ATTACHMENT #1

SGS Yarsley
International Certification Services Limited

Certificate Number

Q15066

This is to certify that the
Quality Management systems of

MDS Nordion Inc.
Isotope Products Division
Ontario, Canada

have been assessed and registered as meeting the requirements of ISO 9001

The scope of registration is detailed on the Assessment Schedule bearing this certificate number.

SGS Yarsley International Certification Services Ltd
Signed by

11 November 1998
This certificate remains valid subject to satisfactory maintenance of the system

Registered Office:
SGS Yarsley
International Certification Services Limited
SGS House, 217/221 London Road,
Camberley, Surrey GU15 3EY, United Kingdom.

NATIONAL ACCREDITATION OF CERTIFICATION BODIES
Registration Number
005

SGS Yarsley
International Certification Services Limited

ASSESSMENT SCHEDULE

Q15066

Assessment Standard: ISO 9001: 1994

Company: MDS Nordion Inc.
Isotope Products Division

Location: 447 March Road
Kanata
Ontario, Canada
K2K 1X8

Product Area Assessed: Design and manufacture of Medical Devices, utilising radiation for its medical application and sealed sources for diagnostic and therapeutic applications.

Authorised by R. R. Carey.
Director

Issue No: 1

11 November 1998

The date of the accompanying certificate, indicates the date of original registration against the above assessment standard.

NATIONAL ACCREDITATION OF CERTIFICATION BODIES
Registration Number
005

SGS Yarsley International Certification Services Limited is accredited by the following authorities:

UK - United Kingdom Accreditation Service (UKAS)

NUCLEAR MEDICINE QUALITY MANUAL

Signatures

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	6	General update			

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1. PURPOSE

This manual serves as a link in the MDS Nordion Quality System documentation. It is considered the guiding document that describes quality activities required to meet the Quality Policy. As a direct result of our company's unique businesses and our corporate structure we have tailored our Quality System documentation to facilitate description of Quality Assurance activities at each level of the organization where responsibilities and activities are undertaken. Additionally, we have endeavored to connect each tier of documentation from the Corporate Quality Policy through to and including, work instructions for all our quality processes. A pictorial representation of how this documentation unites with the Nuclear Medicine business unit can be found in Appendix "A" of this manual.

2. SCOPE

This manual describes the interrelationships of the matrix organization that supports the Nuclear Medicine operations through the provision of Quality Assurance, Quality Control, Procurement, Calibration and Maintenance services. The operating procedures and work instructions as described herein are approved and controlled by the technical authorities and responsible personnel in their functional groups. These operations, procedures and documents are designed and executed to meet the requirements of their internal customers in keeping with the Corporate Quality Policy, Quality Commitment and MDS Nordion employees dedication to teamwork.

3. RESPONSIBILITIES

The Vice-President, Quality and Regulatory Affairs has been appointed the Management Representative for the Company's Quality System. This includes meeting the requirements defined by EN 46001, ISO 9001, ISO 13485 and the U.S. FDA "Good Manufacturing Practices" as defined by Part 211 and Part 820 of the Code of Federal Regulations.

The Management Representative is responsible for:

- ensuring that the Quality System, as defined in this manual is in accordance with the Quality System Standards
- ensuring that the Quality System is established, implemented and maintained
- reporting on the performance of the Quality System to the Company's management for review and as a basis for improvement of the Quality System.

4. PROCEDURE

4.1 Management Responsibility

4.1.1 Quality Policy

The MDS Nordion Quality Policy is stated in the corporate procedure 07, "Quality Policy".

4.1.2 Organization

Responsibility and Authority

The Nuclear Medicine business unit standard operating procedures (SOPs) and policies contain the most detailed responsibilities descriptions in the section of each document entitled responsibilities. The Director, Nuclear Medicine Operations, Production Managers, or their delegates, Manager, Quality Assurance, Quality Control Managers, or their delegates, have the authority to stop further processing, dispensing and or distribution of Nuclear Medicine's products.

The responsibility for following up Corrective Actions and verifying the implementation of solutions that address root cause belongs to the Manager, Quality Assurance.

The organization and reporting structures (Organization Charts) of MDS Nordion, Canadian Operations, are described in the staff list and organization book maintained by the Corporate Human Resources Department. A copy of the Quality Organization as it applies to the Nuclear Medicine business unit at the Kanata site, can be found in Appendix "B".

The following individuals have a primary role and responsibility for quality assurance at Nordion, Kanata Operations.

PRESIDENT: the President has the primary responsibility to ensure that the Nordion quality assurance program conforms to the principles outlined in this Manual, including those principles set out in the Nordion Quality Commitment. The corporate Quality Commitment is reviewed on a timely basis to ensure consistency and relevance with changing corporate objectives and evolving, long-term market conditions.

SENIOR VICE-PRESIDENT, NUCLEAR MEDICINE: is responsible to ensure that all operations are carried out in full compliance with the program including the policies of this present program, the Nordion Quality Commitment, and for adhering to the requirements of all applicable codes and regulations.

DIRECTOR, NUCLEAR MEDICINE OPERATIONS: is responsible for all Kanata isotope processes and their facilities, packaging, shipping and distribution of the finished products. This includes the implementation and ongoing maintenance of GMP and ISO requirements.

VICE-PRESIDENT, HUMAN RESOURCES: that the Nordion Quality Commitment is reflected in sound policies which motivate and support all employees through appropriate rewards and recognition. In addition, the Vice-President, Human Resources is responsible to ensure that systems are in place to select the right people for the job based on qualifications and experience.

VICE PRESIDENT, QUALITY AND REGULATORY AFFAIRS: is responsible for directing the development and implementation of Nordion's quality, regulatory, worker and environmental safety programs. This individual is also responsible for the development and maintenance of the Quality Assurance program, Quality Control services and GMP programs for the manufacturing operations, including approval of related company wide procedures.

DIRECTOR, SUPPLY AND OPERATIONS SERVICES: is responsible for directing Nordion's facilities modifications, maintenance and operations.

MANAGER, FACILITY ENGINEERING: is responsible for all site development, facility development and modifications and space planning activities. Provide systems expertise in nuclear ventilation systems and pharmaceutical and medical device facility engineering.

MANAGER, PACKAGE ENGINEERING: is responsible for directing engineering activities related to the design of sealed sources and radioactive material transport packaging.

MANAGER, QUALITY ASSURANCE: is responsible for overall quality assurance of all Nuclear Medicine products and services by establishing quality plans for the Company, conducting audits and monitoring within the Business Unit as well as for suppliers. This individual is also responsible for quality control functions for the manufacturing areas, completing the analysis of and approving the release of all finished product. This manager is also responsible for approving process/product deviations, raw materials and all changes to process or product documentation.

MANAGER, PROCUREMENT SERVICES: is responsible for working with material and service suppliers as well as users, for ensuring that purchased material and services meet the specifications and quality standards. The Manager is also responsible to ensure that materials and services meet the specifications for the process or products, and that they are delivered on a timely basis.

PRODUCTION MANAGERS: Lead process teams, support, coach and enable Production Technicians in the completion of their operations to control processes and ensure product quality. Participate as members of the Production Management Team under the leadership of the Director , Nuclear Medicine Operations with front line responsibility for compliance with quality and regulatory programs for Nuclear Medicine processes and products.

QUALITY CONTROL MANAGERS: Lead quality control teams, support, coach and enable Quality Control Technicians in the completion of their duties testing and controlling raw materials, in process and final products. Participate as members of the Quality Control Management team under the leadership of the Manager, Quality Assurance with front line responsibility for quality control of materials and products in the Nuclear Medicine business unit.

ALL EMPLOYEES: Work as team members, both within process and cross functional teams. Follow established, approved procedures and practices to execute their assignments while continuously identifying opportunities for improvement in quality of work life, processes and products. Responsible for identifying any barriers to achieving quality standards and requesting immediate assistance from the Manager to overcome these barriers.

Resources

Resource requirements for performing work, audits and verification activities as well as for managing, are documented in various procedures such as Standard Operating Procedures and Standard Test Methods. Resource planning is an integral part of both the annual business planning and the project planning processes. All personnel are qualified through a combination of education, experience and training.

Management Representative

The Vice-President, Quality and Regulatory Affairs is responsible for implementing and maintaining the Quality System in the Nuclear Medicine business unit.

4.1.3 Management Review

The performance of the Quality System is reviewed regularly by the Management Review Team (MRT). This team is comprised of the Senior Vice-President, Nuclear Medicine, Vice-President, Quality and Regulatory Affairs, Manager, Quality Assurance, Director, Nuclear Medicine Operations, Director, Therapeutic Products, Process & Product Development, Manager, Customer Service/Supply Management and Quality Specialist Nuclear Medicine or their delegates. Information prepared for these meetings according to QAP AP-15 "Management Review Team", is presented. This material is discussed in relation to the Quality System, actions are assigned when required and recorded in the minutes. The minutes of these meetings are retained as Quality Records in the Quality Assurance Department files.

Annually, all of the data that is reviewed at the MRT meetings is summarized and analyzed by the MRT. This summary of data is used to determine the effectiveness of the quality systems with respect to meeting the company quality policy and objectives.

4.2 Quality System

4.2.1 General

Nuclear Medicine Quality Systems documentation begins at the corporate level with the Quality Policy, the Quality Assurance Program and at the divisional level in the Quality Manual (see Appendix "A"). Increasing levels of detailed procedures and instructions are documented starting with system level procedures, Standard Operating Procedures, Standard Test Methods and Specifications to work instructions for operations that affect quality in the Nuclear Medicine business unit.

4.2.2 Quality System Procedures

Quality System elements are described in controlled documents that are designed to address that element at the level in the organization where responsibilities and activities occur, i.e., system elements such as purchasing, nonconforming product and internal quality audits are addressed in the Quality Assurance Program and this manual. The functional procedures describing purchasing activities are contained in the Procurement Services Procedures, the procedures for nonconforming product are found in the Nuclear Medicine business unit documents and the procedure for internal quality audits is found in the Quality Assurance Procedure, QAP AP-6 "Quality Audits". The matrix organization that carries out the activities which support Nuclear Medicine's production and quality control operations follows the appropriate documentation for each task being performed.

4.2.3 Quality Planning

Each product in the Nuclear Medicine business unit has its own quality plan that specifies all the specifications, standard operating procedures and standard test methods that are followed to produce and test the final product. These are called manufacturing plans and are designated by the suffix MFP, in the document numbering system.

Products that are in development and projects, each have their own quality plan that describes all the specific procedures, resources and sequence of activities relevant to that new product or project. In the case of new products, a manufacturing plan will be one of the outcomes of the documentation that is developed relevant to that product. These quality plans are developed in compliance with QAP AP-12, "QUALITY PLANS".

The successful culmination of these activities, each functional group in collaboration with the others, results in products and services that consistently satisfy our customers requirements in fulfillment of the MDS Nordion Quality Policy.

4.3 Contract Review

4.3.1 General

Documented procedures are maintained by the Nuclear Medicine business unit to describe the activities, responsibilities and requirements for contract review for existing standard and nonstandard products, as well as for new products. The appropriate documents are 000018.SOP, "Contract Review" and 000006.SOP, "Contract Review for New Products" respectively. The level of activity and documentation is balanced with the impact of the order or contract on the operations.

4.3.2 Review

These reviews, conducted by the cognizant technical and financial authorities, ensure that customer requirements are adequately defined and documented before tenders are submitted, or a contract or order is accepted. Requirements differing from those in any tenders are resolved prior to contract acceptance. These reviews also ensure that MDS Nordion has the capability to meet all contractual requirements.

4.3.3 Amendment to Contract

When amendments to contracts or orders are required, these amendments must be reviewed as per 000018.SOP, "Contract Review" by the same technical and financial authorities that reviewed the originals.

4.3.4 Verbal Orders or Changes

When verbal orders or changes are received they must be reviewed as if they were written orders or changes. Records of these activities must be documented and maintained.

4.3.5 Records

All pertinent documents related to contract review are maintained as Quality Records.

4.4 Design Control

4.4.1 Medical Devices

This applies to those products that require design control. For MDS Nordion this will include all medical devices. Currently, this encompasses I-125 sources, stents and TheraSphere® in the Nuclear Medicine business unit. For these products, any design or change to an existing design, even if the original design was not subject to these requirements, must go through design control. For guidance on Design Control refer to procedure IN/OP 0352 Z000, "Procedure for Design Control and Configuration Management".

4.4.2 Non-Medical Device Products

Design control does not apply to pharmaceutical, bulk pharmaceutical or radiochemical products. Changes to these processes will be handled by 000033.SOP, "Change Control Program". However, design control may be invoked, if deemed appropriate.

4.5 Document and Data Control

4.5.1 General

The standards and requirements for all Kanata Operations controlled quality system documents are defined in QAP AP-30, "Corporate Document Control". External regulations and other documents are controlled primarily through the activities of the Safety and Environment and Regulatory Affairs groups. These activities are described in documents: SERA-OP-001-017, "Management of Transportation Certificates", and SERA-OP-001-015, "Review of External Regulatory Information".

Nuclear Medicine manufacturing and quality control documents are controlled in accordance with 000000.SOP, "Format and Control of Documents". Procurement Services documents are controlled according to Procurement Services procedure P-010, "Objectives/Purpose/Maintenance and Distribution of Procedures". Quality Assurance documents are controlled according to QAP AP-11, "Quality Assurance Document Control". Pertinent documents related to sealed sources and transport packaging are controlled according to IN/OP 0053 Z000, "Policies and Procedures for the Industrial Irradiation Business Unit Technical Publications Department".

All information that is stored on the LAN System is protected by the LAN Backup, which backs up and secures the information. The backup is described in QAP AP-44.

4.5.2 Document and Data Approval and Issue

The above referenced procedures prescribe and describe the activities that are undertaken to ensure that:

- documents are reviewed and approved by the appropriate personnel prior to issue
- current approved revisions are available where operations are being conducted
- superseded and obsolete documents are promptly removed from all points of issue and use and destroyed or suitably marked
- archive files of superseded and obsolete documents are maintained to provide traceability to previous revisions.

4.5.3 Document and Data Changes

When changes are required, documents are reissued. Changes are reviewed and approved by the same authorities, or designates that reviewed and approved the original documents. Changes are assessed for impact prior to implementation as described in 000033.SOP, "Change Control Program". All pertinent information is accessible to the cognizant authorities. A marked-up copy of the previous document is circulated with the draft document for the reviewers information regarding the nature and extent of the change.

Master lists and data bases of documents have been created and are maintained so that they can be used to determine the current version level of any controlled document.

4.6 Procurement Services

4.6.1 General

Procurement is carried out according to documented procedures described in the Procurement Services Procedures Manual. Production is responsible for developing and maintaining current specifications for materials and/or services that are required. Production is also responsible for accurately communicating these requirements to Procurement Services who are responsible for procuring the materials and/or services as required.

4.6.2 Evaluation of Subcontractors

Suppliers are selected based on their ability to meet MDS Nordion's exacting requirements. Procurement Services qualifies suppliers as described in the Procurement Services Procedures Manual. For controlled materials used in the Nuclear Medicine business unit, an Approved Suppliers List, by material, is maintained.

4.6.3 Purchasing Data

Each P.O. is processed in accordance with Procurement Services procedures P-195, "Processing Purchase Requisitions", P-210, "Order Writing - Inventory Purchases" and P-220, "Order Writing - Non-Inventory Requisition Purchase". Each P.O. is reviewed for accuracy and completeness by the Buyer, Senior Purchasing Agent or Manager, Procurement Services and approved prior to issue.

Purchase orders clearly specify the materials or services requested. Where a MDS Nordion specification is indicated, a copy is provided to the supplier.

4.6.4 Verification of Purchased Product

Supplier Verification at Subcontractor's Premises

Should Nuclear Medicine wish to verify product at a subcontractor's premises, this would be documented in the procurement documentation. At this time, this section of this element is not applicable.

Customer Verification of Subcontracted Product

Due to the nature of Nuclear Medicine's products, customers do not check or inspect purchased product prior to receipt.

4.7 Control of Customer Supplied Product

Product supplied by customers is an uncommon phenomenon for the Nuclear Medicine business unit. When this does occur, the materials are treated using documented procedures and activities governed by 000017.SOP, "Verification, Storage and Maintenance of Customer Supplied Product".

These procedures ensure that materials received from customers are verified upon receipt and that any nonconformance, damage or loss is recorded and that this information is communicated to the appropriate contact at the customer's facility. Customer supplied materials are handled and stored in a manner designed to prevent damage or deterioration while in the custody of MDS Nordion.

4.8 Product Identification and Traceability

Raw materials, in-process and finished products are clearly identified by labelling and/or location. When traceability is required, documentation is maintained to ensure lot and/or batch traceability to constituent components. This documentation becomes Quality Records that are used for release and as an element of batch history records. These activities follow the guidelines of 000022.SOP, "Identification and Traceability of Controlled Raw Materials, In-Process Product and Final Product".

Due to the nature of the Nuclear Medicine business unit processes and products, the methods and procedures that are used to provide identification and traceability are adapted to suit the product and location. These activities are described in more detail in the product specific documentation for processing and dispensing.

4.9 Process Control

All processes affecting quality have been identified and are documented providing the necessary instructions for production, inspection and testing. MDS Nordion's facilities are designed and constructed beyond standard manufacturing requirements due to the nature of our products. MDS Nordion's facilities are subject to the requirements of the Atomic Energy Control Board (AECB), Labour Canada, Environment Canada, the Ontario Ministry of Environment and the appropriate building codes. All facilities and processes comply with the requirements set out in this legislation and in MDS Nordion's radioisotope licenses.

Due to the severe environment inside the cells, some processing equipment is discarded after each run, every other run, weekly or operated to failure and then replaced. More permanent equipment is inspected weekly, adjusted, repaired or serviced as required. Maintenance of cell windows is planned and scheduled. Records of servicing, adjustments and repairs are created and maintained.

Production is planned and scheduled based on known and anticipated customer orders. Equipment is dedicated for use, or otherwise identified. Critical process parameters have been identified, are monitored and recorded. When necessary, witnessing of critical steps is executed and signed off. Approval signatures are obtained as required for processes, materials, equipment and documents. Workmanship criteria in the form of written specifications are available in the working areas.

When the results of a process cannot be verified by subsequent inspection, i.e., sealed source welding, the processes are carried out under continuously monitored conditions by qualified personnel using qualified equipment. Specific set-up procedures and tests are conducted for each run to ensure equipment and critical process parameters are all in proper adjustment.

The guiding document for process control meet customer requirements is 000019.SOP, "Identification, Planning and Control of Production Processes".

4.10 Inspection and Testing

4.10.1 General

Inspection and testing activities are conducted in accordance with the system level documents 000015.SOP, "Material and Component Control" and 000023.SOP, "Finished Product Release". Specific inspections and tests procedures (SOPs and STMs), are governed by these documents and address the activities required in detail.

4.10.2 Receiving Inspection and Testing

All incoming materials are inspected according to approved, documented procedures before release to production. Controlled materials are quarantined upon receipt. These controlled materials are received, tested and released to production according to 040801.SOP, "Raw Materials - Receiving, Testing, Release of Archives".

The activities undertaken to verify and qualify materials are based on regulatory requirements and the understood impact of the material on product quality. Materials are sorted into three lists for this purpose, controlled materials, critical materials and archive samples.

Controlled materials: Those which can affect either the safety or efficacy of the final product or the efficacy of the production process.

Critical materials: Those which can affect the safety and performance of the final product by being a component of the final product, by touching the final product for a significant period of time, or by being the final product.

Archive samples: Those which require "reserve samples", (as defined by the U.S. Code of Federal Regulations 211.170) for potential future testing in addition to QC inspection and testing before use.

The Nuclear Medicine business unit does not perform inspection at its subcontractors premises and conducts its incoming inspection sampling accordingly.

4.10.3 In-Process Inspection and Testing

In-process inspection and testing is conducted according to documented procedures against documented criteria for acceptance per 040853.SOP, "In-Process Materials - Receiving, Test, Release and Storage". Nonconforming in-process materials are identified, segregated and dispositioned according to documented procedures.

4.10.4 Final Inspection and Testing

All finished product is tested according to approved documented procedures (STMs). Results are documented and evaluated against approved documented criteria (SPEs) prior to release. In those special cases in the bulk radiochemical, bulk radiopharmaceutical business, product is shipped prior to completion of testing, it is kept under recall until passing results are obtained. The governing document is 400801.SOP, "Final Product - Receiving, Testing, Release and Reserve Sample Retention".

Any nonconforming product is identified, segregated and disposed of according to documented procedures.

4.10.5 Inspection and Test Records

Records of all testing are maintained in QC for the useful life of the raw material or product. Archive records are maintained as quality records (4.16). Only the Quality Control Manager, the Manager, Quality Assurance, and their designates, are authorized to release Nuclear Medicine's products. The records of all product releases clearly indicate the identity of the authorized individual who signed to release the product.

Control of Inspection, Measuring and Test Equipment

Appropriate equipment, providing the relevant accuracy and precision, is selected for all measurements that could affect quality. Calibration procedures, intervals, schedules, standards and acceptance criteria are documented for all equipment. Additionally, identification and location are documented for each piece of equipment. Each piece of equipment is uniquely identified and each has its calibration status clearly identified on the equipment and/or in its log. Records of each calibration are kept and are treated as Quality Records (4.16).

Calibration is directly traceable to an international standard, (NIST, NRC, etc.) whenever possible. Where international standards do not exist, national standards are used.

If any piece of equipment is found to be out of calibration, or beyond its calibration period it is immediately removed from service. When an out-of-calibration condition is discovered, the validity of previous test results are assessed to determine if there are any possible nonconforming materials or products. Appropriate corrective action to address nonconformances and root cause removal are undertaken.

As in 4.9, Process Control, MDS Nordion's facilities are conducive to the controlled environments required for proper calibrations, inspections and tests. Suitable methods are used for handling and storing test equipment so that accuracy and fitness for use are maintained.

Calibration results, investigations and corrective actions are all documented and maintained as Quality records (4.16). The governing documents are CP-6, "Master" and 400802.SOP, "Calibration and Maintenance of Analytical and Dispensing Instrumentation".

4.11 Inspection and Test Status

Due to the nature and size of Nuclear Medicine's processes and products, each batch or lot of product is uniquely separated from other products and from other batches or lots of the same product in time and usually in space. Due to the dedication of facilities cross contamination and product mix-ups between product lines is extremely unlikely. Different batches of the same product are uniquely labelled one from the other and are stored in separate locations accordingly.

The inspection and test status of product is also indicated through labelling and/or location. Final product release is executed by the appropriate QC authority. The methods and procedures are described in the product specific SOPs, PCRs and STMs.

Records of inspection and testing activities, including review of production records are maintained as quality records (4.16).

4.12 Control of Nonconforming Product

Nonconforming product is identified per Inspection and Test Status (4.12), and handled according to 000024.SOP, "Handling of Nonconforming Materials". These procedures ensure that nonconforming product cannot be inadvertently released to customers and that any reworked product is inspected and tested in accordance with approved procedures at least to the same level as regular production.

4.12.1 Nonconformity Review and Disposition

The responsibilities, authorities and methods for managing nonconformities is documented in 040701.SOP, "Handling of Nonconforming Material for Product and Related Material".

After review, nonconforming product may be:

- rejected, or
- accepted without rework or repair by concession, or
- re-graded for alternative use, or
- re-processed in accordance with product specific procedures.

4.13 Corrective and Preventive Action

4.13.1 General

MDS Nordion maintains a corporate Corrective Action Request (CAR) system managed and monitored by the Quality Assurance department. This system described in QAP AP-4, "Corrective Action Requests", is available and open for any employee to raise a CAR. The system for preventive action is defined in the QAP AP-28, "Preventive Action". Customer complaints in the Nuclear Medicine business unit are handled in accordance with 000007.SOP, "Customer Complaints".

4.13.2 Corrective Action

Each person receiving a Corrective Action Request (CAR) is responsible for undertaking an investigation to determine the root cause of the nonconformance. Responses to CARs are evaluated to ensure that the root cause of the nonconformance has been addressed.

CARs are monitored and followed up with recipients to ensure timely completion. When responses or actions are not timely, the issues are escalated to the cognizant management personnel for action.

Any changes to documented procedures that result from corrective and preventive action must be implemented and recorded. In order to close a CAR, the follow-up activity must confirm that the action taken has addressed the root cause of the nonconformance and that the solution was effective.

All production information for each lot or batch is reviewed by the Production Manager. For most products the batch records, containing both production and QC information is also reviewed and signed off by the Quality Control Manager. These reviews are to ensure compliance with requirements and to identify unfavourable trends to head off nonconformances. Any material nonconformances or procedural deviations are reviewed by the cognizant authorities, documented and dispositioned in accordance with 000024.SOP, "Handling of Nonconforming Material for Product and Related Material" and QAP AP-35, "Deviations from Approved Procedures" respectively. In addition to these immediate reviews, identification of root cause and action to prevent recurrence, each of these incidents is tabled and discussed at the Management Review Team Meeting.

4.13.3 Preventive Action

The Manager, Quality Assurance in conjunction with the MRT, establishes the Preventive Action Plan. Selected categories of quality records are reviewed to identify adverse trends and/or opportunities to prevent the occurrence of problems. Once identified, preventive actions are determined, responsibility is assigned, action is taken and resolution is confirmed.

The status of actions outlined by the Preventive Action Plan are reviewed and tracked by the MRT.

4.14 Handling, Storage, Packaging, Preservation and Delivery

Due to the nature of the Nuclear Medicine business unit processes and products, the methods and procedures that are used to handle, store, package and ship products are documented in local and product specific procedures (SOPs & PCRs), in post-production operations. Due to the short shelf-life of most of Nuclear Medicine products, storage is very short term and usually in the production facility dedicated to the product. These procedures were developed to prevent damage and/or deterioration of product and packaging.

Packaging materials are handled as controlled materials according to 000015.SOP, "Material and Component Control". All packaging is designed to protect the product from damage and to expose all handlers of the packages to as low a field of radiation as reasonably achievable. Again due to the nature of Nuclear Medicine's products, this packaging is designed to withstand "worst case scenarios", and therefore far exceeds what is normally experienced in the handling and delivery of the products.

4.15 Control of Quality Records

The identification of Quality Records, including minimum retention times and disposition requirements for the Nuclear Medicine business unit is in 000014.SOP, "Quality Records". When required, supplier quality records are also retained. All quality records must be legible and identifiable to the product involved.

Quality records are stored in readily retrievable format under conditions that will prevent loss, damage and or deterioration.

In the Nuclear Medicine business unit, Quality Records which demonstrate the effectiveness of the quality system will consist of at a minimum:

- Inspection Reports
- Test Data
- Qualification Reports
- Validation Reports
- Audit Reports

- Material Review Reports
- Calibration Data
- Management Reviews
- Training Records
- Corrective Action Request Files
- Batch or Device History Records
- Purchasing Data
- Certificates of Analysis
- Certificates of Compliance.

When required by contract, Certificates of Compliance or Analysis are supplied to customers. Quality records are also made available to customers, when required by contract, in the course of on site quality systems audits.

4.16 Quality Audits

MDS Nordion maintains a Corporate Quality Systems Audit program, administered by the Quality Assurance department, that includes the Nuclear Medicine business unit. This program is documented in QAP AP-06, "Quality Audits". Audits must be conducted by personnel who are independent of those who have direct responsibility for the activity being audited.

Within the Nuclear Medicine business unit, other audits are scheduled and conducted to complement the corporate audit schedule and as required, for new processes and/or in response to current needs.

Results of internal Quality Systems Audits are reported to senior management in the form of audit close out meetings and written reports. Audit results, Corrective Actions and follow-up are discussed at the Management Review Team meetings.

4.17 Training

Education and training requirements are identified for all production and quality control activities that could have an impact on quality. Generic training, such as Safety, WHMIS, Employee Indoctrination and Atomic Radiation Worker, for all personnel is identified in 000016.SOP, "Isotope Operations Training". Specific process training is identified in process specific documents. The cognizant management personnel in the functional groups (Safety, Production, Quality Assurance, Quality Control, Corporate Records and so on) are responsible to determine and record the training requirements for each of the activities for each of the positions in their jurisdiction.

Personnel performing these activities are selected, trained and evaluated accordingly. Records of these personnel's education and training is retained. The governing documents for these activities in the Nuclear Medicine business unit are 000016.SOP, "Isotope Operations Training" and 000011.SOP, "Recording and Tracing of Controlled Document Training".

The Manager, Quality Assurance is responsible for ensuring that the quality system training required for Nuclear Medicine personnel is performed. This will include, but necessarily limited to training on EN 46001, ISO 9001 and ISO 13485. Records of this quality systems training are maintained in Quality Assurance.

4.18 Servicing

The nature of the Nuclear Medicine business unit products does not lead to after sales service in any traditional sense. On occasion, technical trouble shooting and advice is provided to customers, primarily researchers working in new applications. Since these type of services are not contractual in nature, they are not considered part of the Quality System.

4.19 Statistical Techniques

It is the responsibility of the manager of each process, to identify the need for any statistical techniques required to establish, control and verify process capability. When a need is identified, the procedure for execution of the statistical technique is documented. These procedures define the work instructions for the measurement and tracking of efficiency indicators for a particular product or line of products.

4.20 Buildings, Facilities and Equipment

Buildings, facilities and equipment are designed and constructed in such a way as to facilitate the storage handling, manufacturing and cleaning processes. Lighting, heating, plumbing and ventilation systems are designed to meet the requirements set out for the processes involved. Maintenance and cleaning requirements are documented and records are kept of work completed.

The design and construction of a building for pharmaceutical and medical device production incorporates features which prevent hazards that might adversely affect the quality of the drug or medical device. These features provide suitable environmental conditions, promote good sanitary practices, permit adequate cleaning and sanitation, minimize migration of extraneous material, prevent access to insects and animals, and allow employees to fulfill their duties.

The equipment with which a lot or batch of a drug is produced is designed, constructed, maintained, operated and arranged in a manner that permits the effective cleaning of its surfaces, prevents the contamination of the drug or medical device, the addition of extraneous material to the drug or medical device, and permits it to function in accordance with its intended use.

Any drug or medical device that is intended to be sterile is produced in a separate and enclosed area, under the supervision of personnel trained in microbiology, and by a method scientifically proven to ensure sterility.

5. REFERENCED DOCUMENTATION

Corporate

- 07 - Quality Policy

Nuclear Medicine

- 000000.SOP - Protocol for Format and Control of Documents
- 000007.SOP - Customer Complaints
- 000011.SOP - Recording and Tracking of Controlled Document Training
- 000014.SOP - Quality Records
- 000015.SOP - Material and Component Control
- 000016.SOP - Isotope Operations Training
- 000017.SOP - Verification, Storage and Maintenance of Customer Supplied Product
- 000018.SOP - Contract Review
- 000019.SOP - Identification, Planning and Control of Production Processes to Meet Customer Requirements
- 000022.SOP - Identification and Traceability of Controlled Raw Materials, In-Process Product and Final Product
- 000023.SOP - Finished Product Release
- 000024.SOP - Handling of Nonconforming Materials
- 000033.SOP - Change Control Program
- 040701.SOP - Handling of Nonconforming Material for Product and Related Material
- 040801.SOP - Raw Materials - Receiving, Testing, Release and Archives
- 040853.SOP - In-Process Materials - Receiving, Testing, Release and Storage
- 400801.SOP - Final Product - Receiving, Testing, Release and Reserve Sample Retention

- 400802.SOP - Calibration and Maintenance of Analytical and Dispensing Instrumentation

Supply & Operations Services

- CP-6-Master - Instrument Maintenance and Calibration

Industrial Irradiation

- IN/OP 0053 Z000 - Responsibilities and Procedures for the Technical Publications Department
- IN/OP 0352 Z000 - Procedure for Design Control and Configuration Management

Procurement Services

- P-010 - Objectives/Purpose/Maintenance and Distribution of Procedures
- P-195 - Processing Purchase Requisitions
- P-210 - Order Writing - Inventory Purchases
- P-220 - Order Writing - Non-Inventory Requisition Purchase
- P-241 - Quality Program Orders

Quality Assurance

- QAP AP-04 - Corrective Action Requests
- QAP AP-06 - Quality Audits
- QAP AP-11 - Quality Assurance Document Control
- QAP AP-12 - Quality Planning
- QAP AP-15 - Management Review Team
- QAP AP-28 - Preventive Action
- QAP AP-30 - Corporate Document Control
- QAP AP-35 - Deviations from Approved Procedures
- QAP AP-44 - Information Technology Network Backup

Regulatory Affairs

- SERA-OP-001-015 - Review of External Regulatory Information
- SERA-OP-001-017 - Management of Transportation Certificates

Other

EN 46001	-	Application of EN ISO 9001 to the Manufacture of Medical Devices
ISO 9001	-	Quality Systems - Model for qualify Assurance in Design, Development, Production, Installation and Servicing
ISO 13485	-	Quality Systems - Medical Devices - Particular Requirements for the Application of ISO 9001

APPENDIX "A"

QUALITY SYSTEM DOCUMENTATION HIERARCHY

Corporate — **QUALITY POLICY**

Nuclear Medicine — **QUALITY MANUAL**

Product Quality Plans	**Mo-99**	**I-131**	**I-125**	**Xe-133**	**Y-90**	
	C-14	**Ni-63**	**Ir-192**	**Fe-55**	**Cl-36**	
	S-35	**Sr-82**	**I-125 CC49**	**TheraSphere**	**I-125 Sources**	**Ir-192 Sources**

Supporting Systems

DOCUMENT CONTROL
INSPECTION, MEASURING AND TEST EQUIPMENT
IDENTIFICATION & TRACEABILITY
QUALITY RECORDS
PROCESS CONTROL
CONTROL OF NONCONFORMANCES
QUALITY SYSTEMS AUDITS
CORRECTIVE ACTION
TRAINING

Standard Operating Procedures	**PRODUCTION**	**QUALITY CONTROL**
	PROCUREMENT SERVICES	**STORES**
	CALIBRATION	**QUALITY ASSURANCE**

APPENDIX "B"

NUCLEAR MEDICINE QUALITY ORGANIZATION