MILLS BIOPHARMACEUTICALS, INC.
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Quality Manual

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MBI Quality Manual

Foreword

Mills Biopharmaceuticals, Inc. (MBI) is a Manufacturer of medical devices based in Oklahoma City, OK. Established in 1993, MBI provides production capabilities which include radioisotope handling, labeling, and finish product manufacturing and distribution. In addition, non-radioactive processing of medical devices, finish product manufacturing and distribution provide total production capabilities.

MBI is committed to controlled growth by providing consistent processes, safe products and meeting our customers requirements through the implementation of our quality policy.

Our Quality System is an integrated effort at meeting cGMP requirements as set forth by the FDA. MBI is specifically structured to ensure full and continuous implementation of our quality policy. Our Quality System documentation has been designed to meet a diversity of quality requirements, while maintaining full compliance with the Code of Federal Regulations, Title 10, Part 21, Subpart 820.

MBI personnel and resources are dedicated to customer satisfaction. The ultimate measure of our success is the on-time delivery of a safe and effective product to our customers.

Quality Policy

MBI is committed to meet our customer's requirements by providing on-time scheduled delivery of a high quality defect-free product.

Mission Statement

Discipline, commitment, and perseverance through the full implementation of our Quality System will ensure that our Customers consistently receive the highest level of Product Performance and Product Quality.

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MANAGEMENT RESPONSIBILITY (4.1)

The MBI management group is responsible and committed to the full implementation of a company-wide system of quality and continuous improvement for achieving customer satisfaction and safety. The management group ensures that this system is fully understood and maintained at all levels of the organization.

ORGANIZATION (4.1.1)

MBI's Quality Policy clearly defines the company's responsibility and commitment to Quality Products and Customer Satisfaction. MBI, being a small organization, requires Dr. Stanley L. Mills the President/CEO to also serve as Quality Assurance Director. His responsibilities include: providing the Facilities, necessary Resources and Qualified Personnel to consistently maintain an effective Quality System to produce defect-free products and maintain MBI's Quality Policy.

Dr. Mills commitment to responsible implementation of MBI's written procedures and controls ensures that products meet quality standards established by customers requirements, internal company specifications, and regulatory agencies. Additionally, it is Management's responsibility to identify, plan, implement and evaluate on-going process improvements, set specific goals, provide related guidance, and support open communications at all levels of the organization to achieve customer requirements.

Management conducts regularly scheduled reviews to assess progress and effectiveness of the Quality System. These reviews include, but are not limited to reviewing internal audit results, customer complaints, production performance, nonconformance and personnel job functions. These reviews are conducted as a mean of achieving and maintaining MBI's Quality Policy.

PERSONNEL (4.1.2)

All employees at MBI are responsible for ensuring the manufacturing of a quality product and support the company's commitment to customer satisfaction. Ultimately, it is the responsibility of the total management to verify compliance with the Quality System and provide guidance in the identification, verification and implementation of solutions to correct/prevent nonconformance and the improvement of process control.

All personnel employed by the facility shall be trained in the operations of the department to which they are assigned. Established documented procedures for identifying training needs are maintained. Training for all personnel performing activities affecting quality shall be provided.

Personnel responsible for performing quality related activities are instructed as to the purpose, scope and implementation of the QA program, and Standard Operating Procedures.

Personnel performing specific assigned tasks will be qualified on the basis of appropriate education, training and/or experience, as required.

The scope, objective and method of implementing the indoctrination and training program are documented. Proficiency of personnel performing specific activities is maintained by retraining and re-certification. Documentation of appropriate training records are maintained by the responsible management personnel, as well as complete personnel files which may include medical records, if necessary.

QUALITY ASSURANCE PROGRAM (4.2)

A quality assurance program has been established to cover all the operations of Mills Biopharmaceuticals, Inc. This program is in effect throughout the entire company and is documented by written procedures.

All products are issued lot numbers and are manufactured in accordance with the Quality System Regulation (10 CFR 21 Part 820), using formal manufacturing documents. The control of these documents are in accordance with an established written procedure.

All raw materials and final products are released based upon a series of tests and specifications. Until release, the raw materials or final products are segregated by lot number and disposition (i.e., Quarantine, Release, Accept, Reject, In-Process), until testing and review is completed. All testing and specifications are established in a series of documents, in which, any changes must under go a revision and review/approval process.

Non-conforming materials are documented and reviewed by the Material Review Board (MRB). The MRB is made up of members from all departments involved in the process. The board will assign corrective action and/or preventive actions to eliminate the recurrence of the failure or non-conformance.

Departmental procedures are formalized and available to the areas and individuals having designated responsibilities. The procedures cover all functions of the given department.

Customer inquiries and complaints are investigated by the Quality Control and Quality Assurance. Products that have been distributed and not meeting specification are subject to a recall procedure, if applicable.

All activities affecting product quality are carried out under conditions which are suitably controlled to ensure that the right equipment and materials are used in the correct area and manner. Personnel in these areas are properly trained in the use of equipment as well as in the importance of Quality to the organization.

The status and adequacy of the Quality Assurance Program is reviewed periodically to insure that the quality of all products produced by this facility is maintained and continues to meet regulatory requirements. This is accomplished by review of each Standard Operating Procedure every two years or earlier as necessary (with revisions as necessary), and internal audits.

This Quality Assurance Manual is a formal and factual representation of the Quality Assurance Program and is reviewed by executive management every two years from issue date, with revisions and updates as necessary, to reflect the current program status.

Contract Review (4.3)

Documented procedures shall be established and maintained for contract review and for the coordination of these activities. Each tender, contract and/or order will be reviewed to ensure that:

a) the customer's requirements are adequately defined;

b) any differences between the contract or accepted order requirements and those in the tender are resolved; and

c) the company has the capability to meet the contract or accepted order.

How an amendment to a tender, contract or order is made and correctly transferred to the functions concerned within the organization will be identified and documented. Records of contract review will be maintained.

Following documented procedures, contracts are reviewed by quality assurance prior to being accepted. Contracts are reviewed to ensure: that customer requirements are understood, that differences between the customer's requirements and MBI's performance claims/policies/capabilities are discussed and resolved, that all regulatory requirements are adhered to, and that, ultimately, MBI can provide goods and services which meet or exceed the customer's specified requirements. Records of contract reviews are maintained.

EQUIPMENT (4.4)

Documented procedures to control, calibrate, maintain inspection, measure and test equipment used to demonstrate the conformance of product to the specified requirements shall be established and maintained. All such equipment that requires calibration is calibrated in a manner traceable to NIST standards, Accredited Dosimetry Calibration Laboratory, U.S.P., B.P, E.P, J.P. or equivalent where necessary.

Where test software or comparative references are used as suitable forms of inspection, analysis will prove that they are capable of verifying the acceptability of the product, prior to release for use during production, installation or servicing, and shall be rechecked at prescribed intervals. The extent and frequency of such checks shall be established. Records shall be maintained for document control.

Calibration activities are conducted in accordance with documented procedures, to ensure that all equipment requiring calibration is identified and calibrated on schedule. Calibration data and associate corrective action are recorded and maintained by quality assurance. Calibration labels, including last and next calibration dates, are attached to calibrated equipment, if possible. Any equipment, not requiring calibration, is labeled as such.

Calibrations may be performed by an approved calibration vendor. Other calibrations are performed by trained MBI employees, the equipment manufacturer/authorized dealer, or other qualified (third-party) personnel.

Some equipment used in the manufacturing of the device may be checked for accuracy and/or acceptable operation on a periodic basis. Equipment history logs will be maintained for each piece of equipment, which requires calibration, use, and maintenance as described in the written procedures.

DESIGN CONTROL (4.5)

In order to ensure that the specified requirements are met, documented procedures to control and verify the design of the product shall be established and maintained.

Design input requirements relating to the product, including applicable regulatory requirements, shall be identified, documented and their selection reviewed for adequacy. Design output shall be documented and expressed in terms that can be verified and validated against design input requirements.

At defined stages of the design process, formal documented reviews of the design results shall be planned and conducted. Participants at each design review shall include representative of all functions concerned with the design stage being reviewed. Records of such reviews shall be maintained.

MBI establishes, implements and maintains documented design control procedures to ensure that specified design requirements are met. These procedures address design and development planning, organizational and technical interfaces, establishing design input requirements, evaluating design outputs, reviews, verification, validation, and design changes. A design history file is maintained to ensure the device is developed in accordance with the approved design plan.

DOCUMENT CONTROL AND DATA CONTROL (4.6)

Documented procedures, that control all documents and data relating to the requirements of the Quality System Regulation shall be established and maintained.

All documentation required to ensure MBI's products and processes meet internal and regulatory requirements is controlled and available at the point of use either in hard copy or electronically. All controlled documents are clearly identified by a unique control number. Status of all controlled documentation is available either electronically or in hard copy to assure that only the most current versions of documents are in use. Not all copies of a controlled document are required to be controlled, if clearly identified as uncontrolled copies. Uncontrolled copies are for reference use only and may not be used in the final acceptance of products. It is the responsibility of the user to ensure they have the latest copy of any controlled document.

A documentation approval and distribution process exists at MBI to ensure that all responsible and affected departments review and approve internal documents prior to release and that they are made available for use in a timely manner.

The distribution, purging and obsoleting of all controlled documentation is accomplished as necessary through on-going database and hard copy management. Approval, storage, distribution, updating, purging and obsoleting of all controlled documents are the responsibility of Quality Assurance and the functional department's management for which they are generated. Documents of external origin are also controlled within the Document Control system.

MATERIAL and SERVICE PROCUREMENT (4.7)

MBI establishes, implements and maintains documented procedures to ensure that purchased products conform to specific requirements. Documents contain or reference the material and component identification requirements, drawings, specifications, test and inspection requirements, and special instructions, as needed.

Changes and revisions to procurement documents are subject to the same review and approval procedure as the original document. Procedures are established for the requirements for reporting and approving disposition of nonconformance.

Suppliers are selected on the basis of their ability to meet specified requirements for product, delivery and technical support. Quality assurance and/or qualified personnel maintain an effective system for selecting qualified suppliers and for monitoring supplier performance to ensure on-going capability.

INVENTORY (4.8)

MBI establishes, implements and maintains documented procedures to ensure proper handling of all inventory, purchased raw materials, in-process materials, and/or finished devices.

Identification, special handling, labeling, and segregating are all part of the process inventory prior to being released for use. Documentation for the handling of all inventory is maintained on hard copy as well as electronically. Any non-conforming materials which are identified, either in-process or finished device, it is immediately labeled quarantined and segregated to prevent usage of the wrong material. There are written procedures which describe the handling of non-conforming materials.

When applicable, traceability to a supplier's lot number or material identification number is established at the time of product receipt or during receiving inspection, and maintained throughout the subsequent product processing. Also, when applicable, the inventory is labeled with an expiration date to provide for First In, First Out (FIFO).

Finished products are identified and controlled through the use of a unique lot numbering system to ensure traceability as well as the release for distribution.

PROCESS CONTROL (4.9)

MBI has identified production processes and maintains documented procedures to ensure that these processes are carried out under controlled conditions (i.e., suitable environment, appropriate equipment, etc.). Prior to initiating and/or approving new processes, equipment and material, MBI performs qualifications to ensure their efficiency. Qualifications are controlled document, and the data is recorded and kept on file.

Procedures are provided and readily available in all manufacturing processes. Trained employees shall manufacture products and monitor process and product quality in compliance with current documented procedures and applicable standards and/or regulations. Flowcharts have been established to describe the flow of material as well as the process, which include quality verification points. These flowcharts are posted, when possible, in the production areas.

PRODUCT IDENTIFICATION and TRACEABILITY (4.9.1)

All finished devices are labeled through a controlled process and given a lot number which provides traceability. MBI maintains written procedures which describes the product lot numbering system.

INSPECTION, TESTING and LABELING (4.9.2)

To prevent nonconformance and ensure product integrity, MBI has documented procedures for the inspection and testing of incoming materials, in-process materials, and finished products.

In-process testing is performed per written procedures by either manufacturing or quality control. Nonconforming materials are identified and segregated until a disposition is established. This ensures that only products which conform to specification are used for further processing.

Final inspection and testing is conducted by the quality control department in accordance with written procedures. Final inspection and testing requires evidence that the product has been tested and approved, providing evidence that the product meets all specified requirements. Any product that does not conform is identified and secured in a designated quarantine location until a final disposition is determined. As per written procedures, all inspections are performed by someone other than the person who performed the work.

No product is shipped until a) all the documented procedures in the device master record have been completed, and b) all the documentation has been reviewed and authorized for release by the appropriate personnel (i.e., quality control and/or quality assurance).

CONTROL OF NONCONFORMING MATERIALS (4.10)

MBI has written procedures for the identification, documentation, segregation, evaluation, disposition, and destruction of a nonconforming product.

Nonconforming products are identified and placed into a designated quarantine location, until a final disposition is determined. A nonconforming Materials Report (NCMR) is prepared and tracks the status of the product.

A disposition to 'return to supplier' or 'destroy' will be prepared and approved by the appropriate personnel. Nonconforming material which is reworked, according to written procedures, is subject to the same level of inspection and testing as the original process.

Records of all non-conforming materials/finished devices are kept for trend analysis and for verification that the materials or device were not used or released for use.

CORRECTIVE and PREVENTATIVE ACTION (4.10.1)

Corrective action is defined as those actions initiated to permanently correct problems and nonconformance related to specific processes and products. Preventative action is defined as those actions initiated that prevent the occurrence or reoccurrence of problems and nonconformance across a wide range of products or processes.

The corrective and preventative action effort identifies the root cause of a problem or nonconformance, develops an effective solution, and verifies that the problem or nonconformance has been resolved. The effort may include changes to existing procedures as well as the application of process controls to ensure prevention.

The Quality Assurance department or designee is responsible for ensuring the effectiveness of the corrective and preventative action effort and for evaluating unresolved issues to appropriate levels of management.

PACKAGING and TRANSPORTATION (4.11)

Throughout the Quality System, MBI has written procedures for the handling, storage, packaging, and delivery of finished products to prevent damage, deterioration, or unsafe handling.

To prevent damage and/or deterioration, all products which require it are stored in temperature-controlled storage areas. Reagents, chemicals, in-process materials, or other consumables that have a shelf life, are assigned expiration dates which are supported by real-time studies and stability data.

Packaging and shipping containers are designed and constructed to assure that the product is adequately protected during storage and distribution, and to conform with any applicable regulator requirement of both the shipping and receiving destinations. Qualification studies of the shipping container and packaging material are performed prior to the approval of the container.

Only products which have been released for shipment are available in the appropriate storage areas. Written procedures are detailed to ensure compliance with regulations.

Carriers of hazardous materials are selected to ensure that final products arrive at the intended destination in the best condition possible.

DEVIATIONS and CUSTOMER COMPLAINTS (4.12)

Written procedures, describing the handling of all written and oral complaints, inquiries, or requests for information regarding a product manufactured and distributed by the facility, have been established.

These procedures include provisions for review and evaluation by Quality Control / Quality Assurance, and an investigation by the appropriate department/personnel.

A written record of each complaint shall be maintained in a file and will include, but not limited to, the product name, catalog number, lot number, customer location, and name of the individual/facility using the product. The appropriate response to the complaint will be prepared according to written procedures and all applicable regulations.

CONTROL OF INTERNAL AUDITS (4.13)

MBI's Quality System includes internal monitoring to ensure the system is effectively implemented and maintained. Audits are performed in accordance with preestablished written procedures or check lists and conducted by personnel not having direct responsibilities in the areas being audited. Each element of the QA manual is audited at least every two years.

Quality System audits are scheduled on the basis of the status and the importance of the activity performed. Audit observations are documented and corrective actions reviewed for compliance and adequacy. Audit observations are reviewed with management having responsibility in the area audited. Deficient areas shall be re-audited on a timely basis to verify implementation of corrective actions.

QUALITY RECORDS and DOCUMENTATION (4.14)

Our quality system requires maintaining readily accessible and legible historical files of documents pertaining to quality. The retained information includes, but is not limited to records of customer requirements, contract reviews, management reviews, operating logs, audit reports, inspections, tests, material analysis, qualification of personnel, standard operating procedures, and equipment qualification. Other documentation including: drawings, specifications, purchasing documents, calibration procedures and reports, nonconformance reports, deviation reports, and corrective action reports are maintained within the department they are generated and periodically audited to insure their integrity. Internal quality records are retained for a period of not less than (3) months. Quality records required to satisfy various regulatory mandates or customer requirements are retained in accordance with the applicable regulation or contract specification.

All records pertaining to each product lot are maintained in a designated controlled area. Records are available for review by authorized personnel only and are filed in numerical order by Product/Catalog Number and Lot Number. Records pertaining to production lots shall identify the person performing the test, inspection, or manufacturing step, as well as identifying the product by name, product number, and/or lot number.

CONTROL OF QUALITY RECORDS (4.14.1)

Written procedures are in place to control all records, data and procedures generated at MBI.

TRAINING (4.14.2)

Employee training, combined with documented procedures and instructions, provide the foundation for assuring consistency and conformity in all tasks which impact the quality of our products.

All training performed is based on an in-depth process of needs assessment which evaluates the training, education and experience required for positions which may potentially impact the quality of MBI products. As new or repetitive training requirements are identified, they are applied to their respective areas under a rolling schedule.

It is the responsibility of all functional managers to assure that employees are qualified and training needs are fulfilled.

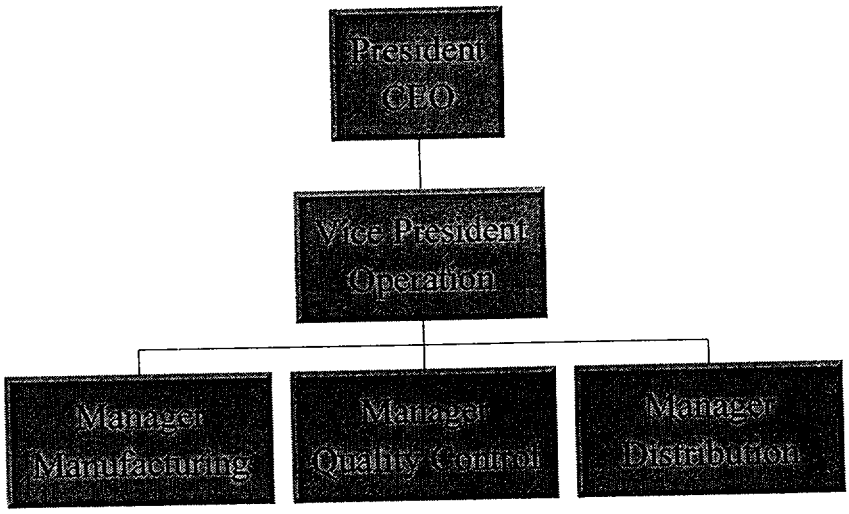
Training records are maintained for all employees. Training criteria and materials are maintained for all training performed and evaluated for content prior to use by the instructor/manager.

STATISTICAL TECHNIQUES (4.15)

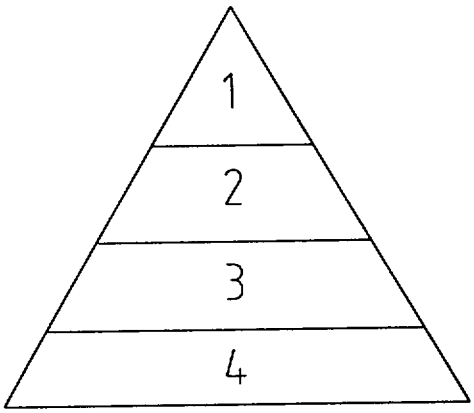
Statistical techniques are strategically selected and applied at MBI, so nonconformance can be prevented. Emphasis is placed on controlling the variability, which causes nonconformance, and on preventing defects to subsequent stages of the process.

The quality system includes the use of appropriate statistical techniques. These techniques include methods for monitoring and improving processes through the evaluation and analysis of statistical data. Results of statistical data analyses provide guidance in the continuous improvement of our processes as well as corrective and preventative action. Statistical methods used at MBI are derived from established standards.

Appendix I: Organizational chart



Appendix II: Quality System Documentation



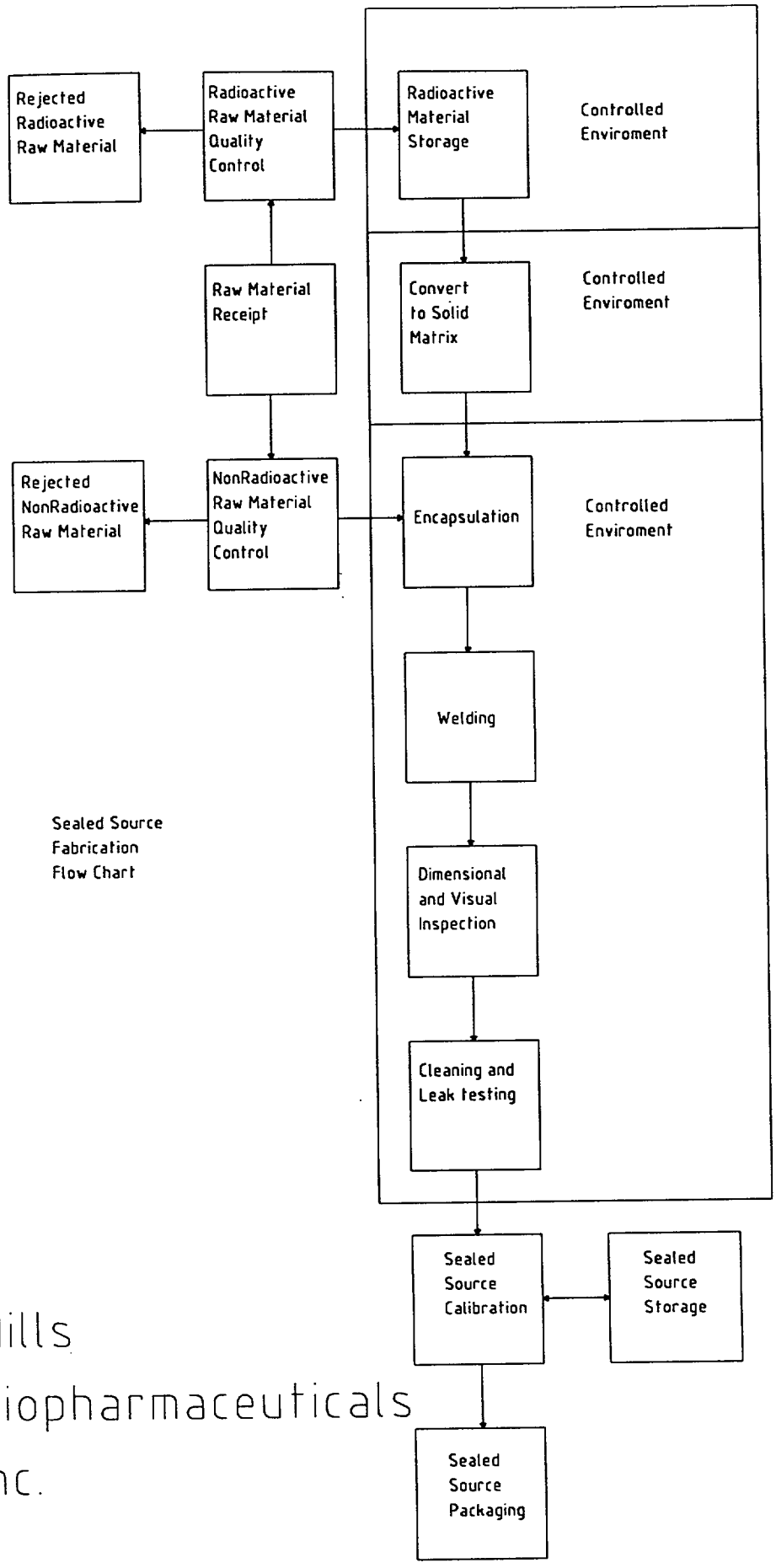
Level 1 - Quality Policy and Quality Manual

Level 2 - Quality system processes

Level 3 - Procedures and Work Instructions

Level 4 - Records and Forms

Appendix III: Product Process Flow Chart



Sealed Source Fabrication Flow Chart

Mills Biopharmaceuticals Inc.

NRC FORM 577 (5-1998)

U.S. NUCLEAR REGULATORY COMMISSION

LICENSE FEE REQUIREMENTS

ATTN: Sandra Kimberley, T-9E10
U.S. Nuclear Regulatory Commission
License Fee and Accounts Receivable Branch
P. O. Box 954514
St. Louis, MO 63195-4514

Mills Biopharmaceuticals Inc
ATTN: Stanley L. Mills, Ph.D., R.Ph.
President and CEO
120 N.E. 26th St.
Oklahoma City, OK 73105

TYPE OF ACTION

- [x] NEW LICENSE
- [ ] RENEWAL OF LICENSE
- [ ] AMENDMENT TO LICENSE

REQUESTED DATE: 06/13/1999

LICENSE NUMBER: New

CONTROL NUMBER: 99-41

I. APPLICATION FEE DUE

Your request for a licensing action is subject to the fee(s) in the category(ies) noted below in accordance with Section 170.31 of 10 CFR Part 170. Payment of the fee is required prior to the issuance of the license, renewal, or amendment.

FEE CATEGORY	APPLICATION	RENEWAL	AMENDMENT
9A	$ 3,600.00	$	$
	$	$	$
	$	$	$
	$	$	$
	$	$	$
	$	$	$
	$	$	$
	$	$	$
	$	$	$
	$	$	$

FEE(s) DUE	$ 3,600.00
PAYMENT RECEIVED	$ 0.00
AMOUNT DUE	$ 3,600.00

- [x] Your request was received without the prescribed application fee.
- [ ] We received your check listed below. Payment of the additional fee noted above is required.
  - _____ Check Number
  - $ 0.00 Amount
- [ ] Your request will increase the scope of your license program. Therefore, your request is subject to the application fee(s) noted above. Refer to Section 170.31 and Footnote 1(d)(2).
- [ ] Your license expired prior to the receipt of your application for renewal. Therefore, your request is subject to the application fee(s) noted above. Refer to Section 170.31 and Footnote 1(a).

MAKE PAYMENT OF THE FEE(S) TO THE U.S. NUCLEAR REGULATORY COMMISSION AND MAIL THE PAYMENT TO THE ADDRESS LISTED AT THE TOP OF THIS FORM. IF WE DO NOT RECEIVE A REPLY FROM YOU WITHIN 30 CALENDAR DAYS FROM THE DATE LISTED BELOW, WE SHALL ASSUME THAT YOU DO NOT WISH TO PURSUE YOUR APPLICATION AND WILL VOID THIS ACTION.

II. FEE NOT REQUIRED

- [ ] _____ Check Number — Enclosed is your check which accompanied your request. The fee is not required because:
- [ ] _____ Check Number — We received your check listed in payment of the fee.
- [ ] _____ Date of Request; _____ Control Number — The Licensing staff has informed us that your request is to be considered as a continuation of the request listed.
- [ ] _____ Date of Request; _____ Control Number — Your request was combined, prior to review, with the request listed.

III. CHECK RETURNED

- [ ] _____ Check Number — Enclosed is your check which was returned to us by the bank for:
  - [ ] INSUFFICIENT FUNDS
  - [ ] ACCOUNT CLOSED
  - [ ] OTHER

MAIL THE REPLACEMENT CHECK TO THE ADDRESS LISTED AT THE TOP OF THIS FORM AND REFERENCE THE ABOVE CONTROL NUMBER.

IV. LICENSE ISSUED WITHOUT THE REQUIRED FEE

- [ ] _____ License Number; _____ Amendment Number; _____ Date Issued — The listed license was issued without the required fee being collected. The fee required is noted in Section I of this form.
- [ ] The scope of your licensed program was increased. Therefore, your request is subject to the application fee(s) noted in Section 1 of this form. Refer to Section 170.31 and Footnote 1(d)(2).
- [ ] Because of the urgency of your request, the license was issued without remittance of the prescribed fee noted in Section 1 of this form.

SIGNATURE -- LICENSE FEE ANALYST	LFDCB	LFDCB
Sandra Kimberley, 301-415-6096	sk	
	6/18/99	

Distribution:
OC/DAF/LFARB S/F (LF-3.2.7)
OC/DAF/LFARB RF
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Pending Cy: MBurgess

DATE: 06/18/1999