SELF INSPECTION AND AUDIT

SELF INSPECTION

- Part of Quality Management System, Chapter 8, CPOB, 2012

Principle and Purposes:

- To evaluate the manufacture Compliance and Incompliance with GMP
- To detect opportunity for improvement the GMP implementation and to recommend the necessary corrective action.

SELF INSPECTION

- Routinely
- Should be conducted in an independent and detail way and Qualified person/competent person.
- Management Should appoint auditor teams.
- Written instruction for self inspection should be established.

Proposes, Scope, Roles and responsibility, Team, Audit program and schedule (yearly bases), Procedure including check list.

- Self Inspection result should be recorded (Finding and CAPA)
- Effective CAPA follow-up and Management review.

SELF INSPECTION

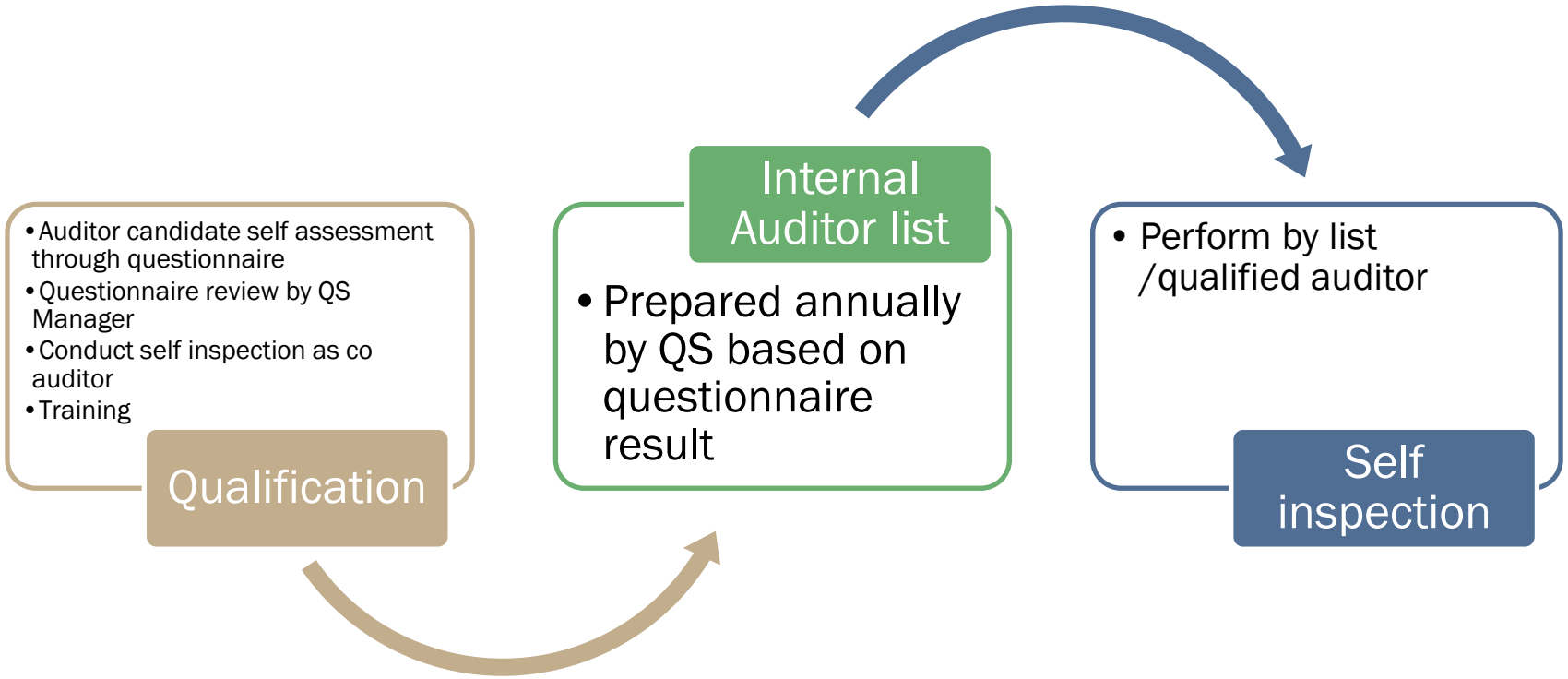
Example of implementation → Schedule :

- ❑ Annual Self Inspection Schedule → max end of first quarter
- ❑ Each department should be audited at least once a year.
- ❑ Quality System Function is responsible to ensures the execution of self inspection is in accordance with predetermined schedule with tolerance plus minus one months from scheduled.

AUDITOR

- Audit shall be conducted by independent individuals not having direct responsibility for the area being audited.
- All auditors shall be properly qualified/competent through experience, education, training and or combination thereof.
- Auditor should maintain their knowledge of internal and external regulations and develop their audit skills.
- Assessment is needed each year to maintain auditor qualification status.

INTERNAL AUDITOR QUALIFICATION



AUDIT TEAM

- Lead auditor
  - Co-ordination of the audit date with the auditee and the audit team.
  - Preparation of the audit with the audit team
  - Explanation of audit method and procedure to auditee
  - Start and closure the audit
  - Ensure adequacy and completeness of the audit report.
  - Assess the proposed CAPA
- Co auditor
  - Co auditor is supporting the lead auditor during preparation, performance and follow up the audit.
- Observer
  - An observer may be part of audit team upon invitation by the audit unit. The observer is not actively involved in the audit process.

TO BE PREPARED BEFORE AUDIT

a) Audit plan or agenda

b) Initial communication with the Auditee to determine more detailed audit schedule.

c) Documentation review (history, trends, procedures, etc).

d) Tools/ techniques, for example:

- Self inspection checklist can be used as a guideline for inspection (Petunjuk operasional CPOB 2012, Jilid I, hal 345-376)
- Other tools that can be prepared with any format according to auditor needs and comfort (e.g : mind mapping, fish bone diagram, etc).

Checklist Manufacturing

INSPECTION

- An opening meeting / discussion is needed prior the inspection to discuss inspection agenda and scope.
- Open communication between the auditor and auditee should be maintained.
- Audit observations should be based on objective evidence, such as direct observations of on-going processes, personnel interviews or evaluation of recorded data.
- If during inspection a critical incompliance is observed, an immediate action must be taken.
- At the end of inspection, through wrap up / closing meeting the Auditor delivers the observations and recommedations of the audited area

INSPECTION REPORT

- Auditor prepare self inspection report within one months after the inspection performed.

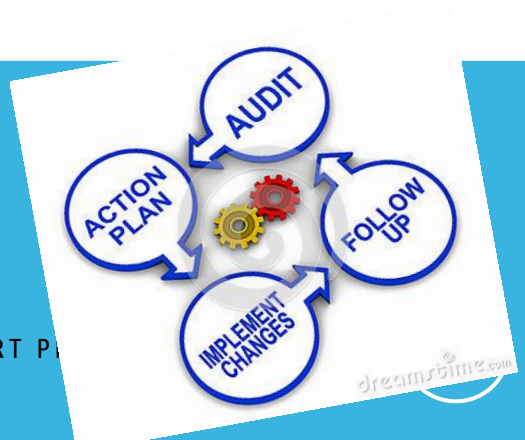
- Audit observation shall be objective, fair and balanced, recorder in adequate detail and easy to understood. Reference is made to underlying documents, if applicable.
- Observation should be classified to “critical, “major” and “minor”, and for recommendation is classified as “N/A”.

Inspection Report

CAPA SELF INSPECTION

- All self inspection and CAPA should be recorded and follow up effectively.
- Monitored by Company management

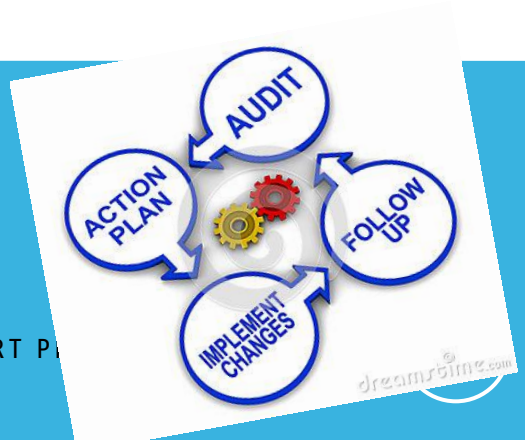
- Example implementation:
- Auditee should prepare CAPA form within one month after self inspection report approved.
- For CAPA which should be coordinated to other department, it is responsibility of auditee for the coordination process.
- The proposed CAPA should correspond with the observation, lead auditor is responsible to review the adequacy of proposed CAPA.
- Part of Quality Management review (CAPA SI as one of Key Performance Indicator)



CAPA SELF INSPECTION

- All self inspection and CAPA should be recorded and follow up effectively.
- Monitored by Company management

- Example implementation:
- Auditee should prepare CAPA form within one month after self inspection report approved.
- For CAPA which should be coordinated to other department, it is responsibility of auditee for the coordination process.
- The proposed CAPA should correspond with the observation, lead auditor is responsible to review the adequacy of proposed CAPA.
- Part of Quality Management review (CAPA SI as one of Key Performance Indicator)



QUALITY AUDIT

- Supplement of self inspection with consist of examination and assessment, all or part of QMS with specific propose to improve it.
- Conducted by outside or independent specialist or internal team designated by Management.

CGMP: AUDITING

Independent Audit Group

- Resources
- Authority

Global Approach - Harmonization of Quality Standards

Audit priority systems / specific issues

Follow-up audits

WHAT WILL BE INSPECTED ?

Process Equipment
- Design and construction
- Equipment maintenance and cleaning
- Calibration
- Computerized system

Documentation and records
- Documentation system and specification
- Equipment cleaning and use records
- Record of raw materials, intermediate, API labeling and packaging materials
- Master production instruction (Master production and control record)
- Laboratory control record
- Batch production record review

WHAT WILL BE INSPECTED ?

Material Management
- General control
- Receipt and quarantine
- Sampling and testing of incoming production materials
- Storage
- Re-evaluation

Production and in-process control
- Production operation
- Time limit
- In-process sampling and control
- Blending batches of intermediate or API
- Contamination control

WHAT WILL BE INSPECTED?

Material Management
- General control
- Receipt and quarantine
- Sampling and testing of incoming production materials
- Storage
- Re-evaluation

Production and in-process control
- Production operation
- Time limit
- In-process sampling and control
- Blending batches of intermediate or API
- Contamination control

Packaging and Identification labeling of API and intermediate
- Packaging material
- Label issuance and control
- Packaging and labeling operation

WHAT WILL BE INSPECTED?

Storage and distribution
- Warehousing procedure
- Distribution procedure

Laboratory Control
- Testing of intermediate and API
- Validation of analytical procedure
- Certificate of analysis
- Stability monitoring of API
- Expiry and re-test dating
- Reserve/retention samples

WHAT WILL BE INSPECTED?

Validation
- Validation policy
- Validation documentation
- Qualification
- Approaches to process validation
- Process validation program
- Periodic review of validated systems
- Cleaning validation
- Validation of analytical method

Change Control

WHAT WILL BE INSPECTED ?

Rejection and Re-use of Materials
- Rejection
- Reprocessing
- Reworking
- Recovery of material and solvent
- Returns

Complaint and Recall

Contract Manufacturers (including laboratories)

SUPPLIER QUALIFICATION SYSTEM (AUDIT AND APPROVAL)

Requirement

- Responsibility of Head of quality for approving supplier to ensure reliable supplier and quality material (meet established specifications.
- A list of approved suppliers of starting material should be established and reviewed.
- For new supplier, should be evaluated (history and nature of the materials.
- And if audit is required, it should determine the suppliers ability to confirm with GMP standard.
- All established supplier should be evaluated regularly.

Purpose & Scope

PURPOSE

To provide consistent approach for evaluation, qualification, approval and certification of the suppliers.

Scope

This procedure is applicable to all supplier who supply products and services which may affect the quality of products, as follows:

1) **Supplier/manufacturers of components, packaging material and critical manufacturing materials**
2) **Supplier of manufacturing and packaging equipment.**
3) **Contract manufacturer (manufacturing of single step)**
4) **Distributor**
5) **Contract laboratories**
6) **Warehouse**
7) **Carrier / freight forwarders**
8) **Service which may affect the quality of drugs substance and drug product, e.g. Maintenance and calibration services, validation services, pest control.**
9) **Supplier of processing aids**
10) **Supplier of equipment used to maintained defined environmental conditions (e.g, HVAC)**
11) **Supplier of software application**

SCOPE

1. CPM / Processing aid
2. Utility (including suppliers form preventive maintenance)

RESPONSIBILITY

A. QUALITY SYSTEM FUNCTION

Coordinate supplier qualification execution.

Prepare supplier qualification plan and report.

B. RELATED DEPARTMENT, E.G : PURCHASING, QUALITY CONTROL, REGULATORY, PRODUCTION TECHNOLOGY, PACKAGING DEVELOPMENT, VALIDATION, EHS, PPIC, WAREHOUSE

Initiate supplier qualification plan once needed.

Review supplier qualification plan and report.

Perform qualification step as required in qualification plan

C. QUALITY SYSTEM MANAGER

Review and approve supplier qualification plan

Review and release supplier qualification report.

SUPPLIER QUALIFICATION PROCESS_01

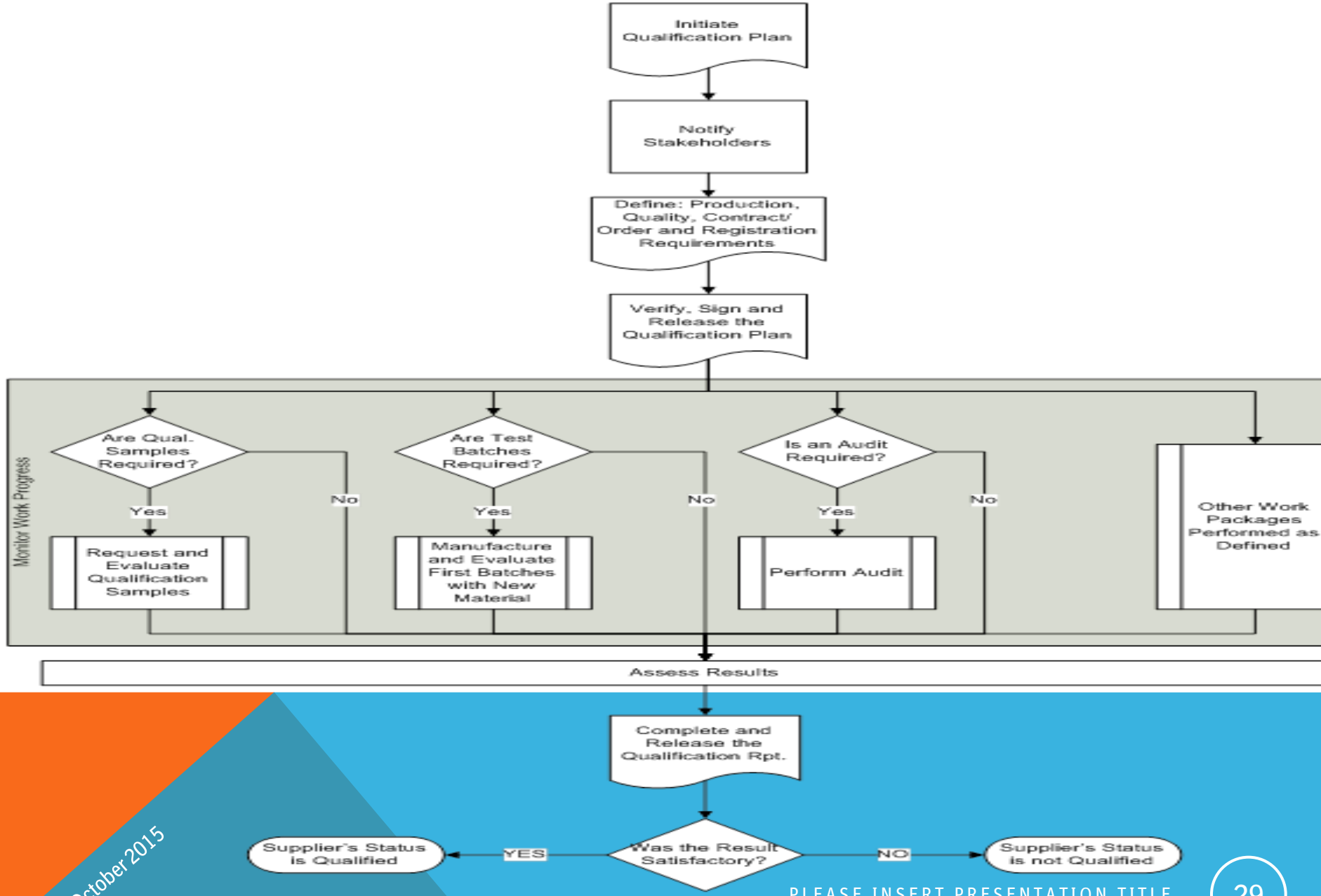
Process	Responsibility	Deliverables/ Documents
Identification the needs for supplier qualification	Business Partner, Purchasing	Change Request (if applicable)
Start qualification (or re qualification) Set up Qualification plan, identify corresponding business partner (e.g Purchasing, Auditor, Production, Regulatory Affairs, Quality Control, Production Technologies, Packaging Development) and distribute plan for completion	Quality System (R)	Supplier Qualification Plan
Create supplier material/service and data in the appropriate data base or system to enable the single steps of the qualification. Grant supplier status "Under Qualification"	Quality System (R)	Supplier list Supplier data base (BPCS)
Release qualification plan Every business partner confirms the information entered into the qualification plan with his/her signature, a final release of the qualification plan is done by the quality system.	Business partner (R) Quality system (A)	Supplier Qualification Plan

SUPPLIER QUALIFICATION PROCESS_02

Process	Responsibility	Deliverables/ Documents
Request qualification samples and information Purchasing orders the specified samples and necessary documentation from the supplier. The quality should be agreed upon by Quality Unit and/or pertinent business partner	Purchasing (R)	Material Samples
Evaluate qualification samples Quality control performs full analytical testing of the new component on three unique lots (less than three lots only upon justification) and compares the result to the suppliers CoA or product specification or critical quality attributes. In case sample have been evaluated during the supplier selection process, these may be taken into consideration.	Quality Control (R) Quality System (C)	Result of Analysis
Evaluate first batches manufactured with newly sourced material. Quality control and or production or production technology evaluate the first batches manufactures with the newly sourced compound. The number of test batches should be defined by risk assessment. The result and the recommendations are forwarded to quality system for acceptance or rejection.	Quality Control (R) Production Technology (R) Validation (R) Quality System (C)	Trial report, validation report, evaluation report

SUPPLIER QUALIFICATION PROCESS_03

Process	Responsibility	Deliverables/ Documents
Decide where an audit is necessary Depending on the supplier material/service categorization Quality Unit decides if an audit is necessary or not.	Quality System (R) EHS (R)	Supplier qualification plan
Perform Audit The identified auditor prepares and performs the audit according 028-OCS-0189 and informs the Quality System on the audit result	Auditor (R) Quality System (I)	Supplier Audit Report
Finalize qualification report Set up qualification report togehter with the corresponding business partner and distribute report for completion.	Business Partner(R) Quality System (A)	Supplier Qualification Report
Release Qualification Report Every business partner confirms the information entered into the qualification report with his/her signature, a final release of the qualification report is done by Quality system A supplier status is granted and entered into the appropriate data base or system. If the qualification fails, the supplier status is set to not approved.	Quality System (R)	Supplier Qualification Report


Initiate Qualification Plan
Notify Stakeholders
Define: Production, Quality, Contract/ Order and Registration Requirements
Verify, Sign and Release the Qualification Plan
Monitor Work Progress
Are Qual. Samples Required?
Yes
No
Request and Evaluate Qualification Samples
Are Test Batches Required?
Yes
No
Manufacture and Evaluate First Batches with New Material
Is an Audit Required?
Yes
No
Perform Audit
Other Work Packages Performed as Defined
Assess Results
Complete and Release the Qualification Rpt.
Was the Result Satisfactory?
YES
Supplier's Status is Qualified
NO
Supplier's Status is not Qualified

Thank you!