Guidelines for Selection of External Auditor Team For Site Assessment and Preparation For EU-GMP inspection leading to EU-GMP Certification

1. AIM

To assess and prepare KAPL manufacturing sites to meet EU GMP standards leading to EU GMP certification

2. SCOPE

Evaluate and Assess four manufacturing blocks of KAPL to be prepared for the EU GMP Inspection

- **Cephalosporin Dry Powder Block**
- **New Non ParenteralBlock**
- **Liquid Injectable Block and**
- **Beta Lactum Dry Powder Block**

This document will detail the scope of work to be carried out as part of the assessment/ audits and beyond. It will also include the audit process employed by EU competent authorities (CAs) in charge of GMP inspections, manufacturing authorizations, and quality defects of medicinal products.

1. Procedure

1.1 Objectives

The objectives of the approved vendor – auditors will be to assess compliance of the site in line with Commission Directive 2003/94/EC, of 8 October 2003, laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use.

From here on this document, aims to explain the work and methodology the Vendors-Auditors team shall employ in achieving this target.

1.2 Scope

Each individual audit is based on a clearly defined scope.

The scope of the audit covers all elements of defined objectives and needs to cover all the elements described in the audit scope; ***See section 3.1***
The Vendor-Auditors shall identify the Gaps, perform Gap-Analysis. They shall also propose Corrective action to bridge the gaps with potential time lines required to address the gaps. Resources in terms of infrastructure and manpower must be outlined along with approximate cost implications to ensure EU-GMP compliance

1.3 Requirements

The requirements of the audit are those specified in the relevant audit documents.

1.4 Feasibility of the audit

The Vendor-Auditor team shall identify the overall resource necessary such as the team leader, the audit team members, and make provision for any other resources required for the authority inspection.

2. On-site auditingactivities

2.1. Audit plan

The Vendor-Auditor team shall prepare the audit plan, which shall be reviewed and accepted by the auditee [KAPL]. The audit plan includes:

- The audit objectives and scope
- The audit requirements
- The date and place where the audit is to be conducted
- The identification of functional units to be audited
- The identification of the individuals within the auditee having significant direct responsibilities for the units to be audited
- The expected time and duration for audit activities, including meetings with auditee's management, observed inspections and audit team meetings
- The working and reporting language of the audit
- The identification, roles and responsibilities of auditors and any accompanying persons (if any)
- The confidentialityrequirements
- The audit report topics, format and structure, expected date of issue and distribution
- The amount of details provided will differ between initial, re-assessment or follow-upaudits.
- The audit plan is adapted to suit the size and complexity of the auditee. The amount of details and depth of the audit will differ depending on the type of theaudit.

2.2. Audit teamwork assignments

If necessary, the Vendor-Auditor team shall assign to each member of the team responsibility for audit specific elements. Such assignments take into account the efficient use of the resources. Changes to the work assignments can be made to ensure the achievement of the audit objectives.

3: Performing the on-site auditing activities

3.1 Audit Scope

The Audit will aim to ascertain the site meets requirements laid down in the following EU GMP Chapters of Volume 4 EU GMP as required under the Commission Directive 2003/94/EC

- *European Union (EU) GMP guide part I: Basic requirements for medicinal products: Chapter 3: Equipment*
- *European Union (EU) GMP guide part I: Basic requirements for medicinal products: Chapter 3: Shared manufacturing facilities*
- *European Union (EU) GMP guide part I: Basic requirements for medicinal products: Chapter 5: Qualification of suppliers*
- *European Union (EU) GMP guide part I: Basic requirements for medicinal products: Chapter 8: Complaints, Quality Defects and Product Recalls*

- *EU GMP guide part II: Basic requirements for active substances used as starting materials: GMP compliance for active substances*
- *EU GMP guide part II: Basic requirements for active substances used as starting materials: GMP compliance for active substances in investigational medicinal products (IMPs)*
- *EU GMP guide annexes: Supplementary requirements: Annex 1: Manufacture of sterile medicinal products*
- *EU GMP guide annexes: Supplementary requirements: Annex 6: Manufacture of medicinal gases*
- *EU GMP guide annexes: Supplementary requirements: Annex 8: Sampling of starting and packaging materials: Glycerol*
- *EU GMP guide annexes: Supplementary requirements: Annex 8: Sampling of starting and packaging materials: Use of near-infrared (NIR) technology for container-wise identity testing*
- *EU GMP guide annexes: Supplementary requirements: Annex 11: Computerised systems*
- *EU GMP guide annexes: Supplementary requirements: Annex 13*
- *EU GMP guide annexes: Supplementary requirements: Annex 16*
- *EU GMP guide annexes: Supplementary requirements: Annex 19: Reference and retention samples (Updated)*
- *General GMP*
- *GMP certificates and manufacturing authorisations*
- *Data integrity*

3.2 Collecting information

Information can be obtained in different ways from several sources such as:

- interviews
- observations of activities (as observed inspections) and the surrounding work environment and conditions
- internal documentation
- records, reports, meeting minutes

3.3 Evaluating evidence

The information collected during the audit shall be verified or confirmed by the Vendor-Auditor team, using alternative sources where possible. Such information, after verification, can be considered as objective evidence, which will then be evaluated for significance relative to the specified requirements. Information that appears relevant but cannot be verified shall be identified and recorded. Copies of working documents shall be provided during the audit, if necessary.

Evidence suggesting non-conformities shall be noted and investigated as part of the audit.

If a significant concern arises which is outside the scope of the audit, it must be reported to the auditee.

4: Reporting on the audit

Audit report preparation

The Vendor-Auditor team shall ensure that the preparation of the report is homogeneously distributed among the KAPL team.

Report content

The Evaluation –Assessment audit report shall provide all interested parties with an accurate record of the audit findings and conclusions. These can include whether:

- The system conforms to the specified requirements
- The system is properly implemented and maintained
- The implemented quality system is effective in meeting stated policy and objectives
- Recommendations for improvement when agreed shall then be drafted by the Vendor Auditor Team and presented to KAPL team for review, approval and implementation.
- Corrective action to bridge the gaps with potential time lines required to address the gaps must be presented
- Resources in terms of infrastructure and manpower must be outlined along with approximate cost implications to ensure EU-GMP compliance