

Guidance 079 Use of a Risk-Based Approach To Establish External Quality Assurance Audit Frequency

- “What are the patients, product quality, and business risks associated with materials/components/services used in the production of medicinal products in relation to their supplier’s audits, and how could these audits be prioritized and scheduled to minimize such risks?”
3. **Assess Method to be Used**

There are several simple to intermediate QRM tools that could be applied to this assessment; for this example we are using Risk Ranking and Filtering (RRF). In using this simple tool we will limit the assessment to a review of the severity and probability associated with each hazard.
 4. **Determine the Potential Risk Factors and related Hazards**

In order to determine the potential risk factors and related hazards, one might need to answer:

 - a. What are the risk factors (e.g. patient safety, regulatory compliance, and business) from which each scenario must be viewed to ensure that all potential or related hazards are identified?
 - What are the sources of potential harm related to each risk factor?
 - Could the material sourced have a potential impact on patient safety?
 - Could the material sourced have a potential impact on product quality and conformance to registered specifications?
 - Could the supply of the material have an adverse impact on the business?
 - b. What are the related hazards?

For the purpose of prioritizing the EQAA schedule, each material supplier represents a potential risk to the finished product(s) in which the material(s) sourced are used, therefore, all material suppliers can be viewed as hazards for the purpose of this assessment.
 5. **Define the Risk Assessment Scales for Probability and Severity**

In order to perform an assessment of the risk posed by each hazard (material supplier) the probability and severity characteristic of each hazard must be defined.

Severity and probability scales must first be defined by determining the range of possibilities and differentiations for each as indicated below:

 - a. **Severity:** Severity is the measure of the consequence (impact) that a defect or failure borne of the material supplier (hazard) may have on your operation/products.

Assessing the severity requires an understanding of how the material supplier might impact the risk factor. For example, when looking at material suppliers and their potential impact on finished product quality, an API supplier may be assigned a higher severity scale than a tertiary packaging supplier since the API may impact potency or dissolution of the

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based supplier audit schedule, each action threshold will represent a different audit frequency. Delineation of the thresholds should be based on perception of risk and an organizational acceptance of the represented risks. For instance, the threshold containing the range of lowest risk scores will correlate with the lowest audit frequency.

An example of a risk evaluation matrix and corresponding action thresholds is shown in Figure 1 below. In this example the values in the green boxes (risk scores 1-4) represent low risk, and could be audited every 5 years. The values in yellow (risk scores 5-14) represent medium risk and could be audited every 3 years. And the values in red (risk 15-25) are high risks to be audited annually.

Figure 1: Example of Risk Evaluation Matrix



Threshold Interpretation: need to include how threshold was determined (i.e. rationale)

- Scale 1-4 represents: LOW risk
Audit every 5 years
- Scale 5-14 represents: MEDIUM risk (Action Threshold)
Audit every 3 years
- Scale 15-25 represents: HIGH risk
Audit every year

7. Assess Probability and Severity Scale for Each Supplier Construct the EQAA assessment table and determine the severity and probability score for each material supplier (hazard) based on the available data gathered in Step 1. For example, the supplier of LDPE bottles, Ajax, has a probability score of 3, taking into account that this supplier has been inspected by the sponsoring site, there have been as many as 7 observations and the observations have not been

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Table 7: Example of Suppliers EQAA Prioritization and Frequencies

Hazard (Supplier's List)		Risk Assessment Scale Results				Risk Control
Name	Material/ Service	Probability (P)	Severity (S)	Total Risk (P×S)	Risk Category	Proposed Audit Frequency
Ajax	LDPE Bottles	3	5	15	High	Annual
ABC	IFC's	1	3	3	Low	Every 5 years
Acme	Labels	1	5	5	Medium	Every 3 years
Astro	Boric acid	1	1	1	Low	Every 5 years
Zap It	Irradiation	1	5	5	Medium	Every 3 years

Risk Acceptance is achieved through approval of the audit EQAA prioritization and frequencies matrix and scheduled by the Site Quality Team.

9. **Communicate and Document**
Communication and documentation of the risks associated with suppliers is achieved upon finalization and distribution of the audit EQAA prioritization and frequencies matrix and schedule to the key stakeholders (Site Quality Team, Procurement, audit staff, etc).
10. **Review the Risks**
Risk Review is a continual process comprised of performance monitoring and the result of periodic supplier audits. If through an audit or routine performance monitoring of a supplier the need exists to re-categorize the supplier, the EQAA prioritization and frequencies matrix and schedule would be revised to accurately reflect the current degree of risk associated with a supplier.