should reside and operate in Nigeria and is responsible for the establishment and maintenance of the local pharmacovigilance system. **(Please refer to the Good Pharmacovigilance Practice Guidelines 2021 and the abridged QPPV Guidelines for more details on the QPPV requirements).**

5.2 The MAH should ensure that the QPPV has adequate theoretical and practical knowledge for the performance of pharmacovigilance activities. The QPPV should have skills for the management of pharmacovigilance systems as well as expertise or access to expertise in relevant areas such as medicine, pharmaceutical sciences as well as epidemiology, and biostatistics.

5.3 All Local Representatives/MAHs with registered products and those who have submitted new applications are subject to pharmacovigilance inspections. Therefore, both have responsibilities concerning inspections, including but not limited to the following:

i) constantly be prepared for inspection as inspections it might be unannounced.

ii) To maintain and make available to inspectors on request, no later than 14 calendar days before the scheduled inspection date, the pharmacovigilance system master file as required.

iii) To ensure that the sites selected for inspection, which may include firms contracted by the Local Representative/MAH to perform pharmacovigilance activities, agree to be pre-inspected before the inspection is performed.

iv) To make available to inspectors any information and/or documentation required for the preparation of the inspection within the deadline given or during the conduct of the inspection.

v) To ensure that relevant staff involved in pharmacovigilance activities or related activities are present and available during the inspection for interviews or clarification of issues identified.

vi) To ensure that relevant pharmacovigilance data is accessible from at least one point.

vii) 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.

6.0. REGULATORY ACTIONS AND SANCTIONS

The following regulatory sanctions shall be applied in the case of non-compliance.

6.1 Local Representative/MAH may be informed of non-compliance and advised on how this can be remedied.

6.2 Non-compliant Local Representative or MAH may be inspected to determine the extent of non-compliance and then re-inspected to ensure compliance is achieved.

6.3 Warning; The Agency may issue a formal warning reminding Local representative/MAH of their pharmacovigilance regulatory obligations.

6.4 Blacklisting non-compliant Local representative/MAH

6.5 Product recalls e.g. where important safety warnings have been omitted from product information.

6.6 Deferral of processing of applications for registration of product(s) until corrective and preventive actions have been implemented.

6.7 The Agency may consider making public a list of Local Representatives or MAHs found to be seriously or persistently non-compliant.

6.8 Urgent Safety Restriction.

6.9 Variation of the Marketing Authorization.

6.10 Suspension of the Marketing Authorization.

6.11 Revocation of the Marketing Authorization

7.0 PENALTIES

Non-adherence to the requirements of these guidelines by Local Representative and Marketing Authorization Holders will result in the Agency imposing penalties and sanctions as prescribed by the Good Pharmacovigilance Practice Regulations, Section 20.

8.0 INSPECTION FEES

MAH scheduled for inspection are required to pay an inspection fee as prescribed in the NAFDAC tariff. This payment is to be paid two (2) weeks before the inspection date and the receipt is presented to the desk officer responsible in the PV Directorate for confirmation.

APPENDIX I: Format for the Pharmacovigilance System Master File

Cover page

The name of the MAH or Local Representative

The date of preparation and last update

Section I: Administrative Information

A signed statement that the Local Representative or the Marketing Authorization Holder (MAH) has the necessary means to fulfill the tasks and responsibilities enumerated in the under-listed references;

1. NAFDAC Mandate, Act Cap N1 LFN (Laws of the Federation of Nigeria) 2004
2. Good Pharmacovigilance Practice Regulations 2021
3. Good Pharmacovigilance Practice Guidelines 2021
4. Guidelines for Conducting Pharmacovigilance Inspections 2024

Section II: The QPPV

1. The details of the Qualified Person for Pharmacovigilance (QPPV), i.e. name and contact details [address, telephone number, fax number, email)
2. The CV (curriculum vitae) of the QPPV
3. The job descriptions of the QPPV
4. The proof that the QPPV has attended the prescribed PV training program
5. The proof that the QPPV has been officially designated
6. Back-up procedure to apply in the absence of the QPPV and the training provided for the backup
7. A signed contract between the Local Representative or the MAH and the QPPV
8. The list of tasks that have been delegated by the QPPV and to whom these have been delegated

Section III: The organizational structure of the MAH

1. The description of the organizational structure of the Local Representative or the MAH relevant to pharmacovigilance showing the position of the QPPV in the organization
2. Diagrams showing the organizational charts will be helpful and preferred
3. Any pharmacovigilance-related activities performed by third parties
4. Description of co-marketing agreements and contracts of pharmacovigilance activities, if any.
5. List of products for which the QPPV is responsible

Section IV: Sources of Safety Data Inflow of adverse reaction reports and safety information

1. Description of the stages involved in the processing of ICSRs including the timelines for submission to regulatory authorities including NAFDAC
2. Outflow of safety data to regulatory authorities including NAFDAC
3. List of the sources of safety data, including but not limited to spontaneous reports, study sources, including any studies, registries, surveillance, or support programs sponsored by the marketing authorization holder

Section V: Computerized systems and databases

1. Description of the functionality and operational responsibility for computerised systems and databases used to receive, collate, record, and report safety information and an assessment of their fitness for purpose
2. Responsibility for the operation of the database and training provided including other types of training to be provided to staff(s) involved in the database operations
3. Validation, maintenance, backup, and access control
4. Management of the data for paper-based systems should be described and mechanisms used to assure the integrity and accessibility of the safety data and in particular the collation of information about adverse drug reactions.

Section VI: Pharmacovigilance processes

The list of standard operating procedures

Details of all the current standard operating procedures relating to pharmacovigilance which are expected include but are not limited to the following;

1. SOP for SOPs
2. Corrective and Preventive Action (CAPA) processes for pharmacovigilance
3. Causality assessment, if applicable
4. Coding of Individual Case Safety Reports (ICSRs), if applicable
5. Communication of safety concerns to patients/consumers, healthcare professionals, and regulatory authorities
6. Complaint handling
7. Deviation Documentation
8. Escalation of safety issues
9. Handling of Counterfeits
10. Internal audits
11. Literature searches (scientific and lay media)
12. Management of pharmacovigilance inspections
13. Manual handling of ICSRs, if applicable
14. ICSR collection, collation, follow-up, assessment, and reporting
15. Review and submission of regulatory documents (e.g. PSURs/PBRERs, RMPs)

16. Signal generation
17. Archiving and retrieval
18. Training
19. Implementation of safety variations to the Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL), if applicable
20. Risk management system(s) and monitoring of the outcome of risk minimization measures

Section VII: Pharmacovigilance System Performance

Evidence of ongoing monitoring of the performance of the pharmacovigilance system including compliance of the main outputs of pharmacovigilance should be described.

The description of monitoring methods should include but not limited to the following:

1. An explanation of how the correct reporting of ICSRs is assessed. In the annex, figures/graphs should be provided to show the timeliness of reporting over the past year;
2. A description of any metrics used to monitor the quality of submissions and performance of pharmacovigilance. This should include information provided by competent authorities regarding the quality of ICSR reporting, PSURs, or other submissions;
3. Where applicable, an overview of the methods used to ensure timeliness of safety variation submissions compared to internal and competent Agency deadlines, including the tracking of required safety variations that have been identified but not yet been submitted;
4. Where applicable, an overview of adherence to risk management plan commitments, or other obligations or conditions of marketing Authorization(s) relevant to pharmacovigilance.

Targets for the performance of the pharmacovigilance system shall be described and explained and a list of performance indicators must be provided.

Section VIII: Pharmacovigilance Quality system

The pharmacovigilance quality system should include the following:

General Overview

A general description of the quality management system should be provided, in terms of the structure of the organization and the application of the quality to pharmacovigilance.

Document and Record Control

There should be a description of the archiving arrangements for electronic and/or hardcopy versions of the pharmacovigilance system master file, as well as an overview of the procedures applied to other quality system and pharmacovigilance records and documents.

Procedural documents

The description of the types of documents used in pharmacovigilance (standards, operating procedures, work instructions etc) should be provided. The applicability of the various documents at global, regional or national level within the organisation, and the controls that are applied to their accessibility, implementation and maintenance should be described.

A list of specific procedures and processes related to the pharmacovigilance activities and interfaces with other functions, with details of how the procedures can be accessed must be provided.

Training

Qualification and records of training for members of staff in the pharmacovigilance Departments of the Local Representative or the MAH and any individual that may receive safety reports, including employees of Local Distributors. Updated training materials and records of training programs should be provided including assessment of the effectiveness of the training programs as an Annex in the PSMF.

Auditing

Information about quality assurance auditing of the pharmacovigilance system should be included in the pharmacovigilance system master file.

A description of the approach used to plan audits of the pharmacovigilance system and the reporting mechanism and timelines should be provided, with a current list of the scheduled and completed audits concerning the pharmacovigilance system maintained in the annex to the PSMF. This list should describe the date(s) (of conduct and report), scope, and completion status of audits of third parties including Local Distributors. Where there are findings during the audit, the corrective and preventive action plans for addressing these should be included in the Annex.

As a means of managing the pharmacovigilance system, and providing a basis for audit or inspection, the PSMF should also describe the process for recording, managing, and resolving deviations from the quality system. The master file shall also document deviations from pharmacovigilance procedures, their impact, and management until resolved.

Section IX: Annex to the PSMF

An annex to the pharmacovigilance system master file shall contain but not limited to the following documents:

1. A list of products covered by the pharmacovigilance system master file indicating product name, and the active substance(s).

2. List of written policies and procedures to comply with NAFDAC's pharmacovigilance requirements
3. A list of tasks that have been delegated by the qualified person for pharmacovigilance
4. A list of all completed audits, for five years, and a list of audit schedules
5. Where applicable, a list of performance indicators
6. Updated training materials and records of the training should be provided including an assessment of the effectiveness of the training programs
7. Pharmacovigilance agreement between the MAH/Local Representative and the Local Distributor(s)

Appendix 2: Corrective and Prevention Action Plan

Feedback on inspection findings should be clear and concise and include proposed actions to address both the identified deficiency and its root cause. Consideration should also be given to identifying and preventing similar deficiencies within the pharmacovigilance system.

Feedback should be entered into the table(s) below, without changes to the inspector team's text that describes the findings. The following text is intended as guidance when considering the information that should be entered into each field within the table(s). 'Not applicable' should be entered into the relevant field if the requested information is not appropriate for the finding in question

Finding	
<<inspection team to add text>>	
Root cause analysis	
<< inspected party to add text >>	
Identify the root cause(s) which, if adequately addressed, will prevent the recurrence of the deficiency.There may be more than one root cause for any given deficiency.	
Further assessment	
<<inspected party to add text >>	
Assess the extent to which the deficiency exists within the pharmacovigilance system and what impact it may have on all products. Where applicable, describe what further assessment has been performed or may be required to fully evaluate the impact of the deficiency e.g. retrospective analysisof data may be required to fully assess the impact.	
Corrective action(s)	
<< inspected party to add text >> Detail the action(s) taken/proposed to correct the identified deficiency.	
Deliverable(s) << inspected party to add text >>	**Due date(s)** << inspected party to add text >>
Preventative action (s)	
<< inspected party to add text >> Detail the action(s) taken/proposed to eliminate the root cause of the deficiency, to prevent recurrence. Action(s) to identify and prevent other potential similar deficiencies should also be considered.	
Deliverable(s) << inspected party to add text >>	**Due date(s)** << inspected party to add text >>

Appendix 3: List for Notification of Contract Pharmacovigilance Service Providers (CPSP)

Nigeria DATE
National Agency for Food and Drug Administration and Control (NAFDAC) NO
National Pharmacovigilance Center

Service type	Company name	Date of signing contract and duration	Qualified Person Responsible for Pharmacovigilance	Back-up Person responsible for Pharmacovigilance	Contact information of CPSP representatives	Contact information of company contact persons

References

1. Adapted from Guideline on good pharmacovigilance practices (GVP): Pharmacovigilance inspections– Module III (Rev 1) EMA/119871/2012 Rev 2/2014
2. Food and Drug Agency Ghana Guidelines for Conducting Inspections: FDA/SMC/SMD/GL- PVI/
3. South African Health Products Regulatory Authority-Pharmacovigilance_Inspection_Guidelines_Version-1.0_May_2022/SAHPGL-CEM-PV-01_v1
4. Guideline on Pharmacovigilance Inspections English Version. Version 01. Effective Date 27 June 2019. https://titck.gov.tr/storage/Archive/2022/contentFile/English%20version%20of%20Guideline%20on%20PV%20inspections_7c6a4226-9e92-49a4-8db5-319c4c564a99.pdf