	Title: Guidelines on the GMP Inspection of Local or Foreign Pharmaceutical Manufacturing Companies Marketing their Products in Sierra Leone	
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Approved by Board	

Pharmacy Board of Sierra Leone,

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1.0 INTRODUCTION

A company applying with the Pharmacy Board of Sierra Leone (the National Medicines Regulatory Agency) for the registration of a medicinal product in Sierra Leone must provide acceptable evidence to show that the manufacturer of the product follows an internationally accepted standard of Good Manufacturing Practice (GMP) and recognized by the Agency in Sierra Leone.

GMP inspections are conducted as one of the requirements for registration of medicinal products in the PHARMACY BOARD OF SIERRA LEONE in Sierra Leone. Such inspections are also conducted to verify compliance with GMP requirements. Inspection involves review of documents, records, facilities, etc.

Sections 40 and 41 of the Pharmacy and Drugs Act, 2001 provides the legal basis for the systematic audit of a facility that manufactures drug components or finished drug products intended to be marketed and use in the country.

Consistency in conducting GMP inspection activities are very important in ensuring quality assurance of pharmaceuticals by the PHARMACY BOARD OF

SIERRA LEONE. This results into common decision making by GMP inspectors at the end of inspections and thus avoiding complaints from manufacturer.

This guideline developed in accordance with the WHO/EU/(PIC/S) Good Manufacturing Practice guidelines, and it is intended to control the manufacturing of medicinal products for their importation and use in the country. It defines procedures to be followed when preparing and planning for inspection, reporting requirements, including format and classification system adopted for non-compliances observed during GMP inspection.

Various working documents are also referred to in this guidelines to help inspectors to comprehend matters related to GMP. It is also expected that the guideline shall help inspectors to conduct GMP inspection with integrity and diligence.

2.0 Objective

The objective of the GMP inspection is to assess the conformance of manufacturers to GMP requirements and ensure quality of products that are registered or in the process of registration or re-registration or variation /change of manufacturing site or procedure.

The purpose of this guidance is:

- To provide information on the types of GMP evidence acceptable to the PHARMACY BOARD OF SIERRA LEONE in Sierra Leone.
- To provide the requirements for an on-site inspection of manufacturing facility where GMP evidence of the premise is not available or

acceptable to the PHARMACY BOARD OF SIERRA LEONE in Sierra Leone

3.0 SCOPE

The guideline is applicable for all types of GMP inspections for pharmaceutical manufacturing plants of API and finished Pharmaceutical Product.

4.0 SPECIFIC REQUIREMENT

4.1 Types of inspections

There are different types of inspection as indicated below:

a) Concise inspection
b) Follow-up inspection
c) Special inspection

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 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.

4.3 FOLLOW-UP INSPECTION

A follow up inspection is also referred to as a re-inspection or a reassessment of the manufacturing 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 GMP non compliances that have been observed. A follow up inspection shall be unannounced.

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. Special inspection is conducted under the following circumstances:

a) When there are complaints about a specific product that suggest there may be defects.

b) When there is a product recall due to events such as adverse drug reactions.

c) To gather specific information, or to investigate specific operations of the manufacturing processes.

The inspection shall be unannounced.

FREQUENCY OF INSPECTIONS

The frequency of inspection of local and foreign manufacturers shall be as follows:

4.5 LOCAL PHARMACEUTICAL MANUFACTURERS

According to the risk based:

- Manufacture of vaccines and other biological follows every year,
- Manufacturer of injectable and other sterile products follows every 2 years,

4.6 FOREIGN PHARMACEUTICAL MANUFACTURERS

Prior to initial approval and once every 3 years subjected to waiver of inspections for sites inspected by a Reference Authority.

4.7 PLANNING FOR GMP INSPECTIONS

The preparation for GMP inspection shall be as per the PHARMACY BOARD OF SIERRA LEONE Procedure for Preparation for GMP Inspection (PBSL – SOP - 94) . The guiding principles for the inspection exercise shall include the following:

a) All pharmaceutical-manufacturing sites at which human drug products (finished pharmaceutical products, biologicals, vaccines, medical devices, herbal medicines, etc.) used in Sierra Leone are manufactured shall be subjected to cGMP inspection (that is, inspection of storage of raw and packaging materials, dispensing, formulation, processing, packaging, quality control and release) by the Pharmacy Board of Sierra Leone (The National Drug Regulatory Agency) before the drugs are registered and at least once every three years.

b) The current Good Manufacturing Practices (cGMP) Guidelines as published by the World Health Organization (WHO), Pharmaceutical Inspection co-orperation Scheme (PIC/S) and the Pharmacy Board's statutory requirements for manufacture of drugs shall be the basis against which the Agency shall inspect local and foreign manufacturing sites for GMP compliance.

c) The Factory Inspectorate and Import Control Department of the Pharmacy Board shall coordinate cGMP inspection of all local and foreign pharmaceutical sites at which human drugs used in Sierra Leone are manufactured.

d) Each site of manufacture shall be inspected by at least two qualified cGMP inspectors for at least two days (depending on the number of manufacturing lines at each site) using the approved cGMP Inspection checklist.

e) The inspection shall be announced and based on all plant processes, systems and production lines.

f) While planning for GMP inspection, the following categories of manufacturers will be considered:

i. The domestic manufacturing sites/facilities shall be inspected from time to time with the PHARMACY BOARD OF SIERRA LEONE's recommendation – after that at least once in two years for routine GMP inspection.
ii. All new manufacturing facilities intended to market medicines in Sierra Leone located within the ECOWAS region with their own and contracted manufacturing sites shall be inspected at regular intervals in accordance with the Pharmacy Board of Sierra Leone's recommendation.
iii. facilities located in reference countries of the Pharmacy Board of Sierra Leone shall be inspected when critical issues reported.

g) Inspection of a foreign pharmaceutical may be initiated through re – inspection after a period of three years from the date of the last inspection or by direct application for GMP inspection or re-inspection by the manufacturer or his/her representative before any dossier is submitted or following a critical failure.

h) At least two months prior to the anticipated inspection trip, the Agency shall send to the applicant through their Local Agents the form for "Application for GMP Inspection" accompanied by the respective invoice for inspection fees.

4.8 GMP Schedule

The following criteria shall be used in making a schedule out of those due for cGMP inspection:

a) Sites from which applications for registration (Dossiers) and/or inspection have been received.

b) Companies that were the first to apply for registration and/or inspection.

c) Company that were the first to pay for inspection.

d) Sites whose inspection would be crucial in making an ongoing regulatory decision or meeting an emergency or a public health priority.

e) Other companies may be included on the schedule in order to make a particular inspection trip cost-effective and geographically logical because of their proximity.

f) A balance shall be made between the available human resources for cGMP inspection and other operations of the Agency.

Each inspection trip shall cover at least 3 manufacturing sites, unless expressly authorized by the Registrar of the Agency.

The most current version of the cGMP/Quality Assurance Audit Checklist and the Guide for the cGMP Inspector shall be used in conducting and preparing the report of the inspection.

The Agency shall communicate the findings of the cGMP audit and the decision of the Technical Committee to the management of the inspected sites within 10 working days following the discussion of the audit report.

The summary of the decisions of the Technical Committee and any corrective action from the applicant shall be presented to the Committee on the National Formulary for consideration, and approval by the registrar.

The management of the inspected site shall have a right to appeal the decision of the Technical Committee within one calendar month of communication of the decision.

The appeal shall be considered at the next scheduled meeting of the Technical Committee and subsequently the Committee on the National Formulary (CNF).

The decision of the Agency (The Board) on the advice of the Committee on the National Formulary on the appeal shall be the final NDA position on the cGMP status of the inspected site.

4.9 The composition of the inspection team

The lead inspector and one other inspector should be with enough previous experiences relevant to product category. (Ex: - Vaccines, Sterile product) (SOP-MFR-005)

4.10 Duration of the inspection

Vaccine & other biological products - 5 to 7 days

Non biological sterile products - 3 to 5 days

Other - 2 to 3 days

4.11 INSPECTION REPORT

Inspection report should be written immediately after completing the inspection. The compiled report shall be shared within the members of the pier review committee for GMP inspection within fourteen (14) calendar days upon completion of inspection.

GMP inspection report is sent to the inspected facility within thirty (30) calendar days after completing the inspection. GMP inspection report shall be written according to the WHO TRS 996 Annex 4 Model Procedure for Preparing GMP Inspection Report (SOP-MFR-003) & (SOP-MFR-005) sufficient details should be provided to allow for an independent assessment, comprehension and easy decision making.

Where observations are included in the report, clear distinction should be made between "compliances" and "non-compliances". Non-compliance observations should be classified as "critical", "major" and "minor". These classes are detailed below.

4.12 CLASSIFICATION OF GMP INSPECTION OBSERVATIONS

Overall, the evaluation should commensurate with the nature and extent of the deviations (i.e. severity).

Non-compliances should be noted by Inspectors and classified as critical, major and minor according to the WHO guidelines on quality risk management (WHO Technical Report Series, No. 986, Annex 6, 2014), Procedure for Risk Classification of GMP deficiencies

4.13 RECOMMENDED REGULATORY ACTION(S)

Category of non-compliance	Regulatory action(s)
11 1. Minor Critical given	• Recommend corrective action within a timeframe

	• Request for compliance report
11.2 Major	• Issue warning letter • Recommend corrective action within a given timeframe • Recommend temporary withdrawal or suspension of Marketing Authorization • Follow-up inspection to verify implementation if necessary
11.3 Critical	• Recommend corrective action within a given timeframe • Request for compliance report • Recommend permanent withdrawal of Marketing authorization in case • Recommend suspension of marketing

authorization in case of registered products

- Recommend not to grant marketing authorization for new application

4.14 APPEAL

Any manufacturer may appeal to any decision of the Pharmacy Board of Sierra Leone. When a manufacturer appeals to a decision of the Pharmacy Board of Sierra Leone, the written submission by the manufacturer will be evaluated by the Pharmacy Board of Sierra Leone. The Pharmacy Board of Sierra Leone will then decide whether to accede to the appeal of the manufacturer after evaluating the submitted reason (s) of the appeal. The Pharmacy Board of Sierra Leone may consider the reason (s) and motivation for appeal and accept or reject the appeal according to the national regulations.

4.15 ADMINISTRATIVE REQUIREMENTS

4.14.1 Submission of Application and payment for GMP Inspection

i. An application to conduct GMP inspection in a foreign Pharmaceutical manufacturing site(s) shall be made in writing to the Board. The application shall be forwarded to the office of the Registrar of the Pharmacy Board of Sierra Leone using the under-mentioned address:
   a. C/o Central Medical Stores compound
   b. New England Ville
   c. Freetown, Sierra Leone

d. West Africa

ii. The applicant shall be a registered manufacturer licensed by the Pharmacy Board or a registered manufacturer's representative or local agent in Serra Leone. The application for the GMP inspection shall be accompanied by:

iii. Payment of a Non-refundable GMP inspection fee

iv. Submission of a Site Master File (SMF).

v. On special request and under exceptional circumstances, applicants with products that are manufactured at more than one site may be considered for a reduced fee for the extra site(s) if the extra site is located in the same country as the initial site or does not fully manufacture any other product eligible for cGMP inspection.

vi. Sites that manufacture vital drugs on the Essential Drug Lists of Sierra Leone with no other or one registered source may, on written request and justification, be considered for inspection at a reduced fee.

vii. Payment of fees can be made by Bank Transfer to the Pharmacy Board Foreign Account. A company shall be placed on the schedule for inspection only after receipt of all the information specified in the "Application for GMP Inspection" and the appropriate fee.

4.14.2 COMPLIANCE WITH GMP REQUIREMENTS

A site shall be considered compliant with GMP requirements if it obtains:

a) An average score of ≥70% in the general sections as outlined in the inspection checklist (quality management and personnel, standard operating procedures, self - inspection, premises and equipment, warehousing areas, dispensaries and Quality control/Assurance). (See "Guide to Inspector on Use of GMP Inspection Checklist" for details).

b) A score of ≥70% in each production line.

c) No critical observation in the general sections or each production line following classification of all deficiencies as critical, major and minor (See "Guidelines for Risk Classification of cGMP Non-Compliances" for details).

d) Major and Minor deficiencies may be resolved through submission of written corrective action but critical deficiencies can only be resolved through a re-inspection. The re-inspection shall be after submission of corrective action and an application plus payment of the inspection fee. All the general sections of the facility must be re-inspected.

e) A combination of the following documents may be used to assess and accept the GMP status of companies/sites/production lines in countries with strong DRAs which may not be inspected immediately either as a result of existing mutual recognition agreements, after the first mandatory GMP inspection or as a result of prioritization:

i. Evaluation of cGMP certificate and/or manufacturing license issued by a strong DRA/Institution.

ii. Evaluation of a Site Master File (SMF) approved by a strong DRA/Institution.
iii. GMP inspection report (product based or plant based) from the local Drug regulatory agency or a strong international drug regulatory agency
iv. Photographs of any new room or equipment not used at the time of the previous inspection

4.16 Issuance of GMP Certificate

No critical observation in the general sections or each production line following classification of all deficiencies as critical, major and minor (See "Guidelines for Risk Classification of cGMP Non-Compliances" for details).

5.0 GLOSSARY

5.1 Critical Observation

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.

5.2 Major Observation

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.

5.3 Minor Observation

Minor observation means an observation describing a situation that is a departure from GMP, but has no significant impact on the product quality. It has low probability of affecting the quality or usability of the product.

5.4 GMP inspector

A GMP Inspector is an officer appointed by the PHARMACY BOARD OF SIERRA LEONE for the purpose of inspecting Pharmaceutical manufacturing sites in order to verify their conformity to GMP. The role of the inspector is to evaluate the compliance of site inspected in country and abroad, with the requirements of applicable regulations and guidelines published by PHARMACY BOARD OF SIERRA LEONE.

These sites may be

- Manufacturers and distributor of medicinal products
- Manufacturers of investigational medicinal product
- Site involved in the storage of medicinal product
- Manufacturers of the active pharmaceutical ingredients and certain excipients

The role involves inspecting, reporting and forming conclusions in respect of the suitability of a site for the activities which it has sought or for which it is already authorized.

The inspector provides technical information and advice to relevant individuals and organizations both internal and external to the PHARMACY BOARD OF SIERRA LEONE.

The inspector provides support to the enforcement and execution of national regulations in relation to medicinal products.

5.5 Lead inspector

Lead GMP Inspector is a Senior GMP Inspector who is charged with the responsibility for leading a GMP inspection team to undertake inspection of a specified pharmaceutical manufacturing site(s)

Key responsibilities

• Preparing ,organizing and carry out inspections in accordance with PHARMACY BOARD OF SIERRA LEONE procedures

• Write inspection reports when acting as lead inspector and contributing to preparation of reports

for joint or accompanied inspections.

• Assisting in the compilation of data and preparation of management report as required

• Applying risk management principle

• Submitting reports as required and maintain appropriate records of meetings and activities

5.6 Senior GMP inspector

A Senior GMP Inspector is an officer who by virtue of experience and competence is appointed as such to conduct GMP inspections and train junior officers in inspections after evaluation by the PHARMACY BOARD OF SIERRA LEONE as by the criteria outlined in the assessment form.

Report to lead inspector, the inspector will be primarily responsible for assessing the compliance of manufacturers with PHARMACY BOARD OF SIERRA LEONE guidelines

5.7 Specialized GMP inspector.

A Specialized GMP Inspector is a GMP inspector who possesses specialized knowledge and experience in conducting GMP inspections for specialized areas e.g., Biological, Blood products

6.0 REFERENCES
NONE

7.0 ANNEXES
NONE

Prepared by ***Reviewed by*** ***Approved by***

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