R&D SYSTEMS
a bio-techne brand

Quality & Environment Systems Manual

Authorized by:

Charles Kummeth, Chief Executive Officer/President

8/13/2020
Date

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1.0 SCOPE

1.1 R&D Systems was founded in 1976 in Minneapolis, MN and was 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.

1.2 The Minneapolis, Minnesota location (Bio-Techne Minneapolis) has two operating segments:

1.2.1 Protein Sciences Segment, which manufactures reagents and instruments, primarily for the research market.

1.2.1.1 Bio-Techne Abingdon in Abingdon, UK is the Authorized European Representative for R&D Systems products manufactured by Protein Sciences Segment.

1.2.2 Diagnostics and Genomics - Minneapolis, which manufactures controls, calibrators and linearity products for hematology analyzers.

1.2.2.1 Bio-Techne France, 19 rue Louis Delourmel, 35230 Noyal Chatillon / Seiche, 35092 Rennes Cedex 9, France is the Authorized European Representative for R&D Systems Diagnostics products.

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

1.4 In April 2019, Bio-Techne Minneapolis received ISO 14001 certification of the site's Environmental Management System (EMS), holding certificate EMS 699287. The scope of the EMS is:
The management of environmental risks associated with the manufacture of biotechnology reagents, hematology controls, and calibrators for R&D Systems Minneapolis, MN Site.

1.5 This manual continues to pertain to the Quality and Environment Management Systems of both segments which operate at the Minneapolis location, being applicable to the manufacture, sale, support and distribution of products manufactured at Bio-Techne Minneapolis.

1.6 The manual also applies to the Environmental Management System which governs the Bio-Techne Minneapolis facility. The facility occupies approximately 600,000 square feet with approximately 750 employees.

1.7 The facility Manual (540308 - this document) describes the Quality and Environmental Management Systems (Q&EMS) used by Bio-Techne Minneapolis for the design, production and distribution of products manufactured at this facility. The Bio-Techne Minneapolis Quality Policy and Environmental Policy are documented in this manual and compliance is achieved through specific reference to local procedures and the effective implementation of the Bio-Techne Minneapolis Q&EMS.

1.8 The Quality and Environmental Management Systems (Q&EMS) applies to all processes, activities and employees at 614 McKinley Place NE, Minneapolis, Minnesota.

1.9 Bio-Techne Minneapolis has determined the following sections of ISO 13485 are not applicable to the Bio-Techne Minneapolis, Minneapolis Q&EMS:

1.9.1 7.5.3 Installation Activities: Bio-Techne Minneapolis products do not require installation

1.9.2 7.5.4 Servicing activities: Bio-Techne Minneapolis products do not require servicing

1.9.3 7.5.5 Particular requirements for sterile product and 7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems - Bio-Techne Minneapolis products do not have a sterility claim.

1.9.4 7.5.9.2 Particular requirements for implantable medical devices - Bio-Techne Minneapolis products are not implantable.

2.0 QUALITY & ENVIRONMENTAL MANAGEMENT SYSTEM REFERENCES

2.1 The Quality and Environmental Management Systems 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 13485:2016[1]

2.1.2 ISO 9001:2015

2.1.3 MDSAP 654945

2.1.4 ISO 14001:2015

2.1.5 21 CFR § 820 – Quality System Regulation (US FDA)

2.1.6 RDC ANVISA 16/2013 – Brazilian Health Regulatory Agency (ANVISA)

2.1.7 MHLW Ministerial Ordinance No. 169 – Japanese Ordinance on Standards for Manufacturing Control and Quality Control of Medical Devices and *In Vitro* Diagnostics

2.1.8 Australian Regulatory Guidelines for Medical Devices (ARGMD) – Australian Therapeutics Good Administration (TGA)

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

2.1.10 European Union Council Directive 98/79/EC concerning *In Vitro* Diagnostics Devices (IVDD)

2.1.11 Applicable laws regulations of Countries where Bio-Techne Minneapolis products are registered and distributed

2.1.12 Local, state, and federal environmental and safety guidelines in accordance with Occupational Safety and Health Administration (OSHA) and the Minnesota Pollution Control Agency (EPA).

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

2.2 Company History:

2.2.1 In 1993, Bio-Techne's subsidiary, Research & Diagnostics Systems, Inc. (Bio-Techne Minneapolis), established R&D Systems Europe, Ltd. (now Bio-Techne Ltd.) in Abingdon, UK. Bio-Techne Ltd. received ISO 9001 certification in July 2007 (certificate # 951 07 4360).

2.2.1.1 Bio-Techne Ltd. has five sales subsidiaries or branches: Bio-Techne, GmbH, Wiesbaden, Germany; R&D Systems France, located in Lille; Bio-Techne AG in Zug Switzerland; Space Import-Export in Milan, Italy; Bio-Techne R&D Systems s.r.o. in the Czech Republic. Several other subsidiaries are currently being established in Hungary, Spain and Poland.

[1] Specific reference to the dated ISO standards (ISO 13485:2016, ISO 9001:2015, and ISO 14001:2015) is provided here; henceforth, in this document and other Quality and Environmental Management System documents, reference to these ISO standards are understood to refer to these revisions.

2.2.2 In 2005, Bio-Techne Minneapolis purchased BiosPacific, located in Emeryville, California. BiosPacific became a strategic business unit of what was then the Diagnostics Division. The site received ISO 9001 certification in 2011 (FM 574663).

2.2.3 Bio-Techne Minneapolis established a wholly owned subsidiary in the People's Republic of China in May 2007, Bio-Techne China Co., Ltd., which opened its Warehouse and Distribution Center in Shanghai on October 1, 2007 and in Hong Kong in February 2011. In April 2014, Bio-Techne China acquired Shanghai PrimeGene Bio-Techne Co., Ltd., which manufactures proteins for sale in China and elsewhere. This site is ISO 9001 certified.

2.2.4 In 2011, Bio-Techne Minneapolis purchased Boston Biochem in Cambridge, Massachusetts and Bio-Techne Ltd. purchased Tocris located in Bristol, UK. Both Boston Biochem and Tocris became strategic business units of what was then the Biotech Division.

2.2.5 In 2013, Bio-Techne Minneapolis purchased Bionostics, Inc. (Devens, Massachusetts) as a strategic business unit of what was then the Diagnostics Division; the facility is certified to ISO 13485 and MDSAP.

2.2.6 In 2014, Bio-Techne purchased Novus Biologicals, LLC in Littleton, Colorado as a strategic business unit of what was then the Biotech Division.

2.2.7 In 2014, Bio-Techne purchased ProteinSimple in San Jose, California and Ottawa, Ontario, Canada; Bio-Techne purchased CyVek Inc., located in Wallingford, Connecticut. These sites became part of what was then the Protein Platforms Division.

2.2.8 In 2015, Bio-Techne purchased Cliniqa in San Marcos, California. Cliniqa is a strategic business unit of what was then the Diagnostics Division and is certified to ISO 9001 and ISO 13485.

2.2.9 In 2016, Bio-Techne Ltd. purchased Space Import Export Srl in Milan, Italy as a distributor for the greater EU. In addition, ProteinSimple acquired Zephyrus Biosciences, Inc. and merged the assets and employees with ProteinSimple.

2.2.10 In 2016, Bio-Techne acquired Advanced Cellular Diagnostics (ACD), in Newark, California. ACD manufactures products for the genomics market. The site is ISO 13485 certified.

2.2.11 In 2017, Bio-Techne purchased Trevigen in Gaithersburg, Maryland, a manufacturer of cell culture products. The original location was closed, and manufacturing transferred to Bio-Techne Minneapolis site.

2.2.12 In 2018, Bio-Techne purchased Atlanta Biologicals, a serum manufacturer located in Flowery Branch, Georgia. The site holds ISO 9001 certificate FS 707254. The site has been renamed Bio-techne Flowery Branch.

2.2.13 In 2018 Bio-Techne purchased Quad Technologies located in Woburn, Massachusetts. The site manufactures microparticles modified with antibodies which serve as the substrate for cell separation or cell activation.

2.2.14 In 2018 Bio-Techne purchased Exosome Diagnostics located in Waltham, Massachusetts, which manufactures and performs testing in the liquid biopsy diagnostics arena.

2.2.15 In 2018 Bio-Techne purchased Euro-Cell Diagnostics s.a.s. located in Rennes, France. In April 2019, the legal name was changed to Bio-Techne France, s.a.s.

2.2.16 In 2019, Bio-Techne purchased B-MoGen, located in Minneapolis, MN. B-MoGen develops and manufactures gene editing technologies.

2.2.17 In July 2020, the Diagnostics Division was renamed Diagnostic Reagents Division. As documents are updated, the necessary change will be made.

2.2.18 Bio-Techne has more than 2300 employees worldwide.

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 & ENVIRONMENTAL MANAGEMENT SYSTEMS

4.1 General Requirements

4.1.1 R&D Systems, Bio-Techne Minneapolis, is committed to the highest level of quality in the manufacture, sale and support of our products. In addition, the organization is passionate about carrying out activities in a manner that minimizes environmental impacts, conserves natural resources and provides effective stewardship of the environment.

4.1.2 In addition, with the decision to pursue ISO 14001 certification, environmental considerations were integrated into this manual and the site overall management system. The synergies between ISO 9001:2015 and ISO 14001:2015, are noted graphically in Figure 1.

Figure 1 – ISO 9001 and ISO 14001 Synergy

4.1.3 Bio-Techne Minneapolis applies a risk-based approach to the control of the appropriate processes needed for the Quality and Environmental Management Systems.

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

4.1.5 Changes made to the Quality and Environmental Management Systems processes are evaluated for overall impact on the Q&EMS and are evaluated for impact on *in vitro* diagnostic medical devices produced under the Q&EMS. Changes are controlled in accordance with the requirements of applicable standards and regulations. An impact assessment process is in place to document these evaluations.

4.1.6 Bio-Techne Minneapolis considers outsourcing as any process, product or service that is obtained by contract from a source outside Bio-Techne Minneapolis that affects key processes and /or product conformity to requirements.

4.1.7 Bio-Techne Minneapolis outsources the following: contract ethylene oxide processing, pest control, contract lab testing when needed including (environmental, microbiology, residual viruses, etc.), deionized water servicing, calibration for specialized instruments and equipment. Other outsourced services may be utilized as needed.

4.1.8 Bio-Techne Minneapolis 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
540009	Management Review - Quality Management System and Environmental Management System
541138	Quality Assurance Organization
541614	Quality Planning

4.2 Documentation Requirements

4.2.1 General

4.2.1.1 The Q&EMS documentation includes the Bio-Techne Minneapolis Quality and Environmental Systems Manual (document 540308) and Standard Operating Procedures (SOPs) needed to establish, maintain and support the Q&EMS, Device Master Records of finished product manufactured at the Minneapolis locations, policies and procedures needed to establish, maintain and support the Q&EMS System, and all records used to provide evidence of the effective implementation of the Q&EMS.

4.2.1.2 The documentation hierarchy is described in the following manner.

4.2.1.2.1 Level 1 Documents

Bio-Techne Minneapolis Manual
Bio-Techne Minneapolis Policies (Quality and Environmental)
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 and Diagnostics 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 Q&EMS
Quality and Environmental Management Systems Review Records
Internal Audit Reports
Technical Reports
Validation Documentation
Device History Records
Forms, Templates, Records and Data

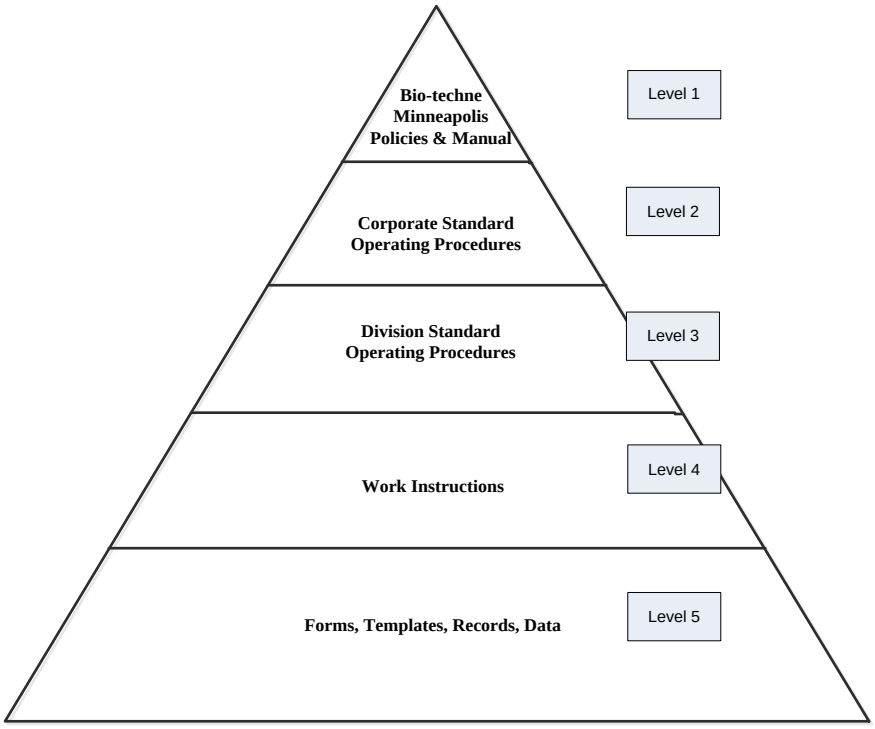


Figure 2 – Document Hierarchy

4.2.2 Quality and Environmental Systems Manual

4.2.1.3 This Quality and Environmental Systems Manual has been prepared to describe Bio-Techne Minneapolis' Q&EMS. This includes Protein Science Segment - Minneapolis site and Diagnostics and Genomics Segment - Minneapolis site. The scope and purpose of the Q&EMS are described in Section 1.0. Each section of the manual references documented Q&EMS procedures relating to the requirements outlined in that section.

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

4.2.1.5 This Quality and Environmental Systems Manual is part of the Bio-Techne Minneapolis Document Control System and is controlled and distributed in accordance with the DCR System in MasterControl™.

4.2.1.6 The Management Representative shall review this document minimally on an annual basis 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; TDI (Technical Documentation Indexes) are also maintained for IVD products. These files contain, or reference, documents generated to demonstrate conformity to the requirements.

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 Q&EMS documents are reviewed for adequacy and approved prior to issue in accordance with appropriate procedures. Bio-Techne Minneapolis 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: Q&EMS and Quality System and Environmental 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, Data from Biomarker Testing Services (BTS) Studies, Essential Requirements Checklists, Technical Document Indexes, Environmental Risks and opportunities, Compliance obligations records; 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 at locations where they are intended to be used. Obsolete documents are prevented from unintended use through archiving in MasterControl™.

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 managed by Senior Manager, Quality Assurance / Regulatory Affairs.

Document	Description Corporate
540643	Standard Operating Procedure (SOP) Review
540578	Record Keeping Guidelines
540146	R&D Systems' Document Formatting
540748	MASTERControl™ Electronic Documentation System
540750	MASTERControl™ Functions
540205	Document Change Request (DCR)/Form Submission Request (FSR) Procedure
540120	Access and Control of Documents of External Origin
Document	**Description Protein Sciences Segment**
540382	Preparation and Maintenance of Document Master Files
Document	**Description Diagnostic Reagents Division**
2006005	Diagnostic Reagents Documents Organization (Document Control)

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. Bio-Techne Minneapolis ensures the quality and legibility of its records by following good documentation practices.

4.2.5.2 All records required to maintained by Q&EMS 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 Q&EMS 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, and the environmental management system is operated in accordance with requirements.

4.2.5.4 Records shall be established and maintained to provide evidence of conformity to requirements and of the effective operation of the Q&EMS. 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 and Environmental 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 Vendor 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 BTS Sponsor Notebooks
4.2.5.5.15 Process and Equipment Validations
4.2.5.5.16 MRB Minutes
4.2.5.5.17 Deviations

Document	Description Corporate
540008	Record Retention
540122	MasterControl™ Functions for Document Control
540534	IT Backup Policy
541138	Quality Assurance Organization
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 Q&EMS, product quality, GMP compliance for all products manufactured and distributed from Bio-Techne Minneapolis, and for maintenance of the environmental controls and records in accordance with all applicable laws and regulations, and in conformance with ISO 14001 requirements.

5.1.2 Senior Management is actively involved in implementing the Q&EMS and ensuring its continual improvement and effectiveness. Senior Management provides the vision and strategic direction for the growth of the Q&EMS and meeting established quality and environmental objectives with regard to the stated policies.

5.1.3 Senior Management provides leadership and shows commitment to the improvement of the Q&EMS through:

- communicating the importance of meeting customer expectations
- statutory and regulatory requirements
- establishing quality and environmental objectives
- supporting the Quality Policy and Environmental Policy
- conducting regular management reviews
- ensuring the availability of resources
- providing Q&EMS training for all associates

5.2 Customer Focus

5.2.1 Bio-Techne Minneapolis 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 DiagnosticReagents Division**
2008035	OEM Technical Service Protocol / Complaints
2008034	Diagnostics Division – Minneapolis Technical Service Protocol/Complaints

5.3 Quality and Environmental Policies

5.3.1 Senior Management ensures the **Quality Policy** and the **Environmental Policy** 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 Environmental Policy is:

Bio-Techne is passionate about carrying out activities in a manner that minimizes environmental impacts, conserves natural resources and provides effective stewardship of the environment. Environmental management is an integral core value and vital part of the Bio-Techne EPIC culture, including:

Meet or exceed pertinent environmental regulations.
Continual improvement of the environmental management system.
Provide training to ensure awareness of environmental issues and collaborate to improve the Company's performance relevant to resource reduction and pollution prevention.
Empower employees to minimize waste. Promote the effective use of innovative environmental technologies and practices.
Promote pollution prevention and waste minimization by recycling both internally and through collaboration with customers and suppliers.

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

5.4 Planning

5.4.1 Quality and Environmental 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 and Environmental Policies during Management Review.

5.4.1.1 Quality effectiveness checks are made 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 and Environmental Management Systems Planning

5.4.2.1 Senior Management ensures quality and environmental planning is carried out to meet the requirements as well as agreed upon objectives. The integrity of the Q&EMS is maintained when changes to the Quality and Environmental Management systems are planned and implemented.

Document	Description Corporate
541614	Quality Planning
541347	Continual Improvement
541881	Job Hazard Assessment
540478	Disposal of Biohazardous Material
541483	Hazardous Materials and Dangerous Goods Handbook
541125	Security and Storage for Controlled Substances Used in Manufacturing
502007	Hazardous Waste Disposal Procedures
S109	Emergency Injury and Hazard Exposure Protocol

5.5 Responsibility, authority and communication

5.5.1 Responsibility and authority

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

5.5.1.2 The CEO has executive responsibility for the Q&EMS and is responsible for creating an atmosphere where product quality and environmental protection is the highest priority.

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

5.5.1.4 The Senior Director of QUALITY, REGULATORY AFFAIRS AND SAFETY, the Vice-President of Diagnostics and Genomics Division and President of Protein Sciences Segment, and the Quality Assurance, Safety, and Facilities staff are responsible for ensuring that the Q&EMS is fully maintained and implemented.

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

5.5.1.6 Each employee is responsible for following Q&EMS guidelines and for their work.

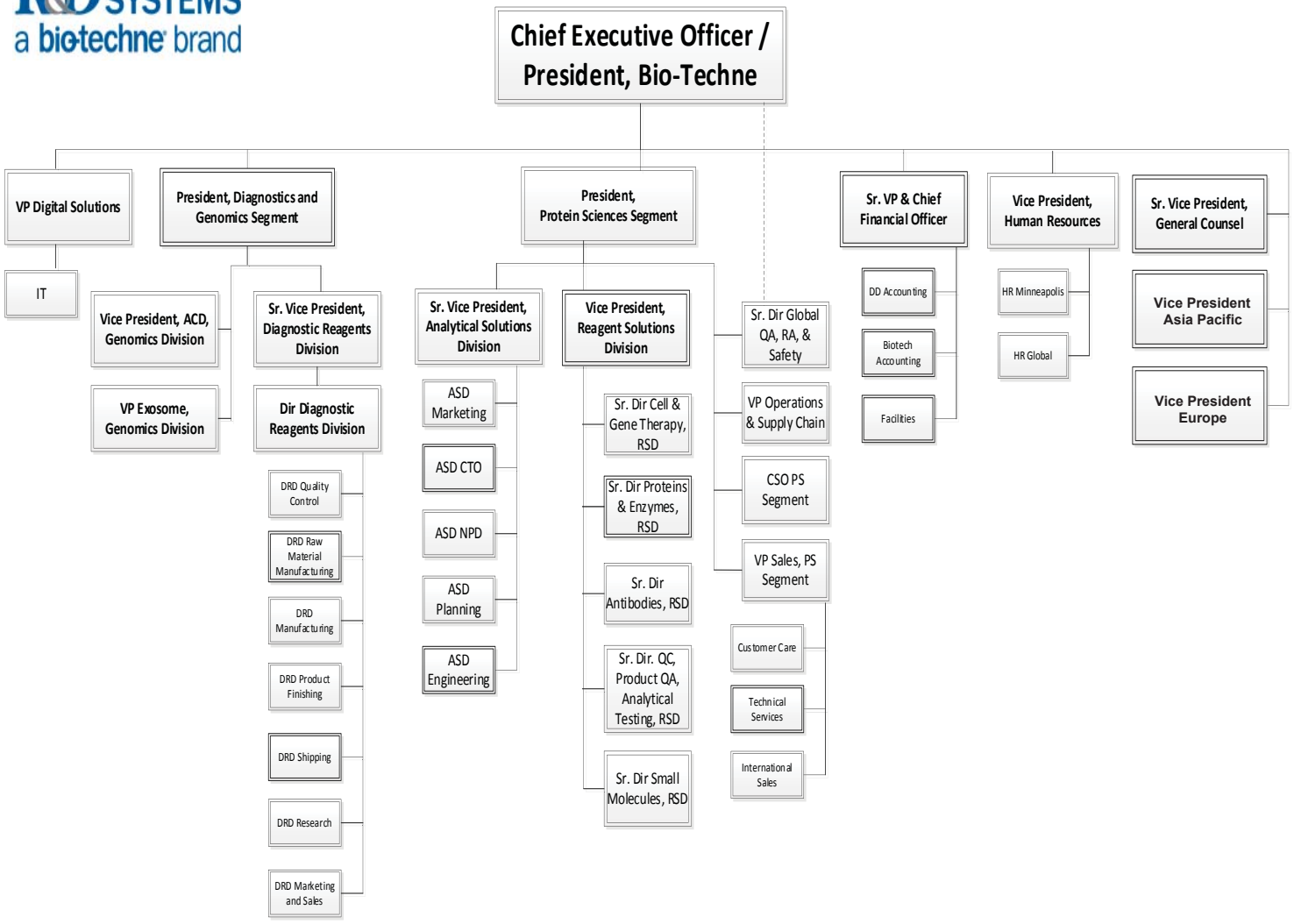
5.5.1.7 Two groups are dedicated exclusively to Quality: Quality Assurance and Quality Control

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.

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 Senior Director of QC, Product QA, and Product Support.

5.5.1.8 The organizational chart describes the functional and organizational structure of the Company. While the structure and organization may vary between the Protein Sciences, and Diagnostics and Genomics Segments, quality and environmental goals are identical.

R&D SYSTEMS, INC.
Minneapolis Departmental Organization



5.5.2 Management Representative

5.5.2.1 The Senior Director of Global Quality, Regulatory Affairs and Safety has been appointed as the Management Representative by the company president and has responsibility for ensuring that requirements are effectively established and maintained in accordance with the appropriate regulations, for reporting on the Q&EMS to upper Management, and for ensuring the promotion of awareness or regulatory and customer requirements throughout the organization.

5.5.3 Internal Communication

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

5.5.3.2 Bio-Techne Minneapolis utilizes a variety of ways to communicate the policies, 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.

5.6 Management Review

5.6.1 General

5.6.1.1 The Q&EMS is reviewed at a minimum annually by the Senior Management Team, the Senior Director of Global Quality, Regulatory Affairs and Safety, and other pertinent management personnel as deemed appropriate. The Bio-Techne Minneapolis Management Review is conducted which includes Protein Sciences Segment and Diagnostics Division, Minneapolis. Management reviews progress to quality objectives that are reviewed 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 Q&EMS and identify potential risks and opportunities for improvement. Any changes to the Q&EMS, including the policies 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 the QA/RA and Safety. Minutes are distributed to those present at the meeting as well as any designees who are absent from the meeting.

5.6.1.5 If corrective and / or preventive actions are identified as a result of the Management Review, Senior Management shall appoint an “Owner” of the issue and determine the level of risk involved. Actions taken are monitored and controlled through regular updates during Management Review and department meetings by the Quality, Regulatory Affairs and Safety organization.

5.6.2 Review Input

5.6.2.1 Management Review Inputs of the Q&EMS 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 and Environmental Management Systems; recommendations for improvement; and applicable new or revised regulatory requirements.

5.6.3 Review Output

5.6.3.1 Management Review Outputs of the Q&EMS are documented at the review meetings and include, improvements needed to maintain the effectiveness of the Q&EMS and its processes, improvement of product related to customer requirements, resource needs and planning and Q&EMS 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 and Environmental 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 Q&EMS and to comply with regulatory and customer requirements. This is evident through resource planning at financial meetings, annual budget preparations, Q&EMS 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 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 Bio-Techne Minneapolis has a Quality System training program (including the applicable requirements of ISO 9001, ISO 13485, 21 CFR 820 and ISO 14001, conducted 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 trainings 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 ensure that current versions of pertinent external standards are identified and available within the organization. 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
540120	Access and Control of Documents of External Origin

6.3 Infrastructure

6.3.1 The infrastructure at Bio-Techne Minneapolis 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 Safety audits are routinely conducted throughout the facility.

6.3.4 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.

6.3.5 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	TAC 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 Temperature Sensor Verification
540306	Calibration of Pipets

Document	Description Corporate
541034	Disaster Recovery Plan, Bio-Techne (Minnesota)
540247	Facilities & Equipment Work Order Request Form and Instructions
541855	Use of Paper Logbooks for Recording Equipment Use and Cleaning
541378	Regulatory Asset Manager (RAM)
542010	Generator Preventive Maintenance

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 required, whereas in other 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
540232	Temperature Monitoring Refrigerators, Freezers and Incubators
541127	Guidelines and Procedures for Animal-Free Laboratories
541130	TAC System: Monitoring and Alarm Response
541276	General Building Cleaning
542083	Cleaning Procedures for Rooms E0-213, E0-213.02, and E0-213.03
542093	Extensive Cleaning Procedures for Rooms E0-213, E0-213.02, and E0-213.03
140210	Deionized Water System Microbial Monitoring
140350	Environmental Monitoring Plan for Viable Organisms

6.4.2 Contamination Control

6.4.2.1 Bio-Techne Minneapolis does not manufacture sterile product. 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 Bio-Techne Minneapolis approaches product realization from a product life cycle aspect with Design Control and Risk Management governing a product's safety and effectiveness from the early stages of research and development through the 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) 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**
540781	Planning Guidelines, Immunoassay Manufacturing
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 those 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 documentation specific to product. All enquiries, contracts or order handling is through Marketing or Technical Service

7.2.3.2 Customer complaints and feedback is handled via Technical Services (Diagnostics) or Customer Care or Technical Service (Protein Sciences Segment), Product Managers and ultimately Quality Assurance. Advisory Notices are communicated to customers through the QA/RA department.

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
541214	Corrections, Removals and Recalls for IVD Products
Document	**Description Protein Sciences Segment**
540260	Field Notification Procedure
540135	Customer Feedback System, Biotech
540775	Medical Device Reporting (MDR) of Injury or Death - US
541053	Reportable Changes, IVD Products
541065	Mandatory Problem Reporting – Canada
541231	Change Control Procedure, Biotech
541886	Corporate Change Control
542118	Adverse Event Reporting – Australia
542119	Adverse Event Reporting – Brazil
542120	Adverse Event Reporting – Japan

Document	Description Diagnostic Reagents Division
2006039	Diagnostics Division Change Control
2008034	Diagnostics Division – Minneapolis Technical Service Protocol/Complaints
2008035	OEM Technical Service Protocol / 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
540215	Validation, Specificity (Cross reactivity and Interference)
541710	Design Control, Cell and Gene 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
540217 - 540221, 540223, 540235 - 540238, 540288, 540337, 540409, 540729, 540804, 541002 and 541273	

Document	Description Diagnostic Reagents Division
2006009	Procedural Elements in a Validation
2006015	DD Design Control

7.4 Purchasing

7.4.1 Purchasing processes

7.4.1.1 Bio-Techne Minneapolis 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 vendors are listed on each raw material specification. Document 540000, vendor Qualification and Monitoring, describes how a new vendor is qualified, including outsourced services and processes, and how vendors are monitored for quality and on-time delivery of goods and services.

7.4.1.3 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.

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 Bio-Techne 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
Document	**Description Protein Sciences Segment**
640xxx	Non-biological Raw Materials Specifications (Biotech)
645xxx	Biological Raw Material Specifications (Biotech)
Document	**Description Diagnostic Reagents Division**
20054xx, 20055xx	Biological Raw Material Specifications
20056xx, 20057xx	Non-biological Raw Materials Specifications

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 the 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
540194	Certificate of Analysis Procedure
541138	Quality Assurance Organization
Document	**Description Diagnostic Reagents Division**
2008855	Instructions For Use (IFU) - Revising, Printing and Inspecting

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 Bio-Techne Minneapolis 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 the 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 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 Project Plan
Document	**Description Protein Sciences Segment**
540124	Inspection of Assembled Kits
550449	Immunoassay Approval / Rejection Criteria
540143	Product Insert Inspection Procedure
540188	Use of Pipettes: Technique and Type of Specific Instructions
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
554350	Treatment of Suspect Test Results Generated During the Testing of Products for Commercial Distribution
540194	Certificate of Analysis Procedure
541138	Quality Assurance Organization
540781	Planning Guidelines, Immunoassay Manufacturing
540207	Label Control, Product Finishing
540072	Fillings Operation Procedure

540186	Cleaning of Cell Culture Labware
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	Special Retail Bottling
540134	Incoming Equipment Validation Procedure
540467	Line Clearance
540124	Inspection of Assembled Kits
Document	**Description Diagnostic Reagents Division**
2008812	Finished Device Inspection Procedure
8855	Instruction Sheet Revising, Printing and Inspecting
2002800	Balance Procedure
2009090	Production Finishing Label Control
2006029	Diagnostics Division, Labeling Control
2009054	Bottling Procedure
2008006	Bottled Product Release
2008809	Assay Sheet Printing and Release
2006039	Diagnostics Division Change Control
2008813	Guidelines for Determining Assay Ranges

7.5.2 Cleanliness of product - Not applicable

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	Internal Notification Procedure: Receipt of New Equipment
541886	Corporate Change Control
540266	Validation Master Plan
Document	**Description Protein Sciences Segment**
540134	Incoming Equipment Validation Procedure
540215	Validation, Specificity (Cross reactivity and Interference)

Document	Description Diagnostic Reagents Division
2006039	Diagnostics 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 Bio-Techne Minneapolis 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 our 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
541104	Labeling Guidelines, IVD
541942	Unique Device Identification (UDI) Guidelines
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	Diagnostics Division, Labeling Control
2009090	Product Finishing Label Control
2008809	Assay Sheet Printing and Release
8855	Instruction Sheets- 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 it 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 by Document Control or 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 the Document Change Request (DCR) Database or PDPT or are assigned at the time of bottling.

7.5.9.3 The Vice President of Diagnostics (Minneapolis) assigns final product lot numbers for DD 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**
2008862	Assigning Final Product Lot Numbers
2006019	Identification and Traceability

7.5.10 Customer property, including intellectual property, is identified, verified and protected while under Bio-Techne Minneapolis' control.

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 product with limited shelf life and 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 QC program and customer complaints.

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

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
540221	Validation, Stability Testing of Immunoassay Kits
Document	**Description Diagnostic Reagents Division**
2010350	Shipping Procedures

7.6 Control of monitoring and measuring equipment

7.6.1 Bio-Techne Minneapolis 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

8.0 MEASUREMENT, ANALYSIS AND IMPROVEMENT

8.1 General

8.1.1 Bio-Techne Minneapolis 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 Q&EMS, and

8.1.1.3 To continually improve the effectiveness of the Quality and Environmental Management Systems.

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 the 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 and R & D 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 A summary report of Protein Sciences Segment complaints is available monthly for review by appropriate personnel. Weekly and monthly summaries of Diagnostics complaints are circulated to Management.

8.2.2.4 Bio-Techne Minneapolis 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 use of the dissatisfaction or non-conformity.

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
2008034	Diagnostics Division – Minneapolis Technical Service Protocol/Complaints
2008035	OEM Technical Service Protocol / Complaints
2008036	Procedure for Investigation of Returned Product
2006025	Investigation Procedure

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, Bio-Techne Minneapolis 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
Document	**Description Protein Sciences Segment**
540775	Medical Device Reporting (MDR) of Injury or Death - US
541065	Mandatory Problem Reporting – Canada
542118	Adverse Event Reporting – Australia
542119	Adverse Event Reporting – Brazil
542120	Adverse Event Reporting – Japan
540260	Field Notification Procedure

Document	**Description Diagnostic Reagents Division**
2006016	Material Review Board (MRB) Procedure - Nonconformance
2008034	Diagnostics Division – Minneapolis Technical Service Protocol/Complaints
2008035	OEM Technical Service Protocol / Complaints
2008036	Procedure for Investigation of Returned Product
2006025	Investigation Procedure

8.2.4 Internal audit

8.2.4.1 Comprehensive, planned quality and environmental 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 and Safety, Facilities personnel.

8.2.4.2 Periodic audits ensure adherence to our Quality and Environmental Management Systems 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 Senior Director of Global Quality/Regulatory Affairs and Safety, 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
502010	Environmental Audit Procedures

8.2.5 Monitoring and measurement of processes

8.2.5.1 Bio-Techne Minneapolis applies suitable methods for monitoring and measurement of the Q&EMS 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 and Environmental Management Systems 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 MasterControl™.

8.3.6 For Diagnostics' products, MRBs are documented using the MRB form. Minutes from meetings of the MRB are published and maintained in MasterControl™.

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 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.

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**
541089	Antibody Re-work Procedure, Dept. 378
540259	Material Review Board (MRB) Responsibility
540265	Rework Procedure
540835	Quarantine of Non-confirming 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
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, QC Laboratory
2008034	Diagnostics Division – Minneapolis Technical Service Protocol/Complaints
2008035	OEM Technical Service Protocol / Complaints
10212	Hematology Shipping's Inventory 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 Protein Sciences**
540819	Risk Management
540865	Statistical Techniques
540537	Test for Outlier Determination (Grubb's Method)
Document	**Description Diagnostic Reagents Division**
2008004	Verification of Bulk Testing

8.5 Improvement

8.5.1 General

8.5.1.1 Bio-Techne Minneapolis continually improves effectiveness of the Q&EMS through the use of the quality and environmental policies, quality and environmental objectives, audit results, analysis of data, corrective actions, and management review meetings.

8.5.2 Corrective Action and Preventive Action

8.5.2.1 Bio-Techne Minneapolis 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 and environmental systems is handled in accordance with the formal change control procedure.

8.5.2.4 Safety and Facilities is responsible for development of an action plan for monitoring and documenting progress related to an environmental non-conformance or failure.

Document	Description Corporate
541886	Corporate Change Control
540552	Corrective and Preventive Action (CAPA Process)

9.0 ADDITIONAL ENVIRONMENTAL MANAGEMENT SYSTEM CONSIDERATIONS

9.1 Context of the Organization

9.1.1 Context of the Organization, pertinent to both ISO 9001:2015 and ISO 14001:2015, takes into consideration persons and groups concerned with, or affected by Bio-Techne's, environmental performance. General context of the organization can be classified as:

9.1.1.1 Internal context, which any actions or products and services that may affect our environmental performance.

9.1.1.2 External context, including legal, economic, social, or political issues.

9.1.1.3 Environmental context, which pertains to all other environmental aspects that may be susceptible to damage by the organization's environmental performance.

9.1.2 The expectations of interested parties, therefore, includes legal and mandatory requirements, as well as investor expectations, customer and contractual expectations, any other expectations held by the local community, and so on. Through the proper implementation and management of the Environmental Management System, Bio-Techne will ensure that we not only meet environmental objectives and expectations, but also have a foundation to ensure we are aware of satisfying all external parties and preparing for the future.

9.2 Identification and Classification of Environmental Aspects

9.2.1 This includes those interactions that Bio-Techne Minneapolis- has with the environment. Any interaction between the organization and the environment, positive or negative must be identified.

9.2.2 The interactions which are significant, and over which we have control or influence.

9.2.3 It is helpful to classify these into four main environmental aspects, including “Air Pollution,” Water Pollution,” “Land Pollution,” or “Use of Natural Resources”.

9.3 Emergency Preparedness and Response

9.3.1 If the event of an emergency, where a negative environmental impact could take place, Bio-techne Minneapolis has a plan in place to deal with this situation to avoid or minimize environmental damage.

9.3.2 Environmental targets and programs are defined for each fiscal year (July 1 – June 30).

Document	Description CORPORATE
541114	Environmental/Waste Management Procedure
542164	Air Quality Program Maintenance Guide
542239	Underground Fuel Tank Monitoring System and Alarm - Buildings E and F
542243	Bio-Techne Headquarters - Operation of Cooling Towers
S110	Emergency Action Plan
S301	Bio-Techne Minneapolis Exposure Control Plan
S302	Bio-Techne Minneapolis Chemical Hygiene Plan
S112	Emergency Coordinator Response

END OF DOCUMENT