ETHIOPIAN FOOD AND DRUG AUTHORITY

GUIDELINE FOR REMOTE GMP INSPECTION

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001	New guideline	02/12/2024
002	Inclusion of Detail Feasibility approaches. Title of the guideline modified.	30/04/2025

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Acronyms

API	Active Pharmaceutical Ingredient
CAPA	Corrective and Preventive Action
EFDA	Ethiopian Food and Drug Authority
FPP	Finished Pharmaceutical products
GMP	Good Manufacturing Practice
GPS	Global Positioning System
GxP	Good x Practice
NRA	National Regulatory Authority
PQR	Product Quality Review
QA	Quality Assurance
QCL	Quality Control Laboratories
QC	Quality Control
SMP	Site Master file

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Abbreviations

API	Active Pharmaceutical Ingredients
CAPA	Corrective and Preventive Action
QCL	Quality Control Laboratory
EFDA	Ethiopian Food and Drug Authority
FPP	Finished Pharmaceutical Products
GMP	Good manufacturing Practice
MVP	Master Validation Plan
NRA	National Regulatory Authority
PQR	Product quality Review

Foreword

The Ethiopian Food and Drug Authority (EFDA) is a national regulatory body established by the Proclamation No 1263/2021, and its mandatesare defined in the Regulation No 531/2023. One of its key responsibilities is to ensure the safety, efficacy and quality of medicines by regulating the manufacturing of pharmaceutical products forcompliance with Good Manufacturing Practices (GMP) requirements.

Globally, various methods are employed to conduct GMP inspection. Remote inspection is one of the inspection processes to enable GMP inspections to continue during the pandemic, resource constraints and others where it has been difficult to conduct these on-site.

Beyond emergency situations, remote inspections have the potential to enhance regulatory oversight by providing a more flexible and efficient approach to GMP compliance assessment. By leveraging advancements in digital communication, EFDA aims to integrate remote inspections as a key component of its regulatory framework, ensuring continuous quality assurance and maintainingcompliance with pharmaceutical manufacturing standards while optimizing resources.

In this context, the EFDA has developed this guideline to outline the provisions for remote inspections of pharmaceutical products manufacturingfacilities. The guideline provides guidance to EFDA, manufacturers and other stakeholders how to conduct remote GMP inspection process and requirements to comply facilitating a transparent and standardized approach in the GMP inspection process.

I hereby call upon healthcare professionals, academia, development partners, associations and other concerned bodies to actively engage implementing this guideline and provide any feedback to the Authority. Your commitment, cooperation, and sustained support will be instrumental in overcoming challenges in ensuring the safety, quality and efficacy medicines circulating in the Ethiopia market.

Definitions

The definitions given below apply to the terms used in this guideline. They may have differentmeanings in other contexts:

1. **"EmergencySituationorstate"**meansunexpectedfactorsincludingpandemics,emergency disaster, wars, among others, that make it impossible for the Authority to conduct on- site inspections either in a particular country or all countries. Late planning for inspection or limited resources shall not be considered an emergency situation.
2. **"Good Manufacturing Practice"** means the part of quality assurance which ensures medical productsareconsistentlyproducedandcontrolledtothequalitystandardsappropriateforthe intended use and as required by the marketing authorization or product specification.
3. **"Manufacturer"** means a company that carries out operations described under article 2 sub-article (54) of the Food and Medicines administration proclamation number 1112/2019
4. **"Marketing authorization"** An official document issued for the purpose of marketing or free distribution of a product after evaluation of safety, efficacy, and quality of the product.
5. **"Marketing authorization holder"** A manufacturer and/or a license holder of the product to whom marketing authorization certificate is issued (by the Authority) to sale or distribute the registered medicine in Ethiopian territory.
6. **"Quality System"**the sum of all that is necessary to implement an organization's quality policy and meet quality objectives. It includes organizational structure, responsibilities, procedures, systems, processes and resources. Typically, these features will be addressed in different kinds of documents as the quality manual and documented procedures.
7. **"Site master file"** means a document containing specific information about the activities undertaken in the pharmaceutical manufacturing site and is usually prepared by the manufacturer.
8. **"Remote inspection"** means inspections that are performed off-site through the use of enhanced communication and information technologyto check the compliance with GMP requirements.

1. Introduction

Globally, National Regulatory Authorities (NRA) implement pre-and post-approval regulatory activities including dossiers evaluation, and inspection of manufacturing sites of Finished Pharmaceutical Products (FPP) and Active Pharmaceutical Products (APIs) manufacturers. These inspectionsareperformedfordossierdataverificationandtoprovideevidencethat the FPP, APIs, QCLs are in compliance with the relevant good practice (GxP) guidelines and regulatory requirements.

During the COVID-19 pandemic, EFDA like other regulatory authorities limited unnecessary contact by only conducting prioritized domestic and foreign facility inspections. These inspections were deemed mission-critical and were not impacted by travel restrictions associated with the public health emergency.

To ensure the GMP compliance, on-site GMP inspections are regarded as effective method for determining a manufacturing site compliance with applicable national and international standards. This provides inspectors with firsthand access to observe operations, evaluate documentation, and assess facility conditions in real-time. However, when on-site GMP inspection are not feasible due to travel restrictions, public health emergencies, or logistical constraints, NRAs and international organizations recommended alternative inspection methods such as remote inspection and desk assessment can be employed

Recognizing the need for a structured approach, the EFDA has developed a guideline to establish clear guidance for conductinga remote inspection.

2. Objectives of the Guideline

This guideline establishes a standardized and structured approach for EFDA to assess GMP compliances through remote inspections ensuring continual regulatory oversight while minimizing delays in product registration and avoiding unnecessary duplication of inspections.

The specific objectives of this document are to:

i. Define a standardized framework for conducting remote inspections

ii. Establish clear criteria and procedures for granting waivers for on-site GMP inspections when virtual inspections provide sufficient assurance of compliance.

iii. Ensure a consistent and transparent methodology for planning, preparing, and executing virtual inspections, including the selection of eligible manufacturing sites and the use of appropriate digital tools to enhance regulatory evaluations.

3. Scope of the Guideline

These guidelines define the regulatory framework for conducting remote inspections as a viable alternative to on-site GMP inspections of local and overseas manufacturers. The remote inspection does not apply to new GMP inspection applications.

Areas of application:

- Travel restrictions, e.g., during pandemic situations, and safety concerns
- Re-inspections if a manufacturer demonstrates good levels of compliance in previous inspections and when the activities of the inspected site are limited
- Verification of certain aspects of Corrective and/or Preventative Actions
- Rapid Assessment of GMP aspects in specific circumstances where there is an immediate need.
- To gather information for an onsite inspection

4. Types of Remote Inspections Considered

The authority may utilize the following type of remote inspections only depending on the level of interaction to be made with the manufacturer during the inspection. However, desktop assessment shall be conducted before conducting the fully interactive, partially interactive and hybrid remote inspections.

4.1. Fully Interactive Remote Inspection: This relies on technology to facilitate live interactions during the entire inspection period. It may use video meetings, document sharing, video streaming (from the plant), and/or other live streaming interactive technology to determine compliance with GMP requirements. The benchmark for activities for a fully interactive remote inspection includes:

- Fully interactive video meetings to resemble live interaction during a face-to-face inspection, including document sharing and video discussions with the inspected manufacturer.

- Opening, daily wrap-up, and closing meetings held with the firm personnel via video meetings to discuss observations found during the interactive assessment, if necessary.
- QA documentation review to start during preparation phase.
- Location verification: SMF, layout versus online satellite maps, usage of GPS coordinates (during inspection if necessary).
- Video interviews of subject matter experts located at the manufacturer.
- Documents may be shared via electronic means such as e-mail or another platform agreed upon. Documents and computer screens may also be screen shared during video meetings to allow first-hand observation.
- Live video streaming from the site of all manufacturing or other areas concerned by the scope of the inspection.
- If live video is not possible, video files of all manufacturing or other areas concerned by the scope of the inspection shared and discussed with inspectors.
- QA documentation, manufacturing records, QC documentation review as comprehensive as during on-site inspections, ideally via document sharing tool and screen sharing; walk through (explanations) by SME, data integrity ideally via screen sharing.
- Assessment of corrective and preventative action plan.
- Issuance of a report.

4.2. Partially Interactive Remote Assessment: inspection of a manufacturing site performed remotely from the site location with some interactive component, such as video or phone meetings and document sharing, to determine compliance with GMP requirements. The benchmark for activities for a partially interactive remote inspection includes:

- Meetings are scheduled with the manufacturer whenever needed, e.g., to facilitate the inspection and request documents such as an opening meeting, a meeting halfway through the assessment and a closing meeting.
- It does not require a fully interactive interaction during the entire inspection period.
- Documents may be shared via e-mail, screen share, or another platform agreed upon.
- wrap-up, and closing meetings are held with manufacturer personnel to discuss observations found during the assessment, if necessary. These are scheduled as necessary during the inspection period.
- Video or phone interviews with subject matter experts located at the plant, if necessary.
- Meetings may be held to allow interactive discussion on documents received & reviewed by inspectors to allow ability to ask follow-up questions and potentially request additional documentation.
- QA documentation, manufacturing records, QC documentation review as deemed necessary.

- Issue a report.

4.3. Hybrid Inspection: An inspection of a manufacturing site performed by EFDA using a combination of on-site inspection and remote assessment.

- Combination could be team of inspector conducts both on-site and remote inspection of the manufacturing site.
- Combination of inspectors on-site and inspectors (may be the same or different authorities) connecting remotely at the same time to the ongoing activities at the facility using a virtual technology.

5. Feasibility Approach or Conditions to Remote Assessment

5.1. Risk Assessment

a) A remote assessment may not be the first choice. Before deciding whether to carry out the remote assessment, it may be appropriate to carry out a risk assessment to determine whether the desired scope may be achieved in the given circumstances. This would also apply to hybrid inspections.

b) Where high and/or multiple medium risk factors are identified, an assessment on whether these risks are deemed acceptable, or whether they require mitigation, could be considered.

c) Where risks are identified that are not considered acceptable (even after any potential mitigation factors have been applied), an alternative inspection approach may be considered.

Table 1: Areas Considered for Risk Assessment, Criteria for Risks Classification and Mitigations

SN	Description	Low	Medium	High	Potential / Mitigation
1	Previous Inspection History (including information from any other regulators)	No significant indicators of non-compliance	Moderate indicators of non-compliance Satisfactory PQS – further assessed case-by-case	Significant indicators of non-compliance The scope was not previously inspected during routine inspection, pre-approval / focused inspection	Familiarity with the site,
2	Activities carried out at site	Non-Sterile Operations Dedicated facility or specific product	Terminally sterilized Low sensitizing /potent in shared facility	Aseptic operations Highly sensitizing / potent in shared facility	Familiarity with the site, e.g., same inspector. Contact with previous inspector.
3	Length of time since last	1-3	3-4	>4	Team

	on-site inspection (years)				inspection for longer duration inspection Onsite /hybrid inspection
4	Information relating to the site from any regulatory authority / source. (e.g. recalls / complaints / intelligence / whistle blower)	No / Minor issues	Moderate issues	Significant issues	Onsite /hybrid inspection based on the seriousness of the risks
5	Changes since last inspection	Minor (e.g., Updated production lines small number of personnel, no adverse metrics)	Moderate (e.g., new production lines, changes in key personnel, some adverse metrics)	Significant (e.g., new building, frequent changes in key personnel, key changes to processes and release testing, numerous adverse metrics)	Onsite /hybrid inspection
6	Extent of scope	Single building / Small number of production lines	Several buildings / Moderate number of production lines	Multiple buildings / Considerable number of production lines	Consider team inspection for large facility On-site / hybrid inspection
7	Site communication style (if known) (Note: Consider including communication and culture together)	Open	Closed	Obstructive	Consider team inspection On-site / hybrid inspection
8	Internet connectivity of site	High Speed and in all areas	Moderate speed / in most areas	Poor connectivity in all areas.	Perform a dry run prior to the assessment
9	Internet connectivity of inspectors	High Speed	Moderate speed	Slow speed	Prior sharing of documents Communication medium consideration (E.g.: Choice of VC platform)
10	Time Difference (hours) (Risk for data integrity issues; inspector fatigue)	1-4	5-7	8-12	Agreed timeframe that is suitable for both inspector and manufacturer
11	Language barriers and difficulty in sourcing	None	Some	Significant	Establish an inventory of

	appropriate/independent translator				reliable translators through experiences

Note:

- Facilities with Low risks (Numbers 3-7) undergo fully or partial interactive remote inspection
- Facilities with moderate risks (Numbers 3-7) undergo hybrid type of remote inspection
- Facilities with high risks (Numbers 3-7) undergo onsite inspection
- If there are combination of risks, the highest risk will prevail

6. Preparation for remote inspection

6.1. Communication

Applicants will be formally notified in writing by the Authority regarding the plans to conduct remote inspection.

6.2. Planning a remote inspection/audit

The following steps will be taken when planning for a remote inspection:

6.2.1. Selecting and notifying the manufacturer

Oncea manufactureisselected forremote inspectionorauditthe followingstepswillbefollowed:

a) EFDA will gather and verify the necessary information required for planning and coordinating the remote inspection

b) Formal notification from EFDA will be sent to themanufactureand, the local applicant. This notification will specify the name and address of the manufacturing site, the scope of inspection, type of the remote inspection, the number of inspection days, and the list of EFDA inspectors.

c) Upon agreement by the manufacturing site to participate in aremote inspection, the Authority will coordinate inspection with thefacilitytoestablish a pointofcontactforrecords transfer and remote interaction.

d) The Authority will assign an EFDAlead inspectorfor the remote inspectionthat will be communicated with the contact point of the manufacturer.

e) Ensure that the necessary logistic aspects of the remote inspection from both the EFDA and the manufacturing site are ready

f) Conduct the remote inspection as per the agreed schedule

6.2.2. Conduct preparatory meeting with the manufacturing site

Once the manufacturer confirms its willingness and ability to participate in the remote inspection / audit, the Authority will schedule a brief virtual meeting to discuss logistics, responsibilities, and expectations. The following discussion areas will be included, but are not limited to:

a) Objectives and scope of the remote inspection.

b) Introduction of the EFDA inspection team and the lead inspector.

c) Identification of the facility'spoint of contact and other key participants
d) Scheduling and setting the duration of the remote inspection.
e) EFDA's expectations during the remote inspection
f) Addressing the time zone differences and translation services for non-English speakers.
g) Conducting remote inspections during normal business hours of the facility.
h) Methods for sharing requested information, including secure documentssharing
i) Technologicalrequirements for conducting an interactiveevaluation duringremote inspection of thesite.
j) Testingboth the EFDA and the manufacturer's internet connectivity to ensure sufficient bandwidth for live video and audio streaming fortheactual remote interactive evaluation.

6.2.3. Logistics arrangement for Remote Inspection

The manufacturer shall ensure that its connectivity including video, image and audio quality, meets the minimum standards required for remote inspection. The EFDA shall also ensure its IT platforms and teleconferencing tools to facilitate remote inspections.

Technological readiness to consider depending on level of remote interaction.

a) Conferencing software, zooming, Teams and other live platforms (this administrative arrangement will be the responsibility of the Manufacture)
b) Secure shared data storage place
c) Data connections at GMP relevant facilities
d) Web cameras, such as mobile phone, head mounted devices, tablets
e) High efficiency scanner
f) Possibility of sharing the screen of computerized systems (data integrity verification)
g) Document camera
h) Audio equipment, such as speakers (where necessary)

6.2.4. Testing of IT systems and inspection site selection

Test of ITsystem andconnectivity isrequired at least one week before the scheduled inspection to check the functionality and suitability of the required technologies. The connectivity test aimed to check whether all GMP relevant areas are well connected with the internet and can therefore be remotely inspected. The feasibility check should include testing of:

a) Security/Access to the Online communication
b) Video Conference Capacity
c) Screen-SharingCapability
d) Connection Strength
e) Checking the functionality of the technologies to be used during the actual remote inspection

6.3. Conducting the Remote Inspection

Manufacturers are expected to maintain the same level of transparency as during an onsite inspection. All relevant personnel shall be available for scheduled interview interactions. The facility shall be operational to the extent possible for the Authority to evaluate key areas such as manufacturing, laboratory, and packaging operations, among others.

As part of a remote inspection, the Authority may:

a) Request and review electronic records, documents, and other necessary information
b) Conduct live-stream and/or pre-recorded video assessments of facilities operations, data and compliance measures.
c) Schedule and conduct interviews through the facility's designated point of contact
d) Assess the facility'scorrectiveandpreventive actions implementation.
e) Provide verbal updates to the facility on observations and outstanding issues, whenever feasible.

6.4. Remote Assessment of Documents and Records

During the remote inspection or audit, the facilities shall comply with the following documentation requirements:

a) Requested documents and records should be provided within a reasonable timeframe, similar to an on-site inspection.
b) Documents shall be submitted in electronic format in secured shared data storage place or made available via secure screen sharing during a live interaction for efficient assessment.
c) For electronic encrypted and password-protected files, facilities shall ensure that EFDA can securely access the required documents.
d) All documents submitted during a remote inspection should be in English.
e) Paper documents should be scanned and submitted as searchable Portable Document Format (PDF) files whenever possible.

7. Application submission process and required documents

The main responsibilities of an applicant for virtual/Remote inspection are listed below:

7.1. Submission of the application

The manufacturer shall submit an application to the Authority through electronic Registration Information System. There shall be not separate application process for remote inspections. The authority will consider applications that have already been submittedfor GMP inspections.

7.2. Required documents for remote GMP inspection

The applicant shall submit the following documents for remote GMP application:

a) Application letter addressed to EFDA
b) Filled and signed GMP Application form as specified by the authority
c) Proof of payment of prescribed fees
d) Site Master File
e) Current manufacturing license of the premises issued by the competent regulatory authority in the country of origin.
f) Current GMP Certificate issued by EFDA
g) List of all the products (medicinal or other) manufactured on-site. The lists should include proprietary names and international non-proprietary names (INN).
h) Quality manual, Procedures, Complaint log, Non-conformance log, Corrective and Preventive Action log, Deviation log, Master Validation Plan (MVP), and certificates in PDF.
i) Facility map that includes the buildings and grounds, infrastructure and equipment layout, storage, maintenance, receiving, shipping, and other areas as appropriate.
j) Copy of the recent GMP inspection report done by the competent regulatory authority in the country of origin and recent GMP inspection report from regional or international bodies if available with a certified translated copy where this is not in English
k) A copy of any warning letter or equivalent regulatory action issued by any authority to which the site provides or has applied to provide the product, if any
l) List of Changes since last inspection, if any
m) Corrective and preventive action (CAPA) and proof of CAPA implementation related to the inspection report(observations/deficiencies)

n) The most recent product quality review(s) (PQR)(s) of the concerned product(s)
o) A confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product(s) has been performed and all matters dealt with.
p) The completed batch manufacturing/packaging record(s) including the analytical part for the most recently released batch of the relevant product(s).
q) A list of any recalls or any Market complaints registers in the last three years.
r) Contract or agreement between the FPP or API manufacturer and the outsourced testing laboratory or sterilization institution (for Outsourced testing laboratory; and Outsourced sterilization).

7.3. Application Fees

Remitting all application fees at the time of application submission

7.4. Submission of additional information

The manufacture shall promptly submit additional information that may be requested by EFDA during the remote assessment. Failure to provide required documents within the specified time, depending on the additional information requested, may result in the application being rejected.

8. Remote Assessments Documentation

- When a report be issued, it should clearly document the inspected areas as well as the mode of the assessment or inspection i.e., on-site, remote or hybrid (including detailed information on type of remote assessment employed). If areas are not covered during the assessment or inspection, then they should also be clearly documented.
- Regulatory databases (where applicable) should describe the type of remote assessment employed including hybrid inspections (if applicable).
- Internal documents (where applicable) should be prepared accordingly for the assessment performed.
- Should a GMP certificate (or similar documentation) be generated as an outcome of the assessment, it should clearly document whether the assessment or inspection was performed remotely, on-site or hybrid.

9. Termination of the Remote Inspection

If a manufacturer is unable to provide satisfactory evidence through the remote evaluation or the author has suspicions on the acts of the manufacturer during the inspection, the EFDA reserves the right to terminate the remote inspection and require an on-site inspection.

10. Follow-up on Remote Assessment Effectiveness

The effectiveness of Remote Assessments may be assessed (if required) during future on-site inspections.

References

- Food and Medicine Administration Proclamation No. 1112/2019
- Medicine Manufacturing Establishment Control Directive
- PIC/S guidance on remote Assessment. PI 056-1, 1 January 2025