Title: Supplier Qualification Program

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1.0 Purpose

Suppliers of raw materials, manufacturing services, testing services, and other service providers must be approved before being used to support GMP manufacturing and testing activities. This SOP defines the procedure to ensure confidence that raw materials and contracted services are supplied consistently and meet pre-determined levels of quality. Components of this program include historical performance of the supplier, supplier audits and, as appropriate, laboratory testing. The program is comprised of an initial 'Approval' step for the supplier, and a subsequent 'Qualification' step involving an assessment of the supplier's ability to consistently supply materials or services that meet specifications.

2.0 Scope

This procedure is applicable to suppliers of CGMP manufacturing associated raw materials, outside testing services, contract-manufacturing facilities, and other service providers. Suppliers already in use prior to the issuance of this SOP will initially be given the status of approved. Changes to their status will be governed by this SOP. This procedure does not apply to those raw materials that are classified as “A Inspection Level Items” and receive only a catalog number verification prior to being approved for use. These items are approved by Biopharmaceutical Quality Assurance (BQA) by approving the Part Number Request.

3.0 Authority and Responsibility

3.1 The Director, Biopharmaceutical Quality Assurance (BQA) has the authority to define this procedure and is responsible for the implementation of this procedure.

3.2 Materials Management and Inventory Control (MMIC) and Biopharmaceutical Development Program (BDP) Operations.

3.2.1 MMIC and BDP Business Operations personnel are responsible for identification of potential new suppliers of raw materials, contract manufacturers, and service providers.

3.2.2 MMIC, BDP Business Operations personnel, and users are responsible for communicating problems with raw materials (suppliers, etc.) to BQA and Management.

3.3 Process Analytics/Quality Control (PA/QC)

3.3.1 PA/QC personnel are responsible for the identification and for assisting in the qualification of new outside testing services.

3.3.2 PA/QC personnel are responsible for communicating problems with outside testing services to BQA and Management.

3.4 Biopharmaceutical Quality Assurance (BQA)

3.4.1 BQA is responsible for performing supplier audits. See ***SOP 21105 - Conducting External Audits.***

3.4.2 BQA is responsible for establishing and maintaining a database of suppliers’ Approval/Qualification status.

3.4.3 BQA is responsible for quality oversight of this procedure.

4.0 Raw Material Supplier Approval and Qualification

4.1 Part Number Requests (Documenting Approval of Suppliers)

4.1.1 The Supplier Qualification Program (SQP) is accessed whenever a new or revised Part Number Request form is submitted to Quality Assurance that designates a unique part number for a raw material and identifies its specific suppliers.

4.2 BQA approval of the Part Number Request is based on the particular specifications being applied to the raw material and on the supplier’s status as an approved vendor.

4.2.1 Initial Approval (of New Suppliers)

Initial approval of a supplier is documented on Form 21109-01. Approval of the supplier may be based on the following considerations.

4.2.1.1 The supplier's performance with similar materials (if the supplier is already a "qualified" supplier for similar materials, the supplier may be considered "approved" for this new material.)

4.2.1.2 The supplier's compliance to a quality system (GMP, ISO-9000, ICH, etc.).

4.2.1.3 The supplier has been audited by BQA or other programs with which the BDP shares information (when the necessary confidentiality agreements are in place).

4.2.1.4 Availability and assessment of FDA inspection documentation, such as Establishment Inspection Reports (EIRs) and Warning Letters, if any.

4.2.1.5 Supplier is sole-source for the part/material.

4.2.1.6 Material is being supplied by a Third Party for use in a specific project.

4.2.2 Conditional Approval (for New Suppliers)

Whenever there is insufficient data to approve a supplier, but there are extenuating circumstances that require the use of that supplier, a conditional approval may be granted. Once sufficient data is obtained that satisfies approval requirements full approval may be granted. Conditional approvals may be revoked by BQA should subsequent data reveal the supplier does not meet requirements and expectations.

4.3 Changes to Approval Status

4.3.1 Changes to supplier approval status are documented and justified on Form 21109-01. If approval for the supplier is being withdrawn, the Part Number Request Form and the Material Specification Sheet are updated to reflect this change.

The following events may cause a supplier to lose approval, be designated as "inactive" or be designated as "probationary approval" depending on the severity, significance, and scope of the identified problem.

4.3.1.1 Confirmed Out-of-Specifications (OOS) with product manufactured and/or distributed by the supplier.

4.3.1.2 Other significant problems with the manufacturer or supplier (such as FDA Warning Letters, Product Recalls, etc.).

4.3.1.3 Materials are no longer obtained from the supplier (designation of "Inactive").

4.3.1.4 Significant changes in the supplier facilities, location, manufacturing methods, or ownership.

4.3.2 Probationary Approval (for Existing Suppliers)

A probationary approval is granted to previously-approved suppliers that have had questionable histories; quality, supply, or other problems; or are in the initial stages of being reinstated into the SQP after having been removed for cause. Probationary approvals may be revoked by BQA should subsequent data reveal that the supplier does not meet requirements and expectations.

4.4 Supplier Qualification Process

4.4.1 Approved suppliers may be "qualified" with additional information regarding the quality of the supplier's product and performance. This additional information includes the following.

4.4.1.1 BDP experience with the supplier's product (the last five consecutively-received lots of product were shown to meet specifications.).

NOTE: The requirement for "consecutively-received lots of product" may be met by other similar products manufactured by the same supplier.

4.4.1.2 On-site audit information that confirms that the manufacturer is in compliance with a quality system that is consistent with GMP requirements for Phase I/II clinical products.

4.5 Revocation of "Qualified" Status

See Section 4.3, Changes to Approval (for Existing Suppliers) when changes to the approved status of a vendor are necessary.

4.6 Requests for Change in Release Requirements for Components/Materials

4.6.1 A reduction in the in-house testing conducted for an approved vendor or vendors may be requested as outlined below in Step 4.6.2. The vendor or vendors must have a positive history of supplying a specific material/component to the BDP that have been inspected, tested and released for use.

4.6.2 The requestor prepares and submits Form 21109-04 Request for Change in Release Requirements for a Component/Material (Attachment 4) to BQA. The form must include the following information.

4.6.2.1 BDP Part Number, Description, Current Inspection Level, and the requested change.

4.6.2.2 **Justification:** Thoroughly explain the reason for the request (e.g., justified by a successful manufacturer audit and material release history).

4.6.2.3 Requestors must provide supporting documentation for reduced release requirements in Section 2 of Form 21109-04.

4.6.2.4 The date of the last acceptable audit of the manufacturer by BQA must be recorded.

4.6.2.5 The user must provide documentation of at least five sequential unique lots of material released successfully by BDP for each manufacturer.

4.6.2.6 The requestor forwards the completed form to BQAD for tracking and approval by BQA.

4.6.2.7 The form is reviewed by BQA.

4.6.2.7.1 If BQA approves Form 21109-04, a revision to the associated Master Specification is initiated as per ***SOP 21903 - Using the Part Number/Master Specification Program to Establish Raw Material Part Numbers and Master Specifications***.

4.6.2.7.2 If BQA rejects the form, the reason for the rejection is given and the form is returned to the requester for correction or withdrawal of the request.

4.7 BQA Oversight of Raw Material Suppliers

4.7.1 Approved suppliers are re-evaluated via an on-site audit at least every three (3) years. See section 4.3, Changes to Approval Status.

4.7.2 Qualified suppliers are re-evaluated via an on-site audit at least every six (6) years. See Section 4.3, Changes to Approval Status.

5.0 Contract Manufacturer Approval

5.1 Selection of Contract Manufacturing Services

5.1.1 Contract manufacturing services are selected by the manufacturer's ability to consistently:

5.1.1.1 Provide product that meets specifications.

5.1.1.2 Meet pre-determined levels of quality.

5.1.1.3 Comply with applicable regulations.

5.1.1.4 Provide product on time and within budget.

5.1.1.5 Sign a mutually-approved Quality Agreement.

5.1.2 Information provided by the manufacturer from its web site or company brochure may be used as an initial assessment of a contract manufacturer's capabilities.

5.1.3 Contract manufacturers must have a quality system in place that is consistent with the CGMP requirements for Phase I/II clinical products as defined in 21-CFR-210/211, 21-CFR-600, and relevant guidelines.

5.2 Approval of Contract Manufacturing Services

5.2.1 Contract manufacturers are approved based on an acceptable audit by BQA and/or on past experience with the manufacturer.

5.2.2 Contract manufacturers will operate under a Quality Agreement approved by BQA as per ***SOP 21108 - Establishing a BDP Quality Agreement with Subcontractors***.

5.3 Qualification of Contract Manufacturing Services

Contract Manufacturers may be "Qualified" with additional information regarding the quality of the supplied product. Contract Manufacturers may be considered for qualification with BDP's successful experience with the vendor's manufactured materials (at least three (3) consecutive lots received with acceptable quality passing PA/QC testing and Batch Production Records reviewed/accepted by BQA). Qualified contract manufacturers are audited less frequently, once qualified, than approved contract manufacturers.

5.4 BQA Oversight of Contract Manufacturers

5.4.1 "Approved" contract manufacturers are evaluated for an on-site GMP audit at least every two (2) years as long as they remain under an active contract with the BDP. Any significant changes or potential impacts to their quality or manufacturing systems require an audit/reassessment. See Section 4.3, Changes to Approval Status.

5.4.2 "Qualified" contract manufacturers are evaluated for an on-site GMP audit at least every five (5) years as long as they remain under an active contract with the BDP.

Any significant changes or potential impacts to their quality or manufacturing systems require an audit/reassessment. See Section 4.3, Changes to Approval Status.

6.0 External Testing Services, Approval and Qualification

6.1 Selection of External Testing Services

Analytical/Testing laboratory services are selected by PA/QC and BQA for their ability to provide accurate and precise results and an appropriate level of compliance and control during sample handling, testing, and reporting.

6.2 Approval of External Testing Services

External testing services are approved based on:

6.2.1 Past history with the service provider.

6.2.2 Information provided by the testing service from its web site, testing manual, or copy of procedure(s) used.

6.2.3 External testing services, must have a quality system in place that supports 21 CFR 211, Subpart I, GMP Laboratory Controls and/or 21 CFR 58, GLP regulations. Other quality systems may be acceptable based on the audit, type of testing needed, and approval by BQA.

6.3 Qualification of an External Testing Service

Approved testing services may be “qualified” by passing an on-site audit and with additional information regarding the quality of the supplier’s service. Contract testing companies may be considered for qualification after a review of BDP’s experience with the service. Results of blinded sample analysis, deviations, non-conformances, sample management, timely processing of samples, and results of on-site audits factor into a decision for qualification.

6.4 BQA Oversight of Contract Testing Labs

6.4.1 Approved external testing services will be evaluated for an on-site GMP audit once every three (3) years.

6.4.2 Qualified outside testing services will be evaluated for an on-site GMP audit once every six (6) years.

7.0 Service Provider Approval

7.1 Selection of Service Providers

Service providers are selected for their ability to provide an appropriate level of control for the service to be provided.

7.2 Approval of Service Providers

7.2.1 Service Providers are approved based on:

7.2.1.1 Past history with the service provider.

7.2.1.2 Information provided by the service provider or company brochure on the type of service provided.

7.2.1.3 Information provided by the service provider on compliance to a quality system or performance standard.

7.2.2 An audit may not be required of the service provider if the service is provided on site (e.g., pest control, on-site calibration) since the performance of duties may be directly observed. However, an audit may be requested by BQA or others.

8.0 Supplier Audits

8.1 Audits of suppliers will be conducted as per ***SOP 21105 - Conducting External Audits***.

8.1.1 **Suppliers are evaluated for whether an on-site audit is needed based on the frequencies described in the sections above. This evaluation includes:**

8.1.2 Criticality of the material or service supplied

8.1.3 Experience with supplier and audit history

8.1.4 Need/Use Frequency

8.1.5 Interval since last audit

8.2 An audit schedule is developed based on the evaluations in step 8.2. Significant changes to the audit schedule (postponements or cancelations) will be documented and included with the schedule.

9.0 Supplier Database

9.1 Supplier information that contains the approval status of raw material suppliers, contract manufacturers, external testing services, and service providers based on audits conducted by BDP is maintained in the BQA Audit database.

9.2 Additional information on suppliers may also be obtained from the Part Number, Master Specification and Accession Log databases located on BDP Public.

10.0 Definitions

10.1 **Approved Supplier –** A supplier that has been designated by Quality Assurance as providing materials or services meeting BDP requirements.

10.1.1 **Conditional –** Supplier that may not have met all requirements to be approved, but needs to be added to the supplier database so that a performance history can be established.

10.1.2 **Probationary –** Supplier, who depending on severity, significance and scope of identified problems, has had its approved or qualified status revoked.

10.2 **Audit –** An inspection of the supplier's operation, facilities, and quality system to assess whether the controls in place ensure that a quality product is being produced.

10.3 **Contract Manufacturer –** A manufacturer that performs manufacturing operations under contract to the BDP.

10.4 **Disapproved Supplier –** A supplier whose approved status has been rescinded, typically as a result of inconsistent product quality or inadequate compliance to requirements.

10.5 **Inactive Supplier –** Supplier that was once approved or qualified, but is no longer used or no longer supplies the material or service.

10.6 **Manufacturer –** A business engaged in manufacturing, preparing, propagating, compounding, processing, packaging, or labeling of a desired commodity.

10.7 **External Testing Services –** A laboratory that performs analytical testing for the BDP.

10.8 **Qualified Supplier –** A supplier that has a successful history of providing materials or services meeting BDP requirements and has been audited by Biopharmaceutical Quality Assurance.

10.9 **Supplier –** A business that furnishes or provides materials or services. Suppliers may be the manufacturer of the product provided or they may provide materials manufactured elsewhere.

10.10 **Vendor –** A business that sells raw materials. A vendor may also be a manufacturer of raw materials.

NOTE: The term "Supplier" will be utilized throughout this document to represent a manufacturer, supplier, distributor, or vendor.

11.0 Documentation

11.1 BQA will complete Forms 21109-01, 21109-02, 21109-03 as needed to document the supplier evaluations conducted. Form 21109-04 is completed by the requestor and the form is subsequently reviewed and approved by BQA.

12.0 References and Related Documents

12.1 **SOP 21105** *Conducting External Audits*

12.2 **SOP 21108** *Establishing a BDP Quality Agreement with Subcontractors*

12.3 **SOP 21903** *Using the Part Number/Master Specification Program to Establish Raw Material Part Numbers and Master Specifications*

13.0 Attachments

13.1 **Attachment 1** Form 21109-01, Supplier Evaluation (Approval/Qualification)

13.2 **Attachment 2** Form 21109-02, Supplier Evaluation (Event Notification)

13.3 **Attachment 3** Form 21109-03, Supplier Evaluation (Reclassification)

13.4 **Attachment 4** Form 21109-04, Request for Change in Release Requirements for a Component/Material

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

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Attachment 1

FNLCR
Form No.: 21109-01
SOP No.: 21109
Revision 04: DEC 04 2015

SUPPLIER QUALIFICATION PROGRAM
Supplier Evaluation (Approval/Qualification)

Supplier Name

Address:

Classification of Supplier □ Raw Material Manufacturer □ Raw Material Supplier
□ Contract Analytical Lab □ Contract Manufacturer □ Contract Service

Approval

Criteria:

□ **Past Performance:** (□ NA)
□ Acceptable □ Unacceptable

□ **Quality System;** (□ NA)
□ 21 CFR 210/211 (Drug GMP) □ ISO-9000
□ 21 CFR 600 (Biologics GMP) □ ICH
□ 21 CFR 58 (GLP) □ Other (List): _____

□ **BQA On Site Audit** : (□ NA)
Date_____ Status: □ Acceptable □ Unacceptable
Comments: _____
_____

□ **FDA Inspection:** (□ NA)
Date_____ Status: □ Acceptable □ Unacceptable
Comments: _____
_____

□ **Sole Source:** □ Yes □ NA □ **Third Party Supplied**: □ Yes □ NA

Supplier Status □ Conditional □ Approved □ Other: _____

Assigned By_____Date_____

Qualification

Criteria:

□ Past lots / service acceptable (list date released and status or attach supporting documentation)

	Item	Cat. No.	Status
1.			
2.			
3.			
4.			
5.			

□ Quality Agreement In Place (Contract Mfg) □ Yes □ No

□ BQA On-site Audit □ Date_____ Status □ Acceptable □ Unacceptable

Supplier Status □ Qualified

Assigned By: _____ Date: _____

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Attachment 2

FNLCR
Form No.: 21109-02
SOP No.: 21109
Revision 04: DEC 04 2015

SUPPLIER QUALIFICATION PROGRAM
Supplier Evaluation
(Event Notification)

Supplier Name:

Address:_____

_____

Contact Person: _____

Event Notification

- ☐ OOS (OOS Number(s):_____
- ☐ Problem w/Supplier
- ☐ Material No Longer Available form Supplier
- ☐ Change Notification
  - ☐ Facilities
  - ☐ Location
  - ☐ Mfg Method
  - ☐ Ownership
  - ☐ Other_____

Comments

_____

_____

_____

Evaluation

- ☐ Maintain Current Status of_____
- ☐ Reclassify Supplier-Complete Form 21109-03 _____

Approved By_____**Date**_____

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Attachment 2

FNLCR
Form No.: 21109-03
SOP No.: 21109
Revision 04: DEC 04 2015

SUPPLIER QUALIFICATION PROGRAM
Supplier Evaluation
(Reclassification)

Name_____

Address_____

_____

Reclassification from a status of _____

To: ☐ Approved
☐ Unapproved
☐ Probationary
☐ No Longer Used/Inactive
☐ Other (explain): _____

Reason for Reclassification

☐ Confirmed OOS OOS Number(s): _____
☐ Unresolved (Explain below)
☐ Problems w/Supplier (Explain below)
☐ Material No Longer Obtained from Supplier
☐ Supplier Changed:
☐ Facilities
☐ Manufacturer
☐ Method
☐ Ownership
☐ Other_____

Comments: _____

_____

_____

_____

Approved By_____ **Date**_____

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Attachment 2

FNLCR
Form No.: 21109-04
SOP No.: 21109
Revision 04: DEC 04 2015

Request for Change in Release Requirements for a Component/Material

Section 1. Background

BDP Part No.: _____

Description: _____

Current Inspection Level Category: _____

Justification: Describe the event or history that supports the request to modify the Release Requirement.

_____
_____
_____
_____
_____

Affected Manufacturer(s):

Manufacturer	Current Release Requirements	Proposed Release Requirements

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Attachment 4 (Continued)

FNLCR
Form No.: 21109-04
SOP No.: 21109
Revision 04: DEC 04 2015

Request for Change in Release Requirements for a Component/Material

Section 2. Supporting Documentation for Reduced Release Requirements

Part 1. Manufacturer Qualification: List the manufacturer(s) that are affected by this request, and their audit dates.

Manufacturer	Audit Date by BQA	Approved Manufacturer?
		YES / NO
		YES / NO

Part 2. Material History: List at least five sequential unique lots for each manufacturer listed above that have been successfully approved by BDP.

Manufacturer	Manufacturer Lot Number	BDP Lot Number	Material Meets RMMS Requirements?
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO
			YES / NO

Comments:

_____
_____
_____
_____

Section 3. Approvals

Requestor Signature/Date: _____

BQA Approval/Date: _____

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