



GLOBAL VENDOR QUALITY MANUAL



Dear Charles River Vendor:

We are committed to sustaining our reputation as a quality organization by upholding the standards and requirements of regulatory compliance of all business units by:

- Assuring the quality and integrity of research products and services
- Assuring data integrity, data accuracy, precision, reliability, timeliness, and preservation
- Assuring the protection of human subjects and the welfare of laboratory animals
- Partnering with customers, vendors and employees to continually improve quality and meet regulatory requirements

This Vendor Quality Manual establishes Charles River's quality expectations for our vendors. We believe the requirements described in this Manual are essential for the effective management of the services and products we provide to our clients.

We recognize that Charles River (CR) has a wide variety of vendors; hence, the requirements and expectations stated in this manual may apply in different ways, depending on the Product or Service supplied. The requirements within this Vendor Quality Manual supplement executed agreements, purchase orders, drawings and specifications between CR and Vendors. To the extent the provisions of this Vendor Quality Manual are inconsistent with an agreement, statement of work, purchase order, drawings or specifications, the latter will prevail over the Vendor Quality Manual.

After reviewing this manual, please sign off the Acknowledgement Letter, located at the end of the document, and return it to CR. A copy of this manual can be accessed from Charles River's external website via the link - [Charles River Vendor Quality Manual](#)

We look forward to working with you.

DocuSigned by:
William Drummond
Signer Name: William Drummond
Signing Reason: I approve this document
Signing Time: 22-Oct-2021 | 12:06:26 EDT
2B2E60CFB9E34B8494C561075C792992

William Drummond

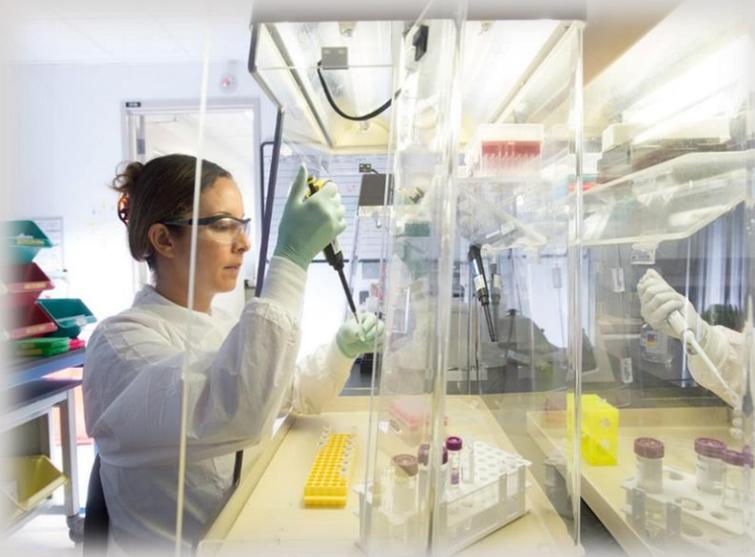
Sr. Director, Global Quality Systems
Charles River Laboratories

DocuSigned by:
Kanwar Singh
Signer Name: Kanwar Singh
Signing Reason: I am the author of this document
Signing Time: 22-Oct-2021 | 10:20:29 EDT
12019E586A0546D0AEC613006103682F

Kanwar Singh

Director, Global Vendor Quality
Charles River Laboratories

TABLE OF CONTENTS



- 1.0 VENDOR MANAGEMENT RESPONSIBILITIES**
 - 1.1 Management Commitment
 - 1.2 Customer Focus
 - 1.3 Quality Principles
 - 1.4 Responsibility, Authority and Communication
 - 1.5 Pharmaceutical Supply Chain Initiative

- 2.0 VENDOR QUALITY AGREEMENTS**

- 3.0 REGULATORY**
 - 3.1 Good Manufacturing Practices
 - 3.2 Good Laboratory Practices
 - 3.3 Vendor Certificates
 - 3.4 Regulatory Inspections

- 4.0 QUALITY MANAGEMENT SYSTEM**
 - 4.1 Production and Process Control
 - 4.2 Equipment Calibration
 - 4.3 Pest Control
 - 4.4 Audits and Inspections
 - 4.5 Sub-Tier Vendor Control
 - 4.6 Control of Nonconforming Product
 - 4.7 Customer Complaints
 - 4.8 Corrective and Preventive Action

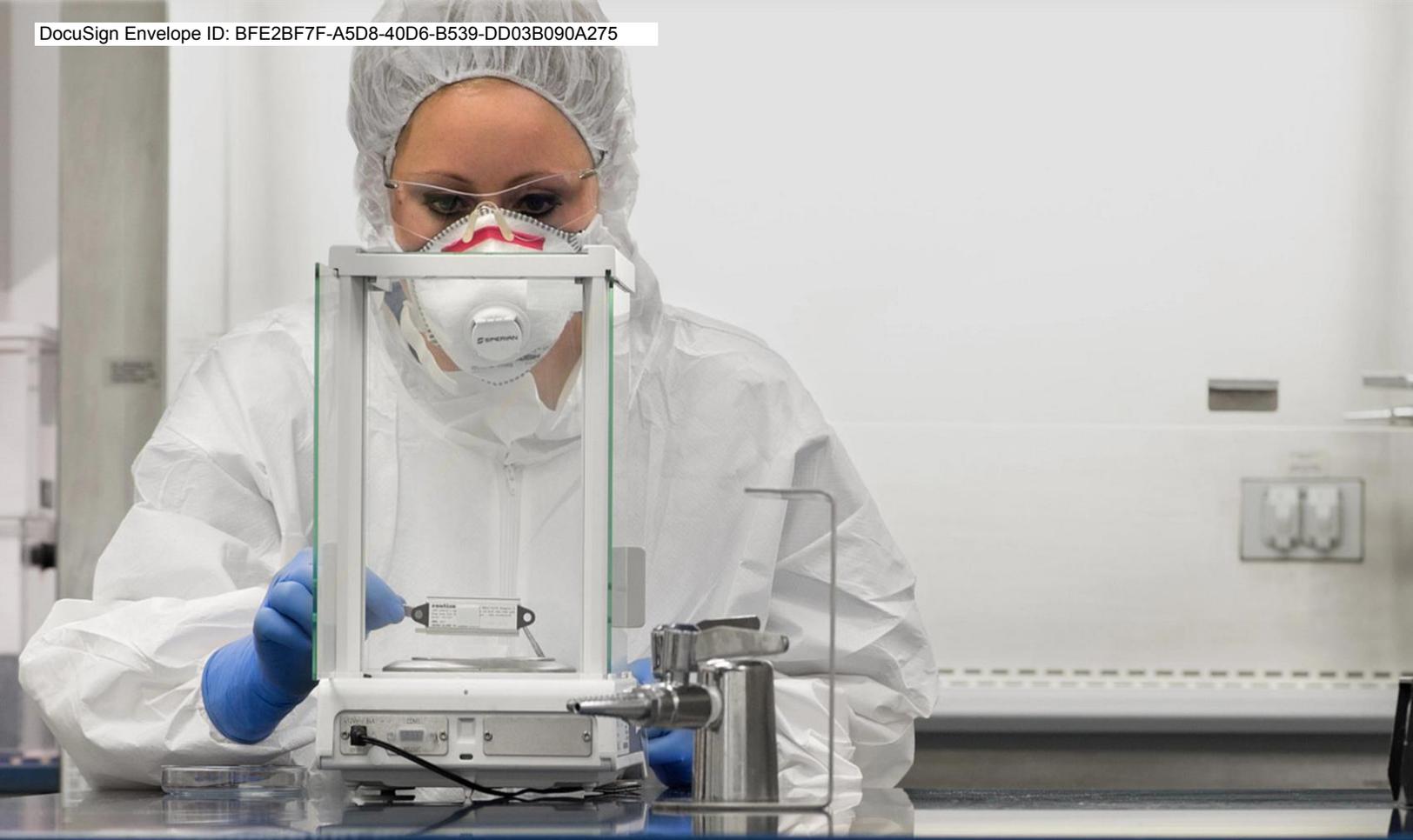
- 5.0 DATA AND DOCUMENTATION CONTROL**
 - 5.1 Data Integrity
 - 5.2 Control of Records & Documents
 - 5.3 Change Control

- 6.0 PRODUCT IDENTIFICATION & TRACEABILITY**

- 7.0 PRODUCT HOLD AND STORAGE**

- 8.0 EMPLOYEE TRAINING**

- 9.0 FACILITY AND INFRASTRUCTURE**



GxP – is an abbreviation for “good practice” regulations and quality guidelines, including but not limited to GMP, GLP etc.

Vendor refers to:

- **Service Provider** – is an organization or individual outside of the CR corporation that performs services such as equipment servicing, maintenance, calibration, testing, delivery etc.
- **Subcontractor** – is an organization or individual outside of the CR corporation that signs a contract to perform part of a CR contract or performs testing activities
- **Contract Manufacturer:** An outside manufacturer who uses materials or/and packaging materials and converts them into a branded finished product for Charles River
- **Supplier:** A company or an organization that manufactures and supplies or distributes materials/products for use at Charles River facilities
- **Consultant:** An individual or an organization that provides expert advice professionally in support of Charles River GxP related activities

1.0 Vendor Management Responsibilities

1.1 Management Commitment

The Vendor will establish a policy that incorporates quality principles and objectives (“Vendor Quality Principles”). The Vendor Quality Principles will take the form of a Quality Management System as required by all applicable regulations in the locations where product (services) is manufactured, stored, and distributed. The principles will be expressed to include a statement of the Vendor’s commitment to:

- Providing products and services that conform to specifications
- Compliance with applicable laws and regulations
- Continuous improvement
- Customer safety and satisfaction

To demonstrate this commitment, the Vendor may, as appropriate:

- Communicate to the organization the importance of meeting customer as well as regulatory expectations and requirements
- Establish measurable goals and objectives for the appropriate functions and level
- Conduct regularly scheduled management reviews on the effectiveness of the quality system and taking appropriate action when indicators are unfavorable
- Ensure availability of necessary resources to implement and maintain an effective Quality System
- Ensure staff have the appropriate training, education, and experience to perform their assigned duties

The Vendor will establish a documented organizational structure that assigns responsibilities of employees who manage, perform, and verify compliance with the Vendor’s quality standards.

The policy and employee responsibilities will be communicated and understood by management and employees and made available to Charles River upon request.



1.2 Customer Focus

The Vendor will ensure that Charles River specifications are met through a robust quality process.

Vendors will have a management representative for reviewing this manual and ensuring compliance to the expectations. The Vendor will confirm receipt of this manual by signing the acknowledgement letter and returning it to Charles River contact within 60 days of receipt. Vendor will maintain updated contact information with Quality contacts at Charles River.

1.3 Quality Principles

In addition to the content described above, Vendor Quality Principles will:

- Establish a structure for reviewing and reporting the performance of the Quality system to operations and senior management
- Include a commitment to meet customer specifications and drive continuous improvement
- Communicate quality compliance obligations to relevant personnel

1.4 Responsibility, Authority and Communication

The Vendor will have a documented organizational structure that describes the responsibilities, authority, and interactions of the people who manage, perform, and verify work related to quality. These may include, where appropriate, specific quality indicators and goals, and processes for tracking and monitoring trends to facilitate continuous improvement. The Vendor is expected to ensure that communication takes place at all levels and to all functions regarding compliance to the Quality System and its effectiveness.

1.5 Pharmaceutical Supply Chain Initiative (PSCI)

As a member of PSCI for responsible Supply Chain Management, Charles River believes in promoting better social, health, safety, and environmental outcomes across its supply chain. The Vendor is expected to support CR's initiative of expanding the market focus on five key pillars of social responsibility – ethics, human rights and labor, health and safety, environment, and management systems. The Vendor is further expected to comply with all applicable laws, rules and regulations as well as the requirements of the Charles River Supplier Code of Conduct and the PSCI Principles for Responsible Supply Chain Management.

2.0 Vendor Quality Agreements

In addition to the requirements and expectations contained in this Manual, Charles River may determine if a Quality Agreement is needed with our vendors.

Quality Agreements will outline the Vendor-specific quality requirements in the form of a stand-alone Quality Agreement. Where a Quality Agreement is required, the parties will negotiate in good faith to establish reasonable terms and conditions to assure the quality of the products or services provided by the Vendor. Requirements listed in a quality agreement will prevail over requirements outlined in this manual in case of any inconsistencies.

3.0 Regulatory

3.1 Current Good Manufacturing and Tissue Practices (cGMP, cGTP)

This requirement is applicable to the Vendor providing GMP based products or services. The Vendor may be required to enter into a Quality Agreement that will address responsibilities for specific activities to control product quality as required under the applicable regulations. See, for example,

- 21 CFR Part 210 and 211
- 21 CFR Part 1270, 1271
- 21 CFR Part 11
- 21 CFR Part 600-680, 820
- EC Directive 2003/94/EC
- Applicable ICH Requirements

3.2 Good Laboratory Practices (GLP)

Charles River requires the Vendor performing GLP regulated activities to comply with GLP regulations to assure the regulatory authorities of data they receive in Safety studies are of good quality and can be relied upon when making assessments of risks to humans, animals, and the environment.

To ensure that Charles River data are reliable, Charles River may include a requirement in a Vendor agreement or purchase order that the Vendor complies with certain GLP requirements even if quality agreements are not a GLP requirement. The Vendor Qualification Program provides a proactive approach by Charles River to document that suppliers of critical product/services consistently apply high standards necessary to support work performed by Charles River in compliance with GLP regulations. See, for example,

- 21 CFR Part 58; 40 CFR Part 160; 40 CFR Part 792
- OECD Principles on Good Laboratory Practice and Compliance Monitoring
- OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring Number 5
- OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring Number 11
- OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring Number 13

3.3 Vendor Certificates

In addition to regulations listed under the GMP and GLP sections, Charles River may request certificates and documents. For Vendors, which are not required to adhere to the GMP or GLP requirements, Charles River may request certificates and documents based on the product and services the Vendor provided to confirm compliance to other accredited, certifying, and regulatory bodies, such as ISO, OSHA, Global Trade Management (GTM), Health Canada, etc.

3.4 Regulatory Inspections

The Vendor is expected to notify Charles River within two business days of any proposed or commenced inspection or visit of the facility related specifically to Charles River activities by any governmental authority, including, without limitation, any Agency or any environmental regulatory authority. In addition, Charles River may request the Vendor to provide the summary of the inspection results related to Charles River activities.

The Vendor will immediately (no more than 48 hours) notify Charles River about any warning letters or major or critical citations issued during an inspection or visit by a third-party inspecting body which has or could potentially impact product or services being provided to Charles River.

4.0 Quality Management System

General: The Vendor will meet generally accepted or contractually agreed upon quality levels in providing goods and services. As applicable, the Vendor will meet the following requirements to ensure that the products and services meet specification:

4.1 Production and Process Control

The Vendor will have systems in place to define and maintain the manufacturing process and associated controls, so that all products conform to their specifications, including, but not limited to: Approved and documented production processes, instructions, and methods that define and control the manner of production.

Plant personnel will have access, as needed, to the most current process control procedures, product requirements, and specifications. In-process and finished products will be inspected and tested to ensure conformance to these requirements and specifications:

- Monitoring and control of process parameters and product characteristics during production
- Compliance with specified reference standards or codes
- Approval of processes and process equipment

The Vendor will validate processes used for the manufacture or delivery of any finished products or services for compliance with applicable regulatory requirements.

The Vendor will have procedures for acceptance of incoming product, including inspection, testing, and verification that the product conforms to Charles River specifications. The Vendor will document acceptance or rejection of incoming product.

The Vendor will have in-process and final product acceptance procedures to ensure that in-process and final products are controlled and meet Charles River's acceptance criteria. Finished product will be adequately controlled until released.



4.2 Equipment Calibration

Every Vendor facility will have a documented calibration program. The program will meet any applicable regulatory and industry requirements.

Facilities will maintain an inventory record of critical (related to product safety, quality, and regulatory) equipment requiring calibration. The following information will include the following, at minimum:

- Equipment Identification (ID)
- Description
- Type of calibration (conducted internally or externally)
- Manufacturer
- Serial Number
- Location
- Calibration Frequency
- Standard/Reference of known accuracy
- Date of Calibration
- Calibration Company (if calibrated externally)
- Printed name and/or initials or signature of the person who conducted the calibration
- Re-Calibration Due Date
- Acceptance Limits
- Regulatory Requirements (if applicable)

Critical equipment not maintained/available on calibrated equipment inventory record will be automatically deemed not calibrated.

Equipment will be identified with a label. The label will include, at minimum, the equipment ID. Where possible, the label should also include the date of calibration, initials of the person who conducted the calibration, and re-calibration date.

Internal calibration records and external calibration certificates will be maintained for inspection, measuring, and testing equipment related to product safety, quality, and regulatory compliance.

Each facility will have a documented process in place for equipment that is deemed out of calibration. Any material produced or service performed with out of calibration equipment will be placed on hold and assessed for impact to applicable processes and/or products.





4.3 Pest Control

The Vendor will have a documented program in place to effectively control pest activity and risks at the Vendor's facilities. Charles River expects the Vendor to have a program that will be managed and executed by trained, licensed/certified plant personnel and/or approved outside contractors. Only certified pest control operators (PCO) or personnel with documented equivalent training will perform pest control activities. The program will meet all applicable federal, state, and local regulations.

Internal assessments will be conducted (recommended at least yearly) to ensure the PCO is following pest control program procedures and verify the program effectiveness. Results of the assessment will be documented and used to facilitate process improvements if necessary.

4.4 Audits and Inspections

The Vendor will plan and conduct routine facility, product, and process inspections. These inspections may include areas such as production start-up, GMP/GLP or other applicable industry regulation checks, quality management systems, and product evaluations. Any deviations will be documented along with appropriate corrective actions.

The Vendor will establish an internal audit program to assess and review compliance with internal procedures/policies, Charles River requirements, and industry best practices related to quality. Internal audits will be conducted at minimum annually by individuals at the facility and, where possible, those individuals will be independent of the area they are auditing. Results of the audit will be communicated to appropriate management and responsible parties. Records of audit findings and corrective / preventative actions will be maintained. Follow-up activities will be conducted and documented to verify corrective / preventative actions have been completed.

Charles River may audit the Vendor's manufacturing and Quality Systems at a frequency deemed necessary per Charles River's internal standards, client/study requirements, vendor class, and other relevant factors.

The Vendor will be audited against the requirements and expectations listed in this Manual and any other requirements based on the vendor type and service provided.

Audit rights will be negotiated in individual contracts and will address access to the Vendor's:

- Facility
- Quality System
- Processes
- Data Management
- Computerized Systems

In addition to assessment of Vendor's Quality Systems, Charles River may require IT Security and/or IT Compliance assessments based on the product and its application or services provided by the Vendor. For example, products and applications connected to Charles River network, vendors collecting, processing, storing, or disposing Personally Identifiable Information (PII) etc.

The Vendor will not charge Charles River any fee for an assessment performed by Charles River and provide full support during the audit as deemed appropriate by Charles River. The assessment may be performed via a questionnaire or a combination of a questionnaire and onsite or remote audit. The Vendor will provide a written response for all Charles River audit findings in a timely manner. The Vendor is expected to provide access to regulatory authorities for inspections or audits, as applicable. Activities pertaining to audits and inspections will be documented and will be made available to Charles River upon request.

When requested by Charles River, the Vendor will provide support to Charles River during regulatory authority inspections.

4.5 Sub-Tier Vendor Control

The Vendor will manage sub-tier vendors (sub-contractors) with controls commensurate with risk. The Vendor will ensure that products manufactured utilize only authentic, conforming, and specified material as stipulated in the specification.

Charles River expects the Vendor to have formal purchasing and control processes to manage sub-tier vendors. These controls are expected to include:

- Selection, evaluation, and approval
- Product qualification
- Procurement
- Product acceptance
- Performance measurement and monitoring, including sub-tier auditing programs
- Nonconforming Product and CAPA processes
- Change control

The Vendor is responsible for ensuring and controlling the quality of all components and raw materials that are purchased to manufacture product or deliver services to Charles River. Charles River reserves the right to perform assessment of sub-tier vendors, when deemed necessary.

4.6 Control of Nonconforming Product

The Vendor will establish and maintain procedures to control product that does not conform to their internal and Charles River specifications. The procedures will address the identification, documentation, evaluation, segregation, and disposition of nonconforming product, including the need for an investigation, which will be documented.

Production defects that exceed established process control/ action limits are expected to be investigated within Vendor's CAPA system. Production defects are expected to be recorded and analyzed for trends to identify need for further CAPA.

The Vendor will have control systems in place to prevent nonconforming product from being integrated with conforming product. If product or packaging materials are inadvertently or improperly released from hold status, Charles River must be notified immediately. The Vendor is expected to fully cooperate in any investigation of containment action.

When delivery commitments are at risk of not being met, a process will be in place to notify Charles River Procurement immediately.

The Vendor will have procedures covering disposition of Nonconforming Product, including review and documentation of decisions.

Disposition will be determined and completed in a timely manner and will include date and/or material codes and quantities involved.



4.7 Customer Complaints

The Vendor will have a documented program in place for handling customer complaints. The program will address responsibilities, response time and corrective actions based on the nature of the complaint.

All complaint types whether quality or safety will be investigated within an agreed upon timeframe with Charles River Quality Representatives.

A log will be maintained to track complaints by product identification, production dates, cause, and origin of complaint. Complaint data should be analyzed for trends and used to improve product safety and quality and to avoid recurrence.

Charles River may issue a request for a Corrective Action Report if a non-conformance is observed in a product or service procured from the Vendor. When a formal reply is requested, the Vendor will promptly acknowledge receipt of notification and communicate to Charles River the immediate containment actions to be taken. The Vendor will perform a thorough investigation to determine the root cause of the issue and appropriate corrective actions.

If the Vendor repeatedly fails to meet delivery and/or Quality performance requirements, Charles River may require preparation and implementation of improvement plans. Recurrence of quality issues and/or unresponsiveness to customer complaint requests may result in a vendor audit.

4.8 Corrective and Preventive Action (CAPA) System

The Vendor is expected to establish and maintain a CAPA system. The CAPA system is expected to include the following requirements:

- Analysis of sources of quality data (e.g., Manufacturing processes, production defects, Product disposition records, quality audit (internal and external) records and reports, complaints, adverse events, environmental monitoring, Vendor Corrective Action/ Preventive Action to identify existing and potential causes of Nonconforming Product or other quality problems
- Investigations to identify the root causes of nonconformances
- Identification of the actions needed to correct nonconformances and to prevent their recurrence
- Verification and validation of corrective and preventive actions to assure their effectiveness and to confirm that Product is not adversely affected by the action(s) taken
- Management review of identified quality problems and associated CAPA activities
- Documentation of CAPA activities and results

These procedures will ensure that:

- Current documents are available at locations within the facility essential to the effective functioning of the product safety and quality system
- Invalid and/or obsolete documents are promptly removed from all points of use to prevent unintended use
- Obsolete documents are expected to be destroyed or appropriately identified as such for limited distribution suitably identified

The Vendor will maintain records for at least seven years or for the time required by applicable federal, regional, state, or local regulations, whichever is greater. In addition, the Vendor will retain records per contractual agreements with Charles River. Records are expected to be stored in an environment that will prevent deterioration, damage, or loss, and are expected to be readily accessible to Charles River upon request.

5.0 Data & Documentation Control

5.1 Data Integrity

The Vendor will have robust systems and controls to ensure all data are complete, consistent, and accurate throughout the data life cycle. The data life cycle comprises of:

- Data creation
- Processing and Manipulation of data
- Semi Active Storage or Transmittal
- Long-Term Retention

The Vendor will follow the ALCOA+ principles (Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, and Available) and data will be collected and recorded automatically or by trained personnel, when appropriate, for product safety and quality tasks/activities (tests, monitoring, verifying, evaluations, audits, inspections, reviews, or analysis).

The Vendor will follow the ALCOA+ principles and data will be collected and recorded automatically or by trained personnel, when appropriate, for product safety and quality tasks/activities (tests, monitoring, verifying, evaluations, audits, inspections, reviews, or analysis).

The Vendor will provide formal training to the employees using the electronic/computerized systems or any other systems, devices or equipment used in the data life cycle.

Electronic systems and equipment used for collecting data must be validated and in compliance with the applicable local regulations. The Vendor will maintain a “good data integrity” policy and will adhere to General Data Protection Regulation (GDPR), where applicable. Charles River may ask the Vendor processing or exchanging Personal Identifiable Information to complete PII assessment for highlighting privacy standards and practices to allow CR to understand how its employees and customer data is being collected, processed, stored, and disposed so that any possible risks can be identified and resolved appropriately.

Charles River may choose to audit the Vendor’s data management systems at a frequency deemed necessary per Charles River’s internal standards, client or the study requirements, etc.

5.2 Control of Records & Documents

The Vendor will establish and maintain documented procedures to control and secure all documents, data, and records that relate to raw materials, production, processing, and finished product. This includes, but is not limited to, regulatory requirements, specifications, label approvals, standard operating procedures, laboratory manuals, product testing results, and quality records.

5.3 Change Control

The Vendor will have a documented system in place to manage changes in materials, specifications, processes, systems, suppliers for raw materials, equipment, management, and/or production facilities to avoid any impact on product safety, quality, and legality.

The system will include communication to Charles River of any changes that have a potential adverse impact on product safety, efficacy, quality or operations. The Vendor is expected to report key management changes to the appropriate Charles River’s Procurement and Quality contacts.

6.0 Product Identification and Traceability

The Vendor will have a system in place to identify product during all stages of supply chain - receipt, production, storage, and distribution. This system will also ensure that product in different stages of the manufacturing process is properly identified to avoid mix ups. This includes any raw materials, in-process materials, inspected product, nonconforming product, and product ready for shipping or storage.

The system will also ensure that the raw material and components used to manufacture the product shipped to Charles River can be traced through the Vendor's system throughout the production process from receipt to shipping.

A unique traceability identifier such as a lot or batch number should be included on the product labels.



7.0 Product Hold and Disposition

The Vendor will have effective documented controls in place to prevent the inadvertent shipment of non-conforming products, raw materials, or packaging materials to Charles River. Withheld, expired, or rejected products or materials will not be shipped to Charles River.

The Vendor will have documented procedures to withhold products suspected of non-conformance or are awaiting test results from the chain of distribution. These documented procedures will be current and pertain to the entire hold and disposition process, including responsibility for communicating information between internal and external parties, including Charles River as applicable. Each non-conformance that led to a product or material hold will be evaluated for root cause. Corrective action will be taken and documented to prevent recurrence.

When delivery commitments are at risk of not being met, a process will be in place to notify Charles River Procurement immediately.

If product, packaging materials, or ingredients are inadvertently or improperly released from hold status, Charles River must be notified immediately.

8.0 Employee Training

The Vendor will have a planned, functional, and effective training program for all personnel including, but not limited to, full time, seasonal, part-time, and temporary employees and contractors.

Training may include the following topics: Applicable regulations and compliance (GMP, GLP, GCP, ISO etc.), data integrity, change control, computer and electronic systems use and validation, calibration, laboratory practices and testing, pest control, animal care, internal auditing, and maintenance. Employees will be trained on job specific responsibilities and evaluated on competency. Training will be conducted by qualified and/or certified individuals.

Training programs will be documented and maintained. Training records will be kept and include a list of participants, completion date, training contents, and effectiveness evaluations to prove employee competency. Refresher training will be conducted at frequencies required to maintain competency.

9.0 Facility & Infrastructure

Buildings will be designed with a logical flow for air, materials, products, equipment, personnel, and waste to reduce or eliminate product contamination. An updated plant layout will be kept on file showing all entrances, exits, and roof access points. All areas of the facility and infrastructure will comply with applicable local and federal regulations.

Walls, ceilings, and floors will be maintained in good condition, kept clean, and free of pits, cracks, and crevices.

Drains will be cleaned and maintained to prevent build up, odors, and pest harborage, and will be routinely sanitized.

Ceilings and overhead structures will be maintained in good condition, be free of rust, peeling paint, plaster, dust, debris, cobwebs, mold, and kept clean. Roof leaks will be identified, controlled, and fixed in a timely manner.

Stairs, catwalks, platforms, pipes, ducts, fixtures, and conduits will be located, designed, and maintained in a manner that does not contaminate product, raw materials, or processing tools or equipment.

Construction and maintenance projects will be effectively managed and temporary structures (if used) designed, constructed, located, and adequately controlled to prevent product contamination and maintain product safety.





Charles River Vendor Quality Manual Receipt and Acknowledgement

I, _____, as a representative of my organization and a vendor to Charles River, understand and agree to the following:

- This manual is intended as a general guide to Charles River’s Vendor Quality expectations and that it is not intended to create any sort of legal contract between Charles River and any of its vendors.
- The manual states that the Charles River Vendor Quality practices and expectations as outlined in the manual are in effect on the date of publications of this manual.
- That requirements listed in a quality agreement or any other legal contract will prevail over the requirements listed in the Vendor Quality manual.
- I acknowledge that I, as a representative of my company, have read and comprehend the information contained in the manual and will contact Charles River’s Vendor Quality personnel if I have any questions concerning contents of this document.

Company Name

Company Representative Name (Printed)

Company Representative (Signature)

Date