1 Purpose

To provide guidance on assigning Lead Audit Team/Site responsibilities, establishing an external supplier's audit program, and the high level principles involved in conducting supplier audits.

2 Scope and Applicability

This Guideline is applicable to all manufacturing Operations and Research and Development sites performing audits of suppliers used by the buyer company. This includes routine audits, "for-cause" audits and initial supplier selection audits.

Note: this document does not cover computerized systems supplier audits.

Note: this document does not cover the certification process for materials/services supplied to the

3 Definitions

3.1 Audit

A systematic and independent examination to verify that the quality influencing activities comply with relevant regulations as well as company policies, standards, procedures and guidelines.

3.2 Lead Audit Team (LAT)

The team that is accountable for conducting audits of vendors facilities on behalf of Operations

3.3 Active Pharmaceutical Ingredient (API)

Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product that when used in the production of a drug becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure and function of the body.

3.4 Certification

Is the act of approving (accepting) quality control results provided by the supplier in relation to a specific material, thereby eliminating the need to undertake some or all laboratory tests on receipt of that material unless specifically required to meet regional/local GMP and/or import regulations.

3.5 Decertification

Is the act of reverting back to full or partial analysis on receipt of the material from the supplier.

3.6 Material

manufacture of an API or finished product that is not a process chemical (solvent), API raw material/intermediate, excipient or packaging material. Examples are filters, and disposable tubing used in the manufacturing process.

A GMP critical consumable is defined as where failure to specify and control quality requirements could adversely affect product quality/patient safety.

3.14 Non-Contributory Raw Material (NCRM)

Is a raw material used in the production of an API that does not contribute to the final molecular structure of an API (e.g. catalyst, water/solvents that are dried off in process, cleaning fluids).

3.15 Lead Team only applicable to Contracted Materials

The Lead Team/Site is the team/site accountable for conducting specified material related QA activities. Usually the QA Management of the buyer site acts as a Lead Team for the buyer (Lead site). Lead site/Team would be responsible for GMP related interactions and issues, conducting audits, and development of the Quality Assurance Agreement.

3.16 API Starting Material [Contributory Raw Material (CRM)]

A raw material or intermediate, that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API Starting Material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. API Starting Materials are normally of defined chemical properties and structure.

3.17 Packaging Component - Critical (PCC)

Is any printed packaging component, primary (product contact) component or device. Furthermore any secondary packaging component critical to the microbiological integrity, stability and/or administration of the product (e.g. aluminum pillow packs around semi-permeable).

3.18 Packaging Component - Non-Critical (PCNC)

Is any non-printed or secondary (non-product contact) packaging component or device that does not fall within the definition of a PCC.

3.19 Sterile Active Pharmaceutical Ingredient (SAPI)

Is an API isolated and stored in a way that ensures its sterility for subsequent use in the preparation of a sterile formulated product that is not subjected to further aseptic or terminal sterilization.

3.20 API Intermediate (INT)

A material produced during steps of the processing of an API that undergoes further molecular change or purification before it becomes an API. Intermediates

5 Guideline

5.1 Selection of Lead Audit Team

The Lead Audit Team shall be assigned on the following basis: knowledge/experience of the type of manufacture/service being supplied, the proximity to the supplier and the cultural awareness of the supplier.

5.1.1 Availability of Resources

After accepting the Lead Audit team assignment, Operations and QA are accountable for establishing the appropriate level of trained personnel and resources to conduct the audits.

5.2 Change in Lead Audit Team Assignment

It is Supply Chain responsibility to re-assign Lead Audit team.

5.3 Audit Program

The designated LAT should establish a rolling routine scheduled audit program. This program should be recorded. Changes can only be made with the agreement of the Receiving Sites involved with that supplier.

5.4 Audit Frequency

On-site supplier selection audits of critical materials/services will be conducted for all new suppliers, preferably before the use of material in manufacture.

The minimum assigned routine scheduled audit frequency should be based upon criticality and the following guidelines are provided:

Suppliers of	Audit Frequency (months)		
	12	24	36
Sterile Finished Products	X		
Non-Sterile Finished Products		X	
General Services*			X
Sterile API and Sterile Excipient for Sterile Finished Product	X		
Non-Sterile API and Non-Sterile Excipient for Sterile Finished Product		X	
Non-Sterile API for Non-Sterile Finished Product			X
Non-Sterile Excipient for Non-Sterile Finished Products			X
XIntermediate			X
API Starting Material (CRM)			X
NCRM			X**
Consumables (critical)			X
Consumables (non critical)			X***

During the audit, the Lead Auditor shall ensure there is a review of the Quality Assurance Agreement, the issues associated with the supplier's laboratory test methods and specifications agreed with buyer.

Observations shall be discussed with the relevant facts at hand, preferably when and where observations are made.

At the end of the audit (e.g. the 'Closing Meeting'), comments (including observations) to be included in the report should be discussed with the supplier.

5.9 Audit Reporting

Immediately upon return to the office the Lead Auditor should record the date of the audit and the auditor's name and mark the materials covered by the scope of the audit. Additional audit related information should be added to the database as it becomes available.

All Receiving Sites should be informed on critical observations as soon as possible.

Each audit shall be documented in a report. Audit reports are confidential and shall be marked as such. The report should not to be shared with other companies. The only exception is when Authorities request a copy of the audit report.

The Lead Auditor shall make the audit reports available to the Receiving Sites.

The audit report shall include paragraphs specifically addressing the issues on laboratory test methods and conduct of quality control tests on materials supplied to buyer as a basis for making/re-confirming the LAT certification recommendation.

The audit report shall be available in English or, in the case of a local supplier, in the local language (an English summary may be included). Audit reports should be issued within 30 calendar days after the audit, unless critical observations have been identified. The report should be sent to the supplier (signed and in pdf format) and its inclusion notified to the receiving site(s). The supplier should be requested to provide a formal response to the audit observations within 30 calendar days of its receipt, unless critical observations have been identified.

Audit observations may be presented in the form of a table at the Closing Meeting (see below) by hand or by electronic form (like Word format) at the Closing Meeting.

The table can then be typed and formally issued with the audit report. The audited supplier may then complete their proposed follow-up action, by whom and when, in order to formally track the responses progress through to closure). Once the Lead Auditor is satisfied with progress, the "date observation closed out" and "closed out by" can be added to the observation table and the formal audit closure record.

5.10 Audit Follow-up

Once the initial audit response and resultant actions, including timescales, have been agreed with the supplier, the Lead Auditor (or designated nominee) that conducted the audit shall track progress of outstanding Critical and Major audit observations and resultant actions. Critical observations should generate immediate corrective actions. If no response is received by the due date the LAT/QA Site will issue a reminder to the supplier and agree upon a new date for the response. If no response is received 30 calendar days from the agreed new date a formal complaint may be raised.

Upon satisfactory response to actions and/or observations by the supplier, the LAT/QA Site, after recording the supplier's response, can close the audit, sending out an audit closeout letter. The LAT/QA Site may then inform the supplier of its status within the buyer company. Receiving Sites should be informed when the audit is closed.

5.11 Archiving of audit documentation

Master copies of audit reports, questionnaires, SQR, etc. should be retained by the LAT/QA Site for a minimum of 6 years past audit (including postal audits). Electronic copies should be made available.

5.12 Audit Standards

The standards in the following table are those that are recommended for an audit of the listed material. The supplier should be requested to meet any agreement made with buyer regarding the audit standards, which are those included in a Quality Assurance Agreement or those presented during the audit preparation or at the opening meeting.

