ETHIOPIAN FOOD AND DRUG AUTHORITY

GMP INSPECTION MANUAL

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1. Introduction

The Government of Ethiopia has been actively working to strengthen the regulatory system at both the national and regional levels. Ensuring the comprehensive regulation of all aspects related to the safety, efficacy, and quality of pharmaceutical products is a key priority. Effective medicines regulation encompasses various critical activities, including the inspection of pharmaceutical facilities such as manufacturers. These inspections play a vital role in safeguarding public health by ensuring compliance with Good Manufacturing Practices (GMP), Good Distribution Practices (GDP), Good Storage Practice (GSP) and Good dispensing practices other regulatory standards.

Conducting inspection and enforcement of inspection activities is essential to ensuring that medicines and other health products on the market comply with prescribed safety and quality standards.

Good Manufacturing Practice (GMP) refers to a set of principles and procedures that, when properly implemented by pharmaceutical manufacturers, ensure that medicinal products consistently meet standards of high quality, safety, and efficacy.

This manual has been prepared to guide inspectors in preparing for and performing Good manufacturing inspection activities. It also serves as reference document for GMP inspectors before, during and after inspections. The manual highlights general conditions and other pertinent requirements that are necessary for carrying out inspections of medicine manufacturing,

1.1. Objectives

The objective of this GMP (Good Manufacturing Practice) inspection manual is to provide inspectors with a structured and standardized framework, clear guidance, and essential requirements for planning, conducting, documenting, and following up on inspections of medicine manufacturing facilities. It aims to ensure consistency and quality in inspection practices, enhance inspector competency, strengthen regulatory compliance, and support evidence-based regulatory decision-making. Additionally, the manual promotes a risk-based approach to inspections, facilitates effective

communication and reporting, and contributes to the overall improvement of inspection services.

1.2. Scope

This manual applies to the inspection of both local and foreign pharmaceutical facilities.

1.3. Terms and definitions

In this manual, the following terms and definitions shall apply, unless the context indicates otherwise.

Inspection: is a systematic process conducted by inspectors to evaluate whether pharmaceutical manufacturers and related facilities comply with applicable laws, regulations, and standards, particularly those related to Good Manufacturing Practices (GMP).

Inspection team: is a group of qualified and authorized personnel assigned by Authority to plan, conduct, and report on inspections of pharmaceutical manufacturing and related facilities. The team is responsible for assessing compliance with Good Manufacturing Practices (GMP) to ensure that products are consistently produced and controlled according to quality standards.

Inspector: person appointed by the authority, based on their competency, to perform inspection activities in accordance with Proclamation No. 1112/2019. The hierarchical classification of inspectors based on their experience, expertise, and responsibility within the inspection process, categorized as follows: Level I –Level IV

Lead Inspector: A senior inspector assigned with the responsibility of leading an inspection team to conduct the inspection pharmaceutical establishment site.

Medical products: Refers to medicines, medical devises, cosmetics and other health products.

Critical observation: means an observation describing a situation that will most likely result in a non-compliant product or a situation that may result in an immediate or

latent health risk and any observation that involves fraud, misrepresentation or falsification of products or data.

Major observation: means an observation describing a situation that may have an impact on the product but is not as significant as a critical observation. It may have an indirect impact in the strength, identity, purity or safety of the product. There is reduced usability of the product without a probability of causing harm to the consumer. Observation of a major deficiency puts a question mark on the reliability of the firm's quality assurance system.

Minor/Other observation: means an observation describing a situation that is a departure from procedures and requirements but has no significant impact on the product quality. It has low probability of affecting the quality or usability of the product.

Authority: The Ethiopian Food and Drug Authority

2. Pharmaceutical Manufacturer Regulatory Inspection

2.1. What is inspection?

Inspection is a systematic and independent examination to determine whether quality activities and related results comply with the planned arrangement and whether these arrangements are implemented effectively and are suitable to achieve the objectives. To inspect is to look closely at something, especially to check that everything is in good order and ensure that it meets certain prescribed or known standards and specifications.

Thus, medical products inspection is the act of examining or looking closely at all the attributes of the products and the condition of all the facilities and/or premises as well as the personnel that deal with products. This helps ensure companies are meeting Ethiopia's safety, effectiveness and quality requirements. The inspection activities are meant to safeguard and promote the health and safety of the patient and public. This will be reinforced through enforcement of laws and regulations. Inspectors shall give emphasis on how inspections are operated as describe in the laws, inspection guidelines or manuals, procedures, work instructions, checklists or any other quality documentation.

2.2. Objectives of inspection

The primary objective of pharmaceutical manufacturing inspections is to ensure that products adhere to established standards of quality, safety, and efficacy, while also ensuring compliance with relevant regulatory requirements. This involves assessing product quality and safety, identifying and mitigating potential risks, verifying the accuracy of documentation and records, overseeing corrective and preventive actions, evaluating operational procedures, fostering continuous improvement, and, ultimately, safeguarding public health.

2.3. What needs to be inspected

In pharmaceutical manufacturing inspections, several key areas need to be thoroughly inspected to ensure that products meet regulatory standards and are safe for public use. these areas include: quality management system (QMS), facilities and equipment, personnel and training, raw materials and components, production processes,

documentation and record keeping, in-process controls and testing, finished product testing and release, storage and distribution, corrective and preventive actions (CAPA), waste management, compliance with regulatory requirements, and others.

2.4. Types of inspection

Inspection is the act of conducting official review of documents, facilities, records, and any other resources to assess their conformity to the requirements. In general term inspection can be classified as post and pre-licensing inspections. Recognizing this, there are five types of inspections, as outlined and described below:

1. Routine inspection
2. Concise inspection
3. Follow-up inspection
4. Special inspection
5. Investigative inspection

2.4.1. Routine inspection

Routine inspection is a full or comprehensive review/inspection of all aspects and components of the pharmaceutical manufacturer. This form of inspection is applied for conducting when a new pharmaceutical establishment is applying for a license to operate, applied when a pharmaceutical establishment seeks the renewal of its license or an extension of its operations beyond the originally approved scope; when there are significant changes within the establishment, such as changes in key personnel and relocation to new premises or modifications to existing premises; or when establishment has not been inspected for a long period; or when there are reports of serious gaps, deficiencies, or lapses in operations. This type of inspection should be announced.

2.4.2. Concise inspection

Concise inspection is the evaluation of limited aspects relating to GMP compliance within a facility. A limited number of GMP requirements are selected by the inspector to serve as indicators of the overall GMP compliance by the manufacturer. The inspector also has to identify and evaluate any significant changes that could have been introduced by the manufacturer since the last inspection. Collectively, the selected

indicators and the changes identified indicate the manufacturer's attitude toward GMP. A concise inspection is conducted under the following circumstances:

a) Where a manufacturer has a consistent record of compliance with GMP through routine inspections in the past.

b) Where a sample of aspects can be taken as a good indication of the overall level of compliance with GMP. However, if the concise inspection uncovers evidence that the level of GMP compliance has fallen, a more comprehensive or full GMP inspection should be performed soon after the concise inspection. These inspections can be announced or unannounced.

2.4.3. Follow-up inspection

A follow up inspection is also referred to as a re-inspection or a reassessment of the facilities. It is performed specifically to monitor the result of corrective actions of the manufacturer following a previous inspection. Depending on the nature of the defects and the work required, the follow-up inspection could be carried out within the agreed timeframe after the previous inspection. The follow-up inspection is limited to specified non compliances that have been observed during the previous inspection. A follow up inspection shall be unannounced.

2.4.4. Special inspection

A special inspection is undertaken to do spot checks which could focus on one product, a group of related products, or specific operations e.g. mixing, or labeling or specific documentation. A special inspection is triggered by customer complaints, adverse events, or reports of unexpected side effects from medical product. Special inspection is conducted under the following circumstances:

a) When there are complaints from consumers, healthcare professionals, or regulatory bodies regarding the safety, efficacy, or quality of medicines.
b) When there is a product recall due to events such as adverse drug reactions or unexpected side effects are reported that may indicate issues with the product's safety or quality.
c) When post-market surveillance identifies new risks or safety issues that were not observed during clinical trials or pre-market assessments.

d) When there are unusual variations or failures in the manufacturing process that may compromise medicines quality or safety, requiring immediate investigation.
e) If there are concerns regarding the traceability of pharmaceutical products, investigative inspections may occur to track the product's origins and handling.
f) Suspicion of violating dispensing rules, storing and distribution practices or regulations around controlled substances.
g) Suspicion of fraudulent activities, such as dispensing, storing distributing and manufacturing of falsified, expired, improperly stored unapproved medications or falsifying records etc
h) Suspicious of fails to meet certain licensing requirements
i) If a product is considered high-risk, such as biologics, vaccines, or new medicines that require close monitoring, a special inspection may be conducted.
j) To gather specific information, or to investigate specific operations of the manufacturing processes. The inspection shall be unannounced.

2.4.5. Investigative inspection

This type of inspection is undertaken to deal with specific complaints received about gaps or non-compliance with standards of professional practice or performance of new establishment whose scope of operation was previously unknown, complaints, product failure or recall. The inspection should be unannounced and special inspection is conducted under the following circumstances:

a) Complaints from patients or healthcare providers regarding poor service, or product quality defect or ineffectiveness/treatment failure of medicines can result in an investigation.
b) Issues with tracing the origin or movement of pharmaceutical products (such as imports or batch tracking)
c) Special inspection is conducted under the following circumstances:
d) When there are complaints about a specific product that suggest there may be defects.
e) When there is a product recall due to events such as adverse reactions to an immunological product.

f) To gather specific information, or to investigate specific operations of the manufacturing processes.
g) In cases where previous inspections revealed problems, an investigative inspection to ensure that the problems have been addressed and that the facility is now in compliance.

2.5. Frequency of inspection

Risk based inspection is a methodology that is based upon the concept of rating manufacturing sites on the basis of an estimated risk that they may pose to patients and users of medicines. A risk based approach to inspection planning will improve to allocate the resources more efficiently such as optimized use of time and manpower and preventing resource waste and conduct deeper, more focused inspections where they are most needed. Risk based inspection planning uses a historical inspection data, audit findings, and reports to help build a risk profile for each facility. Regularly updating risk profiles of facilities based on new data allows for continuous improvement of the inspection process.

The principles of quality risk management should be applied when planning risk-based inspections of manufacturing facilities. Institutions that demonstrate consistent compliance over a specified period (as determined by the regulator) may not require annual routine inspections. For establishments with a strong compliance record, inspections may be conducted less frequently. However, for facilities where violations are frequently observed, inspections should be scheduled more often.

Every licensed pharmaceutical manufacturer shall undergo Good Manufacturing Practice (GMP) inspections at intervals not exceeding three years. However, the inspection frequency may vary based on the risk level. Any new applicants, whether local or abroad, shall be planned for inspection without evaluation of the risk associated with intrinsic and compliance.

The following risk rating methodologies can be implemented to determine appropriate inspection intervals.

The risk ratings assigned to manufacturing sites are based on the assessment of two types of risk: intrinsic risk and compliance-related risk. The intrinsic risk estimated for

a site reflects the complexity of the facility, its manufacturing processes and products, as well as the criticality of the products it manufacturers. The compliance-related risk estimated for a site reflects its GMP compliance status as determined during the most recent routine inspection. When estimating this risk, both the classification and the number of deficiencies identified during the most recent inspection are taken into account.

The intrinsic risk and the compliance-related risk associated with a site are combined using a simple matrix to generate a relative risk rating for the site. This risk rating is then used to determine the frequency of the next routine GMP inspection. Then, Determine the scope of the next routine inspection by considering the following factors: the required focus and depth of the inspection, the estimated duration, the number of inspectors needed, and whether any specific competencies or technical expertise are required on the inspection team.

To determine the appropriate focus and depth of the next routine inspection, the inspector shall consider the following factors before making a recommendation:

- Areas where deficiencies—particularly major or critical—were identified during the most recent inspection at the site;
- Areas that were not inspected, or not inspected in sufficient detail, during the most recent inspection;
- Areas previously found to be inadequately resourced at the site; and
- Any other areas the inspector deems necessary for detailed review during the next inspection.

The quality risk management methodology enables continual updates to the frequency and/or scope of the next routine inspection as new information becomes available. A well-prepared worksheet is used to complete the Quality Risk Management (QRM) methodology for each site. The worksheet consists of seven sections (A to G), and is documented by the previous lead inspector.

- **Part A** provides preliminary information about the site, including the site name and address, and any applicable license numbers.

- **Part B** documents the estimated intrinsic risk associated with the site. Two key risk-indicating factors are assessed:

1. The complexity of the site, its processes, and products.
2. The criticality of the products manufactured (or the services provided) by the site.

Each factor is scored on a scale of 1 to 3:

- For complexity, a score of 3 represents high complexity, while a score of 1 indicates low complexity.
- For criticality, a score of 3 indicates high criticality, and a score of 1 represents low criticality.

These scores are recorded in Part B of the worksheet. A matrix (Table 1, below) is then used to combine the two scores and generate an overall estimate of the site's intrinsic risk, which is also documented in Part B.

Table 1: Intrinsic Risk Matrix

	Criticality		
Complexity	1	2	3
1	1(Low)	2(Low)	3(Medium)
2	2(Low)	4(Medium)	6(High)
3	3(Medium)	6(High)	9(High)

Note: A total score of 1 or 2 represents Low Intrinsic Risk, a total score of 3 or 4 represents Medium Intrinsic Risk, and a total score of 6 or 9 represents High Intrinsic Risk.

Part C is where the compliance-related risk associated with the site is estimated and documented.

The compliance risk (Part C) is solely based on the deficiencies identified during the most recent inspection of the site. (Note: If the most recent inspection was not a routine or full inspection, the deficiencies identified during the last routine (or full) inspection, as well as those identified during the most recent non-routine inspection, should be considered when scoring this risk.)

Table 2: Compliance Risk Table

Deficiency profile	**Compliance-related Risk Score**
1 or more critical deficiencies or ≥ 6 major deficiencies	High
1-5 major deficiencies	Medium
No major or critical deficiencies	low

Note: A score of High, Medium, or Low is assigned to the compliance-related risk associated with the site, and this is documented on the worksheet in Part C.

It is acknowledged that sites with a High Compliance-related Risk Score may need to be inspected again shortly after the inspection that identified the poor compliance status. Such sites may be directed to cease production and their manufacturing license and GMP certificate (for local sites) or GMP certificate (for international sites) may be revoked or modified until they demonstrate a satisfactory level of compliance during a follow-up inspection.

Follow-up inspections, by definition, are non-routine. These inspections, sometimes referred to as for-cause or emergency inspections may be necessary when a site has received critical or multiple major deficiencies (e.g., one or more critical or six or more major deficiencies).

Part D (Overall Risk Rating) is where the intrinsic risk and the compliance-related risk associated with the site are combined to generate the overall risk rating for the site.

A simple matrix, as shown in Table 3 below, is provided on the worksheet to generate this risk rating. The resulting risk rating is then documented in Part D of the worksheet.

Compliance related risk	**Intrinsic Risk**		
	Low	Medium	High
Low	Risk rating = A	Risk rating = A	Risk rating = B
Medium	Risk rating = A	Risk rating = B	Risk rating = C
High	Risk rating = B	Risk rating = C	Risk rating = C

Table 3: Risk Rating Matrix

Part E (Inspection Frequency) is where the risk rating from Part D is used to generate and document the recommended frequency for routine inspections at the site (Table 4).

- Sites with a Risk Rating of A are considered to have lower risk, having at least one Low score in either the intrinsic or compliance risk categories. These sites may be assigned a reduced inspection frequency, typically every 2-3 years, during routine inspection programs.
- Sites with a Risk Rating of B represent a medium level of risk. These sites have no High-risk scores but are not eligible for a reduced inspection frequency. They shall be inspected at a moderate frequency, generally ranging between 1 to 2 years.
- Sites with a Risk Rating of C have at least one High-risk score for intrinsic or compliance risk. These sites may be subject to an increased inspection frequency, typically less than 1 year.

Table 4: Suggested Inspection Frequency for Each Risk Rating

Risk Rating	Suggested Inspection Frequency
A	Reduced Frequency, 2-3 years
B	Moderate Frequency, 1-2 years
C	Increased Frequency, < 1 years

Part F (Inspection Scope) is where the recommended scope of the next routine inspection is documented. To ensure consistency and relevance, Part F should be completed either immediately after the inspection or once the inspection report has been issued, in alignment with Parts D and E of the worksheet. This ensures that the scope reflects both the assessed risk and the planned frequency of inspections.

Part F of the inspection report shall be completed by addressing the following:

1. The required focus and depth of the next routine inspection of the site.
2. The required duration of the next routine inspection of the site.
3. The required number of inspectors to be assigned to the next routine inspection of the site.
4. Whether any specific competence or expertise is required on the inspection team when performing the next routine inspection of the site.

Once Parts E and F have been completed, the recommended frequency and scope of the next routine inspection will be documented on the worksheet. The inspection planning staff can then use this information when planning the next routine inspection program.

Part G is where the names of the individuals who completed the Quality Risk Management exercise are documented. The signature and date of the person who completed the worksheet form should also be recorded in this section.

The outputs of Quality Risk Management exercises performed using this methodology should be reviewed whenever new information becomes available to the inspectorate that may alter the risk profile of the site.

3. Conducting Inspection

3.1. Planning for inspection

Before conducting the inspection, the inspection team shall be responsible for planning the inspection, following the approval of the work plan and budget. The planning process shall include the preparation of an annual or quarterly inspection plan, based on the approved budget and available resources.

During the planning phase, ensure that administrative compliance for manufacturers ready for inspection is verified, including aspects such as the inspection fee, production line, and accurate distance mapping.

Assign trained and qualified inspection teams based on their areas of competence, and approve the inspection schedules. Confirm that inspectors have signed the confidentiality and conflict of interest declaration forms.

The lead inspector is responsible for communicating and notifying the manufacturer(s) of the proposed inspection date(s).

Once the manufacturer confirms acceptance of the proposed inspection dates, finalize the inspection arrangements and proceed with the necessary planning.

When preparing an inspection plan (schedule), the following procedure should be followed

3.1.1. Considerations during Planning for Inspection:

- Selection of medicines manufacturers for inspection: This is a critical initial step in the inspection planning process. Ensure the medicine manufacturers to be inspected are selected based on their risk level, urgency, and application order. Consider public health needs or emergency situations that might require prioritizing specific sites for inspection. The inspectorate shall undertake the selection of manufacturers for inspection.
- Risk-Based Prioritization: Prioritize inspections based on the risk assessment of the manufacturer (e.g., sites with higher risk levels should be inspected more

frequently) and adjust the inspection frequency based on the manufacturer's risk score and product/process classification.

- The local technical representative, manufacturer, technical manager, or owner must complete the inspection details on a form, including information such as: the actual site to be inspected, production lines, and contact details of the responsible persons. This information must be provided in the application form prepared for this purpose.
- The local technical representative, manufacturer, technical manager, or owner is also responsible for paying the prescribed inspection fee. Verify that the inspection fee has been paid.
- Inspection for licensing and certification: Inspections shall be conducted in the order of applications. However, post-inspection planning shall follow a risk-based approach, prioritizing medicine manufacturers that are deemed to have a high risk.
- Geographical grouping of facilities: To optimize resources, facilities to be inspected should be mapped and grouped based on their geographical location, allowing for the organization of single inspection trips to multiple sites within the same area.
- Team Selection and Competence: Assign qualified inspectors based on their areas of competence and expertise, ensuring the inspection team has the necessary skills for the specific site and ensure that confidentiality and conflict of interest declaration forms are signed by all inspectors.
- Inspection duration: Determine the duration required for the inspection based on complexity of the site or process, size and scope of the facility, risk level, availability of budget and resources, language barriers and communication needs and special logistical needs (e.g., multiple buildings or locations).
- Inspection Plan: The plan shall include: Names, postal, and physical addresses of the manufacturer, type of inspection, proposed inspection date and Names of inspectors.

3.1.2. Out-of-Site Planning for the Inspection

Inspectors must prepare themselves for the inspection by gathering all the necessary tools and information to conduct the inspection judiciously and thoroughly. The tools shall include the following:

- **Official Communication:** Communicate with the facility (depending on the type of inspection) through the local technical representative, manufacturer, technical manager, or owner, informing them of the proposed inspection date(s) and send an invitation letter to assist in the preparation for foreign inspections, ensuring that the manufacturer is aware of the logistics.
- **Confirm Availability:** Ensure that the proposed dates for the inspections are suitable for all members of the inspection team.
- **Change of Inspection Dates**: Under exceptional circumstances and with proper justification, a facility wishing to change the agreed inspection date must submit the request in writing, proposing a new date that is convenient for both parties.
- **Review Previous Reports**: Review previous inspection and audit reports to understand the facility's history and address any previously identified concerns or improvements.
- **Secure Inspection Tools**: Ensure that inspection tools such as checklists, guidelines, sampling kits, and other necessary resources are secured and prepared for use during the inspection.
- **Arrange Travel Logistics**: Plan and arrange all necessary travel logistics for the inspection team, including transportation, accommodation, and any other travel-related needs.
- **Secure Relevant References:** Ensure access to important reference materials such as: Relevant laws, regulations, guidelines, and standards, Pharmacopeias, and other lists and reference materials relevant to the inspection.
- **Inspector Identification**: Ensure that all inspectors have their identification cards ready for the inspection.
- **Stationery Supplies**: Prepare necessary stationery supplies for inspectors, including pens and inspection writing books to document findings and observations.

3.2. Conducting an inspection

Upon reaching the premises where the inspection is to take place the inspection team shall make a courtesy call to the respective person in charge of the facility or the facility management to officially announce their presence. After the courtesy call and confirmation the following shall be conducted:

3.2.1. Opening meeting

- The Lead Inspector should express sincere gratitude to the facility for their interest in exporting to the Ethiopian market or for their efforts in manufacturing products for Ethiopia.
- The Lead Inspector should also thank the facility for their hospitality and cooperation in facilitating the inspection process.
- The Lead Inspector shall introduce the inspection team to the facility's management and staff and clearly explain the objective and purpose of the inspection, ensuring the facility understands the scope of the inspection and and request company representatives to introduce themselves.
- Inspectors must present their credentials to the facility to establish their authority and official capacity to conduct the inspection.
- The facility should give a brief presentation about their operations and activities. This should include: Organization structure and detailed activities carried out in the facility
- After the facility's presentation, the inspection team may pose questions to clarify any unclear points or to gain a better understanding of the facility's operations.
- The Lead Inspector should kindly inform the facility that all requested items (such as documents, records, equipment, etc.) should be readily available on-site or provided before the audit concludes.
- Inspectors should ask for assistance from facility staff when necessary to facilitate the inspection.
- The Lead Inspector should present an outline of the inspection schedule, including the specific areas of the facility that will be inspected and the order in which the inspection will proceed and clearly communicate the estimated timeline for each phase of the inspection, ensuring that the facility is aware of the structure and duration.
- The Lead Inspector should clearly inform the facility about the standards that will be applied during the inspection.
- In case the facility refuses to undergo the inspection, the Lead Inspector should clearly explain that refusal is a criminal offense under the relevant regulations.

- The lead inspector should ensure that an opening meeting form is circulated to all individuals present at the inspection.

3.2.2. Performing Actual Inspection

- After the opening meeting, the inspection team shall conduct the inspection by following the Aide-Memoire as a guideline.
- Use diplomacy, tact, and persuasiveness to acquire the necessary information and all necessary inspection details.
- The inspector can gather data by asking questions or conducting an interview directly with the supervisor or operator, reviewing the existing documents, and observing the operation.
- The inspectors shall review the company's overall documentation management system, including its change control practices. They should also evaluate the batch release procedure and the role of the person responsible for this duty. The following are a (not exhaustive) list of documents that may be reviewed:
  - Site Master File
  - Quality Manual
  - Master formula and processing instructions
  - Specifications for starting materials, primary packaging materials intermediate,
  - Bulk products and finished products.
  - Batch manufacturing records
  - Complaints
  - Deviation reports
  - Relevant SOPs and records (e.g., recall procedure)
  - Relevant contracts
  - Job descriptions and training records
  - Validation information
  - Laboratory books
  - Stability data (including ongoing stability)
  - Self-inspection program (self-inspection reports may not be reviewed; only check whether they are available)
  - Product Quality Review reports
  - Quality Risk Management reports

- Management Review reports
- Corporate corrective and prevention action (CAPA) program records
- Vendor approval, qualification and maintenance system and list of approved

- Inspectors shall conduct the inspection systematically using the appropriate inspection checklist. If needed, the inspectors can ask to make copies of documents or to take photographs of premises and equipment. During the actual inspection, the inspectors shall scrutinize inspection reports, inspection data, etc.; check whether inspection guidelines, checklists, and working procedures are followed.
- During the audit tour, the inspectors shall consider and check below areas to be covered

a) Buildings and Facilities

- Premises and facilities must be designed, located, constructed, and maintained to suit the operations to be carried out.
- Layout and design must aim to minimize risk of errors and to facilitate cleaning and maintenance to avoid cross-contamination, build-up of dust, dirt, and other adverse effects on the quality of products.
- Make visual observations, review documentation, ask questions, listen, and take notes.
- Check that there are clear restriction signs on doors to restricted areas.
- Verify orderly placement of equipment and materials to prevent mix-ups and contamination, especially for open non-contained systems.
- Confirm visible, clear, and logical provisions for flow of materials, products, processes, personnel, and waste to prevent mix-ups and contamination.
- Verify smooth, cleanable floors and walls, seamless corners, and ceiling and fittings that prevent build-up of dust and dirt.
- Are operating areas of adequate size to prevent contamination or mix-ups?
- Confirm availability of defined areas or other control systems for:
    - Receipt, identification, sampling, and quarantine of incoming materials and intermediates before release/rejection.
    - Holding rejected materials before disposition (e.g., return, reprocessing, and destruction).

  - Storage of released materials.
  - Production, laboratory, packaging, and labelling operations.
  - Adequacy of ancillary area, utility/maintenance space.
- Is ventilation, air filtration, air heating and cooling, and exhaust systems adequate?
- Is lighting adequate for operations? Review schedule for lighting maintenance (e.g., changing bulbs).
- Confirm that adequate particulate and microbial control is achieved.
- Confirm adequacy of air filtration systems, where needed.
- Check air pressure differential gauges and flow directions as you cross different levels of clean areas.
- Check air control monitoring and air system validation records.
- Verify adequacy of air controls/exhaust systems in dusty operations (e.g., weighing, production).

b) Water Supply

- Check water and plumbing systems, monitoring and control records.
- Confirm clear identification of pipe work, (e.g., markings, documentation, computer control systems) to prevent contamination and facilitate cleaning.
- Confirm adequacy and cleanliness of drains: no back siphoning, no build-up of contaminants.
- Check water standards requirement for operations: potable/higher purity (e.g., sterile preparations).
- Check procedures, records, pyrogen test (e.g., deionization, particulate/microbial contaminant, endotoxins).

c) Hygiene/Sanitation

- Review SOPs for hygiene, gowning; visit cloak rooms, toilets; ask questions.
- Review SOPs, schedules, and records for sanitation, washing, and use of toilet facilities.
- Check availability/adequacy of facilities for toilet, showers, clothing, and laundry.
- Verify that hygiene, gowning, and other relevant SOPs are available in all areas and are followed.
- Review health policy; check pre-employment and routine health records.

d) Pest Control, Sewage, and Waste Disposal

- Verify evidence of safe and sanitary disposal of sewage, refuse, and other wastes in/from building and immediate premises.
- Are responsibilities assigned? Are SOPs, cleaning schedules, methods, equipment, and materials to be used in cleaning buildings and facilities available? Are SOPs followed?
- Do SOPs exist for use of suitable rodenticides, insecticides, fungicides, and cleaning and sanitizing agents? Is there documented evidence that are followed?
- Confirm evidence that any rodenticides, insecticides, or fungicides used for pest control
- Review/note procedures to protect personnel and prevent contamination of equipment, components, drug product containers, closures, packaging, labelling materials, or drug products during application and use of pest control agents.

e) Equipment: Design, Construction, Size, and Location

- Equipment shall be of appropriate design, adequate size, and suitable location to facilitate intended operations, cleaning, sanitation (if needed), and maintenance.
- Equipment surfaces in contact with product must not be reactive, additive, or absorptive or alter quality, identity, purity, safety, or strength of regulated products and related materials beyond official or other established specifications.
- Review list of equipment submitted in SMF before inspection; confirm availability and adequacy of equipment; review SOPs, validation/calibration records, etc.
- Is equipment of appropriate design? Adequate size? Suitably located to facilitate operations, cleaning, and maintenance?
- Confirm that equipment is constructed with materials and of specifications to meet standards.
- Examine SOPs for cleaning, sanitation, and maintenance of equipment and utensils; confirm SOPs are followed.
- Review records for maintenance, inspection, and calibration (if needed) for automatic, mechanical, and electronic equipment.
- Are filters (where used) fiber releasing?

f) Control of Materials

- Ensure that SOPs on sourcing, receipt, identification, storage, handling, sampling, testing, and approval or rejection of materials are established and followed. Materials shall at all times be handled in a manner to prevent degradation and contamination.
- Check the SOP index. View all SOPs if possible. Review some SOPs (e.g., sampling and testing of materials).
- Pick a key SOP; if possible, find where, on a Batch Record, a batch of material has been processed as per that SOP. Ask the employee who performed that task to tell you how that specific operation was performed. Compare their account with the SOP. Does the SOP confirm that the Quality Unit approves the SOP? Check records.

g) Materials Management

- Verify that documented procedures exist for sourcing, receipt, identification, storage, handling, sampling, testing, and approval or rejection of materials.
- Confirm that standards and specifications for materials are documented and complied with.
- Verify adequacy of the process in place for the testing and approval/rejection of materials
- Verify that adequate controls are in place to rotate materials approved for use (e.g.,FEFO/FIFO).
- Verify that materials are retested or re-examined, as appropriate, for identity, strength, quality, and purity and approved /rejected by quality unit (e.g., after exposure to extreme conditions).
- Verify that rejected materials are identified and controlled by a quarantine system designed to stop their use in any operations for which they are unsuitable.
- Review procedures for supplier certification and records.

h) Production and Process Controls

- There shall be SOPs for production and process control designed to ensure that the regulated products and related materials have the identity, strength, quality, and purity they purport

- Review documents (e.g., SOPs, batch manufacturing records, record of yield) and signatures of head of quality unit/independent person verifying activities.
- Confirm availability, adequacy, and implementation of SOP for production and process control.
- Verify that systems are in place and followed for report, investigation, and justification of any deviation from SOPs and that quality unit approval is obtained for such deviations.
- Confirm procedures exists for identification, documentation, review, and approval of changes in raw material, components, specification, analytical methods, facilities, equipment, computer hard/software, and processing steps.
- Confirm SOPs for control procedures include batch requirements, component handling, verification, and supervision of operations.
- Verify that each container of components issued for manufacturing, each component added to batch, and calculations performed by one person are independently verified by a second person.
- Review procedure to ensure that actual yield and percentage of theoretical yield are calculated at the end of the appropriate phase of manufacturing, processing, packing, or holding of regulated products and related materials.
- Verify how equipment identification requirements are met.
- Verify there are written procedures for in-process controls, as well as tests or examinations for conducting on appropriate samples of in-process materials of each batch. Are the SOPs followed?
- Confirm that time limits are established to assure the quality of the regulated products and related materials; check records for proof of adherence to time limits for completion of each phase of production.
- Confirm that written procedures are established and followed, prescribing a system for handling batches that fail to meet specifications.
- Are procedures implemented to control microbiological contamination?
- Is any reprocessing done? Who authorizes it? SOP?
- Verify the batch numbering system.

i) Packaging and Labelling Controls

- Detailed SOPs for the receipt, identification, storage, handling, sampling, examination, and/or testing of labelling and packaging materials shall be established and followed
- Are labelling and packaging materials representatively sampled examined and tested upon receipt and before use?
- Are out-of-specification (OOS) material rejected and quarantined?
- Check SOPs for receipt, identification, storage, handling, sampling, testing, and examination of labelling and packaging materials.
- Is there an implemented process for the control of labels issued?
- Examine implementation of SOPs to assure that correct labels, labelling, and packaging materials are used for drugs and related products.
- Review implementation of SOPs for tamper-evident packaging requirements.
- Review documented and implemented SOPs for inspection of drugs and related products.
- Check for documented SOP for assignment of expiration date.
- Verify that regulated products have expiration dates on labels as required.
- Verify process outlining standards/specifications (e.g., protective, non-reactive, clean/sterile) for drug product containers and closures.

j) Holding and Distribution

- Warehousing and distribution of SOPs for drug products shall be established and followed.
- SOPs shall include quarantine before release; storage under appropriate conditions of temperature; and light and humidity to maintain the quality, identity, purity, and strength of the drug product.
- Check SOPs; check storage conditions; interview personnel on recall and other relevant warehousing and distribution procedures.
- Audit warehouse: ask to see records of temperature and humidity to check storage under appropriate conditions of temperature, humidity, and light.
- Confirm SOP exists to manage stock to ensure that oldest approved stock of drug product and related product is distributed first. Check distribution register to verify.

- Is there a documented system for traceability of distribution of each batch of drug product to facilitate recall? Ask to see it.

k) Laboratory Controls

- Review analysts' notebooks, records of equipment qualification and process validation.
- Review training records and personnel qualification records
- Verify that the Quality Unit and other personnel are trained, qualified, and experienced.
- Examine training records to verify initial and continual training on GMP, hygiene and sanitation, and specific job functions.
- Interview trained staff on training.
- Examine consultant records for proof of experience/qualification.
- Check laboratory SOPs index.
- Review a couple of laboratory SOPs
- Do appropriate and scientifically sound specifications exist for all products manufactured at the site?
- Do sampling plans exist?
- Do test procedures exist?
- Does the laboratory perform identity tests (Id) on APIs and excipients as required?
- Verify the following: (examine actual examples, probe, and ask for explanations)
  - Do appropriate written specifications exist for the acceptance of each batch of:
    - API?
    - Starting materials?
    - Packaging components?
    - In-process materials?
    - Finished products?
  - Do specifications include a description of the sampling and testing procedures to be used?
  - How are ***samples*** taken?
    - By whom?

        - Verify chain of custody.
        - Are samples representative of the batch? How?
        - Do sampling plans specify the number of units per batch to be tested?
        - Are samples labelled and identified?
    - How are samples stored to avoid deterioration, cross-contamination, or mix-up?
    - Are samples stored under lock and key?
    - Is there retesting of any material that is subject to deterioration?
- Verify that the laboratory conducts tests on each batch of raw materials, in-process goods, and finished drug products (check products manufactured 2, 12, and 18 months ago).
- Who determines whether a given batch of material conforms to written specifications or should be rejected?
    - Production manager?
    - Quality Unit (QA/QC) manager?
    - Plant manager?
    - Some other company official?
    - Check against documents on released or rejected batches to see who really makes the decisions.
- How are rejected batches disposed of? Ask to see an example!
- Review verification of compendia methods.

l) Microbiology

- What biological indicators are purchased?
- Are populations of organisms confirmed before use? Is there an SOP?
- Are SOPs for media preparation and storage available?
- How is the number of passages for working culture tracked?
- Are growth promotion tests carried out? Review SOPs.
- Review environmental monitoring results and SOPs.
- With regard to SOPs for analysis of water and other ingredients or drug and related products that are susceptible to microbial contamination, is there appropriate laboratory testing, as necessary, of each batch to determine

absence of objectionable micro-organisms and/or levels of pyrogens and endotoxins?

m) Instrument Calibration and Preventive Maintenance

- Are instruments, apparatus, gauges, and recording devices (e.g., analytical balances, ovens, pipettes, and other analytical volumetric glassware; stop watches; pH meters; thermometers; high-performance liquid chromatography (HPLC) pumps, HPLC detectors, spectrophotometers) calibrated at suitable intervals?
- Is there a written SOP for equipment calibration?
- Has a calibration schedule been established for all equipment subject to calibration? Is it followed?
- Check the analytical balance calibration log.
- Verify that it was calibrated on the days when each of the batches you checked earlier (manufactured 2, 12, and 18 months ago) was weighed in the laboratory during testing.
- Is there a preventive maintenance SOP and schedule for equipment? Is it followed? Verify!

Out-of-Specification (OOS) and Investigations

- Ask to see the SOP for OOS
- Examine the Laboratory Investigations Log.
- How many open investigations are there?
- Frequent OOS test results should raise a red flag!

n) Method Validation

- Does the company have a method validation SOP? Is it followed? Ask to see evidence!
- Ask to see validation (or verification) report of the Assay and Degradation Products Test Methods or the Stability Test Methods for the company's product from a risk based perspective

o) Stability Testing

- Recall that a written stability testing program is required by GMP regulations.
  - The results of these tests must be used to determine the labelled storage conditions and expiration dates.

- The tests must be carried out in the container closure system(s) in which the product is marketed.

- Verify that a stability testing SOP with appropriate details exists and is followed.
  - Ask to see the stability storage chambers.
  - Are the chambers appropriately labelled for temperature and humidity conditions?
  - Are temperature and humidity conditions monitored and recorded?
  - Ask to see the records supporting these items.
  - Are the chambers validated? Ask to see the validation reports and data.
  - What happens when there is a stability test failure? How are these investigated?
  - Ask to see an example. Interview the analysts.
  - How long does it take from when a sample is pulled from the chamber to when testing begins? Ask to see records to verify this.
  - Are stability samples waiting testing after being pulled from the chamber appropriately stored? How and where? Verify SOP and practice.

p) Retention Samples

- Ask to see the SOP
- Verify where retention samples are stored. Are these appropriate?
- How often does the company carry out physical inspection of the samples? Ask to see the documented evidence of where it recently did this.
- Do you notice any “off-color” or other evidence of deterioration?

q) Records and Reports

- Records shall provide appropriate history of each batch of products, including its distribution and all other relevant circumstances pertinent to quality of final product.
- Verify SOP on records and reports; check traceability of a batch with personnel; confirm the role of the quality unit in review and approval of records and/or changes. Review SOP for handling and maintenance of

records and reports. Is it followed? Verify SOP on managing container closure and labelling records (if not already done).

- Verify that records are maintained for all components, containers, closures, and labelling for appropriate periods.
- Verify written record of major equipment cleaning, maintenance, and use in individual equipment logs showing date, time, product, and batch number of each batch processed.

r) Returned Products and Product Salvaging

- Returned products shall be identified as such and held. Where there is any doubt on quality of returned drug product, it shall be destroyed unless examination, testing, or other investigation proves that the product meets efficacy, quality, identity, potency, strength, and safety standards.
- Products that have been subjected to improper storage conditions or have expired shall not be salvaged or returned to the marketplace or for use
- Review SOP and records that manage return, handling, and salvaging of drug products.
- Are they followed?

s) Returned Products and Product Salvaging

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- Products that have been subjected to improper storage conditions or have expired shall not be salvaged or returned to the marketplace or for use
- Review SOP and records that manage return, handling, and salvaging of drug products. Are they followed?

▪ Inspectors should take samples and send for analysis whenever there is any doubt on the quality of the product(s). If any samples have been taken for testing, furnish a receipt or provide evidence for taking these samples to the person from whom samples are taken. Normally, the sample size should be sufficient to carry out the test. Samples should be collected as per the laboratory requirements. Inspectors shall also be trained on techniques for sample collection.

- At the end of the working time of each day, the inspection team should make an informal meeting to report the progress of the inspection, exchange findings or observations, and obstacles found during the inspection.
- Inspectors shall write down all deficiencies they encountered during inspection even though facility can correct such deficiency immediately.
- Before the closing/exit meeting, the team members should meet alone to discuss their findings.
  - Contact the Authority for guidance if there is any uncertainty or in the event of a serious noncompliance that requires immediate action..
  - List major findings to be presented to management at the closing/exit meeting.
  - Begin with the most important findings.
  - List findings of areas of strength, areas of deficiencies, and items that require immediate attention.

3.3. Post-inspection briefing or closing meeting

This is an activity that takes place after inspection has been carried out. The objective of this stage is generally to convey inspection findings/observations in brief to the inspected establishment.

- During the closing meeting, express appreciation to the company for their cooperation and share brief feedback highlighting positive observations from the inspection. Clearly explain the timelines for submitting the inspection report and the expected corrective action plan. Summarize the key findings by area, noting that the report will undergo review by the GMP Task Force. Conclude by asking if the company has any questions or requires further clarification.
- On behalf of the inspection team, Inspection leader should repeat the objective and scope of inspection summarize the observations found during the inspection in both strength and weakness, and final conclusion of compliance level of the facility. Explain to facility if having unclear point and adding the facility comments if appropriate;
- Observations should be clearly described and supported by concrete evidence gathered during the audit. The potential impact of each observation should also be explained. At this stage, it is not necessary to classify the deviations (e.g., critical,

major, or other), as such classification may require review and consensus by the GMP Task Force before a final determination is made.

- The closing meeting should generally be limited to one hour, except in exceptional cases where a high number of observations warrant additional time.
- The auditee must be given the opportunity to ask questions. Any disagreements between the auditor and the auditee regarding the audit findings or conclusions should be discussed openly and resolved whenever possible. Any unresolved issues must be promptly documented and reported to the GMP Task Force for further review.
- In case a critical deficiency is found, Lead Inspector shall record, evaluate the risk and order the facility to stop production/ activities related to the deficiency (order must be informed at closing meeting of inspection and written in inspection report). Lead Inspector shall rapidly submit such record to his/her supervisor for consideration and communicate the facility right after regulatory body makes a final decision.
- In case of minor non-compliance observations, the facility will be required to prepare and implement corrective and preventive action (CAPA) that will be followed up during the next inspection as follow up.
- Depending on the respective legislations and regulations, Authority may take action to correct unsatisfactory practices and prevent the distribution and use of products with suspected quality defects or those manufactured under conditions that do not comply with GMP (Good Manufacturing Practice) requirements. In extreme cases, the closure of operations or activities may be required.

However, in practice, these measures are typically employed only in exceptional cases where the risk to health is significant. Such actions are usually taken after a thorough investigation of the situation, and efforts are made to correct the deficiencies before resorting to drastic measures.

These actions could include:

- **Issuing a Warning**: Regulatory bodies may issue warnings to facilities or companies to address non-compliance issues within a given timeframe.

- **Suspension of Activities**: If the risks are high but not imminent, the regulatory body may suspend specific activities or product lines until corrective actions are taken.
- **Product Recall**: If a product is found to be defective or unsafe, the regulatory body may order a recall of the product from the market to protect consumers.
- **Fines or Penalties**: Facilities found in violation of GMP requirements may face financial penalties or other sanctions.
- **Facility Shutdown**: In extreme cases where the risk to public health is high, regulatory bodies may order the shutdown of a manufacturing facility or distribution center to prevent the distribution of unsafe products.
- **Revocation of License**: In cases of severe non-compliance, the regulatory body may revoke the operating license of a facility or company, barring them from manufacturing or distributing products.

3.3.1. Inspection Report

- An inspection report shall be written immediately after completing inspection with the participation of all members of the inspection team under the coordination of the lead inspector.
- Inspection report must attach list of deficiencies which should be described clearly and in detail. All deficiencies must be listed, classified and referred to relevant reference to the national GMP guideline, WHO and PICs GMP guide.
- The inspection report shall be written according to the agreed standardized inspection reporting format.
- The GMP inspection report should be balanced, unbiased, and based on objective evidence. It must be sufficiently detailed to enable the GMP peer review technical team to form an informed opinion on the recommendations made by the inspectors. The Inspection Report should include positive and negative observations for each activity inspected as communicated to the company before the end of inspection.

3.3.2. Classification of GMP Findings

- GMP findings are classified based on their severity and potential impact on product quality, safety, and regulatory compliance as critical, major or other/minor.
- Prioritize risks related to products and patients when classifying the inspection findings.
- Perform an evaluation of factors that would either increase or reduce the risk and categorization regardless of the initial classification as per further evidences. A comprehensive evaluation should be conducted and below factors shall be consider determining whether any factors may increase or reduce initial classification.
    - Historical compliance record – Whether similar deficiencies have occurred in the past and how they were addressed.
    - Additional evidence – Any new information obtained through further investigation.
    - Corrective and Preventive Actions (CAPA) – The effectiveness of measures taken to resolve the deficiency and prevent recurrence.

  - Extent of impact – Whether the deficiency affects a single batch, multiple batches, or an entire production process.
  - Detectability – Could the issue have been detected before product release.
  - Potential risk mitigation – Whether existing controls or procedures sufficiently reduce the risk.
  - Patient safety impact – The potential harm the deficiency could cause to consumers.
  - Regulatory and quality system maturity – The robustness of the company's quality management system in preventing similar issues.
- Document all related information's which will be useful as input for risk-based categorization (Videos, written objective evidence, photos, etc)
- Inspection deficiencies included in an inspection report must reference specific requirements from the current Ethiopian GMP guidelines, the WHO Technical Report Series, and other regulatory requirements. Other findings that cannot be reasonably referenced should not be listed as an observation.
- The non-compliance statement should include the requirement (R), evidence (E) and deficiency (D) and inspectors concern for being deficient.
- Deficiencies should distinguish whether the defect lies in the system itself or in a failure to comply with the system.
- Where more than one deficiency relates to the same basic quality system failure, the deficiencies should be grouped and listed as a single observation, under a heading that reflects the basic system failure.
- When multiple observations are related to a single topic happened, group them under one title or category as described in the example below.

SN	Description of deficiencies		Classification	Reference
1	Equipment maintenance was found deficient in that:		e.g., Major	e.g., EFDA GMP Guideline, 3rd edition, Clause a.b.c.
	1.	Observation evidence 1: Delayed servicing of critical machinery, affecting production timelines.		
	2.	Observation evidence 2: Failure to document maintenance schedules for key equipment.		
	3.	Observation evidence 3: Lack of preventive maintenance schedule		

- The categorized observational findings shall be verified and approved by lead inspector.
- The Lead Inspector circulates the draft inspection report to all other members of the inspection team seeking their agreement to the draft report. Once this is obtained, the lead inspector then finalizes the report.

3.3.3. Contents of the inspection report

In spite of the type and format of the audit inspection report, the report should contain the following information;

3.3.3.1. Title of the report

- Name of facility
- Name of inspectors
- Detailed address of the facility: Facility Name, Street Address, City or Town, Postal Code / Zip Code, Region or Province/State, Country
- Heading of the report indicating place, date and duration

3.3.3.2. Acronyms, as appropriate

- List of abbreviations commonly used in the report.

3.3.3.3. List of figures and tables, as appropriate

- Title of figure/ tables and pages to locate them

3.3.3.4. Table of contents, as appropriate

- List of topics and pages to be located

3.3.3.5. Executives summary

3.3.3.6. Introduction

- Scope of inspection
- Inspected facility details
- Inspection Date
- Purpose of inspection
- Methodology

3.3.3.7. Main body of the report

- Situation analysis, needs, services and systems
- Observations/Findings: compliance status, strengths, non-compliance issues and evidences
- Analysis of the findings

3.3.3.8. Conclusion and recommendations

- A summary of the overall inspection results and Specific suggestions for improvements, changes in practices, or further actions to ensure compliance.

3.3.3.9. Risk rating and frequency of follow-up inspection

- The risk ratings assigned to sites are based on an assessment of two different types of risk: intrinsic risk and compliance-related risk.

3.3.3.10. Signatures

- Name of inspectors and Signature: Names and signature of inspectors participated in that inspection
- Name and signature of the person approving the report

3.3.3.11. Appendices, if required

- List of tools used and Photos and Evidence

4. Decision on Compliance

4.1. When the facility is found on non-compliance observation or with only minor/other non-compliance observation, the facility shall be considered to be operating at an acceptable level of compliance

4.2. In case of minor/other non-compliance observation, the facility will be required to prepare and implement Corrective and Preventive Action (CAPA) that will be followed during the next inspection.

4.3. When there are less than six (<6) major non-compliance observations from different systems, the facility shall be considered to be provisionally operating at an acceptable level of GMP compliance, subject to CAPA implementation, closure and assessment with the agreed timeframe

4.4. When there are six or more (≥6) major non-compliance observations from different systems, the facility shall be considered to be operating at unacceptable level of compliance

4.5. When there are one or more critical non-compliance observations from different systems, the facility shall be considered to be operating at unacceptable level of compliance

4.6. When the facility is deemed operating at unacceptable level of non-compliance another inspection will be required. Therefore, the applicant will be required to apply for re inspection.

4.7. When non-compliances are observed in the manufacturing facility, the inspector has to recommend the Authority appropriate regulatory action as stipulated below table.

Table 1: Recommended Regulatory actions against observed non- compliance

S/N	Category of Non-Compliance	Regulatory Actions
1	Minor/Other	Operating at an acceptable level of GMP compliance
2	Major (1-5)	Provisionally operating at an acceptable level of GMP compliance, subject to CAPA implementation, closure and assessment with the

		agreed timeframe
3	Major (≥6)	Operating at an unacceptable level of GMP compliance Institute withdrawal or suspension or decline of granting of GMP Certificate Institute of withdrawal of market Authorization in case of registered products
3	Critical	Operating at an unacceptable level of GMP compliance Institute withdrawal or suspension or decline of granting of GMP Certificate Institute of withdrawal of market Authorization in case of registered products

5. GMP Inspection Report Peer Review process:

The peer review process plays a critical role in ensuring the accuracy, consistency, and compliance to regulatory requirements of GMP inspection reports. It serves as an internal quality control mechanism before finalizing inspection reports. A GMP inspection report peer review task force will be established to systematically review the inspection findings and ensure that the inspection reports are accurate, consistent, and aligned with regulatory standards, thereby reinforcing the credibility and effectiveness of GMP compliance inspection.

An independent peer review process is convened for each GMP inspection report by the established task force and provides recommendations for decision.

The Peer Review of the GMP Inspection Report ensures the Quality Assurance of the inspection reports and perform at least the following key functions

5.1. Ensures Accuracy and Completeness

- Peer reviews meticulously examine inspection reports to ensure all observations, evidences, and conclusions are factually correct and accurately documented and that no critical information is omitted or misrepresented.

This thorough review helps identify and rectify any factual inaccuracies or gaps in the report.

5.2. Ensures Consistency and standardization:

- By adhering to standardized formats and procedures, peer review promotes uniformity across inspection reports.
- Checks alignment with relevant regulations (National cGMP Guideline, WHO cGMP Guideline, USFDA cGMP, EU cGMP, PICs cGMP Guide, and other recognized cGMP guidelines,

5.3. Validates Regulatory Alignment

- Peer reviewers assesses whether the inspection findings and subsequent recommendations align with current GMP regulations and requirements. This validation ensures that the inspection process remains relevant and in compliance with evolving regulatory requirements.

5.4. Objectivity and Bias Reduction:

- Through independent evaluation, peer review helps in detecting any potential biases or subjective interpretations in the inspection report, fostering objective and impartial assessment.
- Offers an independent perspective, reducing individual inspector bias.
- Helps ensure fair and balanced reporting of findings.

5.5. Improved Report Clarity and Structure:

- Reviews the report for clear, concise, and professional language.
- Enhances readability and logical flow of information.

5.6. Supports inspectors Development

Peer review provides constructive feedback to inspectors, fostering their professional growth and enhancing both inspection and reporting skills. The feedback shared during this process serves as a valuable learning tool, helping inspectors identify areas for improvement in their reporting techniques and inspection practices. This ongoing cycle of reviewing process not only supports individual development but also contributes to the overall improvement of the quality and consistency of GMP inspections.

5.7. Promote Transparency and Accountability

- Peer review introduces an additional layer of oversight that ensures GMP inspection reports are prepared with integrity, clarity, and consistency. By involving multiple qualified inspectors in the review process, the system minimizes individual bias and promotes openness in how inspection findings and regulatory decisions are reached. This collaborative review fosters accountability among inspectors, as their work is subject to evaluation by their peers. It also builds trust among stakeholders such as regulated entities (manufacturers) and the public.

5.8. Strengthen Regulatory Decisions

- Peer review enhances the credibility and robustness of regulatory decisions by ensuring that inspection findings are accurate, well-documented, and aligned with applicable standards. Through critical evaluation by experienced peers, the inspection report is validated for completeness, consistency, and objectivity. This process helps identify any gaps, clarify ambiguities, and confirm that appropriate regulatory classifications and recommendations have been made. As a result, the final report provides a solid basis for regulatory actions such as GMP licensing, enforcement, or request corrective measures.

6. Inspectors Competencies

6.1. Qualification and training of inspectors

Inspectors shall be appointed by the Authority. The inspectors shall have the qualifications necessary to effectively take part in the inspection of medicine manufacturer. These qualifications shall be based on the following;

- Academic education
- Essential Skills
- Training
- Work experience

6.2. Academic Education

A GMP inspector should have a degree in pharmacy, chemistry, microbiology, biotechnology, engineering, or other relevant scientific disciplines. They should possess a solid understanding of pharmaceutical laws, regulations, and international guidelines, including those established by WHO, PIC/S, EU-GMP, and US FDA. A strong foundation in manufacturing processes, quality control, validation, and risk assessment principles is essential. The possibility of having part-time inspectors with special knowledge as part of inspection teams may also be considered if deemed necessary and these inspectors should sign declaration for conflict of interest.

6.3. Training

To be competent in carrying out inspections, inspectors shall be required to undergo training in pharmaceutical inspections. Such trainings shall provide them with knowledge and skills needed when planning for, carrying out, and reporting on inspections.

Apart from basic training, inspectors shall be required to undergo on-the-job training by senior inspector(s). Such trainings shall involve both theory and practice of inspections and will cover inspection techniques, communication and management skills, and conducting inspections and writing reports as trainees. Continuous training shall be provided to inspectors to keep them abreast of current knowledge and techniques in carrying out inspections. This training shall be completed through attending training programs, seminars, scientific meetings, conferences, and exhibitions organized by either the regulatory body or other national and international organizations

6.4. Experience

Experience as a general concept comprises knowledge of or skills in or participation in activities or events, or knowledge or skills gained through involvement in or exposure to those activities or events Inspectors should undergo structured training (theoretical

and on-site) before conducting inspections independently. An inspector will be deemed experienced as per the competency manual of the Authority.

Inspectors shall demonstrated competence in communication skills and report writing.

Such experience will be taken into consideration when planning and assigning inspectors for conducting pharmaceutical supply chain inspection.

6.5. Resource management

A recent assumption in inspection planning is the increasing reliance on risk-based inspection approaches to optimize resources and enhance efficiency. Regulatory agencies now prioritize inspections based on risk assessment models, focusing on high-risk manufacturers, supply chain vulnerabilities, and compliance history. This approach ensures that inspection resources are allocated where they are most needed; reducing unnecessary delays while maintaining regulatory oversight.

6.6. Conflict resolution

The most effective method of solving conflict is to take steps to reduce conflict occurrences. The lead inspector may establish ground rules, for the inspection team, for communication, interaction and performance of the inspection teams before the inspection process. This will help the inspection team to reduce conflicts during the inspection by eliminating misunderstandings, remaining open minded and flexible.

Conflict may develop at any time during inspection process. The best course of action for the team is to temporarily stop the inspection and allow a cooldown period before proceeding and avoiding or smoothing the issue.

6.7. Other competences

The inspectors should also have competences on communication techniques, interviewing techniques, presentation techniques and process verification (verify by examination of records, documents or interviewing) and validation techniques.

7. Code of Conduct for Inspectors

An inspector is responsible for maintaining impartiality and integrity while conducting inspections, ensuring that assessments are objective, unbiased, and free from any conflicts of interest. They must uphold confidentiality in handling sensitive company data, preventing unauthorized disclosure of proprietary or regulatory information. Additionally, inspectors are required to adhere to both national and international regulatory codes of conduct, ensuring compliance with ethical and legal standards in all inspection activities. This commitment to professionalism strengthens regulatory credibility and promotes trust in the inspection process.

Inspectors shall behave, conduct themselves in accordance with, and observe the code of ethics and conduct as stipulated here:

- Strive to achieve the highest ethical and performance standards in carrying out inspection activities.
- Uphold the honor and dignity of an inspector and avoid association with any enterprise of questionable character or apparent conflict of interest.
- Perform duties tactfully, honestly, and impartially to avoid circumstances that may lead to conflict of interest.
- Protect and promote the interests of this/her organization to the best of his or her ability and knowledge, recognizing that the organization has placed trust and confidence in him or her.
- Make every effort to uphold, maintain, and improve the integrity and reputation of the regulatory body and the government of Ethiopia
- Maintain confidentiality whenever accessing confidential information as a result of inspection.
- Adhere to the laid down rules, regulations, and standard operating procedures in executing his or her functions.
- Make decisions in line with authorized standards and procedures.
- Report inspection findings truthfully and accurately.
- Assess facts quickly and make rational and sound decisions without delay.
- Strive to acquire new knowledge and skills continuously and use them effectively.
- Conduct inspections in a manner that will ensure independence from outside influence and interest, which would otherwise compromise the inspector’s ability to render a fair and impartial opinion regarding any inspection conducted.

- Promptly disclose to his/her organization any interest in any business that may affect the quality or the result of the inspector's work or remediation.
- Disclose fraud or abuse of power and corruption to his/her organization.
- Not use his or her position for personal gain.
- Conserve his/her organization's property and not use it for private gain.
- Not solicit, force, or accept bribes from a person whom the inspector is serving, has already served, or will be serving either by doing so in person or by using another person.
- Not receive presents in the form of money, entertainments, or any service from a person that may be regarded as geared toward compromising the inspector's integrity.
- Seek prior approval by your organization before engaging in outside employment or activities or seeking or negotiating for employment that will directly conflict with the duties or interests of the regulatory body.
- Endeavor to avoid any actions that create an appearance or circumstance of violating the law or ethical standards as determined by the perspective of a reasonable person with knowledge of the relevant facts.
- Be committed to work hard for long hours
- Avoid the use of rude and abusive language.
- Maintain personal hygiene and dress in respectable attire in accordance with acceptable norms of the office.

8. Reference materials

Depending on the needs of the medicine facility, inspectors should maintain the following tools or use them as references as needed.

S.no	Topic/Area	Reference Guidance Document
1.	▪ National Drug Policy ▪ Proclamations, Regulations, and Appropriate Directives ▪ Pharmacy Code of Ethics ▪ National List of Medicines, including registered medicine lists, national essential medicines, and other relevant lists ▪ National Standard Treatment Guidelines and Good Dispensing Practice Manuals	**Publication-EFDA** http://www.efda.gov.et/publications-library/#

	▪ Directive for Disposal of Pharmaceutical Products and other appropriate directives ▪ Good distribution and storage practices ▪ Community pharmacy standards ▪ EFDA Good Manufacturing Practices for pharmaceutical products: Main principles	
2. **1**	**GMP main principles**	WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2*** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/ TRS1025 Annex 6

3. **2**	**Water for Pharmaceutical Use**	WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth- six Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2. **Short name: WHO TRS No. 970, Annex 2** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/ TRS 1025 Annex 3: Production of water for injection by means other than Distillation and distillation and water waste treatment
4. **3**	**Heating Ventilation and Air-conditioning, HVAC**	Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/ Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organisation, 2018 (WHO

		Technical Report Series, No. 1019), Annex 8. **Short name: WHO TRS No. 1019** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1019/en/
5.	**Good practice in Quality Control**	WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty- fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 1. **Short name: WHO TRS No. 957, Annex 1** http://www.who.int/medicines/publications/44threport/en/ **Good chromatography practices.** WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025, Annex 4. **Short name: WHO TRS No. 1025, Annex 4**

6.	**Pharmaceutical Microbiology**	WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty- Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2. **Short name: WHO TRS No. 961, Annex 2** http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1
7.	**Sterile products**	WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty- Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6. **Short name: WHO TRS No. 961, Annex 6** http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1 PICS guide to good manufacturing practice for medicinal products, Annex 1 (sterile medicinal products) https://picscheme.org/docview/4590

8.	**Quality risk management**	WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. **Short name: WHO TRS No. 981, Annex 2** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/ International Conference on Harmonisation, ICH, Q9 Quality Risk Management https://database.ich.org/sites/default/files/Q9_Guideline.pdf Include the PICS guidance
9.	**Non-sterile process validation**	WHO Guidelines on Good Manufacturing Practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organisation, 2015 (WHO Technical Report Series, No. 992), Annex 3. **Short name: WHO TRS No. 992, Annex 3** http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

10.	**Data integrity**	Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5. **Short name: WHO GDRMP guidance** or **WHO TRS No. 996, Annex 5** http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_ annex05.pdf
11.	**Hold time studies**	WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. Short name: WHO TRS No. 992, Annex 4 http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_ committee/WHO_TRS_992_web.pdf
12.	**Site Master File**	WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. **Short name: WHO TRS No. 961, Annex 14** http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

13.	**Sampling**	WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4. **Short name: WHO TRS No. 929,** **Annex 4** http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1
14.	**Validation** - HVAC - Water system - Analytical methods - Computerised systems - cleaning - Guideline on qualification of	WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-third report (WHO Technical Report Series, No. 1019). **Short name: WHO TRS No. 1019, Annex 3** https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287- eng.pdf?ua=1

	equipment and systems - Non-sterile process validation	
15.	**Hazardous substances**	WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. **Short name: WHO TRS No. 957, Annex 3** http://www.who.int/medicines/publications/44threport/en/
16.	**Chemical reference standards**	General guidelines for the establishment, maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. **Short name: WHO TRS No. 943, Annex 3** http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

17.	**Technology transfer**	WHO guidelines on technology transfer in pharmaceutical manufacturing. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7. **Short name: WHO TRS No. 961, Annex 7** http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1
18.	**Biological products**	WHO Expert Committee on Biological Standardization Sixty-sixth report **WHO Technical Report Series, No. 999, 2016) Annex 2** https://www.who.int/biologicals/areas/vaccines/Annex_2_WHO_Good_manufacturing_practices_for_biological_products.pdf?ua=1

19.	**Blood products**	WHO guidelines on good manufacturing practices for blood establishments, Annex 4; World Health Organization **WHO Technical Report Series, No. 961, 2011** https://apps.who.int/iris/bitstream/handle/10665/44079/WHO_TRS_961_eng.pdf?sequence=1
20.	**Stability studies**	WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-second report **WHO Technical Report Series, No. 1010, Annex 10** http://apps.who.int/medicinedocs/documents/s23498en/s23498en.pdf
21.	**Biological products**	WHO Expert Committee on Biological Standardization Sixty-sixth report **WHO Technical Report Series, No. 999, 2016) Annex 2** https://www.who.int/biologicals/areas/vaccines/Annex_2_WHO_Good_manufacturing_practices_for_biological_products.pdf?ua=1

22.	**Blood products**	WHO guidelines on good manufacturing practices for blood establishments, Annex 4; World Health Organization **WHO Technical Report Series, No. 961, 2011** https://apps.who.int/iris/bitstream/handle/10665/44079/WHO_TRS_961_eng.pdf?sequence=1
23.	**Stability studies**	WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-second report **WHO Technical Report Series, No. 1010, Annex 10** http://apps.who.int/medicinedocs/documents/s23498en/s23498en.pdf
24.	**Herbal medicines**	WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-second report **WHO Technical Report Series, No. 1010, Annex 2** http://apps.who.int/medicinedocs/documents/s23498en/s23498en.pdf

25.	**Biosimilars**	WHO Expert Committee on Biological Standardization Sixtieth report; **WHO Technical Report Series, No. 977, 2013 Annex 2** https://www.who.int/biologicals/publications/trs/areas/biological_therapeutics/ TRS_977_Annex_2.pdf?ua=1
26.	**Pharmacovigilance**	https://www.fda.gov/media/71546/download
27.	**Inspection report**	Guidance on good manufacturing practices: inspection report https://cdn.who.int/media/docs/default-source/2021-dha-docs/trs996_ annex4.pdf?sfvrsn=c44d141a_1&download=true
28.	**Supplementary GMP resources**	1. PIC/S https://picscheme.org/docview/4590 2. European Medicines Agency, EMA (Eudralex Volume 4), Good manufacturing practice, https://health.ec.europa.eu/medicinal-products/ eudralex/eudralex-volume-4_en 3. USFDA Current Good Manufacturing Practice, https://www.fda.gov/drugs/ pharmaceutical-quality-resources/current-good-manufacturing-practice- cgmp-regulations 4. Other non-regulatory GMP resources like ISPE, PDA, etc