GUIDE TO THE cGMP INSPECTOR

On How To Use The

cGMP/QUALITY ASSURANCE

AUDIT CHECKLIST

For Manufacturing Facilities of Pharmaceutical Products

How to Prepare for, Begin and Conduct the cGMP Audit

*1.0 **Preparing for the cGMP Audit***

1.1 Review of Relevant Documents

At least two weeks prior to the inspection, a review should be made of the documents relating to the company to be inspected. These may include:

- Site Master File
- Registration dossiers for leading products of the company
- Market complaints and recall reports, where available
- Previous cGMP inspection report(s)
- List of products applied for registration in Malawi
- History of product failures during surveillance testing by NDQCL
- Reports of adverse drug reactions, where available
- Compliance reports if available

1.2 Announcement of Inspection

Announced inspections cover regular or routine inspections to evaluate new plants and new production lines and to decide on the renewal of licence or market authorization. In this type of inspection the company management has to be officially notified of the inspection before the visit.

Unannounced inspections may be necessary for Concise, Follow-Up and Special inspection visits. In this case the company management may not be notified.

1.3 Planning and Scheduling cGMP Audits

The cGMP audit/inspection has to be carried out by at least two GMP Inspectors from PMPB. The GMP Inspector shall be a Pharmacist with at least one with an industrial background in pharmaceutical production and with expertise in production, quality control and cGMP.

The estimated time to carry out a thorough, factual and fair cGMP Inspection Audit of a pharmaceutical manufacturing facility in accordance with this checklist is twelve hours. It is therefore strongly recommended that each facility to be inspected be allocated a minimum of **two days subject to the number of production lines**. Planning should take this requirement into account.

1.4 Role of the cGMP Inspector

The primary responsibility of the cGMP Inspector is to perform the cGMP inspection and present a detailed factual report on the standards of manufacture and controls applied to specific products to PMPB in accordance with the PMPB report format described under section 5.0 of this guide.

1.5 cGMP Re-Inspection of a facility

When a facility is re-inspected for a particular production line then **all** the **seven general sections** of this Audit checklist, namely: quality management and personnel, standard operating procedures, self inspection, premises and equipment, warehousing areas, dispensaries and quality assurance /quality control shall be re-inspected and reported.

2.0 *How to begin the Audit*

2.1 Who should be involved in the Audit?

The team to carry out this formal audit should be comprised of at least two PMPB GMP Inspectors. The company team should have representatives from each of the following departments: Production, QC/QA, Warehousing, Maintenance, Administration/Personnel and Marketing/Sales. The General Manager or Managing Director should also attend and any other relevant personnel.

2.2 The Pre-audit Meeting

An entry briefing/pre-audit meeting should be held between the PMPB GMP inspectors and the company team. The PMPB team leader should chair the meeting and guide the audit team. During this meeting, credentials should be presented, the purpose of the inspection discussed and the audit programme developed. The PMPB inspectors should develop and follow this plan independently, without influence from the company.

A list of critical documents that may not be found should be presented to the company team. The latter should gather the documents in one central location for subsequent review by the PMPB GMP Inspectors.

The documents may include the following:

- Site Master File
- Manufacturing License
- Organizational Chart
- Job Descriptions for key personnel
- Appointment Letters
- GMP Training records
- Medical examination records
- Self inspection procedure and records
- SOP for writing SOPs
- SOP for change control
- Market complaints and product recalls procedures (SOP) and records
- SOP for sampling of raw materials, in-process materials and finished products
- Shelf-life determination program and records
- Validation Master Plan

- Protocols for process Validation
- Process validation reports eg products manufactured, equipment
- Cleaning validation protocols and reports
- Analytical method validation protocols and reports for non-pharmacopoeia analytical test methods used.
- Installation and operation qualification (IQ & PQ) reports for critical equipment.
- Seven consecutive batch records (BMRs) of one leading product for each functional production line.
- Manufacturing and QC Equipment preventive maintenance schedule(s) / plan and records.
- Environmental control test reports for clean-rooms and other controlled environments.
- Any other specific document as the PMPB inspector may decide.

3.0 ***How to conduct the audit?***

The audit team has the authorization to review any record that they deem necessary.

3.1 The entire team should as much as possible try to work together during the audit.

3.2 The audit team walks through every section of the plant and carefully reviews every paper, record or area that is specified in the formal audit checklist no matter how familiar one member of the team is with the checklist item or the area. **Nothing is assumed.**

3.3 Each record, procedure and report is challenged. A good tip is to retrieve all forms, records and samples of a given batch selected randomly from one of the batches made within the last six months. The following records should be challenged for **completeness and correctness** for the selected batch:

- Raw materials requisition and weighing records

- Manufacturing records and procedures
- Dosing/filling records and procedures
- Bulk product sampling and release report
- In-process control record
- Packaging and labelling records.
- Packaging materials requisition and accountability records.
- Specimen of packaging and labelling materials used for the batch.
- Line clearance records before and after each critical production stage
- Status labels that identify the materials, equipment and room that were used to produce the batch.
- Sterilization records, in case of sterile preparations, including time-temperature charts in the case of heat sterilization methods.
- Incident /Deviation record
- Finished product Analytical Report/ Certificate of Analysis
- Record for final review of batch manufacturing records by Qualified Persons in Production and QA/QC Departments
- Batch release record by the Qualified Person in QA Department.

3.4 The checklist is provided for use by the PMPB GMP Inspectors to ensure that all areas of the operations are investigated to verify adherence to the cGMPs. Each applicable question is **promptly** marked Yes or No according to the **current actual status observed** by the PMPB audit inspector during the audit and **not** according to the **intent** or the **future plan**.

3.5 Under the observations/comments sections, notes should be recorded of status of conditions as a guide for improvements to be recommended. **Specific observations made** for any quality assurance areas **not covered in this checklist** should also be noted under observations/ comments provided in the checklist.

3.6 Ask questions where appropriate (not necessarily as written in the checklist) and carefully listen to answers. Make observations of work-in-

progress. Crosscheck with SOPs and records available for adherence and positive evidence of compliance.

Promptly record all observations and comments in a legible and retrievable manner in the checklist.

3.7 Under each section of the audit, add up the questions that have positive, negative and not-applicable answers. Enter the scores in the sub-total of each section.

4.0 Exit/Wrap-up Meeting

After the audit and before the PMPB GMP Inspectors leave the premises, a final discussion with company management is recommended. There should list of the main findings, which should be signed for by both the inspectors and the company team. The PMPB GMP Inspectors should list any unsatisfactory findings and outline any deficiencies/violations of cGMP they have found, to which the company management may wish to respond.

5.0 Format *and Content of the Inspection Report*

5.1 Writing the Report

The cGMP/QA Inspection Report Format is shown on page 9 of this guideline. Follow this report format to write the cGMP/QA report of the facility inspected.

The report is written from the observations, answers and notes recorded in the Audit Checklist during the inspection.

The first page of the report should be printed on PMPB headed paper.

5.1.1 Consensus must be achieved on each answer by the PMPB audit inspectors. If part of a multi-party question is answered negatively, then the answer should be NO.

5.1.2 Calculate the percentage score of all questions answered/observed to be YES over the total questions found to be applicable in each section

5.1.3 Transcribe the calculated sub-total percentage score for each applicable section on to the Summary Score of cGMP Inspection form shown.

5.2 Submission and distribution of the Report

The typed report should be submitted to the Registrar of PMPB and copies distributed to all members of the Evaluation Subcommittee not later than **10 working days** after returning from inspections.

5.3 Submission of the cGMP/QA Audit Checklist booklets

The cGMP/QA Audit Checklist booklets that the PMPB cGMP Inspectors used during the inspection should be handed over to the Chief Drug Inspector in case of foreign facilities.

5.4 Confidentiality Undertaking

All cGMP Inspectors and Evaluation Committee members should note that all information, documents, etc submitted to them and observed during the site visits, and the reports made in connection with the cGMP inspections must be treated as strictly confidential and proprietary to PMPB or parties collaborating with PMPB. All reasonable measures should be taken to ensure that such confidential information is not used for any other purpose, other than the assessment of the facility for consistency in production and quality control, through compliance with cGMP.

All Parties concerned are therefore hereby obliged to comply to this confidentiality undertaking. Therefore the inspectors are required to take an oath.

cGMP Inspection Narrative Report Format

1.0 General Information

1.1 Inspected Site(s)
Name, location, full address and manufacturing license of the inspected site or facility.

1.2 Inspection date(s) Date(s), Month, Year

1.3 Purpose of Inspection
Brief description of the objective(s) or reason(s) for the Inspection

1.4 GMP Inspectors
Name of the PMPB GMP Inspectors that carried out the inspection. The PMPB team leader should be specified.

1.5 Company management team
Name, qualifications, positions and signatures of the management team

1.6 Introduction
Short description of the company and the activities of the company.
Date of previous inspection and names of GMP Inspectors involved.
State major changes made on the facility, equipment, products, and senior personnel since the previous inspection should be stated.

2.0 Brief Report of the Inspection activities undertaken

2.1 Scope of Inspection
Short description of the Inspection. State the type of inspection i.e. Routine, Concise, Follow-up or Special Inspection carried out; and whether it was product related inspection and/or general cGMP inspection.

2.2 Observations and Findings
Specify each area of the facility that was inspected. Use headings from the PMPB checklist **relevant** to the scope of the inspection. New headings may be introduced where necessary.

Changes, improvements, and examples of deterioration since the previous inspection should be reported.

Positive observations should take the form of a description of the processes that the firm is carrying out particularly well and that may be considered exemplary compliance to cGMP.

Negative observations (non-compliances with cGMP requirements) should distinguish between whether the defect lies in the system itself or in the

failure to comply with the system. For instance, when cleaning is found to be sub-optimal, it is important to know whether the SOPs are inadequate or lacking, or whether adequate SOPs exist but are not followed by personnel.

Names, designation, Signatures and date

The report should be signed and dated by the cGMP Inspectors that carried out the Inspection.