ETHIOPIAN FOOD AND DRUG AUTHORITY

Guideline on Remote or Virtual GMP Inspection and Extension of GMP compliance certificates

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Contents

Acronyms

API:	Active Pharmaceutical Ingredient
CAPA:	Corrective and Preventive Action
EFDA:	Ethiopian Food and Drug Authority
GMP:	Good Manufacturing Practice
NRA:	National Regulatory Authority
PQR:	Product Quality Review
QCL:	Quality Control Laboratories

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Foreword

Ethiopian Food and Drug Authority (EFDA) is a regulatory body established by the Regulation No 531/2023, which defines its mission, organization, and functions. One of its key responsibilities is to formulate regulations and guidelines for regulating the manufacturing of pharmaceutical products, ensuring with compliance with Good Manufacturing Practices (GMP) quality standards.

The presence of Poor- quality of pharmaceutical products poses a significant global public health risk. The EFDA plays a critical role in protecting the Ethiopian public from threats, including emerging infectious diseases such as the Coronavirus Disease 2019 (COVID-19) pandemic.

In this context, the EFDA has developed this guideline to outline the provisions for on- site GMP inspection waivers and voluntary virtual inspections of pharmaceutical products manufacturing facilities during public health emergencies and Force Majeure conditions

Beyond emergency situations, virtual 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 virtual inspections as a long-term component of its regulatory framework, ensuring continuous monitoring of pharmaceutical manufacturing standards while optimizing resources.

This guideline is expected to provide clear and comprehensive instructions to manufacturers and other stakeholders during the evaluation process, facilitating a transparent and standardized approach to GMP compliance assessments.

Glossary / Definitions

The definitions given below apply to the terms used in these guidelines. They may have different meanings in other contexts:

1. **"Agent or Local Technical Representative"** any applicant who is not resident in Ethiopia shall appoint a local technical representative who must be a company incorporated in Ethiopia and authorized by EFDA to deal in medicinal products and must hold a import/wholesale operating license.

2. **"Emergency Situation or state"** means unexpected factors including pandemics, 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.

3. **"Good Manufacturing Practice"** means the part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate for the intended use and as required by the marketing authorization. GMP standards are directly aimed primarily at diminishing the list inherent in any pharmaceutical production that cannot be prevented completely through the testing of the final product.

4. **"Manufacture"** all operations that involve preparation, processing, filling, transforming, packaging, and repackaging and labelling of medical products.

5. **"Manufacturer"** a manufacturer is a person or a firm that is engaged in the manufacture of medicinal products. It involves operations such as production, packaging, repackaging, labelling and relabeling of pharmaceuticals.

6. **"Marketing authorization"** approval from the authority necessary to market and sell a product in Ethiopia. This is a legal document that establishes the detailed composition and formulation of the product and the pharmacopoeia or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, labelling and shelf-life.

7. **"Marketing authorization holder"** a person granted with a marketing Authorization of a

product by an NRA.

8. **"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.

9. **"Pharmaceutical product"** means any substance capable of preventing, treating human or animal diseases and any other substance intended for administration to a human being or an animal in order to diagnose diseases, restore, correct or carry out modification of organic or mental functions.

10. **"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.

11. **"Stringent Regulatory Authority (SRA)/ WHO Listed Authorities (WLAs)"** a regulatory Authority which is a member of the International Conference on Harmonization (ICH) or an ICH observer, or is associated with an ICH member through a legally-binding, mutual recognition agreement.

12. **"Virtual inspection"** means inspections that are performed off-site through the use of enhanced communication and information technology to fulfil a legal requirement of an on-site inspection. The only difference from on-site inspection is that the inspector is not physically present at the inspection site.

Chapter one: Introduction

1.0 Background

National Regulatory Authorities (NRA), worldwide implements authorization and post- marketing surveillance of medical products. These systems include the assessment of submitted dossiers, and the inspection of Finished Pharmaceutical Products (FPP) and Active Pharmaceutical Products (APIs) manufacturers. These inspections are performed for dossier data verification and to provide evidence that 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.

On-site GMP inspections are widely regarded as the most effective method for determining a manufacturing facility's compliance with applicable standards. They provide 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 alternative inspection methods such as virtual inspection and desk assessment can be employed

Desk assessment primarily relies on reviewing submitted documentation, which may be suitable for facilities with strong compliance histories. However, it lacks real-time observations and may not adequately capture operational deficiencies. Virtual inspections, on the other hand, offer a more interactive alternative by leveraging real-time video streaming and digital document sharing. While virtual inspections enhance regulatory oversight and reduce logistical challenges, they also have limitations, including technological constraints, potential data security concerns, and the inability to conduct certain physical verifications.

Recognizing the need for a structured approach, EFDA has developed these guidelines to establish clear procedures for conducting virtual inspections.

These guidelines ensure that regulatory evaluations remain rigorous and comprehensive while allowing flexibility in situations where on-site inspections are impractical.

These guidelines apply primarily to overseas manufacturers who have applied for GMP inspection but do not meet the criteria for desk review. they serve as short-term decision-making framework during emergency situations and should be considered as a supplementary measure rather than a replacement for on-site inspections. The requirements set forth in these guidelines establish the minimum necessary standards and are designed to complement, rather than replace, existing legal controls.

1.1 Aim and objectives of the guidelines

These guidelines establish a structured approach for EFDA to assess GMP compliance through virtual inspections, reducing reliance on traditional on-site inspection and desk assessments. By leveraging technological advancements, EFDA aims to ensure regulatory oversight while minimizing delays in product registration and avoiding unnecessary duplication of inspections. The approach prioritizes authenticity, reliability, and adherence to global best practices in virtual assessments.

The specific objectives of this document are to:

i. Define a standardized framework for conducting virtual inspections as a viable alternative to o n -site GMP inspection, particularly in emergency situations such as the COVID-19 pandemic.
ii. Establish clear criteria and procedures for granting waivers for on-site GMP inspections when virtual inspections provide sufficient assurance of compliance.
iii. Facilitate the extension of GMP compliance certificates for previously approved manufacturing sites and marketed products with a proven track record of quality and regulatory adherence.
iv. 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.
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1.2 Scope of the guidelines

These guidelines define the regulatory framework for conducting virtual inspections as an alternative to on-site GMP inspections. They apply to facilities that require remote assessment due to logistical constraints, emergency situations, or other justified circumstances. Virtual inspections aim to maintain regulatory oversight while ensuring the timely evaluation of manufacturing compliance.

These guidelines are applicable to:

- Facilities that have submitted renewal applications for GMP inspection but do not qualify for desk reviews and require a Remote inspection to assess compliance.
- facilities seeking the extension of GMP compliance certificates for registered products manufactured on previously approved production lines.
- With a demonstrated history of compliance.

The guidelines outline the information, documentation, and evidence necessary for conducting virtual inspection or granting waivers. It excludes the procedural requirements for on-site inspections and traditional GMP desk assessments.

Chapter 2: Consideration and criteria for extension of GMP compliance certification

The decision to extend GMP Compliance Certificates for renewal applications shall be based on the following criteria:

2.1 History of Previous Inspection and Registration

i. Manufacturers that have successfully undergone a previous round inspection and demonstrated continued compliance with GMP requirements
ii. An extension of GMP Compliance shall be granted for manufacturing lines where at least one product from the same production line was registered and approved during the previous renewal period.

2.2 History of Market Complaint

Prior to granting an extension, a thorough review of the facility's history of product quality, safety and efficacy related complaint shall be conducted to ensure ongoing compliance with regulatory standards

2.3 Application

Facilities seeking an extension of GMP compliance shall submit a complete application to medicine evaluation and market authorization lead executive office in advance, in accordance with the re-registration guideline of the authority. The submitted information will be assessed by EFDA, and pays all the required fees must be paid before the application is considered.

2.4 Extension Period

The GMP Compliance extension period shall be limited to two years and shall be applicable for only one cycle.

2.5 Onsite inspection requirements

Manufacturer granted an extension must undergo an on-site inspection within the extended period to verify continued adherence to GMP standards.

2.6 Cancellation or Suspension of GMP Compliance Certificate

An extended GMP Compliance certificate may be cancelled or suspended under the following circumstances:

i. Failure of the manufacturer to undergo the mandatory on-site inspection within the extended period.
ii. Confirmation by the Authority of a product quality defect directly linked to GMP violations.

Chapter 3: consideration for GMP virtual/remote inspection

This Chapter outlines the criteria, application procedures and communication with regard to virtual/Remote inspections. Upon confirmation of GMP compliance, the facilities shall be issued with GMP compliance certificates with a validity period of not more than five years. However, based on the risk assessment of the facility, the re-inspection timeline may be shorter.

3.1 Criteria for Remote/Virtual Inspection

Applicants for virtual inspections shall be selected based on the following criteria:

a) Foreign non-Sterile Products Manufacturers, that have successfully passed two consecutive EFDA renewal inspection with no major changes to equipment or premises and have recently completed a physical audit but have pending operations due to observed deficiencies requiring audit.
b) Foreign Manufacturing Facilities producing non-sterile, rare, and critical medicines during pandemics
c) Manufacturers that voluntarily request a remote inspection and express their interest in undergoing the virtual evaluation process.

3.2 Application procedures

There shall be not separate application process for virtual inspections; instead, the authority will consider applications that have already been submitted for GMP inspections.

3.3 Communication

Applicants will be formally notified in writing by the authority regarding the plans to conduct virtual inspection.

3.4 Planning a virtual inspection/ audit

The following steps will be taken when planning for a virtual inspection/ audit:

3.4.1 Selecting and Notifying the Facility

Once a facility is selected for virtual inspection or audit the following steps will be followed:

a) Formal notification will be sent to the facility and, the applicant. This notification will specify the name and address of the facility, the scope of inspection, the number of inspection days, and the names of EFDA inspectors, if known.

. Upon agreement by the manufacturing site to participate in a virtual inspection, the Authority will coordinate with the facility to establish a point of contact for records transfer and remote interaction.

b) The Authority will assign an EFDA lead inspector for the virtual inspection/ audit that will be communicated to the facilities.
c) EFDA will gather and verify the necessary information required for planning and coordinating the virtual inspection/ audit.

3.4.2 Preparing for a Virtual Inspection

Once the facility confirms its willingness and ability to participate in a virtual inspection/ audit, the Authority will schedule a brief virtual meeting to discuss logistics, responsibilities, and expectations. Discussion topics may include, but are not limited to, the following:

a) Objectives and scope of the virtual inspection.
b) Introduction of the EFDA inspectorate team and the lead inspector.

c) Identification of the facility's point of contact and other key participants (e.g., monitoring of ancillary operations).
d) Scheduling and duration of the virtual inspection.
e) EFDA's expectations during the livestreaming walkthroughs of the facility.
f) Addressing the time zone differences and translation services for non-English speakers.
g) Conducting Virtual inspections during normal business hours of the facility.
h) Methods for sharing requested information, including secure documents sharing and the use of video-streaming technology.
i) Technological requirements for conducting an interactive evaluation during evaluation of the facility.
j) Testing the facility's internet connectivity to ensure sufficient bandwidth for live video and audio streaming for the actual remote interactive evaluation. Testing the facility's internet connectivity to ensure sufficient bandwidth for live video and audio streaming.

3.4.3 Pre-Testing IT systems and inspection site selection

A pre-test of IT system and connectivity is recommended at least one week before the scheduled inspection. The feasibility study should include testing of:

a) Security/Access to the Online Portal
b) Telephone or Video Conference Capacity
c) Screen-Sharing Capability
d) Wi-Fi Signal Strength
e) Computer Hardware and Connectivity

3.5 Conducting Virtual Inspection

Facilities are expected to maintain the same level of transparency as during an onsite inspection. All relevant personnel shall be available for scheduled interviews 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 virtual 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's corrective and preventive actions implementation.
e) Provide verbal updates to the facility on observations and outstanding issues, whenever feasible.

If a facility is unable to provide satisfactory evidence through virtual evaluation, EFDA reserve the right to terminate the virtual inspection and require an on-site inspection or alternative assessment measures.

3.6 Technological Requirements

The facility must ensure that its online connectivity including video, image and audio quality, meets the minimum standards required for remote evaluation.

EFDA will utilize its own IT platforms and online teleconferencing tools) to host virtual inspections and audits.

3.7 Virtual Evaluation of Documents and Records

During the virtual/Remote inspection or audit, the facilities must 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 must be submitted el e c t r o n i c format or made available via secure screen sharing during a live interaction for efficient assessment.
c) For electronic encrypted and password-protected files, facilities must ensure that EFDA can securely access the required information.
d) All documents submitted during a virtual inspection should be in English.
e) Paper documents should be scanned and submitted as searchable Portable Document Format (PDF) files whenever possible.

Chapter 4: Responsibilities of the applicant

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

4.1 Submission of the application

The manufacturer must submit an application to the Authority through electronic Registration Information System

4.2 Requirements for GMP

Ensuring that all below required documents for GMP application are submitted:

a) Application letter addressed to EFDA
b) Fill and sign the Pharmaceutical GMP Application form available on: (www.efda.gov.et/publication/gmp-application-form/
c) Proof of payment of prescribed fees
d) The Site Master File
e) Agreement with License Holder
f) Current manufacturing license of the premises issued by the competent regulatory authority in the country of origin.
g) Current GMP Certificate
h) List of all the products (medicinal or other) manufactured on-site and List of products intended for supply in Ethiopia. The lists should include proprietary names and international non-proprietary names (INN).
i) 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
j) 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.
k) Corrective and preventive action (CAPA) and proof of CAPA implementation related to the inspection report (observations/deficiencies).
l) The most recent product quality review(s) (PQR)(s) of the concerned product(s).
m) 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.

n) Quality Manual
o) The completed batch manufacturing/packaging record(s) including the analytical part for the most recently released batch of the relevant product(s).
p) A list of any recalls or any Market complaints registers in the last three years.
q) Aseptic validation report (Required for products applied for that are not terminally sterilized).
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).

4.3 Application Fees

Remitting all application fees at the time of lodging an application

4.4 Applications for Renewal

Submitting applications for renewal of a GMP Certificate at least six months prior to the expiry of the current Certificate.

4.5 Submission of additional information

Promptly submitting any additional information that may be requested by EFDA during an assessment. Failure to provide required documents within the specified time, depending on additional information requested, may result in the application being rejected.

References

- Food and Medicine Administration Proclamation No. 1112/2019
- Medicine manufacturing Establishment Control Directive No. 1000/2024