ETHIOPIAN FOOD AND DRUG AUTHORITY

Pharmacovigilance and Clinical Trial Lead Executive Office

Guideline for Good Clinical Practice Inspection

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Foreword

Good Clinical Practice (GCP) Inspection refers to a systematic and independent examination of clinical trial process and documentation to ensure compliance with GCP guidelines and regulatory requirements. Its purpose is twofold**;** Quality Assurance (to uphold the highest standards of GCP, ensuring that trials are conducted ethically, transparently, and in accordance with regulatory requirements) and Continuous Improvement (to foster a culture of learning, where insights from inspections lead to corrective actions, preventive measures, and overall enhancement of clinical trial practices).

This guideline is intended to provide comprehensive information on Ethiopian Food and Drug Authority (EFDA) inspection programme of clinical trial. According to Proclamation No. 1112/2019, Article 4 and Sub-article 11, the authority has the mandate to authorize the conduct of clinical trial, monitor and inspect the process as to its conduct in accordance with good clinical practice. The clinical trial directive also state that the authority shall perform good clinical practice inspections before the commencement of the trial, during the conduct, and after completion of the trial and triggered as necessary.

I would like to extend my heartfelt gratitude to the U. S. Pharmacopeial Convention Promoting the Quality of Medicines Program (USP/PQM) for their invaluable financial and technical support. My sincere appreciation also goes to all experts including clinical trial researchers and ethics committee members who have directly or indirectly contributed their expertise to the development of this guideline. I invite all interested parties to continue their support by sharing their feedback and suggestions with the EFDA at P.O.Box 5681 Addis Ababa, Ethiopia, or by reaching out via telephone at 251-115524122 or email at Contact efda@efda.gov.et.

HERAN GERBA, Director General, Ethiopian Food and Drug Authority

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Abbreviations

CAPA	Corrective and Preventive Actions
CRF	Case Report Form
CRO	Clinical Research Organization
EFDA	Ethiopian Food & Drug Authority
ERC	Ethics Review Committee
GCP	Good Clinical Practice
ICH	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use
TMF	Trial Master File

Definition

Adverse Event

Any untoward medical occurrence in a clinical trial participant after administration of an investigational product, which does not necessarily have a causal relationship with the treatment.

Amendment

A written description of changes made to a clinical trial after being authorized by the authority

Audit Report/Inspection report

A written feedback generated after a systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, data were recorded, analyzed and accurately reported according to the protocol, standard operating procedures, GCP and applicable regulatory requirements.

Clinical Trial

Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

Clinical Trial Site

A controlled environment where clinical research, development and testing can take place safely with appropriate oversight This site is typically responsible for various activities related to the trial, including recruiting and enrolling participants, administering treatments, collecting data, and ensuring the overall conduct of the trial adheres to regulatory and ethical guidelines.

Corrective and Preventive Action

A system plan designed to address compliance issues and prevent their recurrence. Corrective and Preventive Action (CAPA) plans are crucial for ensuring participant safety, protecting their rights, and maintaining the integrity of study data. Corrective Action is reactive, while Preventive Action is proactive and although they both use similar procedures, they are not always used together.

Contract Research Organization

A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more trial-related duties and functions.

Essential Documents

Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

Good Clinical Practice

An international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects

Good Clinical Practice inspection

Is a systematic and independent examination of clinical trial processes and documentation to ensure compliance with GCP guidelines and regulatory requirements.

Informed Consent

A process by which a participant voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the participant decision to participate

Inspection

The act of a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organizations (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority.

Inspector/s

Is someone who is employed by a regulatory authority, for inspection, for the purpose of assessing compliance with the principles of Good Clinical Practice in connection with a clinical trial

Institutional Review Board (IRB)/Independent Ethics Committee

An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial

Investigational Product

A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial

Investigator

An individual responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Monitoring

The act of overseeing the progress of a clinical trial, and ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory Requirements.

Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol-referenced documents.

Protocol deviation

A protocol deviation occurs when activities during a study diverge from the IRB and regulatory authority approved protocol. It includes any change, divergence, or departure from the study design or procedures that affects the subject's rights, safety, or well-being and/or the completeness, accuracy, and reliability of study data. Minor protocol deviations do not significantly impact subject rights, safety, or data integrity.

Protocol Violation

It is a more serious deviation from the IRB and regulatory authority approved protocol that may harm or pose significant risk to research subjects (e.g., wrong treatment, incorrect dose), compromise scientific data integrity (e.g., enrolling ineligible subjects), involve willful breaches of human subject protection regulations (e.g., failure to obtain informed consent) or reflect serious noncompliance with regulations or institutional policies.

Quality Assurance

All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented, and reported in compliance with GCP and applicable regulatory requirements.

Suspension

Refers to a temporary halt in the progress of a clinical trial. The trial is paused but not permanently stopped. The intent is to address specific issues before potentially resuming the trial.

Sponsor

An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial

Standard Operating Procedures

Detailed, written instructions to achieve uniformity of the performance of a specific function

Subject/Participant

An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Suspected/Unexpected Serious Adverse Reaction

An adverse reaction that is both serious and unexpected, occurring during a clinical trial.

Termination

It refers to the permanent cessation of a clinical trial. The trial is stopped permanently, and no further recruitment or data collection occurs.

Vulnerable Subjects

Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples include children, prisoners, and economically disadvantaged individuals.

1. Introduction

Good Clinical Practice (GCP) is a set of internationally recognized ethical and scientific quality requirements that must be observed for designing, conducting, recording and reporting on clinical trials that involve the participation of human subjects. As defined by the ICH GCP E6, GCP inspection is the act by a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the trial site, at the sponsors and/or CRO's facilities, or at other establishments deemed appropriate by the regulatory authority.

GCP inspection is necessary to ensure the protection of the rights, safety and wellbeing of study subjects and to assure the integrity of scientific testing and study conduct. It helps to determine whether the trials are conducted in accordance with GCP guidelines, ethical standards and other applicable regulatory requirements.

According to article 4(11) of Food and Medicine Administration (Proclamation No. 1112/2019); EFDA, is responsible to authorize the conduct of clinical trials, monitor and inspect the process in accordance with good clinical practice, evaluate the results and authorize the use of the result in such a way that benefits the public; also authority may suspended or terminated clinical trial when necessary. As the Clinical Trial Directive 964/2023 states, The authority shall monitor that the sponsor, investigator, contract research organization, or research centers comply with the good clinical practice principle, protocol, applicable regulations and directives. The regulations require that all clinical trials covered by the provisions of the regulations, including bioavailability and bioequivalence studies, be designed, conducted and reported in accordance with the principles of GCP.

2. Purpose

The purpose of this document is to provide guidance to all the stakeholders involved in the trial, particularly for investigators,sponsor,CRO on the overview of GCP inspections by EFDA and institutional review board or independent ethics committee. Clinical trials are primarily inspected to ensure compliance with GCP.

3. Scope

This Good Clinical Practice (GCP) inspection guideline provides a framework for uniform procedures applicable to all locations subject to GCP inspections. The scope encompasses the Pre-commencement activities, During clinical trial conduct activities, Post-Completion activities and triggered inspections related to clinical trials authorized by EFDA, including bioequivalence and bioavailability studies.

4. Objectives

- To Provide guidance to inspectors for conducting effective and efficient inspection, thereby enhancing the quality and effectiveness of the regulatory of the regulatory system`s inspection activities
- To indicate clinical trial team about the procedures, planning, reporting, action taking and communication undertaken in GCP inspection.
- To Ensure GCP inspection is done in accordance with local regulations, ethical standards, and GCP guideline and directives.

5. Types of GCP Inspections

Clinical trial sites may be inspected before the regulatory approval, while the trial is on-going, or completed on a routine basis or sometimes when triggered by a complaint or there is a suspicion of serious non-compliance with integrity issues and/or scientific/ethical misconduct. Inspections are generally announced. However unannounced inspections could be undertaken.

5.1 Routine GCP inspections

Routine inspections are carried out as a regular surveillance of GCP compliance. These inspections plans are announced to the investigators/sponsor prior to the actual conduct of the inspection. Clinical trials and sites for inspection are selected based on a set of criteria to ensure that a range of issues are addressed. Also the duration of the inspection and the number of inspectors will vary depending on the complexity of the clinical trial and activities conducted at the site, it is typically, scheduled for 3-5 days. Routine GCP inspection are conducted before initiating of the clinical trial, during the conduct and at end of trial

5.1.1 Clinical trial pre- initiations inspection

A clinical trial pre-initiation inspection is conducted to ensure that all necessary preparations and standards are in place before a clinical trial begins. The pre-initiation GCP inspection serves as a preliminary inspection before the trial enrollment and screening process begins.

This inspection is crucial for verifying that the site, staff, and procedures meet the regulatory and ethical requirements for conducting the trial. The main purposes include:

Regulatory Compliance; Ensuring that the clinical trial site complies with relevant laws, regulations, and guidelines (such as GCP) before the trial begins.

Site Readiness: Verifying that the clinical site is prepared to conduct the trial. This includes checking that the site has the necessary facilities, equipment, and trained personnel.

Document Verification: Reviewing essential documents such as the study protocol, informed consent forms, investigator's brochures, and ethics committee approvals to ensure that they are accurate, complete, and compliant with regulatory requirements.

Staff Training and Qualifications: Ensuring that the trial's investigators and other key personnel are adequately trained and qualified to conduct the study.

Ethical Considerations: Confirming that the study's ethical aspects, including participant consent processes and data protection measures, are in place and adequate.

Risk Management: Identifying and mitigating potential risks that could affect the integrity of the trial or the safety of the participants.

Drug Accountability: Check that the investigational product (IP) is available on-site, properly stored, and accounted.

Emergency Preparedness: Review emergency procedures, including staff training in advanced life support and cardiopulmonary resuscitation.

Communication Channels: Confirm effective communication channels between the site and the sponsor. Ensure that the site is prepared for internal and external audits.

By conducting this inspection, regulatory authorities can ensure that the trial will be conducted in a manner that protects participants and produces reliable, high-quality data.

A successful pre-initiation site visit sets the stage for a smooth trial initiation. The following points should have to be considered from both authority and clinical trial team during pre-initation inspection.

A. The sponsor/investigor should not commence the study before the authority conduct pre-initiation inspection or EFDA's permit to commence the study based on risk based approaches.
B. The investigator/sponsor should implement all recommendations depending on the finding.
C. The post pre-initiaon decision may be suspension of the study or recommendations that should be implemented while initiating the trial.
D. For studies which are authorized but suspended, the site should submit the CAPA and provide the objective evidences that shows the findings are resolved.
E. If the objective evidences and CAPA are found not to be verifiable, the team of GCP inspectors can be deployed and conduct on site inspection.
F. The authority will provide written report after conducting the pre-initiaion GCP inspection within 15 calendar days.

5.1.2 Inspection during conduct of clinical trial

EFDA conducts clinical trial inspections to determine whether the investigators are conducting clinical trial in compliance with applicable statutory and regulatory requirements. The EFDA investigator typically performs this oversight function through on-site inspections designed to document how the study was actually conducted at the clinical trial site. The inspection will proceed according to the details set out in the inspection plan. This will be negotiated prior to the inspection and can be amended during the inspection to ensure the inspection objectives is achieved. The inspection will take place over several days, typically 3 consecutive days, depending on the complexity of the trial.

EFDA may collect relevant information to support the inspection and verify compliance with the study protocol, the GCP guideline(s) and the National regulations using different ways, for example:

- ✓ Interviewing appropriate staff members regarding trial related activities

- ✓ Reviewing applicable site policies and procedures regarding research governance activities
- ✓ Examination or demonstration of computers, electronic systems, and databases, where required, to obtain clinical trial data
- ✓ Reviewing adverse event case documentation
- ✓ Reviewing internal and external communication relevant to site
- ✓ Reviewing staff training records in relation trial related activities. If the clinical trial team refuse access to any relevant record or documentation that EFDA inspectors have a legal right to access, this will be documented in the inspection report to determine further action and consequences.

5.1.3 Clinical trial close out inspection

Study close-out is an essential element in concluding clinical trials. During a closeout inspection, things required to be covered include data integrity and query resolution, adherence to regulatory requirements, disposition of study material, etc. Close-out may not occur until the last participant's last visit has occurred. For investigational drug or device studies, clinical investigators must retain study records for a period of at least ten years following the closeout of the clinical trial.

The sponsor and/or PI should have to make sure the following points are addressed and all the appropriate measures are taken.

Study personnel: an updated staff information form needs to be sent to the authority indicating any staff are no longer participating in the study trial.

Safety and regulatory: Ensure all adverse event reporting are submitted, all the regulatory files are completed, and all protocol deviations are reported. If any action is pending, ensure to finish it before site-close out.

Data cleaning: The success of a clinical trial depends on the quality of the data. Hence, ensure the data integrity is maintained throughout the clinical trial process. Generate data quality reports towards the end of the study trial and at close-out.

Medication, supplies, equipment: The clinical trial team should have to understand who has disposition authority and include it in the site closeout checklist. The team should also start

working towards maintaining a low supply inventory once the clinical trial team are approaching the study closeout.

Storage and data retention: for both hard copy and/or electronic recorded data,the clinical trial team should ensure all CRFs are completed, collected, and the legible copies are available in study files.

5.2 Triggered GCP inspections

This is an inspection undertaken whenever there is a concern of actual or potential issues or deviations from GCP on the conduct of the study. This may be whole or at a particular site especially when there is a significant non compliance to GCP occurred. This type of inspection may be done announced or unannounced and apply to ongoing or completed clinical trials.

5.3 Risk-based GCP inspection

A Risk-Based GCP Inspection approach is a structured approach used by regulatory authorities or sponsors to prioritize and conduct inspections of clinical trials based on identified risks. This strategy aims to ensure the most efficient use of resources while safeguarding trial integrity, subject safety, and data reliability.The risk-based approach allows a more targeted, flexible, and less costly process. It is followed to select sites for close follow-up and giving priority during GCP planning for inspection.

The risk based GCP inspection approach will depends on the following conditions:

- The number of approved clinical trials or backlog of the approved clinical trials
- The availability of staff to reach out all approved clinical trials
- Level of knowledge about the product to be or being investigated.
- Type of site i.e., located at large institution vs. small clinic in respect to capacity
- Drugs are used in combinations for which interactions are suspected.
- Additional risks identified by inspector in relation with trial conduct, design and methods which include risks to participants' rights and the credibility of data.

Potential high-risk level of the approved clinical trials to be given priority:

- Early phase (Phase I and II) clinical trials will always inspect in routine inspection schedules
- Clinical trials sites having previously identified noncompliance

- Clinical trial sites include large sample size /more than 1000 population
- Clinical trials with investigational products of biological products
- If information received by the EFDA about suspected violations of legislation relating to the conduct of clinical trials for triggered GCP inspection.

Potential low risk clinical trials which needs limited frequency of GCP inspections

- Multi country trials on which there are non-serious AEs or no AE reports was received from all approved clinical trials.
- Identified clinical trial sites which has adequate staff, equipment to give standard of care for the relevant clinical condition and experienced staff

The inspectors identify focus areas before doing actual inspection as part of risk based GCP inspection.

5.4 Remote GCP inspection

During crisis situations, on-site inspections may not be possible due to multiple factors such as difficulties and restrictions related to travelling between and within the borders of countries (including travel warnings / restrictions, border controls, transportation difficulties), restrictions to accessing facilities justified by health hazards and local authorities' recommendations / orders, as well as additional health and/or safety risks for inspectors and inspectees.

In the context of this guidance, a remote / distant GCP inspection is defined as "the process of conducting inspections at a distance / virtually, supported by technology for communicating, sharing, reviewing, and developing documents and accessing systems, without the inspectors being physically present at the sites where the activities subject to an inspection have taken place / where the inspection would routinely be hosted". During the remote inspection initiation phase, the inspectee should provide detailed information as requested by the inspectors to allow a feasibility assessment by the inspection team, taking into account the computerised systems used for the clinical trial.

Remote inspections could be longer in duration than on-site inspections given the particularities of this type of inspection and the fact that inspectors may need to control several systems simultaneously when conducting the inspection. Duration of daily sessions should be agreed

between inspectors and inspectee and adherence to procedures in place by both sides. A host should be assigned by the inspectee to coordinate and manage further requests and queries during the inspection.

Essential components of the inspection include interviews, presentations (by the inspectee) relating to the topics requested by inspectors in the agenda, documentation review and facility tours (if applicable). It is recommended to use an electronic document request form that can be shared among the inspectee and the inspection team. The inspection team may request the inspectee to keep track of all requests and provide a regular update of the electronic document created. Inspection-derived records should be maintained, and the reporting of remote inspections will be followed as per the standard procedure for reporting of GCP inspections

6. GCP inspection process

The regulatory body may conduct GCP inspections typically under the following circumstances:

- ✓ To verify the accuracy and reliability of data that has been submitted
- ✓ To investigate a complaint about the conduct of the study at a particular site;
- ✓ Upon termination of the clinical site;
- ✓ During ongoing clinical trials to provide real-time assessment of the investigator's conduct of the clinical trial and protection of human subjects;
- ✓ Following serious adverse event(s) notification.
- ✓ For Monitoring on safe handling of investigational products and other related items
- ✓ On request by the investigator

The composition of the inspection team will be determined by considering the investigational product, the clinical trial type and phase, and any other relevant factors specific to each case. The inspectors should possess a letter of appointment from the Authority, a valid GCP certification, and continual qualification. During the inspection, the inspectors will act as the regulatory authority's legal representative for inspection.

6.1 Scheduling and notification

A clinical trial's inspectees will typically be contacted one week before the planned inspection. The notification shall specify the intended venues, including any investigator site(s), and, if appropriate, the study to be examined. The regulatory authority may offer a shorter notice time for inspections that are prompted or for cause.

6.2 Conduct of GCP inspection

An inspection typically consists of an opening meeting, document review, interview sessions, site facility visits, and a closing meeting.

6.2.1. Opening Meeting

In initiating the GCP inspection, the inspectors will hold an initial meeting with the study personnel to explain the GCP inspection plan. During the opening meeting, the entire study team member should avail themselves.

At this meeting, the inspectees must provide a basic summary of the clinical trial as well as details about subject recruiting, the informed consent procedure, experimental product management, safety reporting, handling biological samples, and other related topics. The inspectors may visit the facility where the clinical trials are being conducted as well as speak with study personnel to learn more about how the trials are carried out.

6.2.2. During Inspection

In this stage, the inspector should confirm that the facilities, necessary paperwork and resources needed for the inspection are available. Every essential document pertaining to a clinical trial needs to be accessible for review. A clinical trial's trial master file (TMF) needs to include all the records that, both separately and together, allow for an assessment of the trial's management and the caliber of the data generated. The TMF needs to be created at the beginning of the trial and updated continuously as it moves through its various phases. A minimum list of papers created before to, during, and following the trial is included in all necessary documents. These documents need to be kept in the TMF with the sponsor and investigator. If some papers are determined to be irrelevant to the TMF, a prompt explanation for their omission must be provided.

The activities and documents examined during common type of GCP inspection undertaken by the EFDA are outlined below:

Protocol specific inspections may include:

- TMF
- Legal and administrative aspects
- Communication with the ethics Committee
- Communication with the Regulatory Authority
- Other Communications
- Organizational aspects
- Implementation of the trial at the investigator site
- Facilities and equipment
- Management of biological samples
- Organization of the documentation
- Monitoring and auditing
- Use of computerized systems
- Informed consent of trial participants
- Details of impartial witness if any
- Review of the trial participant data
- Adverse event reporting
- Management of the investigational medicinal product(s)
- Protocol violations/deviations
- Other, as required

System Inspection may include:

- Organization and personnel
- Facilities and equipment
- Sponsor/CRO Operating Procedures
- Implementation and termination of the clinical trial
- Monitoring
- Investigational Medicinal Product
- Sample management

Safety and adverse events reporting

Data handling and clinical trial report

Documentation archiving

Sponsor audit and quality assurance system

Management process for protocol deviations

Delegation of duties

Specific clinical trial inspection

Implementation of decisions by the regulatory authority

Investigational Medicinal Product

Case Report Form data verification

Data handling and clinical trial report (CTR)

Clinical trial documentation and archiving

Audit trails

6.2.3. Closing meeting

During the closing meeting, the entire study team member should avail themselves. The closing meeting will be undertaken during which the inspectors will discuss the preliminary findings with the inspectees to make sure that the findings are understood. In addition, the inspectees should be informed during debriefing that Corrective and Preventive Action (CAPA) should be submitted to the authority for the findings, depending on the inspection report.

The following information may be requested from the inspectees to be submitted to EFDA either prior or after the inspection date based on the necessity

- ✓ Participant status at trial start or during the study, broken down by trial site (number randomized, dropout rate, and number of significant adverse events reported per site).
- ✓ Copies of the standard operating procedures (SOPs) for the company, including any revisions (drug supply protocol, informed consent procedure, monitoring procedure, significant adverse event reporting procedure, etc.).
- ✓ Trial specific documents like TMF, Case Recording Format (CRF), Informed Consent Form, a copy of the current protocol, protocol amendment, source data verification guidelines, product handling instructions, laboratory manual, randomization code breaking procedure, monitoring plans, and reports.

- ✓ The trial team updated resume.
- ✓ Make plans for immediate access to any electronic systems that house crucial documents or trial dates.
- ✓ Any further documentation that the inspectors determine to be required.

6.4 Post GCP inspection activities

Every GCP inspection will result in one inspection report. The inspection report will be provided to the inspected parties; clinical trial's primary investigator, the sponsor of the clinical trial, or a representative of the sponsor, upon the completion of a GCP inspection. The examined location, the inspection's history, and its scope all influence the report's content.

The report contains information about the date, time, and location of the inspection, an account of the observations made, a list of inconsistencies found in the guidelines, trial protocol, and internal procedures, as well as a number of recommendations.

Within 15 calendar days following the last inspection day, the inspectees will get a written report detailing the non-compliance found during the inspection. Written reports are often distributed in hard copy and with an electronic copy as applicable. The inspection report will be brought up for consideration or should be reviewed at the next inspection schedule/GCP inspection of the specific trial. In the event of clarification, the Authority inspection team may invite the inspectees for a discussion.

7. Deficiencies

Deficits in the context of GCP inspections are places where protocols or practices fall short of the necessary requirements. These shortcomings can take many different forms, but they frequently involve problems with documentation discrepancies, protocol compliance, and safeguards for human subjects.

For example, the following are some typical flaws found during GCP inspections:

Incomplete documentation: This can include missing or insufficient documents, including blank CRFs or incomplete screening lists.

Absence of simultaneous, independent CRF copies: Throughout clinical studies, timely and accurate record-keeping is crucial.

Anomalies in pharmacokinetics: These might be caused by duplicate profiles or inconsistent data.

Clarity of source documentation: Ensuring accurate and clear source documentation for clinical and bio analytical research.

These flaws might affect patient safety and the integrity of clinical trials, so it's imperative to fix them right away. Contract research organizations (CROs), investigator sites, sponsors, and a few additional types of sites, such as clinical labs and facilities devoted to bioequivalence/bioavailability studies, are all inspected under GCP. The results of these inspections offer important new information about the caliber and compliance of clinical research sites.

There are key points related to the findings of GCP inspections at clinical research sites. These include;

Grading and Categories of Findings: The inspection findings will be categorized based on their severity and impact. The common categories included issues related to protocol adherence, informed consent, data integrity, adverse event reporting, and recordkeeping. The findings will be graded as critical, major, or minor based on their significance.

Types of Sites Inspected: the GCP inspections cover a wide range of sites, including investigator sites where clinical trials are being conducted. The Sponsors, CROs, and other relevant establishments will also be inspected to assess their compliance with GCP requirements.

Responsibility of addressing Findings: The responsible body for addressing the findings varies. It could be attributed to the investigator, the sponsor, or other involved parties. Corrective actions may be required to rectify deficiencies identified during the inspections.

Areas of Inspection: Inspectors will evaluate various aspects of clinical research sites, such as study documentation (ensuring completeness, accuracy, and consistency), informed consent process (verifying proper informed consent procedures), adverse event reporting (assessing, timely reporting, and documentation), data management (checking data accuracy, source

documentation, and data entry), monitoring practices (evaluating site monitoring and oversight), and quality control (ensuring compliance with GCP principles). Findings might be specific to each area and will contribute to the overall assessment of site compliance.

8. Classification of finding

The classification of observation is intended to classify severity of non-compliance observed during clinical trial inspection. Overall, the evaluation should commensurate with the nature and extent of the deviations (i.e. severity). Situations involving fraud, misrepresentation or falsification of source data or records linked with clinical trials will be a critical observation.

Depending on the particulars of each inspection, deficiencies are categorized as follows and assessed in relation to the risk that the deviation poses to the trial participants' safety and integrity as well as the quality of the data.

Critical Finding
Major Finding and
Minor Finding

A summary for the criteria for judging deficiencies as critical, major or other are detailed below.

8.1 Critical Finding

It means that the evidences show that the participant’s/patient’s right, safety and/or confidentiality either have been or have significant potential to be compromised or there is a serious doubts about the accuracy and/or credibility of data. This happens when there are circumstances, procedures, or practices that negatively impact subjects' rights, safety, or well-being, as well as the accuracy and integrity of data. Such serious flaws are completely unacceptable and could lead to data rejection and/or legal action. Fraud, a pattern of deviations categorized as serious defects, a lack of source documents, and poor-quality data are some examples of the observations.

8.2 Major Finding

It means a major non-compliance with applicable regulations and guidelines that may not have developed into a critical issue, but which may have the potential to do so unless addressed. This is when policies, procedures, or practices have a negative impact on subjects' rights, safety, or

well-being, as well as the accuracy and integrity of data. These are flagrant infractions of GCP principles and represent severe inadequacies. The observations could lead to data rejection and/or regulatory actions. They might also comprise a pattern of deviations and/or a cluster of small faults.

8.3 Minor Finding

It is a minor non-compliance with applicable regulations and guidelines that need to be addressed in order to have sustained confidence in the work of the organization. This is any situation, procedure, or method that is not anticipated to have a negative impact on subjects' rights, safety, or well-being, or on the accuracy and consistency of data. A modest observation suggests that conditions, procedures, and practices need to be improved.

Comments: The findings from the inspection, any warning signs of potential flaws, and advice on how to raise standards or lessen the likelihood that a deviation will happen again.

Clarifications: Questions from the trial site or sponsor company on matters that came up during the inspection but don't quite fit into the categories listed above. Depending on the type of clarification, these could be rated as shortcomings.

9. Corrective action and preventive action plan

Within 15 calendar days of receiving the inspection report, the inspectees are required to respond to the shortcomings detailed in it. This response must include a proposal for corrective and preventative activities, along with a schedule for when those efforts must be completed.

10. Regulatory actions

If the inspectees fail to address the deficiencies, particularly the critical and major deficiencies within the specified timelines, the EFDA may proceed to take regulatory measures in accordance with Directive Article 27, Sub Article 3 and 4 of Clinical Trial Directive 964/2013, based on the deficiencies of the GCP inspection the regulatory directive.

The right of an inspector to enter any site(s) involved in a clinical trial to conduct inspections, examine and open any container or package that he believes to contain any article, take samples, examine any book(s), documents, or record, including electronic data found in any place, and make copies or take extracts, as well as seize and detain an article for as long as may be necessary, is granted by Directive Article 27, Sub Article 3 and 4 of Clinical Trial Directive 964/2013. The refusal to provide information or documents, or the deliberate obstruction of one or more inspectors during the course of the inspection, may result in regulatory measures.

If a clinical trial is being conducted in a way that is harming research participants, such as by fraudulently documenting the results, the EFDA may take regulatory actions without waiting for CAPA. In summary, GCP inspections play a critical role in maintaining the integrity of clinical trials and ensuring patient safety. The findings help to identify areas for improvement and drive corrective actions to enhance the quality of clinical research sites.

11. GCP inspection closure

The inspection team evaluates the CAPA responses to decide if they are appropriate or not. A GCP inspection closing letter will be sent by the EFDA once the CAPA is found to be sufficient.

12. Compliant handling

The authority shall handle the compliant of the inspectees as per the compliant handling procedure of the Authority.

Reference

1. European Medicines Agency (EMA). "Guideline on Good Clinical Practice." Available at: EMA GCP Guideline
2. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). "ICH E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1)." Available at: ICH GCP E6(R2)
3. U.S. Food and Drug Administration (FDA). "Guidance for Industry: Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring." Available at: FDA Guidance Document
4. NIH IRB Professional Administrators Committee Version 5.2 pg. Regulatory Process Workgroup 10/27/2011.
5. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32014R0536
6. https://www.ema.europa.eu/en/human-regulatory-overview/research-development/compliance-research-development/good-clinical-practice/good-clinical-practice-gcp-inspection-procedures

List of Workshop Participants

Name of Participants	Position	Institution
Dr. Solomon Mequanente (PhD)	Associate Professor of Pharmacology	AAU
Dr. Shemsu Umer (PhD)	SOP Ethics Committee chairperson	AAU
Mr. Debalke Fanta	Biological Medicine Dossier Evaluator	EFDA
Mr. Abebe Alemneh	Medicine Registration, Clinical Data Assessor	EFDA
Mrs. Demekech Damte	AHRI, Alert, Institution Ethics Committee Secretary	AHRI
Mr. Chalelgn Kassaw	Clinical Trial Authorization and GCP Inspection Expert	EFDA
Mr. Solomon Assefa	Clinical Trial Authorization and GCP Inspection Expert	EFDA
Dr. Mustofa Hassen	Clinical Trial Authorization and GCP Inspection Expert	EFDA
Mr. Fikreselam Habte	Clinical Trial Authorization and GCP Inspection Expert	EFDA
Mr. Yohannes Tadiwos	Clinical Trial Authorization and GCP Inspection Expert	EFDA

ANNEX

Annex 1.Attendance form

	GCP INSPECTION REGISTRATION FORM		**GCP inspection Dates**		**From .....to.....**	
	Title of The Clinical Trial					
Name of The Trial Site				**Addresses**		
Full Name of The PI:			**Mobile No.**		**Email:**	
Ser. No.	**Full Name Of The Study Team**	**Qualification (Edu./Background)**	**Responsibilities**	**Mobile Number**	**Email**	**Remark**
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						
9.						
10.						
11.						
12.						
13.						
14.						
15.						

Annex 2: Status Recording Form(Inspected/Suspended/Stopped CTs)

EFDA ETHIOPIAN FOOD & DRUG AUTHORITY	**Product Safety Directorate**	**FORM-PSD-011.01** **SOP/PSD- CT008**
Title	List Of Inspected/Suspended/Stopped Clinical Trial	
Year : _____		

S/N	**TITLE OF STUDY**	**SITE OF STUDY**	**SPONSOR**	**CONTACT PERSON**	**DATE INSPECTED**	**STATUS (CONTINUED/ SUSPENDED/STOPPED)**

Annex 3 : Form for risk based GCP inspection planning

EFDA ETHIOPIAN FOOD & DRUG AUTHORITY		Pharmacovigilance and Clinical Trial Lead Executive Office					FORM-PVCT-011.01 SOP/PCT- CT004-23	
Title		Form for Risk based GCP inspection planning						
Sr. no	**Tittle of Trial(Short Name if available)**	**Clinical Trial Site/Place**	**Name of PI**	**Contact Address**	**Date of Authorization**	**Planned Inspection Time**	**Next Plan date of inspection**	**Remark**
1.								
2.								
3.								
4.								
5.								
6.								