QUALITY AGREEMENT

Purchase Request # _____
Contract # (when available) _____
Revision: SOP 21108, Form 01(7/9/04)
Supersedes: None

BETWEEN:

SAIC-FREDERICK, INC.

NCI Frederick
PO Box B
Frederick, MD 21702-1201

Approved By SAIC Quality Contact: _____
Printed Name: _____
Title: _____
Date: _____

AND

SUBCONTRACTOR

Company Name (Insert)
Address (Insert)
Address (Insert)

Approved By Subcontractor Quality Contact: _____
Printed Name: _____
Title: _____
Date: _____

SAIC-FREDERICK, INC. CONTACTS

Primary Contact / Contracting Officer's Technical Representative (COTR)
INSERT

Quality Assurance Contact
INSERT

Business Contact
INSERT

Person(s) in the Plant Contact
INSERT

SUBCONTRACTOR CONTACTS

Primary Contact
INSERT

Quality Assurance Contact
INSERT

Business Contact
INSERT

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Supersedes: None

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1. QUALITY AGREEMENT

1.1 This document establishes the expectations that SAIC-FREDERICK, INC. has for its SUBCONTRACTORS in performing manufacturing activities supporting SAIC-FREDERICK, INC. projects.

1.1.1 The SUBCONTRACTOR must design systems and conduct activities in compliance with various laws and regulations including, but not limited to:

- State and local laws/regulations/ ordinances/ standards, etc
- 21 CFR 210 / 211: Good Manufacturing Practice Regulations
- 21 CFR 600, 601, 610: Biologics regulations
- 21 CFR 11, Electronic Records and Signature regulations.

1.1.2 Special attention is required to design systems and conduct activities to prevent cross contamination of product and to generate good documentation that assure the traceability of equipment, materials, personnel, products, processes, etc. in accordance with FDA/ICH Guidance Documents.

1.2 Documentation and records pertaining to SAIC-FREDERICK, INC. product, processes or supporting activities must be made available to SAIC-FREDERICK, INC. when requested for review. Copies must be provided when requested.

1.3 The SAIC-FREDERICK, INC. and the SUBCONTRACTOR will collaborate on overall product performance to assure the consistent and acceptable quality, integrity, purity and stability of the product.

2. TERM OF AGREEMENT

2.1 This agreement will be effective at the time all required signatures are captured on this document. The Quality Agreement shall be completed and executed prior to the full execution of the subcontract or Basic Ordering Agreement. The Quality Agreement shall be made an attachment to the Subcontract or Basic Ordering Agreement, upon the conclusion of negotiations, and full execution of the Subcontract or Basic Ordering Agreement.

2.1.1 After the close of the contract, the SUBCONTRACTOR agrees to provide documents, testing, record review, as needed, to investigate issues of product quality.

2.1.2 After the close of the contract, the SUBCONTRACTOR agrees to notify SAIC-FREDERICK, INC. of any issue that they become aware of that could

adversely affect the quality of the product produced. These events include, but are not limited to, failure of validations or calibrations that affect SAIC-FREDERICK, INC.'s product, or subsequently detected error, deficiencies or inconsistencies with manufacturing or test records.

2.2 Changes to this document may be made as needed with the written approval of both parties. The document will be modified, re-approved and re-signed.

3. PRODUCT

3.1 The product and a description of activities applicable to this agreement are described in its associated technical specification and/or protocol, and subcontract referenced on the cover page of this document.

4. COMMUNICATION

4.1 Names and information for SAIC-FREDERICK, INC. and the SUBCONTRACTOR contacts are stated on the cover page of this document.

4.2 Each party will notify the other party's Primary Contact and QA Contact immediately (within 1 business day) of any issues that impact the SUBCONTRACTOR's ability to conduct SAIC-FREDERICK, INC.-contracted activities.

4.3 Events that require notification by the SUBCONTRACTOR to SAIC-FREDERICK, INC. include, but are not limited to, the events listed below. The SUBCONTRACTOR should also alert SAIC-FREDERICK, INC. of any other issues or information that have (or could have) an effect on the quality of SAIC-FREDERICK, INC. projects. Communication may occur via phone, FAX, or electronic mail. All communications that do not generate a written record (i.e. phone communications or communication at a meeting, etc) must be followed with a written notification within 2 business days.

REQUIRED NOTIFICATION BY THE SUBCONTRACTOR TO SAIC-FREDERICK, INC.		
EVENT	Notification required to SAIC-FREDERICK, INC.'s ….	Timeframe
Changes to critical staff	Technical and QA Contacts	3 business days
Events that would impact the SUBCONTRACTOR's ability to conduct SAIC-FREDERICK, INC.-contracted activities	Technical and QA Contacts	Within 1 business day

REQUIRED NOTIFICATION BY THE SUBCONTRACTOR TO SAIC-FREDERICK, INC.		
EVENT	Notification required to SAIC-FREDERICK, INC.'s ….	Timeframe
Discussion of technical issues	Technical Representative	As needed
Discussion of quality issues	QA Contact	As needed
Request for the convening of a Quality Review Board	QA Contact	As needed
Need anticipated for reprocessing / rework	Technical/QA/ Business Contacts	Before reprocessing / rework
Verified OOS event	Technical and QA Contacts	Within 1 business day
Errors or deviations	Technical/QA/ Business Contacts	Within 1 business day
Product disposition issues	Technical/ QA/ Business Contacts	When recognized
Anticipation of rejecting a batch	Technical/ QA/ Business Contacts	Before the decision to reject
Initiation of an FDA (or other regulatory) inspection during the manufacture of an SAIC-FREDERICK, INC. product.	QA Contact	Within 1 business day
Receipt of an FDA 483, Warning Letter or other regulatory action	QA Contact	Immediately (within 1 business day)
Destruction of contract-associated records	QA Contact	At least 30 days prior to record destruction

4.4 Events that require notification by SAIC-FREDERICK, INC. to the SUBCONTRACTOR include, but are not limited to, the events that are listed below. SAIC-FREDERICK, INC. will also alert the SUBCONTRACTOR of any other issues or information that have (or could have) an effect on the quality of SAIC-FREDERICK, INC. projects. Communication may occur via phone, FAX, or electronic mail. All communications that do not generate a written record (i.e.

phone communications or communication at a meeting, etc) must be followed with a written notification within 2 business days.

REQUIRED NOTIFICATION BY SAIC-FREDERICK, INC. TO THE SUBCONTRACTOR		
EVENT	Notification required to the SUBCONTRACTOR's ….	Timeframe
Events that would impact the SUBCONTRACTOR's ability to conduct SAIC-FREDERICK, INC.-contracted activities	Technical/QA/ Business Contacts	Within 1 business day)
Request for the convening of a Quality Review Board	QA Contact	As needed
Deviations or Errors detected by SAIC-FREDERICK, INC. during review	QA Contact	As discovered
Determination that a batch is unacceptable for release	QA / Business Contact	As discovered

5. ADMINISTRATIVE INFORMATION

5.1 Organizational Structure

SUBCONTRACTORs must maintain an adequate number of qualified personnel to perform and supervise SAIC-FREDERICK, INC. project-related activities and to meet the requirements of the GMPs.

5.1.1 Personnel must have the appropriate education and experience and be adequately trained on all procedures applicable to their responsibilities for the manufacture of SAIC-FREDERICK, INC. products. This training must be in a formal training program that delineates requirements for basic and on-the-job training based on job function. In addition, there must be a requirement for mandatory cGMP training for new employees and refresher training with sufficient frequency to ensure employees remain familiar with requirements as they apply to their day-to-day responsibilities. This training must be documented and available for review.

5.1.2 Changes to Key Personnel relating to the performance of this subcontract must be conducted pursuant to Section G. "Key Personnel" of the Subcontract

5.2 Quality Review Board

5.2.1 A Quality Review Board will be established consisting of the designated contacts of SAIC-FREDERICK, INC. and of the SUBCONTRACTOR and including other appropriate members from each organization. The Quality contacts from each organization will serve as co-chairs of this forum.

5.2.2 The Quality Review Board will meet as needed to provide appropriate quality oversight of the project and will serve as the mechanism for resolving quality matters.

5.2.3 The QA or Primary Contact of either organization can request convening the Quality Review Board.

6. SAIC-FREDERICK, INC. RESPONSIBILITIES

6.1 Technology Transfer Information

6.1.1 SAIC-FREDERICK, INC. will provide available technology transfer documents that pertain to the work the SUBCONTRACTOR will be performing. When available, these may include (but are not limited to) production and test methods, sampling plans, sample handling instructions, specifications, etc.

6.1.2 SAIC-FREDERICK, INC. will provide the information needed to format specific product labels

6.1.3 SAIC-FREDERICK, INC. will provide reference standards where applicable.

6.1.4 SAIC-FREDERICK, INC. will be responsible for establishing and approving any required stability program.

6.2 Participation in Planning for Manufacture

6.2.1 SAIC-FREDERICK, INC. will provide Quality Assurance review and approval of all relevant process-specific procedures including (but not limited to) standard operating procedures, master production and control records, quality control test methods, specifications, etc.

6.2.2 SAIC-FREDERICK, INC.'s COTR is available to the SUBCONTRACTOR to discuss technical issues or recommend changes. As needed, the COTR may ask other SAIC-FREDERICK, INC. qualified staff to participate in technical discussions. Any deviations in the Statement of Work must go through the SAIC Contracting Officer for modification and official approval.

6.2.3 SAIC-FREDERICK, INC.'s QA Contact is available to the SUBCONTRACTOR to discuss quality or regulatory issues. As needed, the QA Contact may ask other SAIC-FREDERICK, INC. qualified staff to participate in these discussions.

6.2.4 The Quality Review Board may be convened at any time at the request of the SUBCONTRACTOR and / or SAIC-FREDERICK, INC. to discuss issues or to plan for future activities.

6.3 Manufacturing Oversight

6.3.1 SAIC-FREDERICK, INC. will verify through batch record review and test record review that all clinical trial material complies with predetermined specifications and has been released to SAIC-FREDERICK, INC. by the SUBCONTRACTOR's QA.

6.3.2 SAIC-FREDERICK, INC. will assist in the evaluation of errors, deviations and out-of-specification events as needed.

6.3.3 SAIC-FREDERICK, INC. will notify the SUBCONTRACTOR of any deviations or errors detected during a review of project-specific documentation. The SUBCONTRACTOR will subsequently document these events according to its established deviation procedure.

6.3.4 In the event SAIC-FREDERICK, INC. finds a batch unacceptable for release, SAIC-FREDERICK, INC. will notify the SUBCONTRACTOR's QA Contact and discuss the reasons for the rejection. A meeting of the Quality Review Board may be convened to discuss these issues.

6.4 Product Release to the Clinic

6.4.1 The SUBCONTRACTOR does not release the final product to the clinic for human use.

7. MANUFACTURING AND LOGISTICS

7.1 Person-in-the-Plant

7.1.1 The SUBCONTRACTOR must allow SAIC-FREDERICK, INC.'s Person-in-the-Plant (PIP) access to the facility to observe various operations and assist in problem solving for the activities specific to SAIC-FREDERICK, INC. project(s). Any such "in plant visits" will be coordinated in advance by both parties.

7.1.2 The SUBCONTRACTOR must allow SAIC-FREDERICK, INC.'s Person-in-the-Plant to verify that all documentation and records are complete and

accurate, including that, but not limited to, raw materials and components are released, equipment is within calibration, and the final training specific to the SAIC-FREDERICK, INC.'s clinical supply run has occurred with appropriate manufacturing personnel. This may also be performed by SAIC-FREDERICK, INC.'s QA during batch record review.

7.1.3 The SUBCONTRACTOR must provide training to the Person-in-the-Plant as needed to comply with any specialized gowning or safety requirements.

7.2 Facilities, Utilities and Equipment

7.2.1 General

7.2.1.1 Facilities, utilities and equipment must be qualified as is appropriate for the work being performed.

7.2.1.2 Equipment, facilities or utilities that support the aseptic filling process must be fully validated.

7.2.1.3 The SUBCONTRACTOR must have and maintain a preventive maintenance program for all critical systems, utilities, manufacturing and QC instrumentation and equipment and the documentation requirements that include a record of the type and frequency and details of service checks. The preventive maintenance program includes verification that the monitoring system alarms and the back-up generator, if so equipped, are functioning properly.

7.2.2 Facilities and Utilities

7.2.2.1 All utilities that could impact product quality (steam, gases, compressed air, and HVAC) are qualified and appropriately monitored and action is taken when limits are exceeded.

7.2.2.1.1 The SUBCONTRACTOR will have and maintain a HEPA filter certification program that routinely tests filter integrity.

7.2.2.2 The SUBCONTRACTOR must have and maintain procedures for ensuring that personnel, raw materials, equipment and waste flows are controlled to prevent cross contamination.

7.2.2.3 The SUBCONTRACTOR must have and maintain a procedure for area clearance and changeover between campaigns.

7.2.2.4 The SUBCONTRACTOR will assure that access to the manufacturing and testing facilities are restricted to authorized

personnel. Authorized visitors must be escorted at all times in areas used to manufacture, test and store SAIC-FREDERICK, INC. product.

7.2.3 Equipment

7.2.3.1 The SUBCONTRACTOR must have and maintain a calibration program. In the event an instrument is found to be out-of-tolerance (OOT), the period in which the instrument was in use starting with the last successful calibration will be evaluated for product impact.

7.2.3.2 The SUBCONTRACTOR will maintain records of equipment usage, cleaning, testing and any maintenance/calibration performed.

7.2.3.3 The SUBCONTRACTOR will provide information to SAIC-FREDERICK, INC. describing how manufacturing equipment was used immediately prior to its use in the manufacture of SAIC-FREDERICK, INC.'s product, how the equipment was cleaned to prevent carryover of the previous product, and test results that document that the equipment was adequately cleaned and suitable for use in the production of SAIC-FREDERICK, INC. product.

7.2.3.4 The SUBCONTRACTOR will use disposable or dedicated equipment whenever possible during the manufacture of SAIC-FREDERICK, INC.'s product.

7.3 Environment

7.3 1 The SUBCONTRACTOR must have and maintain an environmental program for viable surface and air samples, non-viable air particulate samples, personnel monitoring, and water (WFI, clean steam and purified water) that includes scheduled testing, reporting and trending of results, alert and action levels based on historical data and regulatory requirements, and an investigation procedure for excursions.

7.3.2 The SUBCONTRACTOR must have and maintain a procedure that specifies personnel gowning requirements based on room classification and use. There must be a gowning qualification and certification program for personnel performing aseptic operations that includes routine testing, alert and action levels, and data trending.

7.4 Cleaning and Disinfection

7.4.1 The SUBCONTRACTOR must have and maintain a validated procedure for cleaning dedicated equipment that reduces lot-to-lot carryover, eliminates endotoxin and microbial contamination, and removes the residual cleaning agent(s).

7.4.2 The SUBCONTRACTOR must have and maintain cleaning validation for non-dedicated equipment, e.g., filling needles, pump heads, bioreactors, chromatography columns, that demonstrates adequate removal of the previous product.

7.4.3 The SUBCONTRACTOR must have and maintain a procedure for facility cleaning based on room classification and use, including responsibilities, schedules, a list of qualified disinfectants, and documentation requirements.

7.4.4 The SUBCONTRACTOR will conduct a disinfectant effectiveness study that demonstrates approved disinfectants are qualified to effectively reduce levels of indigent microbial contamination and viruses from surfaces within the facility.

7.5 Computerized Processes

7.5.1 The SUBCONTRACTOR must have and maintain procedures for the operation and maintenance of computerized systems.

7.5.1.1 These procedures will include a disaster recovery plan that ensures that data integrity is maintained for all computerized systems in the event of a system failure that results in a permanent loss of electronic records.

7.5.1.2 The procedure will also include the periodic verification of system access privileges.

7.5.2 The SUBCONTRACTOR will assure that the computerized systems used in the production or support of GMP activities are validated appropriately (minimum I/OQ) based on the intended use of the material and based on the application’s diversity, complexity and criticality.

7.5.3 The SUBCONTRACTOR will assure that computerized systems are compliant with 21 CFR Part 11 and have sufficient controls to prevent unauthorized access or changes to the data and to prevent omissions in data. In addition, an audit trail will be maintained that records the original data, any change to the original data, who made the change and when the data was changed. Where critical data are being entered manually, there

is an additional check on the accuracy of the data. This can be done by a second operator or by the system itself.

7.6 Raw Materials, Components, Component Closures, In-process Intermediates, Finished Products

7.6.1 The SUBCONTRACTOR must have and maintain a written, approved procedure for the receipt, inspection, handling, sampling, testing, approval or rejection, and disposition of raw materials, components and component closures, in-process intermediates and finished product.

7.6.2 The SUBCONTRACTOR must have and maintain a procedure for proper segregation, storage, and controlled distribution of raw materials, components and component closures, and in-process intermediates to ensure traceability, and prevent cross contamination or the accidental use of unreleased materials.

7.6.3 The SUBCONTRACTOR must have and maintain a procedure that requires the identification of all animal derived raw materials and documented proof of the country of origin. Raw materials of animal origin should be avoided. Use of any material of animal origin must be discussed with the SAIC-FREDERICK, INC. COTR and Quality Contact.

7.6.4 The SUBCONTRACTOR must maintain relevant Certificates of Analysis, Certificates of Compliance and/or Certification of Origin (as appropriate) for raw materials.

7.7 Product and Lot Numbers

7.7.1 The SUBCONTRACTOR must have and maintain a written, approved procedure for the issuance of part and lot numbers that are used in cGMP documentation so that materials are uniquely identified and traceable.

7.8 Dates of Manufacture and Expiration

7.8.1 The date of manufacture for the final product fill is defined as the date of the final sterile filtration.

7.8.2 The shelf life of the final product will be supported by stability studies.

7.8.3 The SUBCONTRACTOR and SAIC-FREDERICK, INC. will work together to establish any necessary expiration dates for raw material, intermediate products, solutions, etc.

7.9 Reprocessing / Rework

7.9.1 The SUBCONTRACTOR must contact the SAIC-FREDERICK, INC. COTR, the SAIC-FREDERICK, INC. QA Contact, and the Contract's contact before initiating reprocessing or rework on any material. A meeting of the Quality Review Board can be convened to discuss these issues.

7.10 Product Labeling and Packaging

7.10.1 Labeling and packaging operations must be designed to provide component accountability and reconciliation.

7.10.2 The SUBCONTRACTOR will generate a label galley or proof for review and approval by SAIC-FREDERICK, INC. This review and approval by SAIC-FREDERICK, INC. must be documented.

7.10.3 The SUBCONTRACTOR must generate the labeling required to label the product according to the approved label proof. This labeling must be reviewed and approved according to the SUBCONTRACTOR's written procedures before the labeling is issued for use.

7.10.4 The SUBCONTRACTOR must have and maintain written, approved procedures for the control of labels and labeling materials, and for the approval, issuance, use and reconciliation and disposal of labels.

7.11 Storage and Shipment of Product

7.11.1 The SUBCONTRACTOR will assure that product is stored in suitable storage facilities that protect the product from possible deterioration, interference, theft, cross contamination, intermixing with other materials, or accidental use of unreleased material.

7.11.2 The SUBCONTRACTOR will package SAIC-FREDERICK, INC. product for transit as described in the contract. Each shipment will include a temperature-monitoring device unless appropriate shipping validation studies have been conducted and approved by SAIC-FREDERICK, INC. These records will become part of the product's batch production and control record.

8. QUALITY CONTROL

8.1 General

8.1.1 No additional testing or any change to testing specifications may occur without approval by the SAIC-FREDERICK, INC. COTR, the QA Contact,

and the Contract's contact; and the completion of any required change control documentation.

8.2 Test Specifications

8.2.1 The release testing specified for this project must be captured in a master specification document that is approved by SAIC-FREDERICK, INC.

8.3 Test Method Qualification

8.3.1 The SUBCONTRACTOR will assure that compendial test methods are qualified and that product-specific analytical methods have at least an approved test method using, as indicated, controlled reference standards, positive control and/or system suitability check.

8.3.2 Non-compendial methods must be validated.

8.4 Test execution

8.4.1 Testing must be conducted according to the written and jointly approved testing procedures.

8.5 Evaluation of Test results

8.5.1 The SUBCONTRACTOR will evaluate all test results to confirm conformance to established specifications

8.5.1.1 The results of testing by SUBCONTRACTORs must be reviewed and approved by the SUBCONTRACTOR's Quality Assurance Contact to confirm that the test results have been reviewed and approved and meet the specified testing requirements.

8.5.2 The SUBCONTRACTOR will establish a procedure for documenting deviations and the investigation of OOS test results.

8.5.3 The SUBCONTRACTOR must immediately initiate an OOS investigation for any product testing performed by the SUBCONTRACTOR that produces a test result that fails to meet a specification or action limit. This investigation must be documented.

8.5.3.1 The SUBCONTRACTOR must immediately notify the SAIC-FREDERICK, INC. COTR and Quality Contact when an OOS event is verified.

8.6 QC Materials

8.6.1 QC materials must be received according to the SUBCONTRACTOR's receival policies for GMP raw materials.

8.6.2 Qualification of critical quality control materials will be performed according to written and jointly approved specifications.

8.7 Reserve and Retention Samples

8.7.1 The holding of reserve or retention samples will be specified in the contract. Samples must be held in storage conditions that protect the sample's purity, identity, safety, sterility and quality. Holding areas must be regularly monitored for conformance to environmental requirements.

8.8 Stability Program

8.8.1 The SUBCONTRACTOR will execute any stability testing required by the contract and will comply with GMP requirements for Laboratory Controls for this testing.

9. QUALITY ASSURANCE

9.1 Documentation

9.1.1 Master Production Records and Product-Specific SOPs

9.1.1.1 The SUBCONTRACTOR is responsible for generating product-specific manufacturing and testing documentation designed to direct the production of product that is compliant to GMP requirements and to capture appropriate process data.

9.1.1.2 The SUBCONTRACTOR and SAIC-FREDERICK, INC. will jointly approve these documents before the commencement of manufacturing.

9.1.1.3 The SUBCONTRACTOR will provide copies to SAIC-FREDERICK, INC.'S QA Contact of all project-specific documents that have been approved by the SAIC-FREDERICK, INC.

9.1.2 General SOPs

9.1.2.1 The SUBCONTRACTOR's QA is responsible for generating and maintaining all SOPs and other documentation supporting cGMP operations within its facility. SAIC-FREDERICK, INC.

representatives must be permitted to review these documents on request.

9.1.3 Record Retention

9.1.3.1 The SUBCONTRACTOR will retain all manufacturing master production and control records, batch production and control records, production procedures, testing documentation, and shipping records in accordance with its internal record retention requirements and in compliance with 21 CFR 211.180d.

9.1.3.2 At least thirty days prior to record destruction, the SUBCONTRACTOR will alert the SAIC-FREDERICK, INC. Quality contact. SAIC-FREDERICK, INC. may request that the documentation or portions of the documentation be forwarded to SAIC-FREDERICK, INC. for archiving

9.2 Deviations and Investigations

9.2.1 The SUBCONTRACTOR QA must establish a corrective / preventive action system compliant with the requirements of CGMPs.

9.2.2 As part of the investigation into an error or deviation, the SUBCONTRACTOR must assess the event's impact on the affected product's purity, integrity, safety, and quality. The SAIC-FREDERICK, INC. COTR and Quality Contact are responsible for assisting in this evaluation when requested.

9.2.3 The SUBCONTRACTOR is responsible for alerting SAIC-FREDERICK, INC. of any error or deviation events.. This notification must be made immediately and within the next business day of discovery.

9.2.4 Corrective and preventive actions must be completed within 30 days from recognizing the event. If the completion of these actions requires more than 30 days, interim status reports must be filed at 30 days and regularly thereafter until the actions are closed.

9.2.5 Planned deviations may not be executed without being appropriately reviewed and approved by the SAIC-FREDERICK, INC. COTR and Quality Contact.

9.2.6 The SUBCONTRACTOR must have a procedure for handling complaints that requires as part of the investigation an immediate assessment of the batch records, test records and if applicable, stability data.

9.3 Right to Audit

9.3.1 SUBCONTRACTORs should be prepared to host audits by SAIC-FREDERICK, INC. at least annually. SAIC-FREDERICK, INC. will provide the SUBCONTRACTOR sufficient notice of the intent to audit or inspect the facility, manufacturing operations or testing operations for compliance with cGMPs and with the Quality Agreement. Audit duration is typically 2 days.

9.3.1.1 Audits will be scheduled with a minimum of a 2-week lead time with a maximum of 4 weeks from the initial request with the exception of “for cause” audits.

9.3.1.2 For Cause Audits: Scheduling of a “for cause” audit is determined on a case-by-case basis and can occur within 48 hours of the identification of a problem.

9.3.1.3 SAIC-FREDERICK, INC. will coordinate the scheduling of audits with the SUBCONTRACTOR’s management so that appropriate staff are available for the audit. SAIC-FREDERICK, INC.’s audit team may include SAIC-FREDERICK, INC. staff, other government employees, and/or consultants employed by SAIC-FREDERICK, INC.

9.3.2 At the conclusion of the audit, an exit meeting will be held with representatives from SAIC-FREDERICK, INC. and the SUBCONTRACTOR to discuss significant audit findings. A written audit report will be provided to the SUBCONTRACTOR, typically within 30 – 60 days of the conclusion of the audit.

9.3.3 The SUBCONTRACTOR will respond to audit observations within 30 days and detail the necessary corrective actions and timeframes for correction. Alternately, SAIC-FREDERICK, INC. may provide a corrective / preventive action plan to the SUBCONTRACTOR that identifies system deficiencies, corrective actions and timelines for completions.

9.3.4 The SUBCONTRACTOR will provide periodic reports (not less than every 6 months) on the progress of any corrective actions that require an extended period to implement.

9.4 Change Management

9.4.1 The SUBCONTRACTOR must have a written, approved procedure for managing and tracking changes to master production and control records, bill of materials, analytical standards, test methods (for raw materials and product), raw material and product specification and changes to validated facilities, utilities, computer systems, equipment or processes used in the

cleaning, manufacturing, testing, storage or shipment of SAIC-FREDERICK, INC. product. This procedure must require a documented technical and GMP impact assessment for all changes.

9.4.2 Proposed changes to project-specific documentation may only be accepted with the written approval of SAIC-FREDERICK, INC. and may require validation before the change may be implemented.

9.5 Document Distribution

9.5.1 The SUBCONTRACTOR will provide copies to SAIC-FREDERICK, INC. QA Contact of all project-specific documents that have been approved by SAIC-FREDERICK, INC.

9.6 Disposition of Product (Batch Release or Rejection)

9.6.1 Manufacturer's Release

9.6.1.1 The SUBCONTRACTOR's Quality Assurance must review all batch production and test records including label reconciliation, environmental monitoring data and trends, deviations and investigations. The SUBCONTRACTOR'S QA must confirm that the process was executed according to established requirements and that any deviations, etc. have been satisfactorily identified (documented) and addressed.

9.6.1.1.1 The SUBCONTRACTOR has the authority to reject batches, however, the SUBCONTRACTOR will notify SAIC-FREDERICK, INC.'s Technical and QA Contact of any batch being considered for rejection prior to the decision for rejection. A meeting of the Quality Review Board may be convened to discuss this issue and explore possible courses of action.

9.6.1.2 The SUBCONTRACTOR must provide a Certificate of Analysis to SAIC-FREDERICK, INC. which includes:

- Name and address of manufacturer
- Name of product (or product description)
- Batch or lot number
- Date of manufacture

- Quantity (# units and unit volume) available for the clinic
- Expiration date or re-test date based on stability data (if applicable)
- A list of each test performed, method description, specification and result.
- Review and approval signatures (Manufacturing or QC) and QA

9.6.1.3 The SUBCONTRACTOR must provide a Certificate of Conformance to SAIC-FREDERICK, INC. that verifies that the product was manufactured in compliance to cGMPs.

9.6.1.4 The SUBCONTRACTOR must provide a copy of the batch production and control record and all supporting documents including, but not limited to:

- QA reviewed batch record and buffer preparation records.
- All raw data and final reports for in-process and release tests, including all associated OOS reports
- Certificates of Analysis, and Certificates of Origin (or source origin statements), when applicable, for all raw materials, components and component closures
- Environmental and personnel monitoring data and/or trends
- Sterilization and depyrogenation records
- Label issuance and reconciliation records
- Filter integrity test results for sterilizing filter
- Transaction history (inventory at date of manufacture and all changes in inventory subsequent to that date) for bulk drug substance and/or finished drug product.
- Product storage monitoring data

- Copy of any other documentation of any communication between SAIC-FREDERICK, INC. and the SUBCONTRACTOR that have affected the manufacture or testing of the product.

9.6.2 Product Release to the Clinic

9.6.2.1 The SUBCONTRACTOR does not release the final product to the clinic for human use.

10. REGULATORY COMPLIANCE

10.1 Regulatory Documentation

10.1.1 The SUBCONTRACTOR agrees to provide to SAIC-FREDERICK, INC.'s Technical and Quality Contacts all documentation required for regulatory submissions and requested by Regulatory agencies. This may include items such as the Chemistry Manufacturing Control (CMC) section of an IND application, technical bulletins, summary reports, batch production and control records, Certificates of Analysis, source/origin information on raw materials or testing documentation.

10.2 Regulatory Inspections and Correspondence

10.2.1 The SUBCONTRACTOR must notify the SAIC-FREDERICK, INC. QA Contact immediately (within 1 business day) when an FDA (or other regulatory agency) inspection is commencing during the manufacture of an SAIC-FREDERICK, INC.'s product.

10.2.2 For inspections that involve SAIC-FREDERICK, INC. product, the SUBCONTRACTOR will allow a representative of SAIC-FREDERICK, INC. to be present.

10.2.3 The SUBCONTRACTOR must notify the SAIC-FREDERICK, INC. QA Contact, immediately (within 1 business day) on the receipt of an FDA 483, Warning Letter, or other regulatory action from FDA (or similar communication from other regulatory agencies).

10.2.4 Commitments to regulatory agencies regarding SAIC-FREDERICK, INC. product must only be made after agreement has been reached between SAIC-FREDERICK, INC. and the SUBCONTRACTOR. A meeting of the Quality Review Board may be convened to discuss this issue and to develop a mutually agreed-upon course of action.

10.3 Drug or Biologics Master File

10.3.1 If applicable, the SUBCONTRACTOR will provide a letter of authorization to reference the SUBCONTRACTOR's Drug or Biologics Master File.

11. RESOLUTION OF QUALITY-RELATED ISSUES

11.1 Quality-related issues will be discussed at the Quality Review Board where all parties shall strive to reach an agreement.

12. VALIDATION / VERIFICATION

12.1 Validation Master Plan

12.1.1 The SUBCONTRACTOR will have and maintain a Validation Master Plan that identifies critical equipment, systems and processes used to manufacture, test and evaluate product, and the requirements for validation and revalidation.

12.2 Process Validation

12.2.1 The SUBCONTRACTOR will establish and implement a procedure for the development and execution of SAIC-FREDERICK, INC.-specific Process Validation (PV) Test Plans as indicated in the manufacturing contract that appropriately identify critical process parameters to be controlled and monitored. Once validated, changes to critical process parameters will be implemented through a formal change control program that requires SAIC-FREDERICK, INC. pre-approval.

12.2.2 The SUBCONTRACTOR is responsible for assuring that the sterile fill process into final containers is fully validated, documented, and approved. The SUBCONTRACTOR must allow SAIC-FREDERICK, INC. representatives to review protocols and final reports associated with SAIC-FREDERICK, INC.-specific projects.

12.3 Cleaning Verification

12.3.1 The SUBCONTRACTOR is responsible for assuring that residues from previous uses of the equipment have been removed to acceptable levels. This verification activity must be documented.

12.4 Cleaning and Disinfection Validation

12.4.1 See previous section "Manufacturing and Logistics," subsection "Cleaning and Disinfection".