

## PHARMACEUTICAL VENDOR DEVELOPMENT AND QUALIFICATION

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Article Received on  
08 March. 2018,

Revised on 29 March 2018,  
Accepted on 19 April 2018,

DOI: 10.20959/wjpr20189-12050

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### **ABSTRACT**

In the high majority of cases, the Excipients are not prepared exactly for medicinal usage. But maximum of the medicinal excipients the manufacturer quantity fewer than 10% of the over-all manufacture of that certain material for the usage of pharmaceutical. Excipient produce range contains hundreds of goods different in interaction, source and functionality and they are used for several altered purposes. The existences of handling excipients like supplies and purchasing them lacking completely be suitable the source and the whole delivery sequence have absent by a good manufacturing practice guidelines burdens to confirm the quality of further supplies used in the industrial process. The example that exists in nearly medicinal firms nowadays someplace excipients are obtained from distributor short of signing the definite constructor, manufacturing site and fully circulation lifespan sequence to be altered. The present input gives a summary of the present transfers on good manufacturing practice necessities for medicinal excipient and moves towards the requirement of medicinal excipient makers.

**KEYWORDS:** Vendor, APIs, Qualification.

### **INTRODUCTION**

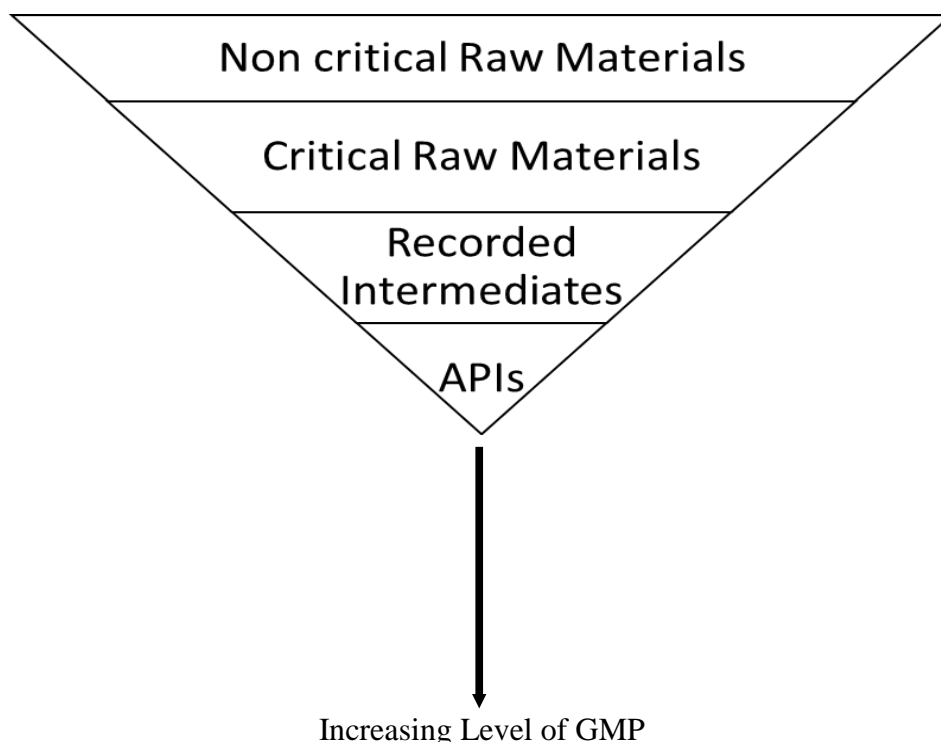
The person who delivers goods or services to a firm or individuals is known as vendor or supplier. A vendor often makes inventorial things and retails those items to a consumer. One who is the intelligence of the thing (raw material, packing material, pharmaceutical components, chemicals etc...) The starting materials used in the production of

pharmaceutical products (active pharmaceutical ingredient's) which are subjected to ensure their quality, safety, and efficacy of the product we must design strict good manufacturing practice regulations. The materials used in the manufacturing of pharmaceutical products can be classified into four based on a characteristic of the starting material Active Pharmaceutical Ingredients industrial method and on hazard associated to possible for an injury to the patients: -

- a) Non-critical raw materials.
- b) Critical raw materials (including API Starting Materials).
- c) Recorded intermediates.
- d) Active Pharmaceutical Ingredients

In each type the quality of the material is possible to reduction as the increases as shown in figure 01:

The quantity of ingredients in each group is possible to reduce as the criticality rises as shown in the below diagram 1:



**Figure 01: Triangle showing criticality of raw materials.**

The final medicinal products according to cGMP regulations are logically explained to each nation and region. The regulation of the content can differ then the objects are the similar:

- To transport high quality, safe medicines manufactured and distributed following measured Procedures to treat disorders and
- To avoid collapses, acute illnesses, adverse incidents or product recalls resulting from defects in the production and delivery processes.

The specifications estimated from the industrial establishments have not been preserved properly. There are many cases around of these cases had very severe consequences.

***E.g.:-***

- In 2008 in the USA lead to around 150 fatalities due to heparin case it I contamination of the active pharmaceutical ingredients with a bogus substance (oversulfated chondroitin sulfate).
- The glycerin with diethylene glycol contaminated with many scandals may lead around 107 expires in the United State of America (1937), in Bangladesh about 300 expires (1990), in Haiti (1996) around 88 deaths (young children), in Panama (2006) 138 deaths. Due to the absence of controls in the delivery network of glycerin and in the therapeutic product industrial places involved.
- In 1994 and 1999 in the USA around 65 deaths due to the contamination of gentamicin sulfate.

In some cases the obtaining Active pharmaceutical ingredients and the Raw materials used in their preparation activity the business pressure to reduce the cost at the lowest price. It does not create non-compliance while this practices, in and itself. But it generates a chance for merchants to introduce themselves to the supply chain and present quality ingredients. This condition also highpoints the want for clearness about potentials and supplies for seller standard and guarantee of the complete supply chain.

The relationship between quality and increased 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 program for qualifying the supplier from whom he will procure the raw materials. All the documents of manufacturer and vendor will be verified during the audit.

#### ***Prerequisite for Supplier qualification***

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 (merchant selection)
2. Quality assessment of all suppliers
3. Supply chain security
4. Ongoing monitoring and evaluation

#### **1. Merchant selection**

The determination of this stage is to describe a fixed of criteria that can be occupied into attention in the choice process of a supplier The supplier choice process beginnings with the definition of the user necessities for the material within scope. The user necessities requirements delivered to procuring would include as a minimum the information: Name of the product (including methods and CAS number when available), material requirements, quantity essential. To select the supplier, the criteria of materials to be procured are determined and the user requirement specification form is developed, stating

- a) Title of the product
- b) Material specifications
- c) Quantity required

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

- i. Specifications
- ii. Manufacturing, packaging and labeling 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 Guarantee of source it is an important section to assure the resource in specified time.

#### **Quality and regulatory compliance**

The supplier should be checked for

- a) cGMP compliance – regulatory track record
- b) Recall – protests
- c) Change control

- d) Material management control
- e) Quality management system
- f) Production facilities and equipment
- g) Process validation
- h) Documentation standards.

**Procurement cost**

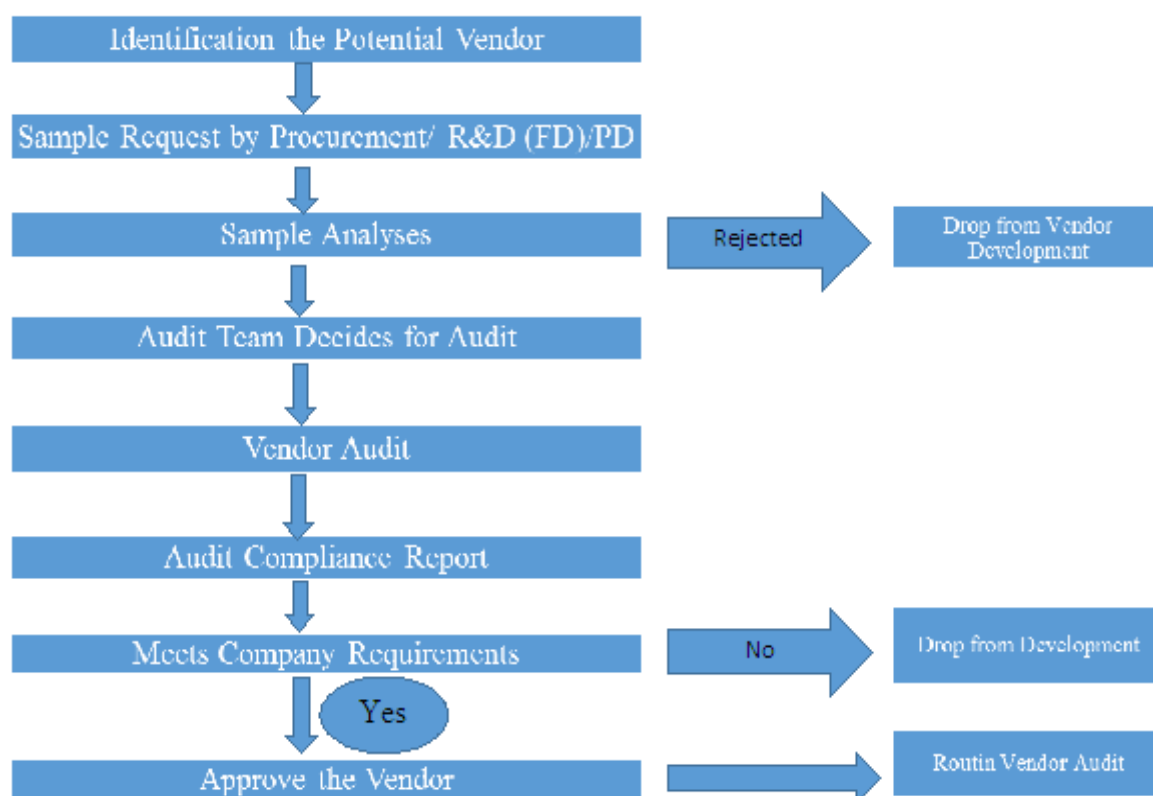
- i. Cost management
- ii. Existence in small - price nations
- iii. Capability to complete target cost

**Practical aspects**

- a) Herbal abilities.
- b) Laboratory abilities.
- c) Occupational program resolving abilities.
- d) Employees qualification
- e) Control systems
- f) Development capabilities
- g) Method improvement capability
- h) Assignment organization
- i) Willingness to innovate
- j) Intelligent property

**Responsiveness and announcement**

- i. Rapidity project assessment
- ii. Resource availability
- iii. Flexibility in attitude
- iv. Openness
- v. Ease of communication
- vi. Pro activeness



**Figure 02: Flowchart for Active Raw Material and Primary Packing Material Vendors**

## METHODS

### *Process for Selection and Evaluation of New Vendors*

For the vendor identification of a new product, the corresponding department shall give the list of new raw materials i.e. APIs, excipients, primary containers etc. with all the material specifications to the department head. After checking the list of raw materials, identify preferably two potential material manufacturers based on the requirements. The Head of the department will procure the shipment sample from the vendor. After procuring the shipment sample, preferably three batches from the vendor, the raw material sample is forwarded to QC department for carrying out the analysis of the sample. Then the samples shall evaluate the material suitability for formulation on an analytical basis. Before taking the scale-up batch the formulation department shall review the analytical results and ensure the performance and suitability of the material with respect to the formulation records. Based on the satisfactory review of material suitability and availability of the documents like vendor surveillance form, DMF, safety statements the QA department will give clearance for execution of scale-up batch. Then the QA will update the approved vendor list of the organization for the procurement of the raw materials.

***Documents collected for Vendor Qualification***

- Vendor registration form
- Vendor Surveillance Form / Vendor Questionnaire
- GMP Certificates
- ISO certificates
- Material safety data sheet
- Certificate of Analysis
- TSE BSE Certificate / Questionnaire

***Document required for vendor qualification***

*The document required during selection of vendor as outlined in Table 0.*

**Table 01: Document for the selection of vendors.**

<i>Sl. No.</i>	<i>Contents of Quality Matrix</i>	<i>Details</i>
1	VRF (Vendor Registration Form)	Registration form to be filled by vendor information about the company such as general information, organization name, list of material to be registered, the name of the contacted person, type of organization, organization structure, performance, latest tax clearance certificate, annual turnover of the company, the quantity of material intended to supply.
2	VQF (Vendor Questionnaire Form)	Questionnaire to be filled by vendor revealing information about the material such as General Information, Quality management system, Hygiene Practices, Lab controls, facility & equipment, production & process controls, shipping & storage of final product, validation regulatory & safety issues
3	cGMP Certificate	Current accreditations by local or international regulatory authorities based on the cGMP.
4	MSDS form (Material Safety Data Sheet)	Material Safety Data Sheet is a manuscript that covers data on the possible risks (well-being, fire, reactivity and environmental) and how to work securely with the organic manufactured goods. It is a vital initial point for the growth of a whole health and safety program.
5	TSE/BSF Certificate	Prion disease also called as Transmissible spongiform encephalopathy, are a set of developing conditions that affect many animals brain and nervous system including humans. The mad-cow disease also known as Bovine Spongiform Encephalopathy (BSE), is a fatal neurodegenerative disease in a cow that causes

		a spongy degeneration in the brain and spinal cord.
6	COA (Certificate Of Analysis)	COA is a certificate given by Quality Assurance that confirms that a regulated product meets its product requirement. They usually include the actual consequences achieved from testing done as a part of quality control of a different lot of a product.

## 2. Quality assessment of all suppliers

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 conforms with “Note for regulation on minimizing the risk of transmitting animal spongiform encephalopathy agents via therapeutic 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 answerable 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 personalized to the raw material being bought, its mode of manufacture, API transported from plant sources, sterile liquids, and biotechnological processes.

- i. The audit must aim to find whether the industrialist being audited has the potential to supply to an altered regulatory standard if it is compulsory for the upcoming?
- 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 making go/no-go decisions.

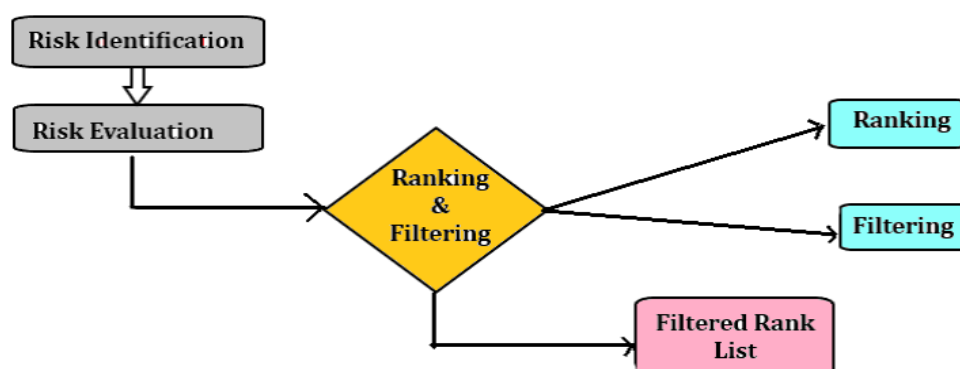


Figure 03: Operation of a Quality Assessment.

The three types of the materials condensation of the quality evaluation process as shown in table 02.

**Table 02: Quality assessment procedure summary.**

Essential Requirements	Non Critical raw materials	Critical raw materials	Registered intermediate API
TSE/BSE Certificates		√	√
Transporter Washing Assessment	√	√	√
Sterile manufacturing Survey	√	√	√
Company Audit	--	**√	√
Historical performance	**√	√	√
cGMP Compliance History	--	**√	√
3 <sup>rd</sup> Party certification	**√	**√	√
Contract Agreement	√	√	√
Condition Agreement	--	**√	√

\*(if accessible)

√- Essential,

\*\*√ - Dependent on risk assessment achieved on the substance being bought.

### ***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 report the essential for***

- i. Any potential changes to the notification that might influence the quality of the product.
- ii. Without prior approval, there is no change.

### ***3. supply chain security***

*Supply chain security discusses to efforts to improve the safety of the supply chain, the transportation, and logistics system for the world's shipment.*

*It combines traditional practices of supply chain management with the security requirements driven by threats such as terrorism, piracy, and theft.*

### ***Supply chain management***

*Supply chain management is a flow of goods and facility contains the movement and storage of Raw materials, of effort -in- method inventory and of complete goods from point of source to point of feeding.*

***Principle***

*The 5R's principles are followed.*

Right place

Right Quality and  
Quantity

Right Period

Right Price

Vendor qualification is a part of supply chain management, where it provides the authority to procure the material only from the known certified approved vendors.

**4. *Ongoing monitoring and evaluation***

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

***Duties***

The estimation must be below the controller of the Quality Part but finished as part of a multi-disciplinary group estimating all characteristics of supply. The current estimation and the re-approval of the supplier the quality unit are responsible. Further branches would provide their input to safeguard that all related features are taken into account.

**1) *Ongoing checking***

According to the defined criteria, each supplied batch should be assessed. These standards should be results of the risk assessment. The resulting characteristics would be occupied into consideration:

- Requirement (results on certificate of analysis and own results)
- Numerical Estimation of Quality Control documents for critical parameters (if applicable) to classify any adversarial trends.
- Packing, sticking
- Stamping
- Transport periods and quantities
- Documentations and further certificates
- Further characteristics

**2) *Regular assessment***

Even, classically on a yearly base, the supplier's performing would be evaluated. For non-critical raw materials, a regular assessment may not be mandatory. Dependent on the nature of the material the resulting information would be assessed:

- Regular complete testing of material
- Quality – for example amount of not correct first-time transports
- Complaint condition
- Product Quality Assessment (recorded intermediates and Active pharmaceutical ingredients)
- Results of SQC/SPC analysis (if applicable)
- Evaluation of variations (critical materials, recorded intermediates, and Active pharmaceutical ingredients)
- Response to audit and remediation idea (if audit had taken place)
- Reaction times for complaints and questions
- Response time if e.g. regulatory requirements change (critical materials, recorded intermediates, and Active pharmaceutical ingredients)
- Regulatory or cGMP/compliance issues (critical materials, recorded intermediates, and Active pharmaceutical ingredients)
- Predefined KPIs with examples in Chapter 4 (recorded intermediates and Active pharmaceutical ingredients)

### 3) *Assessment (category of supplier)*

Later the seasonal assessment the supplier would be categorized according to an objective ranking technique

- **Fully agreeable:** approval
- **Mainly agreeable:** inadequate approval (ongoing supply)
- **Moderately agreeable:** restricted approval (no supply until corrective actions are in place)
- **Not agreeable:** Supplier banned up to activities are taken

The effect of the assessment has an essential power on the occurrence of re-inspections, reassessment, limit of sample and testing.

The important impact

### 4) *Re-audit*

The re-auditing frequency should be active and dependent on the score.

Standard

- **Fully agreeable:** five years

- **Mainly agreeable:** three years.
- **Incompletely agreeable:** one year

### ACKNOWLEDGEMENT

We sincerely thank Jagadguru Sri Shivarathreeshwara University and Dr.T.M.Pramod Kumar, Principal, JSS College of Pharmacy, Mysuru for providing necessary infrastructure and moral support.

### CONCLUSION

In Pharmaceutical industries, Vendor Qualification is a most important process, which acts as a key role for procuring API of good quality and in good price. 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 vendor. Proper vendor qualification cycle 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 and also ensure the quality of the final product.

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