ETHIOPIAN FOOD AND DRUG AUTHORITY

GUIDELINE TO CONDUCT GOOD PHARMACOVIGILANCE PRACTICE INSPECTION

Document No	Version No	Approval Date	Issue Date
EFDA/GDL/072	001	17/04/2025	28/04/2025

Document History

Version No.	Reason for amendment	Effective Date
001	New Version	28/04/2025

Asnakech Alemu,

Pharmacovigilance and Clinical Trial Lead Executive Office

Signature

Table of Contents

Acronyms

ADE	Adverse drug event
API	Active pharmaceutical ingredient
EFDA	Ethiopian Food and Drug Authority
GMP	Good Manufacturing Practice
LEO	Lead Executive Office
GVP	Good Pharmacovigilance Practice
PSMF	Pharmacovigilance system master file
MAH	Market Authorization Holder
QPPV	Qualified Person for Pharmacovigilance
SOP	Standard Operating Procedure

Acknowledgements

The Ethiopian Food and Drug Authority (EFDA) would like to acknowledge and appreciate to all individuals and institutions that contributed to the development of this Guideline for Good Pharmacovigilance Practice (GVP) Inspection – 2025.

We extend our special thanks to the technical working group and representatives from Market Authorization Holders for their dedication, time, and expertise throughout the drafting, validation and finalization process. Their commitment ensured that the guideline aligns with EFDA's regulatory framework and reflects the evolving landscape of pharmacovigilance in Ethiopia.

Foreword

The Ethiopian Food and Drug Authority (EFDA) is committed to safeguarding public health by ensuring the safety, efficacy, and quality of medicines circulating in the Ethiopian market. In alignment with its legal mandate as stipulated under Proclamation No. 1112/2019 and the Pharmacovigilance Directive No. 932/2022, EFDA continues to strengthen its regulatory oversight through robust pharmacovigilance systems and procedures.

This Guideline for Good Pharmacovigilance Practice (GVP) Inspection has been developed to provide a comprehensive framework for planning, conducting, and following up on GVP inspections. It outlines inspection types, processes, expectations from Marketing Authorization Holders (MAHs), and responsibilities of Qualified Persons for Pharmacovigilance (QPPVs). The guideline adopts a risk-based approach, ensuring that inspection efforts are prioritized where they are most needed, and aligns with global best practices.

Pharmacovigilance inspections play a critical role in verifying compliance with regulatory requirements and ensuring that MAHs are actively monitoring and managing medicine-related risks. Through this guideline, EFDA aims to promote transparency, consistency, and accountability across all stakeholders involved in medicine safety monitoring.

I believe that the implementation of this guideline will significantly enhance pharmacovigilance practices in Ethiopia, contributing to the safer use of medicines and the protection of public health. I would also like to call up on all interested bodies/individuals to continue their usual support by forwarding their comments and suggestion for the improvement of this guideline to the Ethiopian food and drug authority P.O.Box 5681 Addis Ababa, Ethiopia, telephone +251-115524122, email: pharmacovigilance@efda.gov.et

Glossary/Definitions

For this document, the following terms and definitions are used.

1. **"Authority"** the Ethiopian Food and Drug Authority.

2. **"Good Pharmacovigance Inspection"** an inspection conducted by the Authority at Market Authorization Holders and health facilities designed to review personnel, systems, facilities and procedures in place and to determine their compliance with regulatory Pharmacovigilance obligations.

3. **"Good pharmacovigilancem practice inspector"** a person who is appointed by the Authority as Good Pharmacovigilance Practice inspector/auditor to verify that the Market Authorization Holders comply with Pharmacovigilance regulatory requirements.

4. **"Inspectee"** any Market Authorization Holder being inspected by the Authority.

5. **"Market authorization Holder"** an individual or a corporate entity/company that has been granted Market Authorization to place a pharmaceutical product in the Ethiopian market.

6. **"Pharmacovigilance"**the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine-related problem.

7. **"Pharmacovigilance self-audit"** an internal review conducted by Market Authorization Holders to assess Pharmacovigilance compliance with regulatory requirements, company SOPs and industry best practices in medicine safety monitoring.

8. **"Pharmacovigilance system master file"** a detailed description of the pharmacovigilance system used by the marketing authorization holder with respect to one or more authorized medicinal products.

9. **"Qualified Person for Pharmacovigilance"** a healthcare professional, usually an employee of Market Authorization Holder, who is responsible for the safety of pharmaceutical products marketed in Ethiopia.

1. Introduction

1.1. Background

According to Proclamation No.1112/2019, the Ethiopian Food and Drug Authority (EFDA) is mandated to protect the public health by ensuring quality, efficacy and safety of medicines. To ensure the safety of authorized medicines, the Authority shall have the responsibility to perform pharmacovigilance inspections and regulate market authorization holders (MAHs) with respect to their monitoring of safety and quality of their medicines as it is clearly stated in the pharmacovigilance directive No. 932/2022.

Pharmacovigilance inspections are crucial for ensuring the safety and efficacy of medicines by verifying that MAHs maintain robust systems to monitor, assess, and manage risks associated with their products. Market Authorization Holders has responsibilities to monitor the safety, quality and efficacy of medicines authorized in the country. By examining procedures, systems, personnel, and facilities, inspections help identify potential safety issues and ensure that appropriate actions are taken to mitigate any risks associated with marketed products.

Pharmacovigilance inspections are not a one-time event but rather a continuous process of monitoring and evaluation, ensuring that safety issues are identified and addressed throughout the lifecycle of a medicine. This guideline is designed to facilitate compliance by the MAH and to enhance consistency in the application of the regulatory requirements regarding Good Pharmacovigilance practices (GVP).

1.2. Scope of the Guidelines

This guideline applies to all Marketing Authorization Holders (MAHs) who are responsible to place their medicinal products for human use in the Ethiopian market.

This guideline serves as a complement to the existing national pharmacovigilance Directive no 932/2022 and national Pharmacovigilance guideline, 2024.

1.3. Objectives of the Guidelines

The objectives of this guideline are:

- To outline the roles and responsibilities of the marketing authorization holders to implement GVP and the GVP inspection process.

- To guide Qualified Person for Pharmacovigilance (QPPV) on their roles and responsibility with respect to Good Pharmacovigilance Practices.
- To provide guidance for the regulatory Authority on how to plan, conduct, report and follow up the GVP inspections considering risk-based approaches.

2. Good Pharmacovigilance Practice Inspections

Good Pharmacovigilance Practice (GVP) refers to a set of measures, standards and practices intended to ensure the safety, quality and efficacy of medicines by systematically monitoring, assessing and preventing adverse effects or any other medicine-related problems. GVP covers all aspects of a medicine's life cycle, from development and marketing authorization to post-marketing surveillance, ensuring that pharmaceutical companies, regulatory authorities and healthcare professionals maintain a consistent and proactive approach to medicine safety. It is the framework of rules, processes, and standards designed to ensure high-quality pharmacovigilance. The ultimate goal is to protect public health by identifying potential risks early and implementing appropriate risk minimization strategies.

Implementation of GVP requires coordinated efforts by multiple stakeholders. The Qualified Person for Pharmacovigilance (QPPV) plays a central role in ensuring the system's integrity. Risk management systems, signal detection, periodic safety update reports (PSURs), and continuous benefit-risk assessments, requirements for the Pharmacovigilance System Master File (PSMF), management and reporting of adverse events and safety communications are integral parts of GVP compliance.

Moreover, training and pharmacovigilance audits are essential to maintain quality standards across all pharmacovigilance systems. In general, a Good Pharmacovigilance system should contain at least the following elements: standard operating procedures (SOPs), training and competence, IT Systems, documentation system and continuous improvement based on audits, inspections, and updates to GVP.

Pharmacovigilance inspections are conducted by regulatory authorities to verify that the Market Authorization Holders have adequate systems in place and comply with the existing regulatory requirements for Pharmacovigilance activities.

Pharmacovigilance inspections can be either system or product-related. System inspections are designed to assess the systems, methods, personnels, and facilities in place to ensure compliance with the regulations. Whereas, product specific inspection primarily focuses on product-related Pharmacovigilance issues, including product-specific activities and documentation, rather than a general system review.

The GVP inspection can be announced or unannounced. Generally, it is anticipated that the majority of inspections will be announced in advance to the inspectee to ensure the availability of relevant individuals for the inspection. However, on occasions, it may be permissible to conduct unannounced inspections or to announce an inspection on short notice (for example, when the announcement could jeopardize the inspection's objectives or when the inspection is undertaken in a short timescale owing to urgent safety concerns).

2.1. Types of Inspection

2.1.1. Routine Inspections

Routine pharmacovigilance inspections are scheduled in advance and are included into the inspection program. There is no specific trigger to initiate this kind of inspection. Routine inspections are usually system inspections and a risk-based approach is implemented.

Routine pharmacovigilance inspections should examine compliance with EFDA legislation and guidelines. The MAH that is expected to have pharmacovigilance obligations should be inspected at least once in three years while following routine inspection. The scope of such inspections should include the review of the following elements, as appropriate:

A. 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 MAH 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 of reported events;
- **iv.** Reporting according to the requirements for various types of reported ICSRs, including onward reporting to the EFDA pharmacovigilance unit and timeliness of such reporting;
- **v.** Record keeping and archiving for ICSRs.

B. Periodic Safety Update Reports/Periodic Benefit Risk Evaluation Reports (PSURs/PBRERs):

- **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 EFDA requirements

iv. Timeliness of submissions

C. 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;

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

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

D. 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 (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;

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;

E. Pharmacovigilance system:

i. Roles and responsibilities of qualified person for pharmacovigilance, 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 MAH in relation to 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 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 adhere to the following points but not limited to:

- The use of pre-selection audits, gap analysis and capacity planning
- Clarity of record / data ownership, and access to source data and the safety database by the MAH
- Defined records management (format, location and timely provision) and document retention periods,
- Terms for transition periods, especially for data transfers, as well as contract termination rules
- Provisions for business continuity
- Proportionate oversight tools (audit, KPIs, deviations)
- QPPV and National Competent Authority access to data and documentation
- Provisions for sharing the outcomes of inspections and audit, CAPA implementation
- Workload metrics and resource / training allocation responsibilities, rules and reports
- Dispute resolution (in relation to pharmacovigilance decisions and activity)

viii. The inspection may include pharmacovigilance quality management 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.

2.1.2. Targeted or "For cause" Pharmacovigilance Inspections

Targeted inspections are initiated when a trigger is recognized. Targeted inspections may be performed to focus on specific pharmacovigilance processes or to examine identified compliance issues and their impact on a specific product. Full system inspections may be performed based on the triggers. Targeted inspections may be conducted on the occasion of one or more of the triggers listed below but not limited to:

A. Benefit/risk balance of the product

i. A change in the benefit risk balance where further examination through an inspection is considered appropriate

ii. An identified risk; or delay or failure in the notification of the risk

iii. Notification of the information including pharmacovigilance problems/concerns to the Authority

iv. Non-compliance or product safety issues identified during the monitoring of pharmacovigilance by the Authority

v. Communication of information on pharmacovigilance concerns to the general public without giving prior or simultaneous notification to the EFDA

B. Reporting obligations

i. Delays or omissions in reporting,

ii. Poor quality or incomplete reports,

iii. Inconsistencies between reports and other information sources,

C. Requests from Authority

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

ii. Inadequate provision of data and documents to fulfil requests for information from the Authority.

iii. Deficiencies or quality issue in reports requested as specific requirements,

D. Fulfillment of commitments

i. Delays or failure to fulfillment of risk management plan commitments,

ii. Delays or failure to carry out specific obligations relating to the monitoring of product safety,

E. Inspections

i. Delays in the implementation or inappropriate implementation of corrective and preventative actions,

ii. Risk identified regarding product safety through other inspections (GCP, GMP and GDP),

iii. Non-compliances identified through other regulatory authorities' inspections,

F. Others

i. Identification of non-compliances as a result of reviewing of pharmacovigilance system master file,

ii. Non-compliance information received from other regulatory authorities identified through non-inspection activities.

2.1.3. Pre-authorization Inspections

Pre-authorization pharmacovigilance inspections are inspections performed before a market authorization 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 MAH in support of the registration application. Pre-authorization inspections are not mandatory; however, the Authority may conduct it in specific circumstances were deemed necessary.

The following aspects shall be considered to decide the need for pre-authorization inspection:

- The MAH has not previously operated a pharmacovigilance system within the country or is in the process of establishing a new pharmacovigilance system;
- Previous information indicates that the MAH has a poor history or culture of compliance. If the 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;
- Due to product-specific safety concerns, it may be considered appropriate to examine the 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).

If the outcome of the pre-authorization inspection raises concerns about the MAH ability to comply with the regulatory requirements, the following regulatory measures will be implemented; non approval of registration application, re-inspection prior to approval of authorization certificate and granting of the authorization certificate with the recommendation to perform an early post authorization pharmacovigilance inspection.

2.1.4. Post-authorization Inspections

Post-authorization pharmacovigilance inspections are inspections performed after a registration certificate is issued and are intended to examine whether the MAH complies with its pharmacovigilance obligations or not. They can be any of the above-mentioned types.

2.1.5. Re-Inspections

A re-inspection may be conducted on a routine basis as part of a routine inspection program. 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.

The triggering factors for re-inspection may include but not limited to the following factors.

- Identification of the significant non-compliance from the previous inspection,
- Inappropriate implementation of the corrective and preventive actions by the inspected MAH,
- 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 QPPV)
- Review of process and/or product-specific issues identified from the assessment of information provided by the marketing authorization holder, or not covered in a prior inspection.

2.1.6. Follow-up Inspection

When non-compliance with pharmacovigilance obligations is identified during an inspection, follow-up will be required until a corrective and preventive action (CAPA) plan is completed.

2.2. Mode of inspections

The Pharmacovigilance inspection can be carried out either onsite or remote. Remote pharmacovigilance inspections are performed by inspectors remote from the premises of the MAH. Communication mechanisms such as the internet or telephone may be used in the conduct of the remote inspection. For example, in cases where key sites for pharmacovigilance activities are located outside Ethiopia 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 pharmacovigilance system master file, via remote access. The remote inspection approach may also be taken where there are logistical challenges to an onsite inspection during exceptional circumstances (e.g. a pandemic outbreak or travel restrictions). Such approaches are taken at the discretion of the inspectors and in agreement with the body commissioning the inspection. The logistical aspects of the remote inspection shall be considered following liaison with the marketing authorization holder. 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

which require on-site inspection or if the objectives of the inspection could not be met by remote inspection.

3. Inspection Process

Pharmacovigilance inspections should be planned, coordinated, conducted, reported on, followed-up and documented in accordance with inspection procedures consistent with the Authority's legal documents, guidelines and pharmacovigilance inspection procedures. Pharmacovigilance inspection starts with the necessary preparation for inspection. The preparation encompasses those activities undertaken after the selection of market authorization holders for a pharmacovigilance inspection and prior to inspection conduct. It involves inspection planning; making the necessary logistical arrangements; announcing the inspection to the MAH and defining the inspection scope and agenda.

Inspector(s) should be appointed for an inspection, taking into consideration National Regulatory Authority procedures. The assignment of good pharmacovigilance practice inspectors and the inspection days should be sufficient to ensure that the inspection objectives are achieved. The Ethiopian Food and Drug Authority has the right to inspect the system, the premises and procedures of market authorization holders at any time.

The inspection process can broadly be classified into pre-inspection, Inspection and post inspection phases.

3.1. Pre-Inspection Activities

The pre-inspection phase is crucial for ensuring a structured and efficient inspection process. It involves preparatory activities by both the Regulatory Authority (RA) and the Marketing Authorization Holder (MAH) to facilitate a thorough and compliant review of pharmacovigilance (PV) systems.

Pharmacovigilance inspections are planned using a systematic and risk-based approach to ensure resources are used efficiently while maintaining public health protection. The regulatory Authority may request information from marketing authorization holders for risk-based inspection planning if it is not readily accessible from other sources.

Factors Considered in Inspection Planning

The Authority will consider the following factors when planning for inspection.

Inspection-Related Factors:

- Past non-compliance found during previous inspections (e.g., PV, GCP, GMP, GLP, GDP)
4. Re-inspection dates set after previous inspections

Product-Related Factors:

- Products requiring additional pharmacovigilance or risk-minimization measures

- Products authorized with post-authorization safety study requirements or additional monitoring
- Products with large sales volume or broad patient use
- Product(s) with limited alternative in the marketplace
- Authorization with conditions associated with safety, e.g. requirement for post-authorization safety studies (PASS) or designation for additional monitoring

Marketing Authorization Holder (MAH) related Factors:

- MAHs that have never had a pharmacovigilance inspection
- MAHs with many products on the market
- MAHs with no prior marketing authorizations in the country
- Negative findings from other authorities or inspections
- Organizational changes, such as mergers and acquisitions
-

Pharmacovigilance System related Factors:

- Transfer of PV activities to third-party service providers
- Changes in the Qualified Person responsible for pharmacovigilance
- Modifications to the pharmacovigilance safety database
- Changes in agreements with Pharmacovigilance service provider or the sites at which is conducted
- Delegation or transfer of pharmacovigilance system master file management.

By considering these factors, EFDA ensures a targeted and effective inspection process, strengthening pharmacovigilance oversight.

A. Preparation of Inspection plan

Pharmacovigilance inspection planning should be based on a systematic and risk-based approach to make the best use of surveillance and enforcement resources whilst maintaining a high level of public health protection. EFDA formulates a detailed inspection plan, outlining objectives, scope, timelines, and key focus areas identified for Pharmacovigilance inspection. In order to ensure that inspection resources are used in an efficient way, the scheduling and conduct of inspections will be driven by the preparation of inspection programs.

During the inspection planning phase, the Authority may notify the MAH about the scheduled inspection and request relevant documents to facilitate the process. This notification is issued within

fourteen calendar days before the inspection date. The inspection date is mutually agreed upon with the MAH.

The Authority may request for the following documents prior to the inspection. This may include but not limited to;

- Pharmacovigilance System Master File (PSMF), reflecting Ethiopian Pharmacovigilance system details (e.g., human resources, organizational chart, job descriptions of QPPV and other staff, SOPs), refer Annex xx for contents of the PSMF.
- List of Important SOPs as per Annex IV
- Minutes of meetings specific to pharmacovigilance
- Individual adverse reaction case files
- Recent PSURs / PBRERs for marketed products
- CAPA records if applicable
- Country-specific RMPs for selected products when applicable
- Line listings of adverse reaction reports

The inspection team is selected based on the inspection scope, and an inspection agenda is prepared. If the inspection is announced in advance, the agenda and list of required documents are sent via email to the MAH before the scheduled date.

B. Determine scope of inspection

The scope of an inspection is determined by the inspection type and any previous inspection history. Key factors to consider may include but not limited to the following points:

- Information obtained from the Pharmacovigilance System Master File (PSMF)
- Information concerning the functioning of the pharmacovigilance system e.g. data for compliance metrics, reporting quality and audit results)
- Specific triggers indicating potential risks
- Supplementary data requests before the inspection to identify suitable sites or clarify aspects of the pharmacovigilance system

C. Selection of Sites for inspection

Any organization or entity conducting pharmacovigilance activities, either fully or partially, on behalf of or in collaboration with the Market Authorization Holder may be subjected to Pharmacovigilance inspection. This ensures their ability to support compliance with pharmacovigilance requirements. Inspections of sites located outside Ethiopia may be necessary if key pharmacovigilance activities, databases, or the main pharmacovigilance center are based abroad.

In such cases, assessing compliance within Ethiopia may not be feasible or efficient. The type and number of sites to be inspected should be selected appropriately to ensure that the key objectives outlined in the inspection scope are met.

The MAH shall also have a responsibility to prepare for the GVP inspection. The MAH is advised to conduct self-audits and confirm readiness at all times and before the planned GVP inspection. In addition, the MAH shall compile and readily avail required documents as well as conduct briefing to their staff regarding the inspection.

3.2. Conduct of Inspection

During a pharmacovigilance inspection, the MAH must take necessary measures to facilitate the inspection process and ensure compliance with Good Vigilance Practice (GVP) guidelines. They are required to provide all requested information and documentation relevant to the inspection scope. The inspection consists of three main phases: the opening meeting, the inspection process, and the closing meeting. The inspection process begins with an opening meeting, where the inspection team introduces themselves, outlines the scope, methodology, and agenda, and confirms key details with the MAH. Representatives from the inspected party also introduce themselves and provide an overview of the pharmacovigilance system. Throughout the inspection, the names, titles, and signatures of participating personnel from both parties are documented.

Inspection activities include a thorough review of the pharmacovigilance (PV) system and processes, interviews with key personnel such as the Qualified Person for Pharmacovigilance (QPPV) and the PV team, and an examination of case processing, including Individual Case Safety Reports (ICSRs), signal detection, and Risk Management Plan (RMP) compliance. Additionally, the Pharmacovigilance System Master File (PSMF) will be verified, compliance with reporting timelines and documentation, risk minimization measures and Corrective and Preventive Actions (CAPA) implementation will be verified.

The inspection may also involve on-site data verification and breakthroughs of relevant facilities. Preliminary findings and initial observations are discussed before concluding the inspection with a closing meeting. During this meeting, the inspection team presents a summary of findings and provides information on the post-inspection process.

3.3.Post-Inspection Activities

An official inspection report will be prepared, classifying the findings and determining whether the MAH complies with regulatory requirements.

The regulatory Authority will prepare the inspection report and share with the MAH within 30 working days. After receiving the official inspection report, if the MAH does not file any complaint on the findings of the inspection within 10 working days, the report will be considered as accepted

by the MAH. The MAH shall provide an appropriate corrective and preventive action plan (CAPA) within 20 working days. 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.
The Authority will review the submitted CAPA and provide feedback to the MAH within 5 working days.

3.3.1. Classification of Findings

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 applicable EFDA legislation and guidelines. (e.g. it includes the MAH engaging in fraud, misrepresentation or falsification of data, Failure to report serious unexpected adverse reactions to the Authority within the regulatory timelines)
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 applicable EFDA legislation and guidelines. (example inconsistently followed SOPs, Missing documentation of minor internal audits and Incomplete training records for pharmacovigilance staff)
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. A deficiency may be minor either because it is judged as minor or because there is insufficient information to classify it as major or critical. (e.g. The procedure for handling safety data exchange agreements does not clearly define the timelines for periodic review and update of agreements)

An inspection report is then generated and internally reviewed to ensure that the classification of deficiencies is consistent before the final report is issued. The Inspection report shall have the content as described on Annex 1.

3.3.2. Follow-up Inspection

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

- review of the marketing authorization holder's corrective and preventive action plan.
- review of the periodic progress reports, when deemed necessary;
- re-inspection to assess appropriate implementation of the corrective and preventive action plan.

- requests for submission of previously un-submitted data, submission of variations,
- requests for issuing safety communications, including amendments of marketing and/or advertising information.
- requests for a meeting with the MAH to discuss the deficiencies, the impact of the deficiencies and CAPA plans.
- Communication of the inspection findings to other regulatory authorities when deemed necessary.
- 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).

Sharing information and communication between GVP inspectors and Dossier assessors is important for the proper follow-up of GVP inspections.

4. Guidance on the QPPV

Pharmacovigilance Directive No.932/2022 states that every Marketing Authorization Holder should have responsibilities to set-up robust pharmacovigilance systems for their medicinal products and to appoint a qualified person responsible for Pharmacovigilance who resides in Ethiopia.

4.1. Responsibilities of the MAH

The MAH should:

- Assign QPPV and appropriate backup QPPV before importation and distribution of its product in the Ethiopian market.
- Provide and/or ensure that the QPPV has received comprehensive training in Pharmacovigilance.
- Ensure that the QPPV has sufficient authority to implement all Pharmacovigilance related activities.
- Ensure that there are appropriate processes, resources and communication mechanisms in place for the fulfillment of the QPPV's responsibilities and tasks.
- Notify the Authority of the absence of the QPPV and substitution plan not later than 14 calendar days after the position becomes vacant.
- Have a signed contract agreement with the QPPV.
- The following QPPV related information should be submitted to the Authority during the assignment of QPPV.
    - Curriculum vitae including proof of qualifications and credentials
    - Contact details including but not limited to the name, telephone, fax and email, postal and official working address

- A description of the roles and responsibilities of the QPPV
- Details of back-up arrangements to apply in the absence of the qualified person responsible for pharmacovigilance
- A list of tasks that have been delegated by the qualified person for pharmacovigilance and to whom these tasks have been delegated.
- Contract agreement between QPPV and MAH as per template attached in Annex V.

- The MAH should have back-up procedures in the case of absence of the QPPV and ensure that the backup QPPV shall meet the basic requirements (a healthcare professional with a minimum of a bachelor's degree in health sciences and received appropriate PV related training).

4.2. Qualification and responsibilities of QPPV

4.2.1. Qualification of QPPV

- The person designated as QPPV should be a healthcare professional with a minimum of a bachelor's degree in health sciences and at least two years of experience in pharmacovigilance-related activities. However, the authority highly recommends that pharmacists and medical doctors with appropriate PV-related training be assigned as QPPV.
- The QPPV should receive formal training in pharmacovigilance from training institutions acceptable by the authority.
- The assigned QPPV should be proficient in English and understand at least one of the national languages of Ethiopia.

4.2.2. Roles and Responsibilities

The QPPV should have the following responsibilities.

- Act as a single point of contact for the authority on all matters relating to pharmacovigilance and safety of marketed products including pharmacovigilance inspections.
- The QPPV should be a full-time employee representing the MAH and should be reachable 24/7.
- Establish and maintain a system that ensures information about all suspected adverse events, which are reported to the marketing authorization holder by any means, are collected, collated, processed, evaluated, and forwarded to the authority in line with the timelines stipulated by EFDA.
- Prepare the following documents for submission to the authority.
  - Periodic Safety Update Reports (PSURs) / Periodic Benefit-Risk Evaluation Reports (PBRER)

- Company-sponsored pre- and post-registration study reports related to pharmacovigilance.
- Risk Management Plans - All RMPs submitted shall be accompanied by a declaration to be signed by the QPPV. The declaration should indicate that the QPPV has read the RMP and will ensure implementation of all activities outlined in the RMP.
- Safety Variations
- Ongoing pharmacovigilance evaluation during the post-registration period

- Review both local and international journals regularly, submit to the Authority in case of published suspected AEs which occur in and outside Ethiopia related to their medical products.
- Ensure that any request from the authority for additional information deemed necessary for the evaluation of the risk-benefit ratio of a marketed product is provided to the authority promptly and fully.
- Oversee the safety profiles of the company's marketed products and any emerging safety concerns.
- Ensure the submission of Pharmacovigilance related documents in compliance with Regulatory requirements and timelines as indicated on the national Pharmacovigilance Directive 932/2022.
- Ensure the proper documentation and archival of Pharmacovigilance related documents.
- Provide Pharmacovigilance training to staff.
- Take continuous professional development training on safety related issues.
- Lead and Coordinate pharmacovigilance self-audits.
- Ensure the quality of submitted data to the regulatory Authority.

5. Regulatory Measures

When non-compliance with pharmacovigilance requirements is detected, the necessary action will be decided on a case-by-case basis. Measures will depend on the potential negative public health impact of the non-compliance(s).

The Authority shall take Administrative, Regulatory or any other form of appropriate measures during violations of pharmacovigilance obligations.

The possible measures may include but not limited to the following:

- The Authority may consider making public a list of marketing authorization holders found to be seriously or persistently non-compliant.
- Actions against a Marketing Authorization(s) or Authorization application(s) e.g. Urgent Safety Restriction; variation of the marketing authorization; suspension or revocation of the marketing authorization; delays in approvals of new marketing authorization applications

until corrective and preventive actions have been implemented or the addition of safety conditions to new authorizations; requests for pre-authorization inspections.

- Product recalls e.g. where important safety warnings have been omitted from product information.
- In the case of QPPVs working as a full-time employee in more than one company, the Authority will take the appropriate administrative actions.
- Action relating to marketing or advertising information based on GVP inspection findings.
- Details are stipulated under Pharmacovigilance Directive No. 932/2022.

6. References

1. egyptian-guideline-on-adr-reporting-for-healthcare-professionals.pdf [Internet]. Available from: https://www.edaegypt.gov.eg/media/pxcanpyk/ca-of-pharmaceutical-care-guidelines-egyptian-guideline-on-adr-reporting-for-healthcare-professionals.pdf

2. Guideline on pharmacovigilance inspections of turkey available from: https://titck.gov.tr/storage/archive/2022/contentfile/english%20version%20of%20guideline%20on%20pv%20inspections_7c6a4226-9e92-49a4-8db5-319c4c564a99.pdf?Bcs-agent-scanner=a80dea51-db7f-2a4e-87d3-012a02930246

3. guideline-good-pharmacovigilance-practices-module-iii-pharmacovigilance-inspections_en.pdf [Internet]. [cited 2025 Mar 30]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-module-iii-pharmacovigilance-inspections_en.pdf

4. Guideline on Good Pharmacovigilance Practice (GVP) in Egypt for Pharmaceutical Products. Available from: https://www.edaegypt.gov.eg/media/g5el0gfa/gvp-guidelines-v-2.pdf

5. Malaysian-Guidelines-on-Good-Pharmacovigilance-Practices-GVP-For-Product-Registration-Holders-First-Edition-August-2021.pdf. Available from: https://www.npra.gov.my/easyarticles/images/users/1047/Malaysian-Guidelines-on-Good-Pharmacovigilance-Practices-GVP-For-Product-Registration-Holders-First-Edition-August-2021.pdf

6. NAFDAC-Guidelines-on-Good-Pharmacovigilance-2021.pdf. Available from: https://www.nafdac.gov.ng/wp-content/uploads/Files/Resources/Guidelines/PVG_GUIDELINES/NAFDAC-Guidelines-on-Good-Pharmacovigilance-2021.pdf

7. REVISED-GUIDELINES-FOR-PV-INSPECTION-PDF. Available from: https://fdaghana.gov.gh/wp-content/uploads/2024/09/REVISED-GUIDELINES-FOR-PV-INSPECTION-PDF.pdf

8. Pharmacovigilance_Inspection_Guidelines_Version-1.0_May_2022.pdf. Available from: https://www.sahpra.org.za/wp-content/uploads/2022/06/SAHPGL-CEM-PV-01_v1-Pharmacovigilance_Inspection_Guidelines_Version-1.0_May_2022.pdf

Annexes:

Annex 1: Template for Inspection Report

GVP Inspection Report Template
Part 1
I. Marketing Authorization Holder Details · Name: · Address: · Name and qualification of Key personnel (QPPV, Backup QPPV, regulatory affairs specialist, Quality and compliance officer, other personnel involved in Medicine safety monitoring as needed) **II. Inspection Information** · Date of Inspection · Previous Inspection Date (if applicable) · Type of Inspection · Scope of Inspection: **III.** Brief Report of Inspection Activities Undertaken: **IV.** Inspectors Information- Name and qualification
Part 2
(A) Brief Summary of the Pharmacovigilance Activities: (B) Use of Outside Technical Assistance in PV activities/ Outsourced activities: (C) Brief Description of the Quality Management System for the PV system: (D). Findings of observations related to: · Pharmacovigilance System Master File (PSMF) · The QPPV and Back up Arrangements

· The Organizational Structure of the MAH
· PV specific meetings · Sources of Safety Data · Pharmacovigilance Processes · Pharmacovigilance system performance · Pharmacovigilance Quality System
Part 3
Summary of Findings and Recommendations
Part 4
Conclusion **Name of Inspectors and Signature** **……...**

Annex 2: CAPA Plan Template

	Food and Drug Authority of Ethiopia **Pharmacovigilance and Clinical Trials Lead Executive Office**	FORM-PVCT-LEO-
	Good Pharmacovigilance Inspection Observation CAPA Clearance Assessment Form	
Revision No.	Issued date:	Next Rev. date:

	Observations	***Proposed CAPAs***	***Timeline***	***Assessment by Inspectors***
	Critical			
1.				
	Major			
1.				
	Minor			
1.				

Annex 3: Pharmacovigilance system master file (PSMF)

EFDA ETHIOPIAN FOOD & DRUG AUTHORITY	**Ethiopian Food and Drug Authority**

Minimum information that the Pharmacovigilance system master file (PSMF) shall contains		
Ser. No.	Topics covered	Remark
1	Cover letter	● MAHs details (name, address and contact) ● QPPV details (name, address and contact) ● The list of PSMFs for the MAH ● PMSF version number and effective date
2	Quality management system	● SOPs, training records, audit schedules and list of audits conducted and completed
3	Organizational structure and responsibilities of MAHs	● Pharmacovigilance team structure ● Outsourcing arrangement and list of contracts and agreement if applicable
4	QPPV	● Roles, responsibilities & organizational support ● Updated CVs ● Contact details
5	Pharmacovigilance process	● Management of individual case safety reports (ICSRs), signal detection, risk management plans (RMPs) and aggregate reporting (PSURs/PBRERs)
6	Sources of safety data	● Clinical trials, spontaneous reports, literature,

		patient support programs, etc.
7	SOPs, Databases and IT systems	● Description of Pharmacovigilance databases ● Data integrity and backup processes
8	Pharmacovigilance System Performance	● Key performance metrics (eg. ICSR, PSUR/PBRER and RMP timeline)
9	Audit and inspection reports	● SOPs, audit schedule, inspection reports, documentation etc.
10	Training plan and business continuity plan	● Pharmacovigilance related annual training plan ● Training matrix
11	Annexes	● List of SOPs covered by pharmacovigilance system ● Organizational chart ● Safety data flow diagram ● Logbook for changes (significant changes made to the PSMF) ● Process workflows (eg. Signal management) ● Document control and version history ● List(s) of products covered by the pharmacovigilance system ● List of MAHs (products covered by PSMF) ● Database validation documentation

Annex 4: List of SOPs

1. Individual Case Safety Report (ICSR) processing.
2. Corrective and Preventive Action (CAPA) processes for pharmacovigilance
3. SOP for safety communications
4. SOP for internal audit
5. Literature searches SOP
6. Management of pharmacovigilance inspections
7. Risk management system(s) and monitoring of the outcome of risk minimisation measures
9. Implementation of safety variations
10. Review and submission of regulatory documents (e.g. PSURs/PBRERs, RMPs)
11. Signal generation
12. Training SOP
13. Pharmacovigilance System Master File (PSMF) Maintenance

Annex V: TEMPLATE CONTRACT FOR QPPV

DD/MM/YYYY

Ethiopian Food and Drug Authority
Africa Avenue, near Wolo sefer, Kirkos sub city,
P.O. Box 5681, Addis Ababa, Ethiopia

CONTRACT FOR QUALIFIED PERSON FOR PHARMACOVIGILANCE (QPPV)

This contract is effective as of [effective date], [name of MAH], a company incorporated in accordance with the laws of [Country of MAH], located at [full address of MAH], (hereinafter referred to as ["short name of MAH if applicable] hereby empowers

[Full Name of QPPV], in his/her function as QPPV of [name of MAH] in Ethiopia, located at [full address of MAH or Local Representative in Ethiopia] (hereinafter referred to as the "Local QPPV") to:

1. Act as a single point of contact for the Ethiopian Food and Drugs Authority (EFDA) on all matters relating to pharmacovigilance and safety of marketed products including pharmacovigilance inspections.
2. Establish and maintain a system which ensures that information about all suspected adverse drug reactions/events which are reported to the personnel of the Marketing Authorization Holder, including medical representatives is collected, collated, processed and evaluated and forwarded to the Authority in line with the timelines stipulated in the EFDA Guidelines.
3. Serve as a point of contact and be available during pharmacovigilance inspections.
4. Prepare and/or submit regulatory documents relating to the safety of marketed products as per the EFDA's Pharmacovigilance Directive No. 932/2022 and the most recent versions of the underlisted EFDA Guidelines.
    i. National Pharmacovigilance Guideline (EFDA/GDL/006/ V 004), July 2024.
    ii. Guideline to conduct Good Pharmacovigilance Practice Inspection (EFDA/GDL/072/ V 001), April 2025
5. This Contract shall be effective as of [the Effective Date] and shall, automatically and without separate notification to third parties, terminate on the earliest of the following occasions:
    i. [Contract End Date] unless extended by [MAH] in writing.

ii. Termination of the contract between the [MAH] and the QPPV by either party.

This Contract shall in all aspects be subject to and interpreted in accordance with the laws of Ethiopia.

MAH	**QPPV**
Signature……..….....	Signature……...……...
Name: ……	Name: ……..……
Title: ……	Title: ……..……
Date: ……...	Date: ……...