QUALITY MANUAL

SECTION TITLE: CONTENTS

TABLE OF CONTENTS

Section 1
  1.1 Page 1 Table of Contents
  1.2 Page 2 Quality Policy
  1.3 Page 3, 4 Company Profile

Section 2
Quality System Requirements:
  2.1 Page 5, 6, 7 Management Responsibilities
  2.2 Page 8 Quality Audits
  2.3 Page 9 Personnel
  2.4 Page 10 Design Controls
  2.5 Page 11 Document Controls
  2.6 Page 12 Purchasing Controls
  2.7 Page 13 Identification and Traceability
  2.8 Page 14, 15 Production and Process Control
  2.9 Page 16 Acceptance Activities
  2.10 Page 17 Non-Conforming Product
  2.11 Page 18 Corrective and Preventive Action
  2.12 Page 19 Statistical Techniques
  2.13 Page 20 Labeling and Packaging Control
  2.14 Page 21 Material Handling, Storage and Distribution
  2.15 Page 22 Records
QUALITY Manual
Section Title: Quality Policy

R&D Systems Inc. Quality Policy:

R&D Systems is committed to the highest level of quality in the manufacture, sale and support of our products. Product quality, compliance to all applicable regulatory requirements, continuous improvement and customer satisfaction shall underlie all of our efforts in development, manufacturing, advertising, sales, shipping and technical support.

Definitions:

- **Quality**: the totality of features and characteristics that bear on the ability of a product to satisfy fitness for use, including safety and performance (§ 820.3 (s)).

- **Quality system**: the organizational structure, responsibilities, procedures, processes and resources for implementing quality management (§ 820.3 (v)).

Assurance of quality and integrity are the responsibility of:

1. the Chief Executive Officer (CEO), who has responsibility for creation of an atmosphere of high standards;

2. the officers, directors, managers and supervisors, who are charged with development and implementation of quality systems; and

3. each employee, who is responsible for the quality of his or her work and for suggesting quality improvements.

This Quality Manual is the top tier of our documentation system. It provides an overview of our Quality System. It is supported by corporate and division standard operating procedures (SOPs) which represent the second tier of our Quality System documents. Relevant SOPs are listed in this Quality Manual. The third tier of the documentation system consists of manufacturing/testing documents, forms and specifications developed by each operating unit.


Sections of the ISO 13485 Standard which do not apply to R&D Systems are as follows:

- Section 7.5.1.2.3 - Service activities (Reason: Applicable to equipment)
- Section 7.5.1.2.2 - Installation activities (Reason: Applicable to equipment)
- Section 7.5.1.3 - Particular requirements for sterile medical devices (Reason: No claim of product sterility)
- Section 7.5.3.2.2 - Particular requirements for active implantable devices (Reason: No implantable devices)

Related Procedures:

- 540007 Canadian Medical Device License, Establishment License and Quality System Certification
- 540120 Required Standards Listing, Maintenance and Review
- 541347 Continuous Improvement
R&D Systems was founded in 1976 in Minneapolis, MN. It is a wholly owned subsidiary of TECHNE Corporation (a holding company with no employees). In July 2014, TECHNE was renamed as Bio-Techne. The stock is traded publicly on NASDAQ’s National Market System under the “TECH” symbol. Bio-Techne has two operating subsidiaries: R&D Systems, Inc. (RDSI) and R&D Systems Europe Ltd. (RDSE).

RDSI has two operating divisions: Biotechnology, which manufactures reagents primarily for the research market, and Clinical Controls, which manufactures controls and calibrators for chemistry (Bionostics) and hematology (R&D Systems) analyzers. The Bionostics manufacturing facility, located in Devens, MA is certified to ISO 13485:2003. Their ISO Certificate number is FM547845.

The Minneapolis manufacturing facility is certified to ISO 9001:2008 and ISO 13485:2003. Their ISO Certificate numbers are FM547845 and FM547846, respectively.


In 2011, RDSI purchased Boston Biochem in Cambridge, MA. It became a wholly owned subsidiary.

In 2014, RDSI purchased ProteinSimple and Novus Corp. ProteinSimple manufactures instruments for running Western blots and Novus manufactures antibodies. Both of these businesses complement the existing RDSI product lines.

RDSE in Abingdon, England distributes Biotechnology research reagents and is the European Representative for the Biotech Division. They received ISO 9001:2008 certification in July 2007. Their ISO Certificate number is 951 07 4360. EuroCell Diagnostics, Village de la Metairie Bâtiment B, 35131 Chartes de Bretagne is the European Representative for the Clinical Controls Division.

RDSE acquired Tocris Holdings Limited in April 2011. Tocris Holding Limited is a Bristol, UK based manufacturer of biologically active chemical reagents. RDSE also has two sales subsidiaries, R&D Systems GmbH, in Wiesbaden, Germany and R&D Systems France in Lille.

RDSI established a wholly owned subsidiary in the People's Republic of China in May 2007. R&D Systems China Co. Ltd. (RDSA) opened its Warehouse and Distribution Center in Shanghai on October 1, 2007 and in Hong Kong in February 2011. RDSA provides products, marketing and technical support to our Asian distributors and directly to major customers. In April 2014, RDSA acquired PrimeGene, which manufactures proteins for sale in China.
R&D Systems’ physical plant in Minneapolis currently occupies approximately 600,000 square feet of laboratory, manufacturing, shipping and office space as of July 1, 2014. Bio-Techne Corporation and subsidiaries had 1293 full- and part-time employees as of July 1, 2014.

Bio-Techne Organization

This Quality Manual applies to the manufacturing and distribution operations at RDSI in Minneapolis, MN.
Quality is the responsibility of each employee throughout our organization.

Management is responsible for communicating our Quality Policy to all employees and for ensuring full understanding of, and commitment to, quality.

- The CEO has executive responsibility for the Quality System and is responsible for creating an atmosphere where quality is the highest priority.
- The Vice-Presidents are responsible for overseeing the development, implementation and maintenance of the Quality System.
- The Director of Quality and Regulatory Affairs (QC/QA/RA) has been appointed as the Management Representative by the company president and has responsibility for ensuring that quality requirements are effectively established and maintained in accordance with the appropriate regulations and for reporting on the Quality System to upper Management.
- The Director of QC/QA/RA, the Vice-Presidents CCD and Biotech, and the Quality Assurance (QA) staff are responsible for ensuring that our Quality System is fully maintained and implemented.
- Each director, manager and supervisor is responsible for ensuring that Quality Systems are followed in his or her area.
- Each employee is responsible for following quality systems guidelines and for the quality of his or her work.

Two groups are dedicated exclusively to Quality:

1. Quality Assurance (QA) assists operating departments in the development of quality systems and conducts periodic audits to ensure that those systems are implemented faithfully and effectively. Quality Assurance has the responsibility to:
   - identify and evaluate quality-related problems;
   - recommend solutions to quality problems and verify that any problems have been resolved (corrective actions);
   - initiate actions to prevent the occurrence of quality problems (preventive actions);
   - control non-conforming products until corrective action has been taken;
   - set quality goals and objectives for the company and develop plans to meet those goals and objectives;
   - report to Management on quality-related issues.

The Quality Assurance Department is responsible for quality systems, but implementation of these systems and quality *per se* is the responsibility of each director, manager, supervisor and employee.

2. Quality Control (QC) inspects and tests products at all stages of the manufacturing process, from raw materials to finished goods. QC Management has responsibility for product release against predetermined specifications. The Biotech QC Departments report to the Director of QC/QA/RA.

The following charts describe the organizational and functional structure of the Company. While the structure and organization of the Quality function varies between the two divisions of R&D Systems, their goals are identical.

Related Procedures:

- 540009 Management Quality Systems Review Procedure
- 541138 Quality Assurance Organization
- 541614 Quality Planning
Quality Systems Flow Chart

Continual improvement of the quality management system

Customers

Requirements

Management responsibility

Measurement analysis and improvement

Resource management

Product Realization

Product

Input

Output

Quality Control

Manufacturing Operations

Research and Development

Customer

Feedback
R&D SYSTEMS, INC.
Department Organization

Chief Executive Officer/President

Sr. VP Clinical Controls Division
Sr. VP Biotech Division

VP Finance & Chief Financial Officer

VP of Sales & Marketing

Business Development

Sr. Director, Quality and Regulatory Affairs (Management Representative)

QA/RA

Sr Director Human Resources

Bioassay

QC/ Microbiology

Biotech Marketing

Biotech Sales

Technical Service

Technical Service BiosPacific

Facilities

IT

Accounting

Raw Material Manufacturing

Quality Control

Laboratory

Manufacturing

Shipping

Product Finishing

Marketing/Sales

Hematology Research

R&D SYSTEMS, INC.
Department Organization

Chief Executive Officer/President

Sr. VP Clinical Controls Division
Sr. VP Biotech Division

VP Finance & Chief Financial Officer

VP of Sales & Marketing

Business Development

Sr. Director, Quality and Regulatory Affairs (Management Representative)

QA/RA

Biotech Marketing

Biotech Sales

Technical Service

Technical Service BiosPacific

Facilities

IT

Accounting

Raw Material Manufacturing

Quality Control

Laboratory

Manufacturing

Shipping

Product Finishing

Marketing/Sales

Hematology Research

Effective 7/1/14
Periodic audits ensure adherence to our Quality System and identify areas for continuous improvement.

Internal Quality System audits are performed by the Quality Assurance staff or by other trained personnel under the guidance of Quality Assurance. Results of audits are reported to the CEO, the Director of QC/QA/RA, the appropriate Vice President, and the operating units involved. It is the responsibility of those units to develop corrective actions, to correct deficiencies and to present evidence of correction.

Vendor audits are performed by Quality Assurance staff on an as-needed basis.

Other Quality System effectiveness checks are made by department managers and senior management, through periodic review of product complaints, non-conforming material tracking/trending and material review board meeting minutes.

To ensure that the Quality System is effective and relevant, it is reviewed annually by the Senior Management Team, the Director of QA/RA, the Regulatory Affairs Manager and other managers, as appropriate. The agenda for the meeting is written by Quality Assurance based upon audit results and other outstanding issues related to the Quality System and product quality. Minutes from the meetings are distributed to those present at the meeting as well as any designees who are absent from the meeting. A copy of the agenda and meeting minutes are maintained on file in Quality Assurance.

Related Procedures:

**Corporate**
- 540009 Management Quality Systems Review Procedure
- 541131 Quality Meetings
- 540167 FDA Inspection Procedure
- 540291 Internal Audit Procedure
- 540335 Vendor Audit Procedure
- 540552 Corrective and Preventive Action
- 541347 Continuous Improvement

**Biotechnology**
- 540135 Customer Feedback System, Biotech
- 540259 Material Review Board Responsibility Procedure
- 540550 Quality Assurance Role in the RDS-BTS Laboratory

**CCD**
- 6016 Material Review Board Procedure
- 8034 Technical Service Protocol/Complaints
It is our policy to hire only qualified personnel and to ensure that they are trained in all aspects of their jobs.

Copies of job descriptions, job applications, resumes and annual performance reviews are kept on file in the Human Resources Department.

The Company has a Quality System training program (including the applicable requirements of ISO 9001, ISO 13485 and 21 CFR 820), conducted by Quality Assurance, which all employees are required to complete. Upon satisfactory completion of this training by an employee, a certificate of completion is given to the employee’s supervisor. Quality Assurance maintains a master log of all certificates of completion issued. Ongoing training, as necessary, ensures personnel are familiar with applicable requirements.

The Company has provided ISO 13485/CMRD, cGMP and risk analysis training to Managers and Directors responsible for the manufacture and testing of our products. It is the responsibility of these trained employees to ensure that all of their employees are familiar with the pertinent aspects of these regulations.

Regulatory Affairs ensures that the latest revisions all pertinent Standards are available. When revisions are available, this is communicated to Quality Assurance and other pertinent personnel so that we can keep up-to-date on the latest regulations and Standards.

Each department maintains job-specific training records for its employees. Supervisors are responsible for job-specific training, for training on new or revised documents, for ensuring that training is effective and for maintaining training records. Notification of document changes is issued as a trigger for training.

Related procedures:

540189 Personnel Training Procedure
540816 Procedure for Generating Personnel Training Reports
540120 Required Standards Listing, Maintenance and Review
We have different Design Controls for different types of products. In general, they cover the following points.

1. Approval of the design goals (Design Input)
2. Review of feasibility studies (Design Review)
3. Approval of the product description (Design Output)
4. Review of process development and preparation of manufacturing documents (Design Verification Review)
5. Review and approval of product validation (Final Design Review/Data Review)
6. Transfer to manufacturing

The specific procedures for the different product lines are referenced below.

Related Procedures:

**Biotechnology**
- 540045 Definition of Product Design Goals for Assay Development
- 540323 Design Control, Protein Products
- 540266 Validation Master Plan
- 540215 Specific Immunoassay Validation Procedures (i.e., Linearity, Precision, etc.)
- 540217 through 540221, 540223, 540235 - 540238, 540288, 540337, 540409, 540729, 540804, 541002 and 541273

**CCD**
- 6009 Procedural Elements in a Validation
- 6009A Testing Protocol Request
- 3421 Procedure for Developing Operational Procedures
- 6015 Product Introduction/Product Improvement Procedure
- 6015A Design Control and Transfer Worksheet
- 6039 Product Development Request Form
- 6026 Design Input
- 6027 Design Output
- 6040 Design Review Procedure

**Corporate**
- 540819 Risk Management
- 540325 Design Control
To ensure consistent quality, we use written, approved procedures for all operations. The Document Control and Quality Assurance departments or their designee(s) are responsible for controlling the issue, distribution, revision and archiving of these procedures.

The documents that must be controlled include:

- The Quality Manual and Quality Systems SOPs
- Device Master Records
- Internal Audit Reports
- Standard Operating Procedures
- Manufacturing Procedures
- Testing/Inspection Procedures and Specifications
- Calibration and Maintenance Records
- Device History Records
- Design Control Records
- Forms
- Data from BTS Studies
- Essential Requirements and Technical Document Indexes

Biotechnology uses a formal Document Change Request (DCR) procedure for creating new documents and revising existing documents. It involves review and approval by multiple departments generally including a technical department, the affected department and the Quality Assurance department. The Clinical Controls Division initiates formal Document Control in each Department. The Department Supervisor reviews a draft with assistance from designated individuals.

Related Procedures:

**Corporate**
- 540643 Standard Operating Procedure (SOP) Review Procedure
- 540578 Record Keeping Guidelines
- 540146 Creating a Document
- 540748 MasterControl™ Electronic Documentation System
- 540750 MasterControl™ Functions

**Biotechnology**
- 540205 Document Change Request (DCR) Procedure
- 540382 Preparation & Maintenance of Document Master Files
- 540532 Data Management: General Procedures & Definitions (BTS Lab)

**CCD**
- 3007 New and Updated Procedure Protocols
- 3008 Manufacturing Procedure Format
- 6005 Document Organization (Document Control)
- 3421 Procedure for Developing Operational Procedures
- 6006 Updating the Device Master Record (DMR)
- 6030 Format for "Product Description/Device Specifications" Documents
- 6031 Format for "Product Type" Documents
Consistent quality of raw materials and contracted services is a key part of our Quality System.

Purchasing Control covers the following areas:

- **Specifications**: Requirements for raw materials are stated in written specifications available to all personnel doing purchasing and receiving activities.

- **Vendors**: Qualified vendors are listed on each raw material specification. Document 540000, Vendor Qualification and Monitoring, describes how to qualify new vendors in the Biotech and CCD divisions, including outsourced services and processes, and how our vendors are monitored for quality and on-time delivery of goods and services. Vendor performance is tracked, with Key Providers and vendors with quality-related returns receiving Vendor Scorecards. Vendors who do not perform well may be disqualified and replaced.

- **Purchasing**: The purchase order includes our part number and a request for a Certificate of Analysis and/or Certificate of Origin where appropriate. All materials used in the manufacture of products are verified against the purchase order. Purchasing interacts with suppliers regarding non-conforming or damaged materials.

- **Contracts and Supply Agreements**: Purchasing, Sales, Legal or Business Development is responsible to ensure customer contracts and supply agreements are in place when required. Intellectual property contracts, customer contracts and supply agreements are managed by Legal or Business Development.

Related Procedures:

- 540687 Purchasing Procedure, R&D Systems
- 540192 Receiving Procedure, R&D Systems
- 540000 Vendor Qualification and Monitoring
- 540335 Vendor Audit Procedure
- 540876 Quarantined Product Procedure
- 540805 Policy Regarding Contracts and Supply Agreements
- 640xxx Non-biological Raw Materials Specifications (Biotech)
- 645xxx Biological Raw Material Specifications (Biotech)
- 54xx, 55xx Biological Raw Material Specifications (CCD)
- 56xx, 57xx Non-biological Raw Materials Specifications (CCD)
The ability to trace each lot of product back to the raw materials used in its manufacture and to trace any lot of raw material to products into which it became incorporated is an essential feature of our Quality System.

A part number and lot number (or receiving number) control all materials used to manufacture products. This provides complete traceability from receipt of raw materials through final shipment to the customer. In Biotechnology, part numbers are assigned by Document Control or through the Product Development Project Tracking (PDPT) database. An MRP System (RenCS) is in place in the kit manufacturing area which is used to track inventory, assign job (lot) numbers and plan the production of the kit products. Lot numbers for all other products may be sequentially assigned from the Document Change Request (DCR) Database or PDPT, or are assigned at the time of bottling.

The Vice President of CCD assigns final product lot numbers for CCD products.

Receiving departments are responsible for assigning receiving numbers to incoming raw materials.

Related Procedures:

540153  Part Number Assignment (Biotech)
540206  Assigning Lot Numbers
540540  Receiving, Entering and Labeling of Samples for RDS-BTS Lab
540831  RenCS, Add and Maintain Part Records
8862    Assigning Final Product Lot Numbers (CCD)
6019    Identification and Traceability (CCD)
We design quality into our products. Areas of the manufacturing process that require control are identified during the development of a product and the effects of variables and appropriate limits are established.

Process Control is accomplished through planning, written procedures, inspection, calibration, training, supervisory oversight and employee awareness. Changes to the manufacturing process, if required, are controlled, qualified and validated.

- Written procedures provide bills of materials, instructions for production, equipment required, working environment, filling and labeling instructions, record sheets, expiration dating, in-process testing, and acceptance criteria.

- Monitoring of product manufacture is accomplished through the use of Batch Records (Device History Records) containing the current revisions of the documents required for the manufacture of a product. Manufacturing and Quality Control departments print official copies of their documents from MasterControl™. In CCD, Operations assembles the batch records. Quality Control verifies compliance through review and approval of completed batch records prior to final product release.

- The Specification Deviation Procedure handles both planned and unplanned deviations from the written procedures.

- All new inspection, measuring and test equipment is inspected and validated, when appropriate, against manufacturer’s specifications and is identified with a permanent preventive maintenance (PM) number. Equipment is calibrated on a regular schedule. Improperly maintained or calibrated equipment will not be used. Records of calibration and maintenance are maintained by the Facilities Department. Quality Assurance audits equipment periodically, to ensure that calibration is proceeding according to schedule.

- The supervisor or lead personnel contributes to quality through training employees, assisting employees with new or specialized processes, interpreting instructions for and communicating process changes to employees.

Related Procedures:

**Corporate**

- 540126 Deviation Procedure
- 540142 Procedure for Documentation of Equipment Maintenance and/or Calibration
- 540310 Software Validation
- 540133 Internal Notification Procedure: Receipt of New Equipment

**Biotechnology**

- 540781 Planning Guidelines, Immunoassay Manufacturing
- 540834 RenCS, Recipe Authorization
- 540833 RenCS, Add, Copy and Maintain a Process Specification
540832 RenCS, Adding and Copying a Recipe
540207 Label Control, Product Finishing
540072 Filling Operations Procedure
540267 Preparation, Completion and Approval of Batch Records
540278 Bottling Procedure for Cytokines and Antibodies Designated for Retail Sale
540256 Labeling Procedure for Cytokines and Antibodies Designated for Retail Sale
540134 Incoming Equipment Validation Procedure

CCD
9090 Product Finishing Label Control
9054 Bottling Procedure
8812 Finished Device Inspection Procedure
8813 Guidelines for Determining Assay Ranges
8006 Bottled Product Release
8809 Assay Sheet Printing and Release
6009A Testing Protocol Request
6017 Product Type, Product Type Revision, Product Change Notification
Acceptance/inspection activities are critical to the manufacture of quality products.

- **Incoming materials** are received in accordance with documented procedure(s).

- **Deliveries are inspected** against the purchase order for type, quantity and external transit damage. Additional inspection may include verification against Certificates of Analysis, Certificates of Origin, in-house material specifications or incoming testing procedures.

- **In-process testing** is specified by the manufacturing and/or Quality Control procedures. Testing may include the recording of physical parameters such as pH and temperature, actual functionality testing and/or visual inspection.

- **Final inspection and testing** are completed before any product is released for sale. Quality Assurance or Quality Control Management sign the product release forms. All documentation is reviewed and the product is physically inspected before release stickers are placed on the product and batch record.

All inspections and testing are supported by completed documentation. Release by exception is documented and approved by the Material Review Board.

Related Procedures:

- 540192 Receiving Procedure, R&D Systems
- 540080 Raw Materials Departmental Receiving and Inspection Procedure
- 540124 Inspection of Assembled Kits
- 540143 Literature and Label Approval Procedure
- 550449 Immunoassay Approval/Rejection Criteria
- 540267 Preparation, Completion and Approval of Batch Records
- 540526 Receiving OEM Products
- 540363 Releasing Retail Product
- 540194 Certificate of Analysis Procedure
- 541138 Quality Assurance Organization
- 8812 Finished Device Inspection Procedure (CCD)
Our Quality System provides for the identification, documentation, evaluation, segregation, and disposition of non-conforming product.

Quality Assurance administers the non-conforming materials system with the participation of the Material Review Board (MRB). Within departments producing research use only materials, appropriate technical personnel will review non-conforming material and make decisions concerning disposition of that material. Any employee with knowledge of non-conforming material may call for a Material Review Board meeting. Minor non-conformities may be released by Quality Control with adequate documentation. Disposition of major non-conformities lies with the MRB. QA is responsible for documenting the activities of the MRB. The Biotech MRB is composed of representatives from Quality, Manufacturing, and Development. Additional representatives from Product Support, Marketing, Technical Service or Sales may also participate as required. All corrective actions must be fully documented. Minutes from meetings of the MRB are published and maintained in MasterControl™.

In CCD, MRBs are documented using the Material Review Board (MRB) form. Minutes from meetings of the MRB are published and maintained in MasterControl™. A summary of MRBs is distributed quarterly to managers for review.

All non-conforming material is clearly marked with Quarantine stickers or labeled appropriately. In addition, it is physically separated from conforming material until final disposition.

A Specification Deviation is issued for any deviation in the manufacturing procedure even if the product ultimately meets final release specifications. If a product is reworked, it must undergo all required inspections and tests as well as any additional inspection or testing required by the MRB. Reworked material must pass the same release criteria as the original product.

Related Procedures:

**Corporate**
- 540126 Deviation Procedure
- 540552 Corrective and Preventive Action
- 541214 Corrections, Removals and Recalls for IVD Products

**Biotechnology**
- 541089 Antibody Rework Procedure, Dept 378
- 540259 Material Review Board Responsibility Procedure
- 540265 Rework Procedure
- 540835 Quarantining Product in Finished Goods Inventory
- 550407 Criteria for the Acceptance of Protein Preparations for Sale
- 550406 Criteria for the Acceptance of Antibody Preparations for Sale

**CCD**
- 3009 Adjustment/Replacement of a Finished Product
- 6016 Material Review Board Procedure
- 1012 Rework Procedure
- 3018 Quarantine Procedure
- 8021 Rejection of a Product, QC Laboratory
- 10212 CCD Shipping's Inventory Quarantine Procedure
We are committed to taking preventive and corrective action to remedy any customer dissatisfaction or non-conformity that is identified. Whenever appropriate, a root cause analysis will be done to identify the root cause of the dissatisfaction or non-conformity.

A Customer Feedback System is maintained by Quality Assurance using the input from Technical and Customer Service. All customer complaints are logged and then classified as to type of complaint (performance, physical, etc.). All complaints are numbered and tracked by QA from receipt of initial call until closure. A summary report of Biotech complaints is available monthly for review by appropriate personnel. Weekly and monthly summaries of CCD complaints are circulated to Management.

In Biotechnology, periodic meetings are held to review performance complaints. Each meeting is attended by members of the appropriate department(s), MRB members and Technical Service. In the CCD, complaints are reviewed weekly by members of the MRB and Technical Service.

Corrective action is taken to remedy non-conformities that are identified and to prevent future recurrences. Preventive action is taken to eliminate the cause of a potential non-conformance. The Material Review Board reviews non-conformities. An action plan is put together with QA being responsible for monitoring and documenting the progress of any corrective or preventive action plan to ensure its completion. A corrective or preventive action that changes approved documents or processes is handled through the Document Change Request and the Change Control systems in Biotechnology and through department-level document control in CCD.

Related Procedures:

540775 Medical Device Reporting (MDR) of Injury or Death
540552 Corrective and Preventive Action
540260 Field Notification Procedure
540135 Customer Feedback System, Biotech
540331 Returned Goods Procedure (Biotech)
541231 Change Control Procedure, Biotech
8034 Technical Service Protocol/Complaints (CCD)
8036 Procedure for Investigation of Returned Product (CCD)
Statistical methods are very powerful tools when used correctly within the quality process. These methods are selected with care to ensure they suit the application required and will produce an objective output.

The motivation to use these statistical methods is a desire to improve quality and to meet customer requirements. The Quality System is subject to variations from components, design and equipment. Statistical methods can assist with the elimination or minimization of these variations.

Statistical methods are used whenever possible or applicable to ensure product consistency.

Test and control are implemented to release product, and to improve the knowledge base to allow for product improvement.

Tools that are used or should be considered are:
- Experimental Design - Design of Experiment(s) software is available and is being used by kit development groups.
- Analysis of Variance/Regression Analysis
- Risk Analysis
- Root Cause Analysis
- Statistical Sampling Inspection
- Histograms - Plot frequency of events
- Pareto diagrams - Assist with sorting crucial problems
- Flow charts - Pictorial diagrams of processes or systems

Examples of where Statistical techniques may be applied:
- Design Input - Determining requirements and expectations
- Design Control - Periodic evaluation to provide assurance of acceptable product performance
- Shelf Life - Determine appropriate dating for products
- Process Control - Determine machine or process capabilities, monitor deviations
- Defect Analysis - Assist with understanding problems
- Data Analysis - Review and understanding of products
- Vendor Monitoring - Analysis of non-conforming product and on time delivery
- Continuous Improvement - Analysis of audit findings and corrective actions

Related Procedures:

540865 Statistical Methods
540537 Test for Outlier Determination (Grubb's Method)
8043 Detecting Outliers (CCD)
We present to our customers only the highest quality labeling and packaging, and ensure that they meet all regulatory requirements.

Labels, literature and packaging are subject to incoming inspection.

Label control is the responsibility of the Quality Assurance and Manufacturing departments. Document Control and our Insert, Certificate of Analysis (ICA) database maintain the Literature Approval system through which new Biotech label and literature copy is circulated for approval prior to printing. The variable information on labels is printed in Manufacturing from password secured files. Each label is assigned a part number and is revision controlled. All labeling operations require label inspection and reconciliation.

The QA/RA Specialist(s) monitors label control in CCD.

Pre-printed labels are stored in locked cabinets or access-controlled areas.

Product packaging is designed to protect the product from environmental stress and physical damage during shipping. The effectiveness of the packaging in protecting the product has been documented and is monitored on every lot by analyzing data received through the external QC program and through customer complaints.

Finished products are assembled according to written procedures. Final product packaging is done so as to protect product integrity through physical separation of different operations. All packaging areas are cleared prior to the start of the next operation. Quality Control or other appropriate personnel inspect finished products using statistically valid sampling plans and release product only after it meets inspection criteria.

Related Procedures:

**Corporate**
- 541104 Labeling Guidelines, IVD

**Biotechnology**
- 540207 Label Control, Product Finishing
- 540256 Labeling Procedure for Cytokines and Antibodies Designated for Retail Sale
- 540143 Literature and Label Approval Procedure
- 540124 Inspection of Assembled Kits
- 540467 Line Clearance
- 541365 Development, Revision and Approval of Protein Inserts using the ICA System

**CCD**
- 6029 Clinical Controls Division Labeling Control
- 6029A Labeling Review Form
- 9090 Product Finishing Label Control
- 8809 Assay Sheet Printing and Release
- 8855 Instruction Sheets – Revising, Printing and Inspecting
It is our goal to minimize damage or deterioration of products throughout manufacturing to delivery to the customer. Stability studies are conducted during development to validate recommended storage conditions.

Storage conditions for raw materials, work in process and finished goods are specified in the appropriate specifications or manufacturing procedures. Storage areas are environmentally monitored to protect product integrity. Backup generators are available in case of a power outage. Products are properly identified with part number, lot or receiving number and acceptance status before they are placed in storage areas.

Materials are handled in a manner to ensure first in-first out use when required. Materials are marked with an expiration date where appropriate. This date is monitored and outdated product is removed from stock for appropriate disposal or retesting.

Products are packaged and labeled for distribution to ensure physical and functional integrity during transportation. The mode of transportation is chosen to protect the quality of the product.

Related Procedures:

- 541178 International Order Procedure, Biotech Shipping
- 541252 Domestic Retail Biotech Shipping Procedure
- 541351 Finished Goods Inventory Cycle Counts, Biotech Shipping
- 541358 Processing Expired Product in Biotech Shipping
- 540180 Identification and Breakdown of Expired Product in Inventory
- 540221 Validation: Stability Testing of Immunoassay Kits
- 541069 RenCS, Removing Expired Components from Inventory
- 540281 CCD Shipping Procedures
- 6100 Storage of Products (CCD)
- 10211 Closing Out Expired Product (CCD)
We believe that it is essential to maintain quality records not only to conform to the regulations, but to also aid management in reviewing the effectiveness of our Quality System and making decisions on how to improve it. The records that are maintained also demonstrate that products were manufactured to specifications and standards.

The quality records that are maintained include:

- Quality System DOCUMENTATION
- Device Master Records
- Device History Records
- Document Change Requests
- Calibration and Maintenance Records
- Internal Audit Reports and Management Reviews
- Customer Complaints
- Vendor Qualifications
- Purchase Orders
- Customer Orders and Contracts
- Personnel Records/Training records
- Design History Files (Validation Data)
- Field Notifications and Recalls
- BTS Sponsor Notebooks
- Process and Equipment Validations
- MRB Minutes
- Deviations

All of our records are stored in conditions to facilitate their preservation and to allow ready access by appropriate personnel. The records are retained for at least three years, or as specified in individual SOPs or customer contracts.

Related Procedures:

541138 Quality Assurance Organization
540008 Quality Record Retention
540539 Archiving Study Documents for the RDS-BTS Laboratory
540534 Computer Servers Back-up Procedures
541303 R&D Systems Server/Application Documentation