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1.0 Purpose

The purpose of risk analysis is to identify the risks associated with each supplier. The intent is to prevent the program from manufacturing a product that does not meets regulatory requirements. The purpose of this procedure is to define the process for the evaluation of risk for suppliers of products and services for the Biopharmaceutical Development Program (BDP).

2.0 Scope

This applies to the evaluation of risk for new suppliers and the continued evaluation of supplier risk for current suppliers.

3.0 Authority and Responsibility

3.1 Development / Project Scientist

- Notifies Quality Assurance of the new materials critical to the process during the development phase
- Provides manufacturer information for new materials critical to the process during the development phase
- Provides contract manufacturer information during the development phase
- Works with Quality Assurance to determine the initial risk score

3.2 Manufacturing Operations

- Provides manufacturer information for materials
- Provides calibration service provider information
- Works with Quality Assurance to determine the initial and ongoing risk score
- Notifies Quality Assurance of any event that may impact a risk score

3.3 Process Analytics / Quality Control (PA/QC)

- Provides manufacturer information for analytical reagents and materials

- Provides service provider information for contract testing laboratories
- Notifies Quality Assurance of any event that may impact a risk score
- Works with Quality Assurance to determine the initial risk score

3.4 Quality Assurance

- Works with Development, the Project Scientist, PA/QC and Manufacturing to identify, quantify, evaluate and mitigate any risk associated with a raw material or service provider
- Uses risks scores to schedule external audits and supplier surveys.

4.0 Procedure

4.1 Supplier risk is evaluated in three main areas

- Criticality of Materials or Services Provided
- Quality System Evaluation
- Actions by Regulatory Bodies

4.2 Scoring

4.2.1 General Scoring Information

4.2.1.1 Score the manufacturer or service provider according to the following guidelines. Not all criteria in each area will be met. Choose the category that best represents that supplier. In the case where two categories equally describe the supplier, select the higher risk category.

4.2.1.2 In Use / Not in Use Score

This score is used to weight those materials and services currently inuse higher than those that have been used in the past with the potential to be used again

4.2.2 Scoring Rubrics[1]

4.2.2.1 Criticality of the Materials or Services Provided

5 **High Risk**	The material or service provided has a direct impact on product quality or compliance. Examples include but are not limited to: API manufacturer (as biologic/drug substance), sterile manufacturer, sterile products, final release testing services (biologic/drug substance or product testing), sterility testing services, stability testing services, or cell banking CMO.
3 **Moderate Risk**	Material or services provided have an indirect impact on product quality or compliance. Examples include but are not limited to: plasmid manufacturers (used as starting materials and not as final product), non-sterile packaging, or API intermediates.
1 **Low Risk**	Materials or services provided do not have an impact on quality or compliance. Examples include but are not limited to Laboratory in-process testing, secondary packaging, warehouse logistics, document storage companies, warehousing companies, and characterization testing labs.

[1] Modified from the *PDA Points to Consider in Remote and Hybrid GMP/GDP Audits, 2022*

4.2.2.2 Quality System Evaluation

5 High Risk	No third-party Quality System Evaluation in the previous 5 years (e.g., does not currently possess an ISO certificate).
	Has never been audited by the BDP, or an audit was unfavorable.
	BDP Quality Survey responses are inadequate or is indicative of quality system inadequacies.
3 Moderate Risk	Third party certification is current (e.g. ISO), but is not robust enough for the material or service provides. (e.g., ISO9001 certification for a calibration service provider rather than ISO17025).
	Audit by BDP is not necessary or an audit by BDP was favorable .
	BDP Supplier Survey responses are adequate. Reviews of the survey are indicative of a need for update or improvement to the quality systems.
1 Low Risk	Third party certification is current (e.g., ISO).
	Audit by BDP is not necessary or an audit by BDP was favorable.
	BDP Supplier Survey responses are favorable.

4.2.2.3 Regulatory Compliance

5 High Risk	Recent regulatory inspections (<3 years) have yielded regulatory actions (e.g., import alerts, import bans, GMP certificates revoked, warning letters) (OAI), or no regulatory history exists for the organization.
3 Moderate Risk	FDA or other Health Authority Inspections have resulted in Voluntary Actions Indicated (VAI), or equivalent categorization during recent (<3 years) inspections.
1 Low Risk	Recent FDA or other regulatory agency inspections (<3 years) are not applicable or have resulted in No Actions Indicated (NAI).

4.2.2.4 In Use / Not in Use Score

10 In-Use	The material or service provider is currently in use.
	The material or service provider is necessary for an upcoming project.
3 Potential For Use	The material or service provider is potentially being used in an upcoming project.
1 Not In-Use	The material or service supplier is no longer in use and will not be used in the future.
	Former suppliers no longer in business.

4.3 Calculation of Risk Score

Risk Score is the product of the scores detailed above.

(Score A) x (Score B) x (Score C) x (Score D) = Risk Score

A = Criticality of the Materials or Services Provided
B = Quality System Evaluation
C = Actions by Regulatory Bodies
D = In Use / Not in Use

4.4 Use of the Risk Score

4.4.1 Risk scores are used for creation of a critical supplier list.

4.4.2 Risk scores are used to prioritize external audits.

4.4.3 Risk scores are used to identify areas of process improvement to mitigate and reduce risk.

4.5 Mitigation of Risk

4.5.1 General

Risk is mitigated in multiple ways. These include but are not limited to:

- Frequency and complexity of material testing upon receipt, or lot pre-testing
- Quality Control review of external testing
- Quality Assurance review of external testing
- Quality Assurance review of calibration results
- Team onsite audit
- Others

4.6 Acceptance of Risk

After mitigating the risk to as low as reasonably practicable (ALARP), the remaining risk is accepted. Re-evaluation of the risk score and additional mitigation measures may occur during the supplier evaluation / re-evaluation cycle.

4.7 Implementation of Risk into the Supplier Program

4.7.1 Not all current manufacturers and service suppliers have a current risk score.The following is an outline of the plan to implement the scores.

4.7.2 Implementation of the plan.

4.7.2.1 Phase 1 -New Suppliers / Service Providers

New suppliers added to the parts numbering database triggers notification to quality. Follow ***SOP 21109 – Supplier Qualification Program***.The calculated risk is included on ***Form 21109-01 Supplier Evaluation (Approval / Qualification).*** This is only done for suppliers categorized as C or D suppliers.

4.7.2.2 Phase 2A Risk Analysis

Complete risk evaluations of current raw material manufacturers and service providers in this order:

- Contract Manufacturers
- Contract Testing Laboratories
- Raw Material Supplier, Risk evaluations will be prioritized based on the materials supplied. Evaluations will be performed on those suppliers that provide materials categorized as “F” followed by those that provide “E” item, “D” items and finally “C” items.
- Material Storage Facilities
- Document Storage Facilities
- Calibration Service Providers

4.7.2.3 Phase 2B Supplier Surveys

Supplier Surveys will be sent in the following order :

- Contract manufacturers in use.
- Contract Testing Laboratories in use
- Raw Material Suppliers
- Material Storage Facilities
- Document Storage Facilities
- Calibration Service Providers
- Risk is recalculated based on survey responses.

4.7.2.4 Phase 3 – Re-evaluation and Maintenance

The implementation of the risk scores is complete. Risk scores are re-evaluated and become an input to the supplier program.

4.8 Risk Re-Evaluation and Maintenance

4.8.1 The risk for new manufacturers or service providers is calculated during the supplier approval process per ***SOP 21109 – Supplier Qualification Program***.

4.8.2 Risk for a current supplier is re-evaluated or recalculated during the following events:

- After onsite external audits
- After new raw materials or services are added
- After notification of site changes
- After business changes made (e.g., buy-out or merger)
- After notification of FDA action (warning letter, recall, OAI)
- After internal customer feedback concerning quality or customer service issues
- After evaluation of a supplier survey.
- After any event that may change the manufacturing or service provided

4.8.3 If none of the above events trigger a recalculation of the risk score, the score is recalculated every five (5) years during a supplier review.

4.8.4 A recalculation of the risk is limited to approved suppliers.

4.9 Records

A supplier risk file is maintained by QA.

5.0 Definitions

Critical Supplier: A supplier of a product or service of which whose failure to meet specified requirements could cause unreasonable risk.

Characterization Testing: Characterization testing is used to gain additional understanding of the physical and chemical properties of a product. Characterization tests are not used for product release and typically do not have acceptance criteria.

6.0 References and Related Documents

SOP 21109 *Supplier Qualification Program*

SOP 21105 *Conducting External Audits*

7.0 Change Summary