Supplier Qualification – A Review

Abstract:
It is a GMP requirement to certify the vendor to deliver high quality and safe medicines, and to prevent recalls, deaths, adverse events, and serious illness due to substandard quality of manufactured medicines. The main aim of business is to generate profit. To achieve good profits, sometimes pressure will be increased to get raw materials of low cost, which sometimes leads to procurement of substandard material. This can be avoided by using supplier qualification as a tool.

Key words: GMP, vendor, quality assessment.

Introduction:
Relationship between quality and increasing risk of raw materials is as follows:

The manufacturer has the ultimate responsibility to qualify the vendor. Internally, the vendor should also have an efficient vendor certification programme for qualifying the supplier from whom he will procure the raw materials. All the documents of manufacturer and vendor will be verified during audit.

Supplier qualification prerequisite:
1. Sample evaluation
2. Evaluation of supplier’s quality system to assure quality and safety of procured materials by checking manufacturing controls.

Steps of Supplier Qualification:
1. Supplier selection
2. Due diligence
3. Quality assessment of all suppliers
4. Change control and production assessment
5. Supply chain security
6. Ongoing monitoring and evaluation

1. Supplier Selection:
The purpose of this step is to define a set of criteria that can be taken into consideration in the selection process of a supplier. The supplier selection process starts with

the definition of the user requirements for the material within scope. The user requirement specifications provided to purchasing should contain as a minimum the information: Name of the product (including formulae and CAS number when available), material specifications, quantity required. To select the supplier, the criteria of materials to be procured are determined and the user requirement specification form is developed, stating:

i. Name of the product
ii. Material specifications
iii. Quantity required

Information to be requested from the supplier for selection should contain:

i. Specifications
ii. Manufacturing, packaging and labelling details
iii. Material safety data sheets
iv. Analytical test methods to examine the sample against the specified criteria.

Supplier Assessment Dimensions:
Dimension Parameters checked for
Assurance of supply It is an essential element to assure the supply in specified time

Quality and regulatory compliance
The supplier should be checked for

i. cGMP compliance – regulatory track record
ii. recall – complaints
iii. change control
iv. material management control
v. quality management system
vi. production facilities and equipment
vii. process validation
viii. documentation standards.

Procurement cost
i. cost management
ii. presence in low-cost countries
iii. ability to achieve target price

Technical aspects
i. plant capabilities
ii. laboratory capabilities
iii. business programme resolving capabilities
iv. staff qualification
v. control systems
vi. development capabilities
vii. process development expertise
viii. project management
ix. willingness to innovate
x. intellectual property

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Responsiveness and communication
i. rapidity project assessment
ii. resource availability
iii. flexibility in attitude
iv. openness
v. ease of communication
vi. proactiveness

A multi-disciplinary team is appointed by buyer to assess all the above characteristics of the vendor. The multi-disciplinary team, after thorough review, shortlists a number of vendors of appropriate competence.

2. Due Diligence:

Purpose:
- This step is not applicable for non-critical raw materials.
- For critical raw materials, including API starting materials, the necessity to perform due diligence can be based on a risk assessment according to ICH Q9.
- Documented evidence will be assembled to support the go/no-go decision process.
- The possibility of establishing a long-term business relationship with the supplier will be evaluated.
- The implemented systems and existing facility will be assessed and challenged in order to evaluate the capability of the supplier to comply with the customer’s requirements.

Due diligence is a legally binding process during which the buyer evaluates the assessments and liability of the vendor. It is essential to assure that the appropriate due diligence is conducted prior to contracting with a supplier, and that documented evidence is created to take decisions such as go/no-go processes. The possibility of establishing a long-term business relationship with the supplier is evaluated during due diligence.

The various supplier challenges that have to be assessed are:
- Process containment
- Process equipment
- Quality of utilities
- Analytical equipment availability and method development
- Process of preparing for regulatory submission.

Selection of Cross-functional Team:
Depending upon the criticality to be evaluated, a cross-functional team is established, consisting of representatives from
- Engineering
- Regulatory
- Environmental / health / safety
- Technical experts
- Procurement department

The cross-functional team will evaluate the vendor for qualification, and recommendations will be sent to the senior management to take go/no-go decisions.

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<thead>
<tr>
<th>Areas to be challenged</th>
<th>To be checked for</th>
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<td>iii. Quality system</td>
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<td>Process</td>
<td>i. It is done to check the ability of the supplier to produce the products continuously on time</td>
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<td>The various areas evaluated are</td>
<td>i. Chemical synthesis</td>
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<td>v. Product quality review</td>
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<td>iv. Waste management licenses</td>
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All the above areas are assured and challenged to evaluate capacity of vendor, to take appropriate decision on go/no-go situations.

3. Quality Assessment:
The supplier must assure that supplies are of quality and can be used at any stage of manufacture, and should assure that the material being produced complies with “Note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via medicinal product” – EME/410/01 (TSE guidelines). The material which is delivered by tanker is assured for its quality. The tanker should be specific for a particular product,
and if not, necessary cleaning is assured by cleaning validation. The quality unit is responsible for evaluating the quality of the vendor. If needed an audit team must be established with appropriately qualified personnel to audit the vendor. The audit questionnaires must be tailored to the raw material being purchased, its mode of manufacture, API delivered from plant sources, sterile liquids, and biotechnological processes.

i. The audit must aim to find whether the manufacturer being audited has the potential to supply to a different regulatory standard, if it is required in the future?

ii. Does this supplier have the potential to be a long-term partner?

The auditor should also decide to what extent the audit must be conducted; if needed, a re-audit must be done with appropriate remediation. The audit finding should address the capability of the vendor, and should assist in taking go/no-go decisions.

Operation of a Quality Assessment:

Establishing Supply Agreement / Contract:
The agreement should address the raw materials and quantities required, and it should also focus on the expected quality of raw materials.

It should address the need for:
i. Notification of any potential changes that may impact the quality of the product

4. Change Control and Production Assessment:
All the changes that impact the quality of product must be evaluated and agreed by both supplier and firm. The change can be initial at any stage, by any department. To track the change a control form form is issued. Contents of control form are:
i. Tracking number
ii. Detailed description of change
iii. Specification for material based on requirements
iv. Defined number of batches being affected
v. Products impacted
vi. Reason for change
vii. Acceptance criteria
viii. Supporting documentation:
   - Outline of changes to master formula record
   - Financial impact
   - Impact on current testing
   - Validation impact

The change control form is evaluated by the cross-functional team, after the approval of the change is implemented. After successful implementation of change, a closure memo is prepared by the assigned coordinating function that verifies and shows evidence that all requirements of the temporary change request have been met.

Change Control and Assessment Process:
The change control and production assessment process follows five main steps: initiation of change, execution of change, evaluation of change, closure of the temporary change control package and preparation for ongoing monitoring as follows.

Initiation of Change
The execution of changes to the process are managed by a cross-functional team according to the following principles:

- The system for change control is overseen by the quality organisation, but may be managed by another function
- All changes are assessed from a technical, quality, regulatory, stability, safety, environmental and business standpoint, with the appropriate personnel involved in the review.
- The impact of the change on the affected areas, processes and systems is evaluated and communicated
- All changes requiring a change to the filed process will be communicated to the appropriate agencies
• For non-critical raw materials, the process may be streamlined to assess the change as there is no regulatory impact, and the impact may be minor to the process.

Mechanism for Review of Change:
For Critical Raw Materials and API Intermediates

The mechanism for review is as follows.
• Tracking number
• Detailed description of change
• Specification for the material based on user requirements
• Defined number of batch that will be impacted
• Products impacted (name and identification code)
• The reason for the change
• Acceptance criteria
• Supporting documentation
  • Outline of changes to master batch records
  • Financial impact
  • Impact on current testing
  • Validation impact
  • Results of use test of material and the follow-on product evaluation

Execution of Change:
Following approval of the temporary change request by the appropriate functions and the completion of all actions required for the change, the process is executed using the new material.

Evaluation of Change:
The evaluation of the change is performed at a number of levels as follows:
• The resulting material produced as part of the temporary change is then evaluated by
• Routine testing of the material for all materials
• Use tests to produce the final product for critical materials and API intermediates
• Extra testing to evaluate the material produced and ensure that it is within expectations for critical materials and API intermediates
• The validation completion report is drafted and approved as per the normal site procedure
• All prior-to-release and prior-to-implementation requirements are assessed and tracked to closure as per the site systems.

5. Supply Chain Security:
Along with supplier and manufacturer, other firms such as agents, brokers, distributors, re-packers, re-labellers and transport companies are involved in contributing to the supply chain. The shorter the supply chain, the more secure it will be.

The entire supply chain from the manufacturer of an API, registered intermediates or critical raw material to the customer should be assessed and qualified from a quality perspective, mainly related to quality system, transportation, storage and related conditions, as well as traceability of the material.3

Apart from the supplier qualification and management activities, the following measures related to packaging can be considered and may increase the supply chain security for APIs:
• Use of tamper-resistant packaging closure by the manufacturer
• Evaluation of the label by the customer: the label on the material matches the reference label provided by the manufacturer.

6. Ongoing Monitoring and Evaluation:
After approval, the vendor has to be checked periodically for compliance. The quality unit is responsible for the evaluation and re-approval of the vendor.

Responsibilities
The evaluation should be under the control of the quality unit, but completed as part of a multi-disciplinary team evaluating all aspects of supply.

i. Ongoing Monitoring:
At least the following aspects should be taken into consideration:
• Specification (results on certificate of analysis and own results)
• Statistical evaluation of quality control data for critical parameters (if applicable) to identify any adverse trends
• Packaging, sealing
• Labelling
• Delivery dates and quantities
• Certificates and other documents
All deviations should be monitored and managed according to the company’s complaints procedure.

ii. Periodic Evaluation:
Regularly, typically on an annual basis, the supplier’s performance should be assessed. Depending on the type of material, the following data should be evaluated:

- Periodic full testing of material
- Quality – for example number of not right-first-time deliveries
- Complaint situation
- Product quality review (registered intermediates and APIs)
- Results of SQC/SPC analysis (if applicable)
- Assessment of changes (critical materials, registered intermediates and APIs)
- Reaction to audit and remediation plan (if audit had taken place)
- Response times for complaints and questions
- Reaction time if, e.g., regulatory requirements change (critical materials, registered intermediates and APIs)
- Regulatory or cGMP/compliance issues (critical materials, registered intermediates and APIs)
- Predefined KPIs with examples in Chapter 4 (registered intermediates and APIs)

iii. Rating:
After the periodic evaluation the supplier should be classified according to an objective rating system.

- Completely satisfactory: approval
- Mainly satisfactory: limited approval (ongoing supply)
- Partially satisfactory: conditional approval (no supply until corrective actions are in place)
- Not satisfactory: supplier disqualified until actions are taken.

iv. Re-audit:
The frequency of the re-audit should be dynamic and depending on the rating.

Example:
- Completely satisfactory: 5 years
- Mainly satisfactory: 3 years.
- Partially satisfactory: 1 year

Conclusion:
The main aim of any firm is to produce the medicinal products which are safe and of good quality. To maintain the quality, the raw material should be purchased from a competent supplier, identified and evaluated for his competence. Proper vendor certification will ensure the quality of incoming raw materials and reduce the cost involved in retesting. The supplier qualification will increase the confidence of the firm to produce the product of good quality.

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