Auditing a Microbiology Laboratory in One Day or Less

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Summary

- Preparing for the audit
  - Defining the audit scope, purpose & standards
  - Selecting the audit team
  - Setting the agenda
  - Collecting information and creating a checklist

- Conducting the audit on the day
  - Opening & closing meetings
  - Process approach to auditing
  - Risk evaluation and prioritisation
The limitations of the audit process

An audit is only a “snap-shot” in time

Tips for success:

- Preparation
- Risk evaluation (before/during)
- Audit skills (questioning/listening/observing/recording/analysing)
Defining the audit scope & purpose

Having a clear audit scope and purpose defines the objective of the audit and defines the audit boundary

- **Scope**
  - Products or materials tested /services supplied

- **Purpose**
  - Qualification
  - Routine
  - For cause
Auditee / Auditor Relationship

The nature of the relationship and reason for audit can have a significant impact on the audit process:

- **Contract manufacturer** – micro lab likely to be a small part of a bigger audit, some aspects of QMS review may be covered elsewhere.

- **Contract test lab** – customer confidentiality will restrict the data you can review / areas you can visit.

- **Qualification** – focus on QMS, no test data available.

- **For cause** – limited scope with in-depth review, auditee may feel defensive.

- **Self inspection** – unlimited access to data, beware of familiarity & conflict of interest.
Defining the audit standards

- Must be able to reference any observations to the audit standards to be able to explain/defend them
- Used to create an audit checklist
- Examples include
  - Regulatory guidelines (EU GMP, FDA CFR, PIC/S, WHO, ISO)
  - Quality agreement
  - Customer specified test methods
  - Pharmacopoeial methods
  - Marketing Authorisation
Selecting the audit team

Given the limited amount of time available it can be useful to have an audit team.

- Define responsibility for areas of review in advance
- Beware of industrial tourism!
- Trained auditors – who will lead
- Subject matter experts – set expectations
Role of the Lead Auditor

The lead auditor is responsible for ensuring the audit is managed effectively and efficiently

Before the audit
- Agreeing the audit date
- Sending out the agenda
- Agreeing responsibilities of audit team members
- Collecting and disseminating pre-audit information
Role of the Lead Auditor

On the day

- Conducting audit opening/closing meetings
- Keeping track of progress of audit team members
- Re-prioritisation of areas for review, if required

After the audit

- Writing the report, with input from the other auditors
- Feedback to management/end-user
- Approving the CAPA plan
- Tracking observations to completion
Pre-audit information gathering

Used to identify areas of risk and prepare a checklist

- Supplier history / scorecard
- OOS
- Complaints
- Changes since previous audit
- Supply chain
- Previous audit report
- Status of observations from previous audit
Pre-audit information gathering

Used to confirm compliance and enable specific test data to be requested

- Details of batches tested
- Example CoA
- Registered test methods
- Product specification
- Regulatory certification
- Regulatory history
Creating a Checklist

A checklist helps you to mentally prepare for the audit and acts as an *aide mémoire* on the day.

Should include:

- Basic QMS elements
- Specific requirements of audit standards
- Areas of interest based on pre-audit information
Audit Agenda

Having a well defined agenda sets clear expectations enables the auditee to prepare any necessary information

- Scope and purpose
- Audit team
- Audit host
- Timing (start/end times, opening/closing meetings, tour vs. documentation review, lunch, auditor-only time)
- Areas/topics/documents for review (identify responsibilities for each auditor)
- Reporting & response times
Opening Meeting

To be held with site management & audit host, ensures the smooth running of the audit and set expectations.

- Introduction of auditors/auditees
- Company presentations (auditor’s should be brief)
- Confirm audit agenda
  - Logistics – which areas to visit and when
  - If the audit team will separate
  - Timings for lunch, auditor only time, closeout meeting
- Advance requests for documentation
Process Approach to Auditing

Input
- Materials
- Machines
- Methods

Process
- Measurement & Monitoring

Output
- Manpower
- Environment

QMS
Issues Management – Change Control – Docs & Records
Process approach to a micro lab audit

Sample Receipt → Analysis → Test Report → Sample Disposal

- Trending, Invalid Assays, KPI, CAPA
- Cultures, Reagents, Utilities
- Equipment
- Methods
- Training
- EM, Area Classification, Housekeeping

QMS
OOT/OOS – Change Control – SOP & Forms
Facility Tour

- Aim to begin with facility tours (helps with understanding during documentation review)
- BUT – may need to re-schedule to observe certain activities
- Restrict to areas related to the scope of the audit
- Select a batch - begin with sample receipt and progress in a logical order
Facility Tour

- Check logbooks, temperature charts etc. in use (ask first!)
- Speak to the people that actually perform the testing
- Use the tour to help request documentation specific to items/activities observed e.g.
  - Equipment documentation (qualification, PPM, calibration, temperature records)
  - Training records related to activities observed in-process
- Clearly state potential observations as you go to allow the auditee to respond
Document Review

- Reviewing of procedures – skip to process flow
- Due to customer confidentiality many only be able to see records related to testing performed for you
- Keep track of documents you’ve requested, tick them off as you receive them
- Advise auditee of order of priority for review
Process approach – sample handling

- Sampling plan – based on statistical methods
- Chain of custody & maintaining sample integrity
- Sample labelling & identification
- Sample checks on receipt
- Stability samples – pull vs. test time
- Retention sample storage/control
- Process for sample disposal
Process approach – testing

- Observe testing being performed where possible
- Specification for test article
- Review of test method & test records
- Method/specification complies with Marketing Authorisation/Quality Agreement
- Test records clearly identify who did what and when – actions attributable to specific analyst
Process approach – result reporting

- Comparison of test result vs. specification control
- COA format / template control
- COA format complies with specification & customer requirements
- Process for release to customer
- Impact of deviations on test result release
- Authorisation for test result approval
- Process for review/approval of outsourced work
- Trend analysis to ensure quality of test results
Process approach – measurement & analysis

- Review of quality KPI:
  - Performance vs. target for turn around time
  - Trend of invalid bioassays > performance of critical reagents
  - Customer complaints
  - CAPA effectiveness
  - Overdue CAPA
- Management review
- Trending of EM/bioburden and feedback (audit of CMO)
Process approach – materials

Materials management

- SOP for material receipt
- Inventory review – stock vs. actual
- Handling of materials supplied without expiry date
- Storage of temperature sensitive materials
- Control of rejects
- Reagent qualification/ certification
- Process for ensuring reagents not used until checked/released
- SOP for qualification of new reagent lots & extending re-test dates
Process approach – materials

Supplier Management

- Procedure for supplier selection/qualification/ongoing management
- List of approved suppliers
- Agreements
- Audit schedule
Process approach – equipment

- Equipment qualification (protocol/report, assessment for re-qualification)
- Equipment ID/calibration tags
- Equipment logbooks
- PPM schedules
- Maintenance reports
- Calibration schedules
- Calibration reports (as found vs. adjusted)
- SOP for calibration OOT events
Process approach – equipment

Computarised systems:
- Process for granting/removing access
- List of authorised users (periodically checked)
- Individual ID & password
- Limited Admin users (not analysts)
- Access levels defined
- Audit trail function switched on and reviewed.
- SOP for back-up/restoration of data
- Has the systems been evaluated for data integrity?
Process approach – methods

- Method validation (or tech transfer) protocol/report – as per ICH Q10
- Qualification of pharmacopoeial methods
- Process for revising test methods with pharmacopoeial updates
- Method change control & evaluation (control of “clarification documents”)
- Deviation from test method only with customer approval
Process approach – methods

Laboratory instruments:

- Instrument interface with SAP/LIMS
- Directory of networked instruments

Method control

- Methods locked
- Method parameters as per SOP
- Authorisation of changes to methods
- Audit trail function switched on, regularly reviewed, validated
Process approach – manpower

- Review records related to activities observed
- Training need identification / matrix
- Annual GMP training
- Assessment of competence:
  - Performance qualification
  - Gowning qualification
  - Aseptic technique qualification
- Job descriptions
- Sufficient trained staff
- Signature list
Process approach – environment

- Sufficient space
- Housekeeping
- Monitoring of environmental conditions where they may impact test results/production
- Effective separation between areas where necessary to prevent cross contamination (positive control vs. test samples)
- Area classification & pressure cascades
- Transfer disinfection
Process approach – QMS Deviations

- Deviation SOP
- Review example deviation investigations is possible
- Impact assessment considers severity & impact on other work & extent of root cause
- RCA investigation commensurate with risk
- Process for customer notification - Annex 16 certification QP “should be aware of and take into consideration any deviations which have the potential to impact compliance with GMP and/or compliance with the MA” – how communicated?
Process approach – QMS OOS/OOT

- OOS / OOT SOP
- Review of selected OOS investigations if possible
- Process for customer notification
- Lab investigation vs. manufacturing investigation
- Authorisation for re-test / re-sampling
- SOP for sterility test failure
- Annex 16 EU Import testing – OOS to consider material shipment qualification process (where shipped separately from batch)
Process approach – QMS Change Control

- Change control SOP
- Review of relevant change controls
- Appropriate pre-implementation/post-implementation actions & evidence of completion
- Pre-implementation approval / sign-off for closure
- Post-implementation effectiveness check
- Requirement to notify customers of significant changes
Process approach – Document Control

- SOP for document control
- Index of documents (revision status and distribution)
- SOPs approved prior to use
- Process for recalling superseded docs
- Periodic document review
- Document changes – altered text clearly identified
- Control of blank forms/records
- Archiving
  - Appropriate facility on/off site
  - Retention times
Risk Evaluation & Prioritisation

Prepare to deviate from your agenda to ensure the most important items are reviewed

- Insufficient time – focus on areas of highest risk
- Potential observation – expand your review to determine if issue is isolated, or systemic
- Critical observations - may need immediate notification/escalation depending on your procedure
- Lead auditor - periodically check progress with the audit team and clarify priorities where required
Follow-up of Previous Observations & CAPAs

- Was CAPA completed?
- Was CAPA completed on time?
- Effectiveness check – was root cause addressed?
- Process for tracking audit CAPA
- Any repeat observations – increase classification?
Preparation for the closing meeting

Useful to have some time alone to prepare for the closing meeting and compose yourself – even if you are auditing alone

- Agree who will say what
- Discuss potential observations within the audit team
- Carefully word any observations that are likely to be contentious
Closing Meeting

To be held with site management & audit host.

- Provide positive feedback if possible
- Clearly explain observations – include document references, explain gap vs. audit standard, check auditee has understood your concerns
- Do not classify observations – except critical observations
- Describe next steps – timelines for reporting & response/CAPA plan
- Say thank you!
Audit Reporting

- Timely issue of the audit report is a mark of professionalism and shows you value the audit process
- Audit report (internal) vs. Observation report (external)
- Be clear on timelines for the auditee response when the audit report is issued
Summary

- Preparation is the key to success on the day
- Focus on what is important / highest risk
- Take a logical process approach
- Items discussed here are not an exhaustive list!
Questions?