R&D SYSTEMS
a bio-techne brand

Quality System Manual

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1.0 SCOPE

1.1 R&D Systems was founded in 1976 in Minneapolis, MN as a wholly owned subsidiary of TECHNE Corporation (a holding company with no employees). In July 2014, TECHNE was renamed Bio-Techne. The stock is traded publicly on NASDAQ's National Market System under the "TECH" symbol. Bio-Techne has two operating segments: Protein Sciences and Diagnostics & Genomics.

1.1.1 Protein Science Segment has manufacturing facilities in Minneapolis and St. Paul, Minnesota.

1.1.2 Diagnostics & Genomics Segment has a manufacturing facility in Minneapolis to manufacture controls, calibrators and linearity products for hematology analyzers.

1.1.3 The Authorized European Representative R&D Systems branded *in vitro* Diagnostic Medical Devices is Bio-Techne SAS, 19 Rue Louis Delourmel, CS 49228, 35230 Noyal Chatillon Sur Seiche, France.

1.2 The Minneapolis facility is Bio-Techne corporate headquarters and manufactures products for both the Protein Sciences and Diagnostics & Genomics Segments. The Quality Management System is certified to ISO 9001 and ISO 13485, holding certificates from BSI: FM547845 (9001), FM547846 (13485).

1.3 This manual pertains to the Quality Management System of both segments which operate at the Minneapolis and St Paul locations, being applicable to the design and development, manufacture, sale, support and distribution of products under the R&D Systems brand name.

1.4 This Manual (540308 - this document) describes the Quality Management System (QMS) used for the design, production and distribution of R&D Systems branded products manufactured at the Minneapolis and St. Paul facilities. The Quality Policy and Risk Policy (for IVD products) are documented in this manual (Section 5) and compliance is achieved through specific reference to local procedures and the effective implementation of the R&D Systems' QMS.

1.5 The Quality Management System applies to all processes, activities, and employees at 614 McKinley Place NE, Minneapolis, Minnesota, and 22 Empire Drive, St. Paul, Minnesota.

1.6 R&D Systems has determined the following sections of ISO 13485 are not applicable to the Quality Management System:

1.6.1 7.5.3 Installation Activities: products do not require installation.

1.6.2 7.5.4 Servicing Activities: products do not require servicing.

1.6.3 7.5.5 Particular requirements for sterile product and 7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems - products are not sterilized and do not have a sterility claim.

1.6.4 7.5.9.2 Particular requirements for implantable medical devices - products are not implantable.

2.0 QUALITY MANAGEMENT SYSTEM REFERENCES

2.1 The Quality Management System Manual also serves as the Quality System Record (QSR) as defined in the FDA Medical Device Quality System Regulations and references key procedures which detail the fulfillment of these requirements. The following documents have been utilized during the development of this manual; their listing as references does not imply compliance with all of them. Their applicability will be dependent on the specific products and regulatory requirements of the countries and regions where products are distributed. Included are:

2.1.1 ISO 13485 [1]

2.1.2 ISO 9001

2.1.3 Medical Device Single Audit Program (MDSAP)

2.1.4 21 CFR § 820 - Quality System Regulation (US FDA)

2.1.5 RDC ANVISA 665/2022 - Brazilian Health Regulatory Agency (ANVISA)

2.1.6 Australian Regulatory Guidelines for Medical Devices (ARGMD) - Australian Therapeutics Good Administration (TGA)

2.1.7 Medical Devices Regulations (SOR/98-282) - Health Canada

2.1.8 European Union Council Directive 98/79/EC concerning *In Vitro* Diagnostics Devices (IVDD) and Regulation (EU) 2017/746 (IVDR)[2].

2.1.9 MFDS (South Korea): Standards for Manufacture and Quality Management of Medical Device and In Vitro Medical Device; Medical Device Act and In Vitro Medical Device Act; Regulation on Management of Safety Information Including Medical Device and In Vitro Medical Device Side Effects.

2.1.10 United Kingdom (UK) Medical Device Regulation (MDR)

2.1.11 Applicable laws regulations of Countries where R&D Systems' products are registered and distributed.

Document	Description
540007	Canadian Medical Device License, Establishment License and Quality System Certification
540120	Access and Control of Documents of External Origin
541347	Continual Improvement
542714	US Medical Device and Annual Establishment Registration
543022	Requirements for Registration of In Vitro Diagnostic Medical Devices in the United Kingdom
543040	EU Requirements for Authorized Representative, Importer and Distributor
542118	IVD Requirements - Australia
542119	IVD Requirements - Brazil

[1] Specific reference to the current standards is provided in SOP 540120; henceforth, in this document and other Quality Management System documents, reference to these standards is understood to refer to these revisions.

[2] The *in vitro* diagnostics devices manufactured are classified Class I self-certified according to the IVDD and will be classified as Class B according to Regulation (EU) 2017/746 - IVDR. As of the date of this manual, the products continue to be sold under the IVD directive.

2.2 Company History

2.2.1 As noted in Section 1.1, the company was started in 1976, as Research & Diagnostics Systems, Inc. (R&D Systems, Inc.) at the 614 McKinley Place NE, Minneapolis, Minnesota facility.

2.2.1.1 Initially the business unit, which manufactures controls, calibrators, and linearity products, which are registered IVD products, for hematology instruments, operated as the Hematology Division. The division name was subsequently changed to Clinical Controls Division (CCD) in 2015, to Diagnostics Division (DD) in 2017, and to its current name, Diagnostic Reagents Division (DRD), in 2018.

2.2.1.2 The current Protein Sciences Segment manufactures proteins, antibodies, kits and IVD-registered kits. This business unit was previously known as Biotech, as noted on the header for procedures and specifications related to PSS products.

2.2.2 In 2021 the facility at 22 Empire Drive, Saint Paul, MN was built for the dedicated manufacture of Animal-Free, GMP-grade products. The facility is part of the Protein Sciences Segment.

3.0 TERMS AND DEFINITIONS

3.1 **Document Change Request (DCR):** a formal process for creating new documents and revising existing documents.

3.2 **Documented:** Written and retrievable; may be in hard copy, electronic or another media form.

3.3 **Device Master Record (DMR):** A compilation of records containing the procedures, specifications and quality management system requirements for a finished medical device.

3.4 **Effective Date:** The date a document becomes effective.

3.5 **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)].

3.6 **Quality System:** The organizational structure, responsibilities, procedures, processes and resources for implementing quality management [(§ 820.3 (v)].

3.7 **Bio-Techne Minneapolis:** R & D Systems, Inc; includes the Protein Sciences Segment and the Diagnostics and Genomics Segment.

3.8 **Shall:** Must (unless, by nature of the business, the subject or requirement does not apply).

3.9 **SOP:** Standard Operating Procedure

4.0 QUALITY MANAGEMENT SYSTEM

4.1 General Requirements

4.1.1 R&D Systems is committed to the highest level of quality in the design and development, manufacture, sale and support of our products. Overview of the Quality Framework is provided in Figure 1 on the next page.

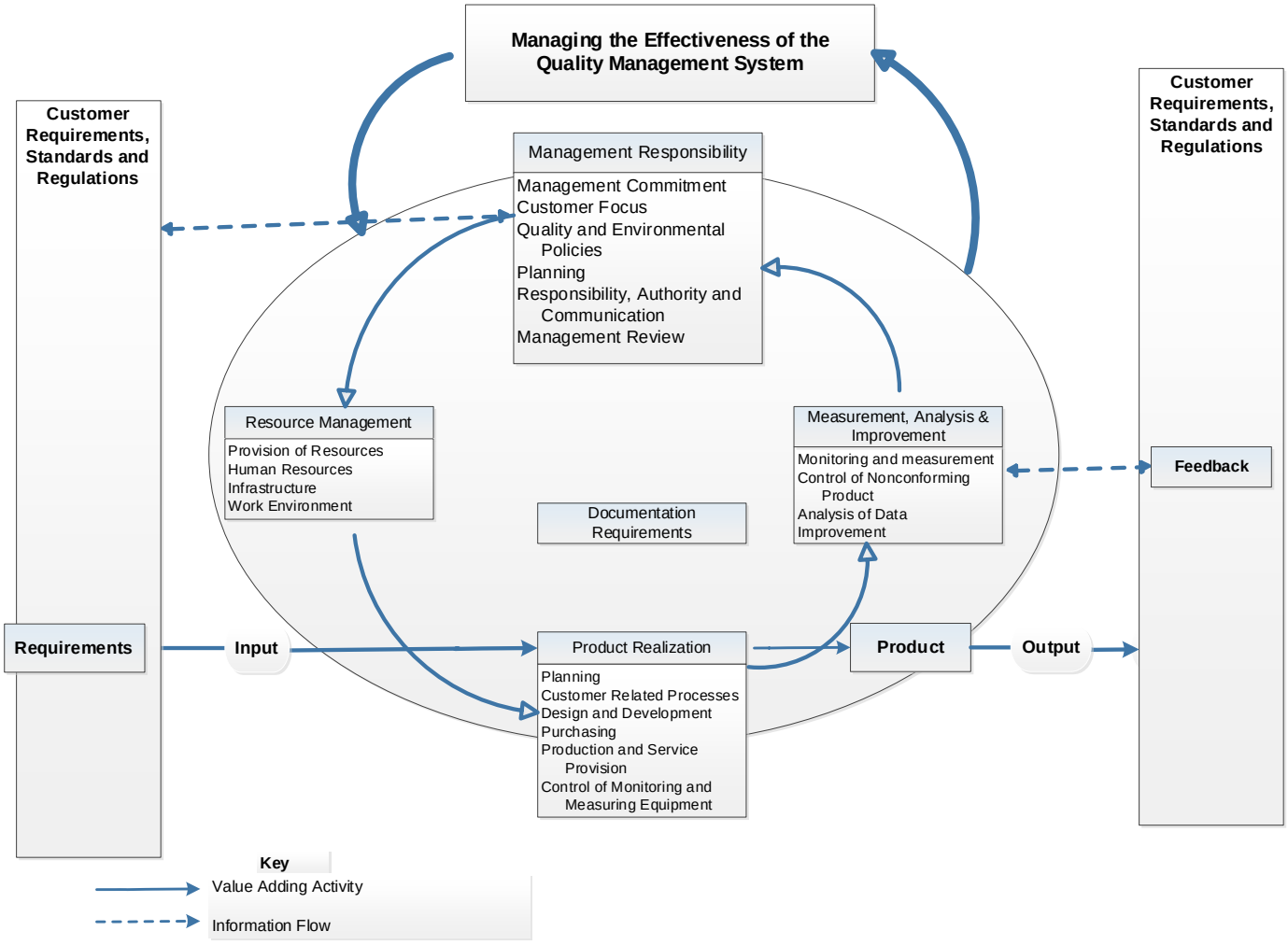


FIGURE 1 – QUALITY FRAMEWORK

This manual outlines the global requirements of R&D Systems Quality Management System, providing an overall framework for the communication and dissemination of quality mission, vision, expectations, policies, supporting procedures and guidelines. This information guides organization-wide quality-related task planning and provides a standard for formal quality system evaluations (Figure 1 above).

R&D Systems has the authority and responsibility to establish and maintain detailed quality system documentation that focuses on the specific needs and expectations of customers and the requirement of regulatory authorities.

4.1.2 R&D Systems applies a risk-based approach to the control of the appropriate processes needed for the Quality Management System (QMS).

4.1.3 Assurance of product/process quality and integrity of the QMS are the responsibility of: The Chief Executive Officer (CEO), who has responsibility for creating an atmosphere of high standards; the Officers, Directors, Managers and Supervisors, who are charged with development and implementation of quality requirements; and each employee, who is responsible for their work and for adhering to quality requirements.

4.1.4 Changes made to the QMS processes are evaluated for overall impact on the QMS and are evaluated for impact on *in vitro* diagnostic medical devices and GMP products produced under the QMS. Changes are controlled in accordance with the requirements of applicable standards and regulations.

4.1.5 R&D Systems considers "outsourcing" as any process, product or service that affects key processes and /or product conformity to requirements which is obtained by contract from a source outside of R&D Systems.

4.1.6 R&D Systems outsources the following: contract ethylene oxide (EO) processing, pest control, contract lab testing when needed, e.g., environmental, microbiology, residual viruses, etc., deionized water servicing, calibration for specialized instruments and equipment. Other outsourced services may be utilized as needed.

4.1.7 R&D Systems has procedures in place which outline the specific approach and activities associated with software validation and revalidation. This falls under the validation portion of this manual.

Document	Description CORPORATE
540009	Management Review - Quality Management System

4.2 Documentation Requirements

4.2.1 General

4.2.1.1 The QMS documentation includes the R&D Systems' Quality Manual (this document, 540308), Standard Operating Procedures (SOPs) needed to establish, maintain, and support the QMS, Device Master Records of finished product manufactured at the Minneapolis and St. Paul locations, policies and procedures needed to establish, maintain and support the QMS, and all records used to provide evidence of the effective implementation of the QMS.

4.2.1.2 The documentation hierarchy, shown graphically in Figure 2, is described in the following manner.

4.2.1.2.1 Level 1 Documents
R&D Systems Quality Manual
R&D Systems Quality Policy
Device Master Records
Technical Files (Technical Documentation Indexes)

4.2.1.2.2 Level 2 Documents
Corporate SOPs

4.2.1.2.3 Level 3 Documents
Protein Sciences Segment (Reagent Solutions Division and Analytical Solutions Division) and Diagnostics and Genomics Segment (Diagnostic Reagents Division) level documents

4.2.1.2.4 Level 4 Documents
Controlled and Non-Controlled Documents including Work Instructions

4.2.1.2.5 Level 5
Records that provide evidence of conformity to the requirements and effective operation of the QMS
QMS Review Records
Internal Audit Reports
Technical Reports
Validation Documentation
Device History Records
Forms, Templates, Records and Data

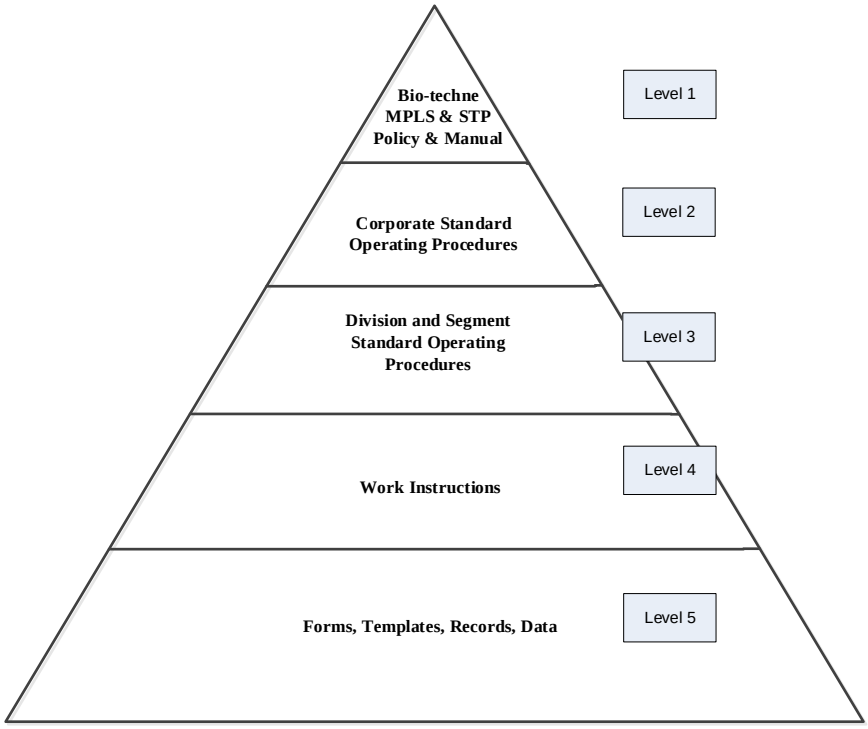


Figure 2 – Document Hierarchy

4.2.2 Quality System Manual

4.2.1.3 This Quality System Manual has been prepared to describe R&D Systems' QMS. This includes the Protein Science Segment - Minneapolis and St. Paul sites and the Diagnostics and Genomics Segment - Minneapolis site. The scope and purpose of the QMS are described in Section 1.0. Each section of the manual references documented QMS procedures relating to the requirements outlined in that section.

4.2.1.4 This Quality Systems Manual has been approved by members of Senior Management.

4.2.1.5 This Quality Systems Manual is part of the R&D Systems' Document Control System and is controlled and distributed in accordance with the DCR System in our eDMS (electronic Document Management System). The process of moving the eDMS from MasterControl to SmartSolve has been completed. (MasterControl will continue to be used to access historical records such as completed validations and technical reports.)

4.2.1.6 The Management Representative shall review this document at a minimum annually and facilitate appropriate changes.

4.2.3 Medical Device File

4.2.3.1 Device Master Records are maintained for all *in vitro* diagnostic (IVD) medical device products; Technical Documentation is also maintained for IVD products. These files contain, or reference, documents which demonstrate conformity to requirements.

Document	**Description CORPORATE**
543023	IVDR Technical Documentation Requirements[3]
Document	**Description Protein Sciences Segment**
542676	Device Master Records (DMRs) - Protein Sciences Segment
Document	**Description Diagnostic Reagents Division**
2006006	Device Master Records (DMRs)

4.2.4 Control of Documents:

4.2.4.1 Internal documents:

4.2.4.1.1 QMS documents are reviewed for adequacy and approved prior to issue in accordance with appropriate procedures. R&D Systems uses a formal Document Change Request (DCR) procedure for creating new documents and revising existing documents. This involves review and approval by multiple functionalities generally including a technical department, the affected department, and the Quality Assurance department.

Documents that must be controlled include: QMS and Quality System SOPs, Device Master Records, Internal Audit Reports, Management Review results; Standard Operating Procedures, Manufacturing Procedures, Testing/Inspection Procedures and Specifications, Calibration and Maintenance Records, Device History Records, Design Control Records, Forms, Chemical Safety, AWAIR (MN-OSHA) requirements, Essential Requirements Checklists, Technical Document Indexes, Competence records; and evidence of communication; Non-conformities and corrective action. SOPs also define controlled documents and records.

4.2.4.1.2 Appropriate documents with their relevant revision status are available in our eDMS. Obsolete documents are prevented from unintended use through archiving in the eDMS.

[3] The *in vitro* diagnostics devices manufactured are classified Class I self-certified according to the IVDD and will be classified as Class B according to Regulation (EU) 2017/746 - IVDR. As of the date of this manual, the products continue to be sold under the IVD directive.

4.2.4.1.3 Document changes can be initiated by anyone in the organization but may only be posted after approval through the DCR process.

4.2.4.2 External standards and regulations that impact products, processes or documentation are maintained through a Tech Street Subscription.

Document	Description CORPORATE
540120	Access and Control of Documents of External Origin
540146	R&D Systems' Document Formatting
540205	Document Change Request (DCR)
540578	Record Keeping Guidelines
540643	Standard Operating Procedure (SOP) Review
542769	SmartSolve QMS Document Management Administrator Instructions
542770	SmartSolve QMS: Document Management - Document Coordinator Instructions
542771	SmartSolve QMS: Document Management - Document Approver Instructions
542772	SmartSolve QMS: Document Management - Viewer Instructions
Document	**Description Protein Sciences Segment**
540382	Preparation and Maintenance of Document Master Files

4.2.5 Control of Records

4.2.5.1 Records provide descriptive, recorded evidence that quarantined items, product, processes, and equipment meet specified requirements. R&D Systems ensures the quality and legibility of records by following good documentation practices.

4.2.5.2 All records required to be maintained by the QMS and regulatory authorities are identified, collected, archived and retrieved in accordance with SOPs established by Document Control procedures. Record retention periods are defined based on product and regulatory requirements.

4.2.5.3 It is essential to maintain these records not only to conform to the regulations, but to also aid management in reviewing the effectiveness of the QMS and in making decisions on how to improve it. The records that are maintained also demonstrate that products were manufactured to pertinent specifications and standards.

4.2.5.4 Records shall be established and maintained to provide evidence of conformity to requirements and of the effective operation of the QMS. Records shall remain legible, readily identifiable and retrievable. A documented procedure shall be established to define the controls needed for the identification, storage, protection, retrieval, retention time and disposition of records.

4.2.5.5 Quality records maintained include:

4.2.5.5.1 Quality System Documentation

4.2.5.5.2 Device Master Records

4.2.5.5.3 Device History Records

4.2.5.5.4 Document Change Requests

4.2.5.5.5 Calibration and Maintenance Records

4.2.5.5.6 Internal Audit Reports and Management Reviews

4.2.5.5.7 Customer Complaints

4.2.5.5.8 Supplier Qualifications
4.2.5.5.9 Purchase Orders
4.2.5.5.10 Customer Orders and Contracts
4.2.5.5.11 Personnel Records / Training records
4.2.5.5.12 Design History Files (Validation Data)
4.2.5.5.13 Field Safety Notifications and Recalls
4.2.5.5.14 Process and Equipment Validations
4.2.5.5.15 MRB Minutes
4.2.5.5.16 Deviations
4.2.5.5.17 Nonconformances
4.2.5.5.18 Corrective and Preventative Actions (CAPAs)
4.2.5.5.19 Change Notices

Document	Description CORPORATE
540008	Record Retention
540578	Record Keeping Guidelines
542868	Introduction of SmartSolve QMS Functions
540534	Corporate IT Backup Policy
541490	Bio-Techne Network Security Policy
541526	Bio-Techne Information Security Policy
542050	Password Policy
541034	Disaster Recovery Plan, Bio-Techne (Minnesota)
Document	**Description Diagnostic Reagents Division**
2008128	Archiving Product Files

5.0 MANAGEMENT RESPONSIBILITY

5.1 Management Commitment

5.1.1 Senior Management has responsibility for the oversight of the QMS, product quality, and GMP compliance for all products manufactured and distributed by R&D Systems.

5.1.2 Senior Management is actively involved in implementing the QMS and ensuring its continual improvement and effectiveness. Senior Management provides the vision and strategic direction for the growth of the QMS and establishing quality objectives with regard to the stated policies.

5.1.3 Senior Management provides leadership and shows commitment to the improvement of the QMS through:

- communicating the importance of meeting customer expectations
- statutory and regulatory requirements
- establishing quality objectives
- supporting the Quality Policy
- conducting regular Management Reviews
- ensuring the availability of resources
- providing QMS training for all associates

5.2 Customer Focus

5.2.1 R&D Systems strives to identify current and future customer needs to meet customer requirements or exceed customer expectations. This may include potential customers and end-users.

Document	Description Protein Sciences Segment
540135	Customer Feedback System, Biotech
Document	**Description Diagnostic Reagents Division**
2006926	DRD Customer Feedback/Complaints

5.3 Quality Policy

5.3.1 Senior Management ensures the **Quality Policy** and the **Risk Policy for IVD Products** are communicated to all associates.

5.3.2 The Quality Policy is:

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 requirements and to maintain the effectiveness of the Quality Management System, continual improvement and customer satisfaction shall underlie all of our efforts in development, manufacturing, advertising, sales, shipping and technical support.

5.3.3 The Risk Policy for IVD Products is:

R&D Systems, Bio-Techne Minneapolis, is committed to the highest level of quality and safety in the manufacture, sale, and support of our products.

The purpose of this Risk Policy is to provide guidance for establishing criteria for risk acceptability. These criteria are used in the evaluation of residual risk associated with in vitro diagnostic (IVD) medical devices manufactured by R&D Systems, Inc. The criteria will ensure that IVD medical devices have a high level of safety consistent with stakeholder expectations.

The policy applies to all persons involved in establishing, reviewing, updating, and approving the criteria for risk acceptability in risk management plans for IVD medical devices designed, developed and/or manufactured by R&D Systems, Bio-Techne Minneapolis. Risk Management processes apply to the lifecycle of the product.

Risk acceptability is defined as the overall risk level (residual risk) that is considered acceptable. In defining the criteria for overall risk acceptability, the Risk Management Team shall take the following elements into consideration:

1. **The purpose and/or intended use of the IVD medical device.**
2. **Applicable regulatory requirements in the regions the IVD medical device is to be marketed.**
3. **Relevant international standards for the particular IVD medical device being designed and developed.**

4. **The generally acknowledged state of the art, which can be determined from a review of international standards, best practices in technology, results of accepted scientific research, publications from authorities, and other information for similar IVD medical devices and similar other products.**

5. **Validated concerns from stakeholders, for example obtained through direct communication from users, clinicians, patients or regulatory bodies, or through indirect communication via news reports, social platforms or patient forums.**

Risk control measure options can include the use of specific international standards, elimination of the risk by making the design of the medical device and its manufacturing process inherently safe, implementation of protective measures in the design of the IVD medical device or in the manufacturing process and/or providing information for safety to the users of the IVD medical device.

Risks are reduced as low as possible using risk control measures without adversely affecting the benefit-risk ratio. Consideration should be given to whether technically practicable measures would reduce the risk without impacting the intended use or the benefit of the IVD medical device. The approach taken can use a semi-quantitative risk matrix to support risk estimation. The risk matrix is divided into three regions corresponding to unacceptable risk (red), insignificant or negligible risk (green) and risks that require investigation to determine if further risk control is feasible (yellow). If risk is in Green Zone - No further action required - risk is determined to be acceptable. If risk is in the Yellow Zone – Investigate to determine if further risk control is feasible. A benefit-risk analysis will be performed to determine if the risk is acceptable. If risk is in the Red Zone - Further risk reduction is required.

5.3.4 The Quality and IVD Risk policies are reviewed during Management Review for continuing suitability.

5.4 Planning

5.4.1 Quality objectives are established to support the organization's efforts in achieving its strategic priorities and are reviewed annually for suitability and alignment with the Quality Policy during Management Review.

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

5.4.2 Quality Management System Planning

5.4.2.1 Senior Management ensures quality planning is carried out to meet the requirements as well as agreed upon objectives. The integrity of the QMS is maintained when changes to the Quality Management System is planned and implemented.

Document	Description CORPORATE
541347	Continual Improvement
540009	Management Review-Quality Management System

5.5 Responsibility, Authority and Communication

5.5.1 Responsibility and Authority

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

5.5.1.2 The CEO has executive responsibility for the QMS and is responsible for creating an atmosphere where product quality is the highest priority.

5.5.1.3 The President and Vice-Presidents are responsible for overseeing the development, implementation and maintenance of the Quality System.

5.5.1.4 The VP of Quality and Regulatory, the Directors of Quality Assurance and Quality Control, Director of Diagnostic Reagents Division and President of Protein Sciences Segment, are responsible for ensuring that the QMS is fully maintained and implemented.

5.5.1.5 Each director, manager and supervisor are responsible for ensuring that the QMS requirements are followed in their area.

5.5.1.6 Each employee is responsible for following QMS guidelines and for their work.

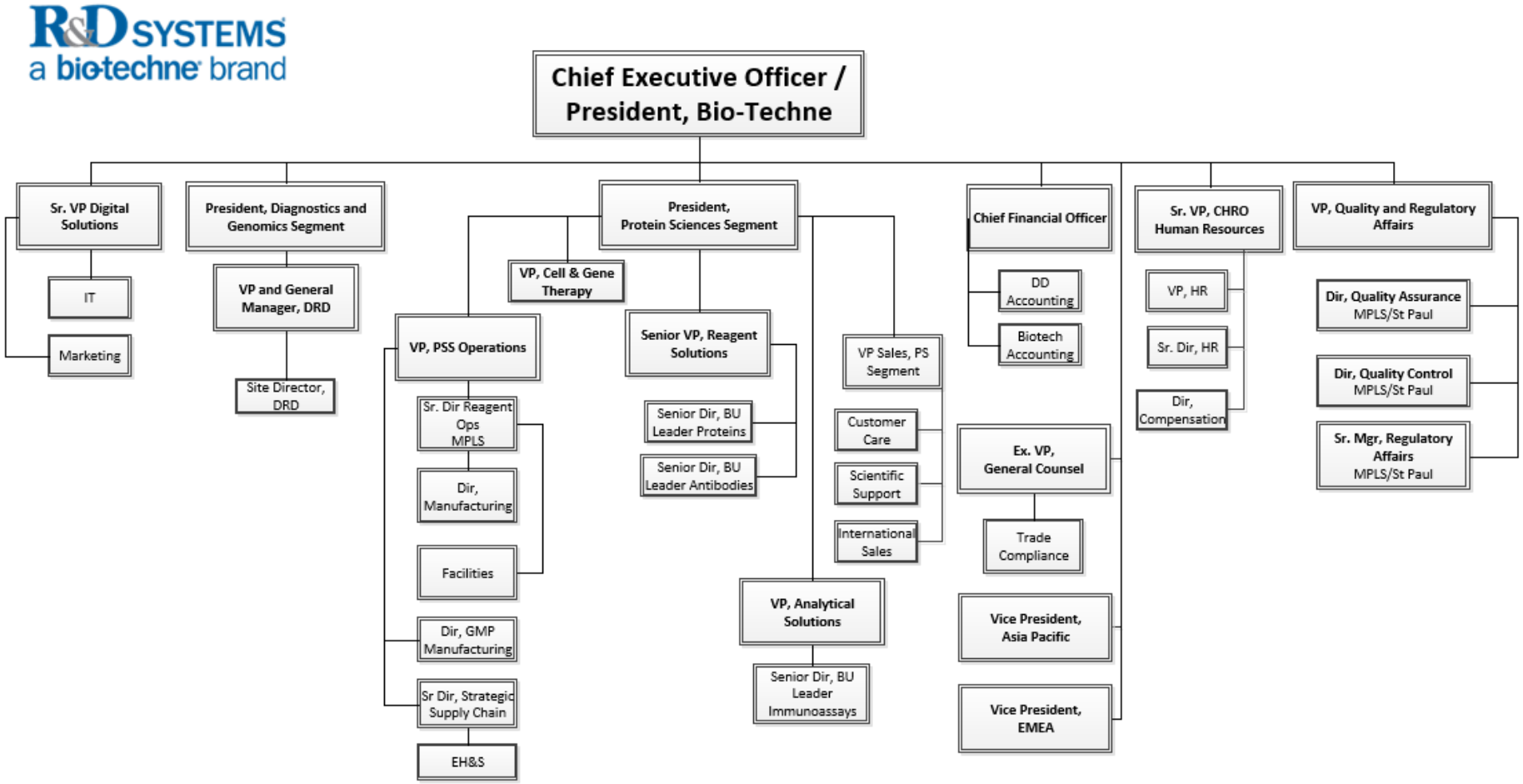
5.5.1.7 Two groups are dedicated exclusively to Quality: Quality Assurance and Quality Control.

5.5.1.7.1 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. Quality Assurance personnel report to the Director of Quality Assurance.

5.5.1.7.2 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 QC Departments report to the Director of Quality Control.

5.5.1.8 The organizational chart describes the functional and organizational structure of the Company.

Organization Chart for Minneapolis and St. Paul



5.5.2 Management Representative

5.5.2.1 Management Representative duties are shared by the Vice President, Quality and Regulatory Affairs and the Director of Quality Assurance. They have responsibility for ensuring that requirements are effectively established and maintained in accordance with the appropriate regulations; for reporting on the QMS to upper Management; and for ensuring the promotion of awareness of regulatory and customer requirements throughout the organization.

5.5.2.2 Person Responsible for Regulatory Compliance (PRRC) for *in vitro* diagnostic medical devices registered and sold in the EU. The PRRC communicates with the European Union Authorized Representative regarding the IVD products on behalf of R&D Systems under IVDR.

5.5.3 Internal Communication

5.5.3.1 Management is responsible for communicating our quality policy to all employees and for ensuring full understanding of, and commitment to the policies.

5.5.3.2 R&D Systems utilizes a variety of ways to communicate the policy, requirements, objectives, and accomplishments to its associates.

5.5.3.3 The communication channels include department meetings, formal announcements, newsletters, associate meetings, and the Bio-Techne intranet.

5.5.3.4 During plant-wide communication meetings, associate involvement and feedback are encouraged.

5.5.4 External Communication

5.5.4.1 The PRRC is responsible for communicating with the European Union Authorized Representative regarding R&D Systems' IVD products sold in the EU under IVDR.

5.5.4.2 The Vice President of Quality Assurance and Regulatory Affairs is responsible for ensuring that all communication with outside regulatory agencies is conducted as per the regulations of the specific countries where R&D Systems' IVD products are sold.

Document	Description CORPORATE
541066	EU Vigilance Reporting
543029	United Kingdom Vigilance Reporting
542714	US Medical Device and Annual Establishment Registration
540775	Medical Device Reporting (MDR) of Injury or Death - US
541065	Mandatory Problem Reporting - Canada
542118	IVD Requirements - Australia
542119	IVD Requirements - Brazil
543038	Person Responsible for Regulatory Compliance

5.6 Management Review

5.6.1 General

5.6.1.1 The QMS is reviewed at a minimum annually by the Senior Management Team, Quality Directors, and other pertinent management personnel as deemed appropriate. The R&D Systems Management Review includes Diagnostic Reagents Division and Protein Sciences Segment, from both Minneapolis and St. Paul. Management reviews progress to current quality objectives at planned intervals.

5.6.1.2 It is not required for all Senior Management to be present; however, the number of attendees must constitute a quorum. If someone plans to be absent, substitutes are encouraged to attend.

5.6.1.3 Management Reviews assess the continuing suitability, adequacy and effectiveness of the QMS and identify potential risks and opportunities for improvement. Any changes to the QMS, including the policy and objectives, are identified and documented during Management Reviews.

5.6.1.4 Conclusions (Minutes and Agenda) of these reviews are recorded and maintained by Quality Assurance.

5.6.1.5 Action items identified as a result of the Management Review will be documented in meeting minutes. Action items are reviewed during the subsequent Management Review meeting.

5.6.2 Review Input

5.6.2.1 Management Review Inputs of the QMS shall include but is not limited to information arising from: feedback; complaint handling; reporting to regulatory authorities; audits; monitoring and measurement of processes; monitoring and measurement of product; corrective action; preventive action; follow-up actions from previous management reviews; changes that could affect the Quality Management System; recommendations for improvement; and applicable new or revised regulatory requirements.

5.6.3 Review Output

5.6.3.1 Management Review Outputs of the QMS are documented at the review meetings and include: improvements needed to maintain the effectiveness of the QMS and its processes; improvement of product related to customer requirements; resource needs and planning; and QMS effectiveness evaluation with stated applicable standards and regulations.

5.6.3.2 The responsibility for the required follow up action items are assigned to owners. These decisions and activities are recorded in the meeting minutes.

Document	Description CORPORATE
540009	Management Review - Quality Management System
540167	On-Site Regulatory Inspection

6.0 RESOURCE MANAGEMENT

6.1 Provision of Resources

6.1.1 Resources are provided as needed to develop, maintain and improve the QMS and to comply with regulatory and customer requirements. This is evident through resource planning at financial meetings, annual budget preparations, QMS meetings, project reviews, business continuity plans, as well as, through organizational structures and associate development and training plans.

6.2 Human Resources

6.2.1 To ensure the competence of our associates, job descriptions have been prepared identifying the qualifications required for each position that affects product quality. Managers ensure jobs are filled based on the necessary education, training, and experience required to perform the jobs. Appropriate qualifications, along with required training and skills, provide the competence required for each position.

6.2.2 Developmental goals are established when additional training is needed and / or weaknesses are detected between the associate's performance and the requirement for the job.

6.2.3 Training

6.2.3.1 Qualifications are reviewed upon hire, when an associate changes positions or the requirements for a position change.

6.2.3.2 Each job description defines the training/skill needed. Annual performance evaluations measure the ability to meet the requirements of the job and ensure that associates are aware of how their activities link to the achievement of quality objectives.

6.2.3.3 R&D Systems has a training program (including the applicable requirements of ISO 9001, ISO 13485 and 21 CFR 820) administered by Quality Assurance, which all employees are required to complete. Ongoing training, as necessary, ensures personnel are familiar with applicable requirements.

6.2.3.4 Specific training for ISO 13485, GMP, MDSAP and Risk Analysis are provided 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.

6.2.3.5 Requalification training is assigned at the Manager's discretion to reacquire knowledge when a failure occurs or in relationship to performance.

6.2.3.6 The QA/RA organization is responsible to train on current documentation related to IVDR and other appropriate external standards and ensure that current versions of pertinent external standards are identified and available within the organization as described in 540120, Access and Control of Documents of External Origin. When revisions are available, this is communicated to Quality Assurance and other pertinent personnel so that associates are kept current on the latest Regulations and Standards.

6.2.3.7 Each department maintains job-specific training records for its employees. Supervisors / Managers 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.

Document	Description CORPORATE
540189	Personnel Training Procedure
542649	How to Perform Annual Training Effectiveness Check using Forms
543064	Procedure for Training Set Up of New and Transferred Employees at R&D Systems
540120	Access and Control of Documents of External Origin

6.3 Infrastructure

6.3.1 The infrastructure of R&D Systems includes buildings, workspace, utilities, process equipment and supporting services. The existing infrastructure is established and maintained to ensure

product conformity through business planning, capital acquisition, facility and equipment maintenance and utility agreements.

6.3.2 Equipment is checked regularly and maintained to ensure continuing process capability.

6.3.3 The building and workspaces are designed to meet particulate and microbiological standards and are defined by the intended operations and equipment, components and products exposed in a particular area.

6.3.4 Utilities are monitored as applicable and as defined in established procedures. Monitoring may be done in-line or through periodic sampling and subsequent testing.

Document	Description CORPORATE
541276	General Building Cleaning
540004	Maintenance of R&D Systems Main Deionized Water Systems (Facilities)
541130	EcoStruxure TAC/EMS System: Monitoring and Alarm Response
540142	Procedure for Documentation of Equipment Maintenance and/or Calibration
540232	Temperature Monitoring Refrigerators, Freezers and Incubators
540312	R&D Systems Deionized Water Systems (End User)
540571	TAC/EMS Temperature Sensor Verification
540306	Calibration of Pipets
541034	Disaster Recovery Plan, Bio-Techne (Minnesota)
540247	Facilities & Equipment Work Order Request Form and Instructions
540133	Equipment Life Cycle at R&D Systems Minneapolis
542010	Generator Preventive Maintenance
Document	**Description St. Paul Facility**
2201011	Equipment Life Cycle for the GMP Manufacturing Facility St. Paul
2201007	Maintenance Program for the GMP Manufacturing Facility St. Paul
2201008	Calibration Program for the GMP Manufacturing Facility St. Paul

6.4 Work Environment and Contamination Control

6.4.1 Work Environment

6.4.1.1 The work environment is established and maintained to achieve conformity to the product requirements and to have a positive influence on personnel to enhance overall performance.

6.4.1.2 Environments are controlled per established procedures. Verifications of laminar flow hoods, biological cabinets and HEPA filters are performed by approved suppliers. Environmental conditions (i.e., air, surface and water) are routinely monitored in the designated production areas during manufacturing as described in the environmental monitoring and water testing procedures. Controlled environments are cleaned in accordance with pertinent established procedures.

6.4.1.3 Production environments are clean and provide a suitable working environment. They are also cleaned on a routine schedule.

6.4.1.4 Special attire is required in the production / laboratory areas. For example, laboratory coats and safety glasses are generally required; in some areas, a laboratory coat, hair net and safety glasses may be needed.

Document	Description CORPORATE
540004	Maintenance of R&D Systems Main Deionized Water Systems (Facilities)
540046	Pest Control Program - Minneapolis
540232	Temperature Monitoring Refrigerators, Freezers and Incubators
541127	Guidelines and Procedures for Animal-Free Laboratories
541130	EcoStruxure TAC/EMS System: Monitoring and Alarm Response
541276	General Building Cleaning
542630	Guidelines and Procedures for Laboratory Cleaning
542786	Universal Gowning Guideline for Lab Spaces and Clean Rooms
140210	Deionized Water System Microbial Monitoring
140350	Environmental Monitoring Plan for Viable Organisms
Document	**Description St. Paul Facility**
2200038	Operation, Maintenance, and Sanitization of WFI Water System (Facilities)
2200073	Pest Control Program for GMP Manufacturing Facility St. Paul
2200074	Gowning Instructions for GMP Manufacturing Facility
2205017	Material and Personnel Flow for GMP Manufacturing Facility St. Paul
2201000	St Paul Facility Environmental Monitoring Plan for Viable Organisms
2201001	St Paul Facility Airborne Particle Monitoring
2200077	Cleaning of the GMP Manufacturing Facility St. Paul

6.4.2 Contamination Control

6.4.2.1 R&D Systems does not manufacture sterile product, although some products are tested in accordance with USP <71> Sterility Tests. Some products contain biological material which entails specific disposal requirements pertaining to safety and environmental requirements. Potential biohazardous material is handled as required by pertinent procedures.

7.0 PRODUCT REALIZATION

7.1 Planning of Product Realization

7.1.1 R&D Systems approaches product realization from a product life cycle perspective with Design Control and Risk Management governing a product's safety and effectiveness from the early stages of research and development through manufacturing stage and a product's post launch and post-marketing performance. Product and process risk management is defined in an established procedure. Risk management principles are also incorporated in management review, corrective and preventive actions, internal audits and training.

7.1.2 Planning is required before new products or processes are implemented. Product requirements are defined in the Device Master Record and incorporated into specifications and device history records. These documents provide complete manufacturing and quality assurance specifications for each product line.

7.1.3 Custom made products are processed in accordance with individual customer requests. Details regarding these products are documented via Statements of Work (SOW) or supply agreement which are agreed upon by the customer and R&D Systems. In the absence of specific Standard Operating Procedures and product requirements maintained in the Electronic Documentation Management System, documented review and approval by both the customer and R&D Systems' representatives is maintained via the SOW.

Document	Description CORPORATE
540819	Risk Management - Product / Process
Document	**Description Protein Sciences Segment**
541174	Lot Identification and Designation Procedure
Document	**Description Diagnostic Reagents Division**
2006011	Product Request Procedure

7.2 Customer-Related Processes

7.2.1 Determination of requirements related to product

7.2.1.1 The right product is manufactured for our markets by building to demand on Finished Goods Inventory.

7.2.1.2 Quality records are utilized to capture production data in order to initiate actions for product yield improvement.

7.2.2 Review of requirements related to product

7.2.2.1 Quality records are reviewed during customer complaint evaluations.

7.2.2.2 Customer requirements are determined prior to manufacture and shipment of products.

7.2.2.3 Purchase orders and contracts are reviewed, and product must meet requirements prior to shipment. Finished product specifications are available for products. As noted in 7.1.3 for custom or made-to-order products, requirements for the finished product are clearly defined in Statement of Work or supply agreement.

7.2.3 Communication

7.2.3.1 Technical Services provide relevant technical product documentation specific to product information requests. Customer inquiries, contracts or order handling is through Marketing, Customer Care or Technical Service.

7.2.3.2 Customer complaints and feedback is handled via Technical Services (Diagnostic Reagents Division) or Customer Care or Technical Service (Protein Sciences Segment), Product Managers and ultimately Quality Assurance with input from Regulatory Affairs as applicable to GMP and IVD products. Advisory Notices are communicated to customers through Quality Assurance and Regulatory Affairs.

7.2.3.3 Any change to a product or process must be appropriately documented including reason for change, possible effects of the change to the product or for customers, and requirements for customer and/or regulatory notifications. Refer to pertinent procedures for required information.

Document	Description CORPORATE
541053	Reportable Changes, IVD Products
541065	Mandatory Problem Reporting – Canada
542118	IVD Requirements - Australia
542119	IVD Requirements - Brazil
541214	Corrections, Removals and Recalls for IVD Products
542174	Post Market Surveillance System - IVD Products
541886	Corporate Change Control Policy
541066	EU Vigilance Reporting
543029	United Kingdom Vigilance Reporting
543023	IVDR Technical Documentation Requirements

543038	Person Responsible for Regulatory Compliance
540775	Medical Device Reporting (MDR) of Injury or Death - US
541053	Reportable Changes, IVD Products
Document	**Description Protein Sciences Segment**
540260	Field Notification Procedure
540135	Customer Feedback System, Biotech
541231	Change Control Procedure
Document	**Description Diagnostic Reagents Division**
2006039	Diagnostic Reagents Division Change Control
2006926	DRD Customer Feedback/Complaints

7.3 Design and Development

7.3.1 Appropriate Design Controls are employed for each specific product type. In general, the controls ensure the following review and approval steps are accomplished:

7.3.1.1 Approval of the design goals (Design Input)
7.3.1.2 Review of feasibility studies (Design Review)
7.3.1.3 Approval of the product description (Design Output)
7.3.1.4 Review of process development and preparation of manufacturing documents (Design Verification Review)
7.3.1.5 Review and approval of product validation (Final Design Review / Data Review)
7.3.1.6 Transfer to manufacturing

Document	**Description CORPORATE**
540819	Risk Management - Product / Process
540325	Design Control - General Guidelines
Document	**Description Protein Sciences Segment**
540323	Design Control, Protein Products
540266	Validation Master Plan
541710	Design Control, Cell and Gene Therapy Products
541786	Design Control of GMP Proteins and Antibodies
541906	Design Control for Development of R&D Systems Antibody Products
541341	Design Goals, DuoSet Products
Document	**Description Diagnostic Reagents Division**
2006009	Procedural Elements in a Validation
2006015	DRD Design Control

7.4 Purchasing

7.4.1 Purchasing Processes

7.4.1.1 R&D Systems assesses its suppliers and purchases only from those who can satisfy the company's quality requirements. The purchasing process is performed in accordance with approved procedures.

7.4.1.2 Qualified suppliers are listed on each raw material specification. Document 540000, Supplier Qualification and Monitoring, describes how a new supplier is qualified,

including outsourced services and processes, and how suppliers are monitored for quality and on-time delivery of goods and services.

7.4.1.3 Supplier performance is tracked, with Key Providers and suppliers with Quality-related returns receiving Supplier Scorecards. Suppliers who do not perform well may be disqualified and replaced.

7.4.2 Purchasing Information

7.4.2.1 Requirements for raw materials are stated in written specifications available to all personnel doing purchasing and receiving activities.

7.4.2.2 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.

7.4.2.3 A purchase order includes R&D Systems part number and a request for a Certificate of Analysis and/or Certificate of Origin where appropriate. Materials used in the manufacture of products are verified against the purchase order. Purchasing interacts with suppliers regarding non-conforming or damaged materials.

Document	Description CORPORATE
540687	Purchasing Procedures, R&D Systems
540192	Receiving Procedures, R&D Systems
540000	Supplier Qualification and Monitoring
540335	Supplier Audit Procedure
540876	Nonconforming, Purchased Material Procedure
542749	Product or Service Supplier Corrective Action Request
542391	Writing a Raw Material Specification
542497	Chain of Custody for Receiving and Handling Infectious Biologicals

7.4.3 Verification of Purchased Product

7.4.3.1 Acceptance / inspection activities are critical to the manufacture of quality products.

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

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

7.4.3.4 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, purity and/or visual inspection.

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

Document	Description Protein Sciences Segment
540192	Receiving Procedures, R&D Systems
540080	Raw Materials, Departmental Receiving and Inspection Procedure
540143	Product Insert Inspection Procedure
540526	Receiving OEM Products

Document	Description Diagnostic Reagents Division
2008855	Instructions For Use (IFU) - Revising, Printing and Inspecting
Document	**Description St. Paul Facility**
2200024	Material Transfer Between Minneapolis and St. Paul Sites
2205006	Incoming Supplies Procedure for GMP Manufacturing Facility

7.5 Production and Service Provision

7.5.1 Control of Production and Service Provision

7.5.1.1 Procedures are established, documented and maintained to identify and plan the production process that directly affects quality and ensure that these processes are carried out under appropriate conditions. Written procedures provide bills of materials, instructions for production, equipment required, working environment, filling and labeling instructions, record sheets, expiration date, in-process testing, and acceptance criteria.

7.5.1.2 Monitoring and measuring of purchased materials, labels, labeling, components, packaging, raw materials components, manufacturing materials, environments, in-process product and finished product are conducted in accordance with applicable SOPs. Records of each batch of finished product provides identification and traceability, manufactured amount and amount released for distribution on the device history records or applicable Quality Records prescribed in the applicable SOPs.

7.5.1.3 Acceptance criteria and quality standards are prescribed in operation-specific SOPs.

7.5.1.4 Incoming components, raw materials, labeling and manufacturing materials are not processed until they have been inspected and verified as conforming to prescribed requirements as listed in raw material specifications.

7.5.1.5 Quarantined items that do not meet the prescribed specifications shall remain on hold until a Material Review Board disposition is received.

7.5.1.6 R&D Systems has established documented procedures to ensure applicable equipment is processed through the autoclave or cleaned by EO processing prior to use where required.

7.5.1.7 Finished products are assembled according to written procedures. Final product packaging is done to protect product integrity through physical separation of different operations. Line clearance procedures are conducted in packaging areas prior to the start of each operation. Quality Control or other appropriate personnel inspect finished products using statistically valid sampling plans, and product is not released unless all inspection criteria are met.

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

7.5.1.9 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.

7.5.1.10 Monitoring of production 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 documents from the Electronic Document

Management System. For the Diagnostic Reagents Division products, batch records are assembled by Operations. Quality Control verifies compliance through review and approval of completed batch records prior to final product release.

Document	Description CORPORATE
540306	Calibration of Pipets
542008	Master Equipment Qualification Plan at Minneapolis
543039	EU Declaration of Conformity Requirements
540133	Equipment Life Cycle at R&D Systems Minneapolis
Document	**Description Protein Sciences Segment**
540124	Inspection of Assembled Kits
550449	Immunoassay Approval / Rejection Criteria
540143	Product Insert Inspection Procedure
542609	Routing IVD Inserts
540363	Releasing Retail Product
550406	Criteria for the Acceptance of Antibody Preparations for Sale
550407	The Criteria for the Acceptance of Bulk Protein and Enzyme Preparations for Sale or In-House Applications
541249	Procedure for Bottling Animal-Free and/or GMP Proteins
541829	QC-Bioassay Acceptance and Validity Criteria
552063	Procedure for Assessing Stability of Bulk Antibody and Protein Lots and Assigning Expiration Dates
543055	Protein, Enzyme, and Antibody Stability and Expiry Assignment
554350	Treatment of Suspect Test Results Generated During the Testing of Products for Commercial Distribution
540194	Certificate of Analysis Procedure
542565	Certificate of Origin (CoO) Procedure
540781	Planning Guidelines, Minneapolis Protein Science Segment
540207	Label Control, Product Finishing
540072	Filling Operation Procedure
540737	Use and Cleaning of Cell Culture Hoods, LAF and BSC
540738	Cleaning of Waterbaths (Cell Culture)
540267	Preparation, Completion and Approval of Batch Records
540278	Bottling Procedure for Cytokines and Antibodies Designated for Retail Sale
540256	Labeling Procedure for Proteins and Antibodies Designated for Retail Sale
540367	Made To Order (MTO) Filling - Special Bottling
540467	Line Clearance
Document	**Description Diagnostic Reagents Division**
2008812	Finished Device Inspection Procedure
2008855	Instructions For Use (IFU) - Revising, Printing and Inspecting
2002800	Balance Procedure
2009090	Product Finishing Label Control
2006029	Diagnostic Reagents Division, Labeling Control
2009054	Bottling Procedure

2008006	Bottled Product Release
2008809	Assay Sheet Printing and Release
2006039	Diagnostic Reagents Division Change Control
2008813	Guidelines for Determining Assay Ranges
Document	**Description St. Paul Facility**
2201024	Preparation, Completion and Approval of Batch Records for GMP St. Paul Facility
2201011	Equipment Life Cycle for the GMP Manufacturing Facility St. Paul
2201002	Procedure for Bottling St. Paul GMP Facility

7.5.2 Cleanliness of product

7.5.2.1 Although R&D Systems' products do not claim sterility, product cleanliness is important. Routine Environmental Monitoring is conducted for all manufacturing areas, and bioburden and endotoxin analysis is required for both in-process and finished products in accordance with product specific documents.

7.5.3 Installation activities - Not applicable

7.5.4 Servicing activities - Not applicable

7.5.5 Particular requirements for sterile medical devices - Not applicable

7.5.6 Validation of processes for production and service provision

7.5.6.1 All new inspection, measuring and test equipment is inspected and validated, when appropriate, against manufacturer's specifications and is identified with a unique, permanent preventive maintenance (PM) number.

7.5.6.2 Validation of processes for production occur per documented procedures.

7.5.6.3 Changes to the manufacturing process, if required, are controlled, qualified and validated.

7.5.6.4 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 through the validation process.

Document	**Description CORPORATE**
540310	Computer System Validation
540133	Equipment Life Cycle at R&D Systems Minneapolis
542455	Validation Numbering System
541886	Corporate Change Control Policy
540266	Validation Master Plan
Document	**Description Protein Sciences Segment**
2201011	Equipment Life Cycle for the GMP Manufacturing Facility St. Paul
541231	Change Control Procedure
Document	**Description Diagnostic Reagents Division**
2006039	Diagnostic Reagents Division Change Control
2006009	Procedural Elements in a Validation

7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems – Not applicable

7.5.8 Identification

7.5.8.1 R&D Systems strives to provide only the highest quality labeling and packaging to our customers, which also is compliant with all regulatory requirements.

7.5.8.2 Labels, literature and packaging are subject to incoming inspection.

7.5.8.3 Label control is the responsibility of the Quality Assurance and Manufacturing departments. Document Control and the Insert, Certificate of Analysis (ICA) database maintain the Literature Approval system through which new Protein Sciences label and literature copy are 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.

7.5.8.4 The QA/RA Specialist(s) monitors label control for Diagnostics products.

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

Document	**Description CORPORATE**
541942	Unique Device Identification (UDI) Guidelines
541104	Labeling Guidelines, IVD
Document	**Description Protein Sciences Segment**
540207	Label Control, Product Finishing
540256	Labeling Procedure for Proteins and Antibodies Designated for Retail Sale
540143	Product Insert Inspection Procedure
540467	Line Clearance
Document	**Description Diagnostic Reagents Division**
2006029	Diagnostic Reagents Division, Labeling Control
2009090	Product Finishing Label Control
2008809	Assay Sheet Printing and Release
2008855	Instructions For Use (IFU) - Revising, Printing and Inspecting

7.5.9 Traceability

7.5.9.1 The ability to trace each lot of product back to the raw materials used in manufacture, and to trace any lot of raw material to products into which it has been incorporated is an essential feature of the quality system.

7.5.9.2 A part number and lot number (or receiving number) is used to maintain identification throughout the manufacturing process, providing traceability from receipt of raw materials through final shipment to the customer. In Protein Sciences, part numbers are assigned through the Product Development Project Tracking (PDPT) database. An ERP System (Microsoft Dynamics AX) is in place in the kit manufacturing area, which is used to track inventory, assign job (lot) numbers and plan the production of kit products. Lot numbers for all other products may be sequentially assigned from PDPT or are assigned at the time of bottling.

7.5.9.3 Operations assigns final product lot numbers for DRD products.

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

7.5.9.5 Particular requirements for implantable medical devices - Not Applicable

Document	Description Protein Sciences Segment
540153	Part Number Assignment
540206	Assigning Lot Numbers
Document	**Description Diagnostic Reagents Division**
2006019	Identification and Traceability

7.5.10 Customer property, including intellectual property, is identified, verified and protected while under R&D Systems' control.

Document	Description CORPORATE
542712	Safeguarding Customer Property

7.5.11 Preservation of Product

7.5.11.1 Procedures are established, documented and maintained for handling, storage, packaging, labeling and delivery of product in such a manner that prevents damage and deterioration to the product. Product design and development include appropriate stability studies to validate recommended storage conditions and shelf life. Finished products with limited shelf life and those due to expire are pulled from inventory and controlled per established procedures.

7.5.11.2 Procedures to minimize raw materials or component damage and deterioration are established. Storage conditions for raw materials, work in process and finished goods are specified in the appropriate specifications or manufacturing procedures. Storage areas are controlled and monitored to ensure proper environmental conditions. 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 being placed into storage areas.

7.5.11.3 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.

7.5.11.4 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.

7.5.11.5 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 each lot by analyzing data received through the external DRD QC program and customer complaints.

7.5.11.6 Finished product packaging is done to protect product integrity through physical separation of different operations.

Document	Description CORPORATE
542712	Safeguarding Customer Property
Document	**Description Protein Sciences Segment**
541178	International Order Procedure, Biotech Shipping

541252	Domestic Retail Biotech Shipping Procedure
541351	Finished Goods Inventory Cycle Counts
541358	Processing Expired Product in Biotech Shipping
542887	Product Source of Truth (PSOT)
Document	**Description Diagnostic Reagents Division**
2010350	Shipping Procedures

7.6 Control of Monitoring and Measuring Equipment

7.6.1 R&D Systems has established a program for the control of monitoring and measuring equipment. All new inspection, measuring and test equipment is inspected and assigned a unique, permanent preventative maintenance number. Equipment is calibrated on a regular schedule. Improperly maintained or calibrated equipment will not be used. The status of calibration is clearly defined. 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.

Document	**Description CORPORATE**
540142	Procedure for Documentation of Equipment Maintenance and/or Calibration
Document	**Description St. Paul Facility**
2201007	Maintenance Program for the GMP Manufacturing Facility St. Paul
2201008	Calibration Program for the GMP Manufacturing Facility St. Paul

8.0 MEASUREMENT, ANALYSIS AND IMPROVEMENT

8.1 General

8.1.1 R&D Systems implements the monitoring, measurement, analysis and improvement processes as needed:

8.1.1.1 To demonstrate conformity to product requirements.

8.1.1.2 To ensure conformity of the QMS, and

8.1.1.3 To continually improve the effectiveness of the Quality Management System.

8.1.1.3.1 These processes are identified in documented procedures and include determination of applicable methods, including statistical techniques, and the extent of their use.

8.2 Monitoring and Measurement

8.2.1 Feedback

8.2.1.1 A Customer Feedback System is maintained by Quality Assurance using input from Technical Service and Customer Care.

8.2.2 Complaint Handling

8.2.2.1 Any employee of R & D Systems who has knowledge of an event which is considered a complaint, or potential complaint about an R & D Systems product, is responsible for contacting the pertinent department (Technical Service for Diagnostics and Customer Care or Technical Service for the Protein Sciences Segment products), who is then responsible for ensuring proper handling of the event.

8.2.2.2 All customer complaints are logged and classified as to type of complaint (performance, physical, etc.). Complaints are numbered and tracked by QA from receipt of initial report of the complaint until closure.

8.2.2.3 Summary reports of complaints are available monthly for review by appropriate personnel.

8.2.2.4 R&D Systems is committed to taking preventive and corrective action to remedy any customer dissatisfaction or identified non-conformity. Whenever appropriate, a root cause analysis will be done to identify the root cause of the dissatisfaction or non-conformity.

Document	**Description CORPORATE**
542174	Post Market Surveillance System – IVD Products
Document	**Description Protein Sciences Segment**
540260	Field Notification Procedure
540135	Customer Feedback System, Biotech
540259	Material Review Board (MRB) Responsibility
Document	**Description Diagnostic Reagents Division**
2006016	Material Review Board (MRB) Procedure - Nonconformance
2008036	Procedure for Investigation of Returned Product
2006926	DRD Customer Feedback/Complaints

8.2.3 Reporting to Regulatory Authorities

8.2.3.1 If applicable regulatory requirements require notification of complaints that meet specified reporting criteria of adverse events or issuance of advisory notices, R&D Systems shall follow established procedures on providing notification to the appropriate regulatory authorities. Records of reporting to regulatory authorities are maintained as per pertinent record keeping procedures.

Document	**Description CORPORATE**
541214	Corrections, Removals and Recalls for IVD Products
542714	US Medical Device and Annual Establishment Registration
540775	Medical Device Reporting (MDR) of Injury or Death - US
541065	Mandatory Problem Reporting – Canada
542118	IVD Requirements - Australia
542119	IVD Requirements - Brazil
541066	EU Vigilance Reporting
543029	United Kingdom Vigilance Reporting
543038	Person Responsible for Regulatory Compliance
Document	**Description Protein Sciences Segment**
540260	Field Notification Procedure
Document	**Description Diagnostic Reagents Division**
2006016	Material Review Board (MRB) Procedure – Nonconformance
2008036	Procedure for Investigation of Returned Product
2006926	DRD Customer Feedback/Complaints

8.2.4 Internal Audit

8.2.4.1 Comprehensive, planned quality system audits (self-inspections) are performed by an individual and / or audit team comprised of the quality assurance staff that has adequate training and is independent of the area being audited. Other trained personnel outside of the local Quality Assurance staff may also conduct audits under the guidance of Quality Assurance.

8.2.4.2 Periodic audits ensure adherence to our Quality Management System and identify areas for continual improvement.

8.2.4.3 Audit criteria, responsibilities and requirements for planning and conducting audits are defined and carried out per approved procedure.

8.2.4.4 Audit findings are issued to the responsible area management and a written response is required.

8.2.4.5 Results of the audit are reported to the Vice President of Quality and Regulatory Affairs and the appropriate Vice President and management of the operating unit which is audited. It is the responsibility of the operating unit to provide a timely corrective action response regarding deficiencies noted during the internal audit. The response should include root cause analysis, correction of deficiencies, and corrective action plan.

8.2.4.6 Follow up verifications to the audit are conducted where necessary. Follow up activities include the verification of the actions taken and the reporting of the verification results.

8.2.4.7 The records of the internal quality audit activity are maintained and are confidential.

Document	Description CORPORATE
540291	Internal Audit Procedure
540552	Corrective and Preventive Action (CAPA Process)
541347	Continual Improvement

8.2.5 Monitoring and Measurement of Processes

8.2.5.1 R&D Systems applies suitable methods for monitoring and measurement of the QMS processes. These methods demonstrate the ability of the processes to achieve planned results. When planned results are not achieved, corrective and preventive action is taken, as appropriate.

8.2.5.2 Production operations are planned and documented.

8.2.5.3 Batch records, validation documents, equipment records, and training records are maintained as per the record retention procedure.

8.2.5.4 Only approved work instructions, product, process and / or product specifications, and environmental conditions are used for production of finished products.

8.2.6 Monitoring and Measurement of Product

8.2.6.1 In-process inspections and testing are carried out in accordance with applicable SOPs. Execution of the SOPs are documented on the appropriate forms.

8.2.6.2 Final product inspection is carried out by designated personnel per established procedures.

8.2.6.3 Inspection and test documents are maintained, and records are kept in the batch record.

8.3 Control of Non-Conforming Product

8.3.1 Our Quality Management System provides for the identification, documentation, evaluation, segregations, and disposition of non-conforming product.

8.3.2 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.

8.3.3 Minor non-conformities may be released by Quality Control with adequate documentation. Disposition of major non-conformances lies with the MRB.

8.3.4 The MRB process is led by QA, including responsibility for convening MRB meetings and documenting activities.

8.3.5 The Protein Sciences MRB is composed of representatives from Quality, Manufacturing, and Development. Additional representatives from Product Support, Marketing, Technical Service or Customer Care may also participate as required. All corrective actions must be fully documented. Minutes from meetings of the MRB are published and maintained in SmartSolve QMS Non-Conformance Module.

8.3.6 For Diagnostics' products, MRBs are documented using the MRB form. Minutes from meetings of the MRB are published and maintained in SmartSolve QMS Non-Conformance and/or Complaint Module.

8.3.7 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.

8.3.8 Rework

8.3.8.1 A non-conformance 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.

Document	**Description CORPORATE**
540126	Deviation Procedure
540552	Corrective and Preventive Action (CAPA Process)
541214	Corrections, Removals and Recalls for IVD Products
Document	**Description Protein Sciences Segment**
540259	Material Review Board (MRB) Responsibility
540265	Rework Procedure
540835	Quarantine of Non-conforming Product
550407	The Criteria for the Acceptance of Bulk Protein and Enzyme Preparations for Sale or In-House Applications
550406	Criteria for the Acceptance of Antibody Preparations for Sale
542810	Non-Conformance (NC) Procedures
Document	**Description Diagnostic Reagents Division**
2003009	Adjustment/Replacement of a Finished Product
2006016	Material Review Board (MRB) Procedure – Nonconformance

2003018	Quarantine Procedure
2008021	Rejection of a Product
2010212	Diagnostic Reagents Division Shipping's Quarantine Procedure

8.4 Analysis of Data

8.4.1 Statistical methods are very powerful tools when used correctly within the quality process. Methods are selected with care to ensure suitability to the application required and will produce an objective output.

8.4.2 The motivation to use these statistical methods is a desire to improve quality and to meet customer requirements. Statistical techniques are employed to identify, understand and minimize or eliminate variation which results from inherent variability associated with design, components, methods and equipment.

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

8.4.4 Tools that are used or should be considered are:

8.4.4.1 Experimental Design – Design of Experiment(s) software is available and is being used by kit development groups.

8.4.4.2 Analysis of Variance / Regression Analysis

8.4.4.3 Risk Analysis

8.4.4.4 Root Cause Analysis

8.4.4.5 Statistical Sampling Inspection

8.4.4.6 Histograms – Plot frequency of events

8.4.4.7 Pareto Diagrams - Assist with sorting crucial problems

8.4.4.8 Flow Charts – Pictorial diagrams of processes or systems

8.4.5 Examples of where Statistical techniques may be applied:

8.4.5.1 Design Input – Determining requirements and expectations.

8.4.5.2 Design Control – Periodic evaluation to provide assurance of acceptable product performance.

8.4.5.3 Shelf Life – Determine appropriate dating for products.

8.4.5.4 Process Control – Determine machine or process capabilities, monitor deviations.

8.4.5.5 Defect Analysis – Assist with understanding problems.

8.4.5.6 Data Analysis – Review and understanding of products.

8.4.5.7 Continual Improvement – Analysis of audit findings and corrective action

Document	**Description CORPORATE**
542713	Analysis of Data-QMS
540819	Risk Management – Product / Process
540865	Statistical Techniques
540537	Test for Outlier Determination-Grubbs Method
Document	**Description Diagnostic Reagents Division**
2008004	Verification of Bulk Testing
2006009	Procedural Elements of Validation

8.5 Improvement

8.5.1 General

8.5.1.1 R&D Systems continually improves effectiveness of the QMS through the use of the quality policy, quality objectives, audit results, analysis of data, corrective actions, and management review meetings.

8.5.2 Corrective Action and Preventive Action

8.5.2.1 R&D Systems acts to eliminate the causes of non-conformities in order to prevent recurrence. Corrective actions are appropriate to the effects of the non-conformities. Preventive action is taken to eliminate the cause of a potential non-conformance.

8.5.2.2 The Material Review Board reviews non-conformities.

8.5.2.3 QA is responsible for the development of an action plan for monitoring and documenting the progress of any corrective or preventive action plan to ensure its completion and effectiveness for product and process related issues. Any change necessary to a document or process which affects the quality system is handled in accordance with the formal change control procedure.

Document	**Description CORPORATE**
541886	Corporate Change Control Policy
540552	Corrective and Preventive Action (CAPA Process)
Document	**Description Protein Sciences Segment**
542811	IVD Product Change Control in MPLS-PSS
541231	Change Control Procedure
Document	**Description Diagnostic Reagents Division**
2006039	Diagnostic Reagents Division Change Control

9.0 ADDITIONAL ISO 9001 CONSIDERATIONS

9.1 Context of the Organization - Quality Management System

9.1.1 R&D Systems is committed to defining our position in the marketplace and understanding how relevant factors arising from legal, political, economic, social, and technological issues influence our strategic direction and organizational context.

9.1.2 R&D Systems identifies, analyzes, monitors and reviews factors that may affect the ability to satisfy customers and stakeholders, as well as factors that may adversely affect the stability of the process, or the integrity of the Quality Management System.

9.1.3 To ensure that the QMS is aligned with strategic direction, considering relevant internal and external factors, pertinent information is collated and analyzed to determine potential impact on our context and subsequent business strategy. The table below lists typical internal and external factors which are considered.

Internal Issues	**External Issues**
Employees	Customers and Suppliers
Market Share	Markets and Competition
Performance	Regulatory and Statutory
Values and Culture	Technological
Innovation and Knowledge	Culture and Social

9.1.4 The organization periodically evaluates itself and its context, with a focus on issues that can affect customer satisfaction and delivery of quality product.

9.1.5 Internal context is the environment in which R&D Systems aims to achieve its objectives, as defined by upper management during annual planning. Internal context considers the organization's approach to governance, its contractual relationships with customers, and other interested parties. Things to be considered are related to the culture, beliefs, values, or principles inside the organization, as well as complexity of processes and organizational structure.

9.1.6 To determine external context, issues arising from the social, technological, environmental, ethical, political, legal, and economic environment are considered. Specific examples include:

- government regulations and changes in the law
- economic shifts in the organization's market
- the organization's competition
- events that may affect corporate image
- changes in technology

9.2 Understanding Needs and Expectations of Interested Parties

9.2.1 R&D Systems recognizes that there are a unique set of interested parties whose needs and expectations change and develop over time. Only a limited number of the respective needs and expectations are applicable to R&D Systems operations or to the QMS. Needs and expectations broadly include those shown in the table below.

Interested Parties	Needs and Expectations
Customers	Price, Reliability, Value
Distributors and retailers	Quality, Price, Logistics
Shareholders	Regulatory and Statutory
Employees	Shared Values and Security
Suppliers	Beneficial Relationships
Regulatory and Statutory	Compliance and Reporting

9.2.2 To ensure that R&D Systems products and processes continue to meet relevant requirements, the potential impact of relevant needs and expectations that may be elicited from the interested parties must be identified and assessed. Where appropriate, to ensure that processes are aligned to deliver the requirements of interested parties, relevant needs and expectations are converted into requirements which become inputs to the QMS and to product design.

9.3 Organizational Knowledge

9.3.1 Organizational knowledge is knowledge specific to the organization, generally gained by experience. The knowledge is used and shared to achieve objectives, both quality and business related. Internally based knowledge includes intellectual property, experience gained from previous failures and successes, and the results of product and process improvements. External knowledge sources include conferences, customer knowledge, or supplier knowledge.

9.3.2 Organizational knowledge is an important resource, similar to people, infrastructure, and monitoring and measuring resources, which must be understood and controlled. Two main sources of maintenance / control of organizational knowledge are the electronic document

management system and PDPT. All information contained in these two databases is routinely backed up in accordance with 540534, IT Backup Policy.

9.3.3 Figure 3 below provides a graphic of sources of organizational knowledge. As per ISO 9001, the requirements for collection and maintenance of organizational knowledge include:

10.3.3.1 Identification of knowledge needed to operate processes and to make products.

10.3.3.2 Compilation and maintenance of the knowledge, and availability of knowledge as needed.

10.3.3.3 Consideration of current knowledge when making changes and determine process to gain additional knowledge or update knowledge if necessary for changing needs.

9.3.4 When addressing changing needs and trends, R&D Systems will consider existing knowledge and determine how to acquire or access any necessary additional knowledge and required updates.

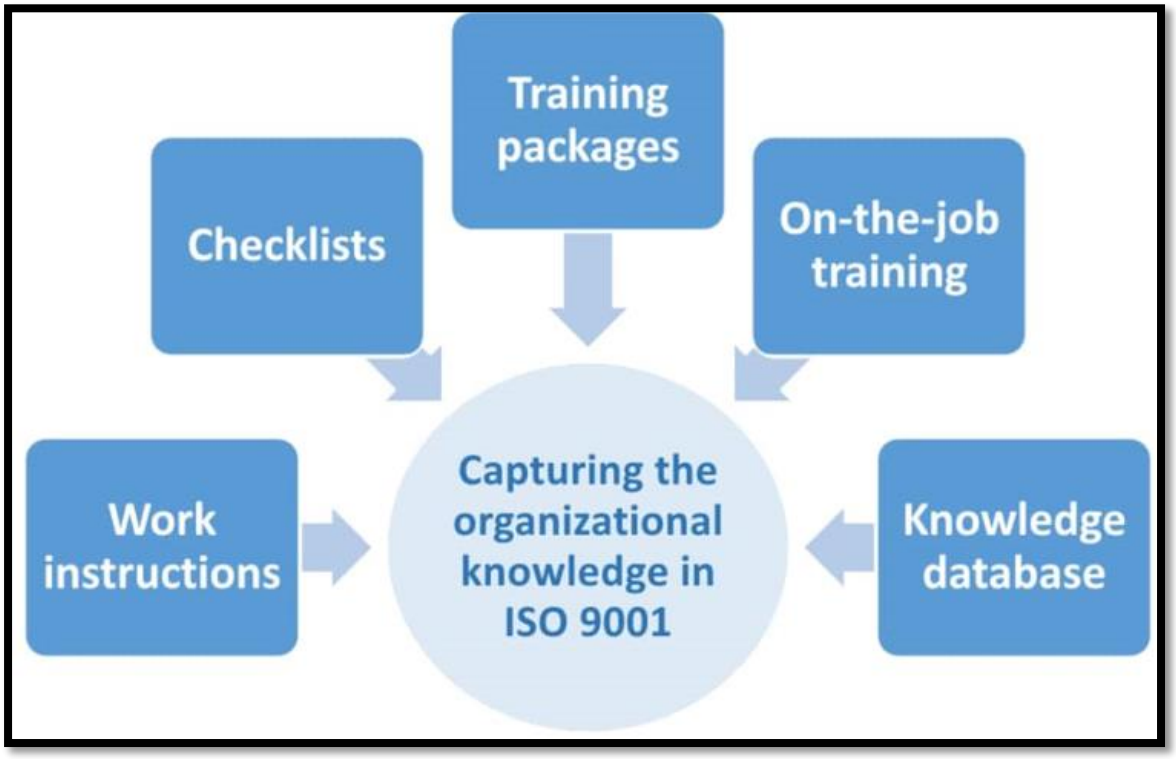


Figure 3 – Sources of Organizational Knowledge

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