1. PURPOSE

The purpose of this document is to provide appropriate design, regulatory and performance requirements for the upgrade of the existing P2000 Production Facility and HVAC System, located in Building P2000 on the South African Nuclear Energy Corporation (NECSA) Complex [Elias Motsoaledi Street Extension (Church Street West), R104 Pelindaba, Brits Magisterial District, Madibeng Municipality, North-West Province, 0240] in compliance with ISO 14644, WHO, PIC/S and SAHPRA standards and guidelines.

ACTION	NAME & EXPERTISE	SIGNATURE	DATE
Originated	T Makate *Facility Review*		2026/03/19
Checked	M Shabalala *Production Review*		2026/03/19
Checked	G Thengwana *Safety Review*		2026/03/19
Checked	S van Niekerk *Maintenance Review*		2026/03/19
Checked	I Maledi *Quality Assurance Review*		2026/03/19
Checked	T More *Engineering Review*		2026/03/19
Checked	M van Vuuren *Engineering Review*		2026/03/19
Checked	K Molebatsi *Waste Control Review*		2026/03/20
Checked	T Ntuli *Maintenance Review*		2026/03/20
QA Approved	P Rametse *Quality Assurance Review*		2025/03/20
Approved	T Matshidiso *Regulatory Compliance Review*		2025/03/20
Approved	M Moloisi *Client Review*		2025/03/20
Approved	Vincent Legoabe *Design Review*		2025/03/20
		Implementation Date:	2025/04/03

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NAME	SIGNATURE	DATE

The URS is compiled to facilitate prospective service providers and/or design engineers in understanding the needs, identifying further requirements, and proposing a suitable design. Appropriate definition and application of these requirements will result in an operational facility in compliance with all user requirements as well as applicable regulatory requirements. The URS is not intended as an exclusive approach, the identification of omissions or alternative suggestions by prospective suppliers and/or design engineers are welcome.

The URS is compiled to facilitate prospective service providers and/or design engineers in understanding the needs, identifying further requirements, and proposing a suitable design. The URS will be used as input into the basis of design and as a point of reference throughout the validation life cycle of the laboratory i.e. Design specification, Quality Risk Management (QRM), and Commissioning and Qualification (C&Q) activities.

2. SCOPE

The scope of this URS is limited to the upgrade of the existing P2000 Production Facility and HVAC System located in Building P2000 on the NECSA Premises, and includes reference to the:

- Modification of the existing layout (incl. area classifications) to establish a Grade B environment in the Radiochemistry room (located in front of the synthesis and dispensing hot cells) and to improve the cascading of personnel into/from the Grade B area.
- Overall improvement/upgrade of the existing facility layout and material and personnel flow.
- Upgrade/Replacement of the existing HVAC system to provide clean and conditioned air to the areas.
- Improvement/upgrade of the facility surface finishes.

The upgrade of the Cyclotron technical area and hall is excluded from this URS and the upgrade project. The scope of the upgrade is provided in Appendix A.

The existing P2000 Production Facility and HVAC System are used to produce aseptically prepared Flourine-based radiopharmaceuticals. Due to the nature of the products being manufactured the premises, services, systems, equipment, and processes must comply to the principles and guidelines of current Good Manufacturing Practice (cGMP), as prescribed by the SA Guide for GMP.

This document specifies the requirements associated with the design, development, installation and qualification of the upgrade of the existing P2000 Production Facility and HVAC System, and all its associated systems and support services.

The URS details the following requirement types:

- Compliance Requirements
- Process Requirements – Capacity
- Process Requirements – Product Physical Properties
- Process Requirements – Critical Quality Attributes (CQAs) and Critical Process Parameters (CPPs)

- Automation and Records
- Design and Consideration
- Equipment
- Utilities and Supporting Systems
- Operations and Maintenance
- Constraints
- Life-cycle Requirements

Whilst every endeavour has been made to list most requirements, and it is recognized that the URS is not intended as an exclusive approach, the identification of omissions or additional cGMP and other related requirements by prospective service providers and/or design engineers are mandatory and remain the sole responsibility of the service providers. NTP has an expectation of a compliant facility from the service providers. Requirements such as environmental Acts are included in the requirements but may not be exclusive; the onus is on the supplier to comply with the laws of the Republic of South Africa, including municipal by-laws not outlined in this document.

An assessment shall be performed by the prospective service provider on the existing P2000 Production Facility and HVAC System to determine the scope of the upgrade required to align the production facility and HVAC system to this document.

3. REFERENCES

This document complies with the requirements of:

ISO 9001: 2015	:	Quality Management System – Requirements, Fifth edition, 2015.
ISO 14644-1:2015	:	Cleanrooms and Associated Control Environments, Part 1: Classification of Air Cleanliness by Particle Concentration
ISO14644-3:2019	:	Cleanrooms and Associated Control Environments, Part 3: Test Methods
ISO14644-4:2022	:	Cleanrooms and Associated Control Environments, Part 4: Design, Construction and Start-up.
ISPE Baseline Guide: C&Q	:	ISPE Baseline Guide: Commissioning and Qualification, Volume 5, 2nd Edition, 2019
ISPE Good Practice Guide: HVAC	:	ISPE Good Practice Guide, Heating Ventilation and Air Conditioning (HVAC), 2009
NTP-PRG-0300	:	Control of Documented Information and Forms
NTP-OTS-9002	:	Operating Technical Specification for the medical and industrial facility
NTP-SOP-6047	:	Procedure for the control of lockers at NTP facilities.
OSH Act 85 of 1993	:	Occupational Health and Safety Act
PE-009-17 (Part I)	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products Part I, August 2023.

PE-009-17 (Annexes) - Annex 1	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 1: Manufacture of Sterile Medicinal Products, August 2023.
PE-009-17 (Annexes) - Annex 3	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 3: Manufacture of Radiopharmaceuticals, August 2023.
PE-009-17 (Annexes) - Annex 15	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 15: Qualification and Validation, August 2023.
SAHPGL-INSP-02_v9	:	SAHPRA Guideline on Good Manufacturing Practice for Medicines, Version 9, August 2025
SANS 10400 XA:2021	:	The application of the National Building Regulations, Edition 2: November 2021

The following documents are referenced in this document:

Act 85 of 1993	:	The Occupational Health and Safety Act 85 of 1993
ISO14644-1:2015	:	Cleanrooms and Associated Control Environments, Part 1: Classification of Air Cleanliness by Particle Concentration
ISO14644-3:2019	:	Cleanrooms and Associated Control Environments, Part 3: Test Methods
ISO14644-4:2022	:	Cleanrooms and Associated Control Environments, Part 4: Design, Construction and Start-up.
ISO 17873-2004	:	Nuclear facilities — Criteria for the design and operation of ventilation systems for nuclear installations other than nuclear reactors
ISPE Baseline Guide	:	Commissioning and Qualification, Volume 5, 2nd Edition, 2019
ISPE Good Practice Guide	:	Heating Ventilation and Air Conditioning (HVAC), 2009
PE-009-17 (Part I)	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products Part I, August 2023.
PE-009-17 (Annexes) - Annex 1	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 1: Manufacture of Sterile Medicinal Products, August 2023.
PE-009-17 (Annexes) - Annex 3	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 3: Manufacture of Radiopharmaceuticals, August 2023.
PE-009-17 (Annexes) - Annex 15	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 15: Qualification and Validation, August 2023.
SAHPGL-INSP-02_v9	:	SAHPRA Guideline on Good Manufacturing Practice for Medicines, Version 9, August 2025
SANS 10114-1: 2020	:	Interior Lighting Part 1, Artificial Lighting of Interiors, 4th Ed.
SANS 10400	:	Application of the National Building Regulations
SANS 10142	:	The Wiring of Premises
SHEQ-INS-0234	:	NECSA QMS Requirement for External Design Organisations
SHEQ-INS-1110	:	Housekeeping and demarcation
SHEQ-INS-1120	:	Lighting (Natural and Artificial)

SHEQ-INS-7010	:	Zoning of facilities with hazardous chemical substances
SHEQ-INS-7030	:	Surveillance programme for workplaces containing hazardous chemical substances
SHEQ-INS-7132	:	Necsa Ventilation Design Specification
SHEQ-INS-7140	:	Management of hazardous chemical waste
SHEQ-INS-8030	:	System for the classification and demarcation of radiological areas
SHEQ-INS-8050	:	Radiological surveillance programme for workplaces
SHEQ-INS-8180	:	ALARA programme
SHEQ-INS-8310	:	Requirements in respect of ventilation systems for nuclear facilities
SHEQ-INS-8920	:	Access Control to NECSA Sites and Its Facilities
WHO Technical Report Series (TRS) No. 957, Annex 3	:	WHO Good Manufacturing Practices for Pharmaceutical Products Containing Hazardous Substances, 2010
WHO Technical Report Series (TRS) No. 1010, Annex 8	:	Guidelines on Heating, Ventilation and Air-Conditioning Systems for Non-sterile Pharmaceutical Products, 2018
WHO Technical Report Series (TRS) No. 1019, Annex 2	:	Guidelines on Heating, Ventilation and Air-Conditioning Systems for Non-sterile Pharmaceutical Products, Part 2: Interpretation of Guidelines on Heating, Ventilation and Air-conditioning Systems for Non-sterile Pharmaceutical Products, 2019
WHO Technical Report Series (TRS) No. 1019, Annex 3	:	Good Manufacturing Practices: Guidelines on Validation, 2019
WHO Technical Report Series (TRS) No. 1025, Annex 2	:	International Atomic Energy Agency and World Health Organization Guideline on Good Manufacturing Practices for Radiopharmaceutical Products.
WHO Technical Report Series (TRS) No. 1044, Annex 2	:	WHO Good Manufacturing Practices for Sterile Pharmaceutical Products, 2022

4. ABBREVIATIONS AND DEFINITIONS

4.1. The following abbreviations are used in this document:

AHU	:	Air Handling Unit
ACPH	:	Air Changes Per Hour
BMS	:	Building Management System
CCTV	:	Closed-circuit Television
cGMP	:	Current Good Manufacturing Practices
CNC	:	Controlled non-classified
CPP	:	Critical Process Parameter
CQA	:	Critical Quality Attribute
C&Q	:	Commissioning and Qualification
DQ	:	Design Qualification
GDocP	:	Good Documentation Practice
GEP	:	Good Engineering Practice
HCS	:	Hazardous Chemical Substances
HSE	:	Health, Safety and Environment
HVAC	:	Heating Ventilation and Air Conditioning

ICT	:	Information and Communication Technology
IQ	:	Installation Qualification
ISO	:	International Organization for Standardization
ISPE	:	International Society of Pharmaceutical Engineers
LED	:	Light-Emitting Diode
MAL	:	Material Airlock
µm	:	Micrometre
NECSA	:	Nuclear Energy Corporation of South Africa
OHSA	:	Occupational Health and Safety Act
OQ	:	Operational Qualification
OTS	:	Operating Technical Specification
Pa	:	Pascal
PA	:	Public Address
PAL	:	Personnel Airlock
PIC/S	:	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PPE	:	Personal Protective Equipment
PTH	:	Pass-through Hatch
PQ	:	Performance Qualification
PVC	:	Polyvinyl Chloride
QA	:	Quality Assurance
QC	:	Quality Control
QRM	:	Quality Risk Management
QMS	:	Quality Management System
RH	:	Relative Humidity
RSP	:	Responsible Pharmacist
RPH	:	Radiopharmaceuticals
SANS	:	South African National Standards
SME/s	:	Subject Matter Expert/s
SAHPRA	:	South African Health Product Regulatory Authority
SANS	:	South African National Standards
SPE	:	Specification
URS	:	User Requirement Specification
WHO	:	World Health Organization

4.2. The following definitions are provided to ensure a uniform understanding of this document:

Acceptance Criteria	:	Numerical limits, ranges or other suitable measures for acceptance of test results.
Action Limit	:	The action limit is reached when the acceptance criteria of a critical parameter has been exceeded. Results outside these limits will require specified action and investigation.
Air Changes per Hour (ACPH)	:	The flow rate of air supplied to a room, in m^3/hour, divided by the room volume, in m^3.
Air-handling Unit (AHU)	:	The AHU serves to condition and filter the air, as well as provide the required airflow within a facility.

Airlock	:	An enclosed space with two or more doors, and which is interposed between two or more rooms, e.g. of differing class of cleanliness, for the purpose of controlling the airflow between those rooms when they need to be entered. An airlock is designed for and used by either people or goods.
Alert Limit	:	The alert limit is reached when the normal operating range of a critical parameter has been exceeded, indicating that corrective measures may need to be taken to prevent the action limit being reached.
At-rest	:	Condition where the installation is complete, with equipment installed and operating in a manner agreed upon by the customer and supplier, but with no personnel present.
Aseptic	:	Aseptic preparation/processing is the handling of sterile product, containers and/or devices in a controlled environment in which the air supply, materials and personnel are regulated to prevent microbial, endotoxin/pyrogen and particle contamination.
Building Management System	:	A computerized system that controls, monitors, and optimizes environmental conditions, through functions and facilities such as heating, air-conditioning, lighting, and security.
Classified Space	:	An area with airborne viable and non-viable particle contamination controlled within preset limits. A cleanroom designated by ISO 14644-1 volume units (“in operation”) or PIC/S Annex 1 Grade A, B, C, D (“at-rest” and “in operation”). A classified space implies ongoing environmental monitoring
Cleanroom	:	An area with defined environmental control of particulate and microbial contamination constructed and used in such a way as to reduce the introduction, generation and retention of contaminants within the area.
Cleanroom Classification	:	A method of assessing the level of air cleanliness against a specification for a cleanroom or clean air equipment by measuring the total particle concentration.
Commissioning	:	A well planned, documented, and managed engineering approach to the start-up and turnover of facilities, systems, and equipment to the end user, that results in a safe and functional environment that meets established design requirements and stakeholder expectations.
Conditioned Area	:	An area where temperature and humidity are controlled and monitored.
Contamination	:	The undesired introduction of impurities of a chemical or microbial nature, or of foreign matter, into or onto a starting material or intermediate, during production, sampling, packaging or repackaging, storage or transport.
Controlled Not Classified (CNC)	:	A cGMP manufacturing area designed to produce a consistent and controlled environment, but not necessarily monitored to a given environmental classification
Controlled Area (Classified Area)	:	An area within the facility in which specific procedures and environmental parameters, including viable and nonviable particles, are defined, controlled and monitored to prevent degradation, contamination or cross-contamination of the product.
Critical Process Parameter (CPP) or Component	:	A processing parameter (such as temperature or relative humidity) that affects the quality of a product, or a component that may have a direct impact on the quality of the product.

Critical Quality Attribute (CQA)	:	A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range or distribution to ensure the desired product quality.
Cross-contamination	:	Contamination of a starting material, intermediate product or finished product with another starting material or product during production, testing or storage.
Design Qualification (DQ)	:	Verification that the proposed design of the facilities, equipment, or systems is suitable for the intended purpose. DQ is a documented collection of activities that define the functional and operational specifications of the facilities, equipment, or system.
Differential Pressure	:	The difference in pressure between two points, such as the pressure difference between an enclosed space and an independent reference point, or the pressure difference between two enclosed spaces.
Direct Impact System	:	A system that is expected to have a direct impact on product quality. These systems are designed and commissioned in line with good engineering practice and, in addition, are subject to qualification practices.
Extract Air	:	Air leaving a space, which could be either return air or exhaust air. Return air refers to air that is returned to the air-handling unit and exhaust air is air that is vented to the atmosphere.
GMP Classified and Controlled Area	:	A cleanroom which is classified space and controlled area as per PIC/S Annex 1 requirements (e.g., viables, non-viables, temperature, humidity, pressure)
Good Engineering Practice	:	Established engineering methods and standards that are applied throughout the project life cycle to deliver appropriate, cost-effective solutions.
Grade A	:	A cGMP Grade A environment is equivalent to an ISO14644-1 Class 5, for both at rest and in operation.
Grade B	:	A cGMP Grade B cleanroom, in operation, is equivalent to an ISO14644-1 Class 7 environment, while at rest, it corresponds to an ISO14644-1 Class 5 cleanroom.
Grade C	:	cGMP Grade C cleanroom spaces are for performing less stringent steps of sterile product manufacturing. The airborne particle classification equivalent for Grade C (at rest and in operation) is ISO14644-1 Class 7 and ISO14644-1 Class 8, respectively.
Grade D	:	For cGMP Grade D, the airborne particle classification is the equivalent of an ISO14644-1 Class 8 cleanroom at rest.
Installation Qualification (IQ)	:	The documented verification that the facilities, systems and equipment, as installed or modified, comply with the approved design and the manufacturer's recommendations.
Normal Operating Range	:	The range that the manufacturer selects as the acceptable values for a parameter during normal operations. This range must be within the operating range.
Operating Limits	:	The minimum and/or maximum values that will ensure that product and safety requirements are met.
Operating Range	:	Operating range is the range of validated critical parameters within which acceptable products can be manufactured.

Operational Condition ("In operation")	:	This condition relates to carrying out room classification tests with the normal production process with equipment in operation and the normal staff present in the specific room.
Operational Qualification (OQ)	:	Verification that the equipment or systems, as installed or modified, perform as intended throughout the anticipated operating ranges.
Performance Qualification (PQ)	:	Verification that the equipment and ancillary systems, as connected, perform effectively and reproducibly based on the approved process method and specifications.
Pressure Cascade	:	Process whereby air flows from one area, which is maintained at a higher pressure, to another area maintained at a lower pressure.
Qualification	:	Action of proving that any equipment works correctly and leads to the expected results. The word validation is sometimes widened to incorporate the concept of qualification.
Recirculation HVAC System	:	A recirculation HVAC system is a design where filtered and conditioned air is continuously recirculated back through the system. The room supply air is made up of a portion of treated outside air mixed with some of the air returned from the room. An equivalent portion of the air supplied to the room is either discarded or lost through leakage to the adjacent area, due to local area pressurization.
Recovery	:	Room recovery or clean-up tests are performed to determine whether the installation is capable of returning to a specified cleanliness level within a finite time, after being exposed briefly to a source of airborne particulate challenge.
Sterile Product	:	A sterile product is essentially free from living microbes and chemical or physical contamination to the point at which it poses no present risk to the patient.
Subject Matter Expert/s	:	This is a qualified and knowledgeable person that is familiar with the equipment/facilities that are being discussed or constructed. This may be a team of varying expertise that are combined to undertake and execute a task.
Uncontrolled (UC) Area	:	Areas where the HVAC systems may be present, but no claim is made or qualified for the specific control of particulate, temperature or humidity. These areas are sometimes referred to as "general" or "comfort Controlled" area within facilities such as offices and technical spaces.
Facility Upgrade	:	The planned process of improving, modifying, or modernizing an existing pharmaceutical production facility so that it meets current regulatory requirements (e.g. current Good Manufacturing Practices (GMP) etc.), operational needs, and technological standards.
Validation	:	Documented series of actions that prove that any procedure, process, equipment, material, activity or system performs its intended functions adequately and consistently, and lead to the expected results of uniform batches that meet the required specifications and quality attributes.

5. GENERAL

5.1. Background

NTP Radioisotopes SOC Ltd. (NTP), a subsidiary of the South African Nuclear Energy Corporation SOC Ltd. (NECSA), is a leading global producer and supplier of nuclear medicine and radiation-based products and services.

The P2000 Production Facility located in Building P2000, on the Pelindaba West site, is used for the aseptic manufacturing of fluorine-based radioisotopes. Building P2000 was built in 1971 and consists of two independent facilities housed in the same building. The northern part of the building houses the Package Irradiation Facility (Co-60 sterilisation facility), and the southern side is the P2000 Production Facility, housing the cyclotron, the production processes together with its support functions. There is no direct internal access from one facility to the other. Opposite the road (to the South) is the Necsa Visitors Centre building and to the western side Entrance Gate 1 of Necsa. The total area of the P2000 Production Facility is approximately 255 m^2.

The P2000 Production Facility is a single storey concrete building and consists of the following areas:

- Cyclotron Technical room, with a Controlled Not Classified (CNC) classification
- Cyclotron Hall, with a Controlled Not Classified (CNC) classification
- Radiochemistry Room (i.e. Hot Cell Operation Area), with a Grade C “at-rest” classification
- 2000 Change Room, with a Grade C “at-rest” classification
- Radiological Change room, with a Controlled Not Classified (CNC) classification
- Dispatch, with a Controlled Not Classified (CNC) classification
- Kitchenette, uncontrolled area
- Toilet, uncontrolled area
- AHU area, with a Controlled Not Classified (CNC) classification

The existing layout and area classifications of the P2000 Production Facility is provided in Appendix A and B respectively.

The synthesis and dispensing hot cells are located in the Radiochemistry room and consists of Grade A area classifications in the “at-rest” state respectively. Both the synthesis and dispensing hot cells are accessed from the front of the hot cells which is located in the Grade C Radiochemistry room, which is in direct violation of cGMP requirements.

The API manufacturing occurs in the Cyclotron Hall, after which the API is transferred from the Cyclotron through tubing into the Grade A synthesis hot cell located in the Radiochemistry room. The radiochemistry room is the area that is covered in the scope.

The manufacturing of the final product is performed via an automated manufacturing process in the Grade A synthesis hot cell. The final product is then transferred to the Grade A dispensing hot cell for

dispensing and discharge into secondary packaging. The overall process flow diagram is provided in Appendix C.

The purpose of this upgrade is to improve, modify, and modernize the P2000 Production Facility (incl. layout, personnel and material flow, area classifications, surface finishes etc.) so that it meets current regulatory requirements (e.g. current Good Manufacturing Practices (GMP) etc.), operational needs, and technological standards. The scope of the upgrade is indicated in Appendix A.

The facility upgrade requires modification of the existing layout (incl. area classifications) to establish a Grade B environment in the Radiochemistry room (located in front of the synthesis and dispensing hot cells) and to improve the cascading of personnel into/from the Grade B area as illustrated in Appendix D (included for illustration purposes only).

The pressure cascade of the existing Radiochemistry Room has been designed at a negative pressure, with controlled pressure differentials between interconnected rooms to control airflow and prevent radiological contamination from uncontrolled areas. The room pressures are monitored by locally installed and calibrated magnehelic pressure gauges and the Building Management System (BMS).

5.2. System Classification and Risk Assessment

The P2000 Production Facility and related HVAC system have been classified as Direct Impact (quality critical) systems, as per the ISPE Commissioning and Qualification Guideline, Vol 5, 2nd Ed, and therefore require commissioning and qualification. Qualification of the modifications of P2000 Production Facility and HVAC system shall include Design, Installation, Operational and Performance Qualification as minimum testing requirements.

The scope of the qualification shall be determined through a risk-based approach. The level of testing required for each requirement shall be commensurate with the risk to product quality and/or other risks as deemed relevant if the requirement is not implemented or implemented incorrectly.

6. RESPONSIBILITIES

6.1. System Owner/Client:

6.1.1. It is the responsibility of the system owner to create and maintain the user specification requirement and ensure that the requirements are clearly stipulated to ensure that it offers sufficient information for proposed outcomes.

6.2. Subject Matter Expert/s (SME/s):

6.2.1. It is the responsibility of the SME to ensure that this document gives sufficient content to the task to allow a clear understanding to be imparted to the prospective service provider without limiting the scope and to allow for newer more advanced technologies.

6.3. Compliance Expert/s:

6.3.1. It is the responsibility of the compliance expert/s to ensure that sufficient consideration is given to compliance of the task to quality, safety and regulatory standards, and the validation information furnished meets requirements for a compliant facility/equipment.

6.4. Prospective Service Provider:

6.4.1. It is the responsibility of the prospective service provider to derive sufficient information from the URS to determine and ensure that all the legal, compliance, safety and regulatory requirements are met in the proposed quote/scope of work supplied.

6.4.2. It is the responsibility of the prospective service provider to request further information where unclear to ensure that the prospective quote gives a final determination that is final in executing the task.

6.4.3. QRM analyses for design decisions.

7. PROCESS

The user requirements for the upgrade of the existing P2000 Production Facility and HVAC system are defined in the tables below.

Each table contains user requirements for a functional area or discipline such as Process, Design and Consideration, Operations and Maintenance, etc.
The tables are structured as follows:

- ***ID Number:*** A unique requirement identification number
- ***Requirement:*** A specific and verifiable requirement for the system/facility i.e. a condition that must be satisfied for the system/facility to meet its intended purpose.

7.1. Compliance Requirements

The P2000 Production Facility and HVAC System shall be upgraded, commissioned, and qualified in accordance with Good Engineering Practice (GEP), current Good Manufacturing Practice (cGMP), sound radiological design requirements and key focus area stipulated herein:

ID No.	Description
7.1.1.	Act 85 of 1993: The Occupational Health and Safety Act 85 of 1993
7.1.2.	ISO14644-1:2015 - Cleanrooms and Associated Control Environments, Part 1: Classification of Air Cleanliness by Particle Concentration
7.1.3.	ISO14644-3:2019 - Cleanrooms and Associated Control Environments, Part 3: Test Methods
7.1.4.	ISO14644-4:2022 - Cleanrooms and Associated Control Environments, Part 4: Design, Construction and Start-up.

ID No.	Description
7.1.5.	ISO 17873-2004: Nuclear facilities — Criteria for the design and operation of ventilation systems for nuclear installations other than nuclear reactors
7.1.6.	ISPE Baseline Guide: Commissioning and Qualification, Volume 5, 2nd Edition, 2019
7.1.7.	ISPE Good Practice Guide, Heating Ventilation and Air Conditioning (HVAC), 2009
7.1.8.	PE-009-17 (Part I): PIC/S Guide to Good Manufacturing Practice for Medicinal Products Part I, August 2023.
7.1.9.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 1: Manufacture of Sterile Medicinal Products, August 2023.
7.1.10.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 3: Manufacture of Radiopharmaceuticals, August 2023
7.1.11.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 15: Qualification and Validation, August 2023.
7.1.12.	SAHPGL-INSP-02_v9: SAHPRA Guideline on Good Manufacturing Practice for Medicines, Version 9, August 2025
7.1.13.	SANS 10114-1: 2020: Interior Lighting Part 1: Artificial Lighting of Interiors, 4th Ed.
7.1.14.	SANS 10400: Application of the National Building Regulations
7.1.15.	SANS 10142: The Wiring of Premises
7.1.16.	SHEQ-INS-0234: NECSA QMS Requirement for External Design Organisations
7.1.17.	SHEQ-INS-1110: Housekeeping and Demarcation
7.1.18.	SHEQ-INS-1120: Lighting (Natural and Artificial)
7.1.19.	SHEQ-INS-7010: Zoning of facilities with hazardous chemical substances
7.1.20.	SHEQ-INS-7030: Surveillance programme for workplaces containing hazardous chemical substances
7.1.21.	SHEQ-INS-7132: Necsa Ventilation Design Specification
7.1.22.	SHEQ-INS-7140: Management of hazardous chemical waste
7.1.23.	SHEQ-INS-8030: System for the classification and demarcation of radiological areas
7.1.24.	SHEQ-INS-8050: Radiological surveillance programme for workplaces
7.1.25.	SHEQ-INS-8180: ALARA programme
7.1.26.	SHEQ-INS-8310: Requirements in respect of ventilation systems for nuclear facilities
7.1.27.	WHO Technical Report Series (TRS) No. 957, Annex 3: WHO Good Manufacturing Practices for Pharmaceutical Products Containing Hazardous Substances, 2010.
7.1.28.	WHO Technical Report Series (TRS) No. 1010, Annex 8, Guidelines on Heating, Ventilation and Air-Conditioning Systems for Non-sterile Pharmaceutical Products, 2018
7.1.29.	WHO Technical Report Series (TRS) No. 1019, Annex 2, Guidelines on Heating, Ventilation and Air-Conditioning Systems for Non-sterile Pharmaceutical Products, Part 2: Interpretation of Guidelines on Heating, Ventilation and Air-conditioning Systems for Non-sterile Pharmaceutical Products, 2019
7.1.30.	WHO Technical Report Series (TRS) No. 1019, Annex 3, Good Manufacturing Practices: Guidelines on Validation, 2019

ID No.	Description
7.1.31.	WHO Technical Report Series (TRS) No. 1025, Annex 2: International Atomic Energy Agency and World Health Organization Guideline on Good Manufacturing Practices for Radiopharmaceutical Products.
7.1.32.	WHO Technical Report Series (TRS) No. 1044, Annex 2, WHO Good Manufacturing Practices for Sterile Pharmaceutical Products, 2022

7.2. Process Requirements – Capacity

ID No.	Requirement
General	
7.2.1.	The upgraded P2000 Production Facility layout shall include the following areas as a minimum: • Preparation Area • Radiochemistry Room (i.e. Hot Cell Operation Area) • Decontamination and Clearance Area • Packaging and Dispatch Area • Street Clothes Change Rooms • Change Rooms (GMP [Grade D, C and B] and Radiological) • Emergency Shower Area • Material Transfer Systems
7.2.2.	Appropriate storage cabinets must be provided in the areas for storage of small quantities of chemicals, flammable solvents, and other consumables that are currently in use.
7.2.3.	Sufficient bench space shall be provided in all areas to place bench-top equipment and performing the required activities.
7.2.4.	Adequate and designated storage of hazardous chemical substances (HCS) and flammables shall be provided, demarcated and/or barricaded in all areas they are used/stored in.
7.2.5.	There shall be adequate space and access for any necessary safety equipment, such as isolation switches, fire extinguishers and safety showers. First-aid facilities shall be readily accessible and suitably equipped/stocked.
Preparation Area	
7.2.6.	The Preparation Area shall provide adequate space for the following operations and processes: • Keep stored incoming or outgoing consumables and packaging materials segregated. • Safety equipment storage and allow sufficient space for personnel movements. • Solid waste storage and segregation during production activities.
7.2.7.	The Preparation Area shall allow sufficient space to be equipped with a GMP compliant conveyor or roller system, to enable the safe and ergonomic handling of the lead pots. The installation of the conveyor/roller system shall be performed by NTP, however, adequate space allowance for this installation shall be provided for in the facility layout design.
Radiochemistry Room (i.e. Hot Cell Operation Area)	

ID No.	Requirement
7.2.8.	The Radiochemistry Room (i.e. Hot Cell Operation Area) shall provide adequate space for following operations and processes: • Performing the preparation activities within the hot cells and primary control interface (incl. manipulations) with the hot cells. • Removal and replacement of the hot cell manipulators. • Administrative activities (lab bench etc.)
7.2.9.	The maintenance area behind the hot cells shall be demarcated and accessible for maintenance purposes.
Decontamination and Clearance Area	
7.2.10.	The Decontamination and Clearance Area shall provide adequate space for following operations and processes: • Contamination monitoring of radioactive materials and containers • Decontamination of radioactive materials and containers
7.2.11.	The Decontamination and Clearance area shall be equipped with a GMP compliant conveyor or roller system to enable the safe and ergonomic handling of the radioactive materials and containers. The installation of the conveyor/roller system shall be performed by NTP, however, adequate space allowance for this installation shall be provided for in the facility layout design.
Packaging and Dispatch Area	
7.2.12.	The Packaging and Dispatch Area shall provide adequate space for following operations and processes: • Packaging of final product into final packaging containers. • Dispatch of final product. • Storage of packaging materials.
Primary Change Room	
7.2.13.	The Primary change room is dedicated to removal of street clothes and shall provide adequate space for the changing of personnel from street clothes into undergarments. A maximum of 1 person will occupy the change room at any given time.
7.2.14.	Adequate storage facilities shall be provided in the personnel change rooms for the storage of street clothes, and protective/cleanroom clothing and shoes.
Change Rooms (GMP [Grade D, C and B] and Radiological)	
7.2.15.	The Change Rooms shall provide adequate space for the donning of cleanroom clothing. A maximum of 1 person will occupy any change room at any given time.
7.2.16.	Adequate storage facilities shall be provided in the change rooms for the storage of protective/cleanroom clothing and shoes.

7.3. Process Requirements – Product Physical Properties

ID No.	Requirement
7.3.1.	The F-18 FDG has the following characteristics: • Radioactive Fluorine-18, plus either a PSMA or Glucose ligand.

ID No.	Requirement
	• Time-sensitive release/QC constraints for short half-life products and the integration of radiological safety with asepsis should be acknowledged, distinguishing features of radiopharmaceutical manufacturing. • Sterile radiopharmaceutical injectable • Aseptic preparation with terminal sterilization via filtration

7.4. Process Requirements – Critical Quality Attributes (CQA's) and Critical Process Parameters (CPP's)

ID No.	Requirement
7.4.1.	The temperature in the facility shall be controlled, continually maintained and monitored between 22 °C ± 3 °C (range: 19 to 25 °C).
7.4.2.	Relative humidity in the following areas shall be controlled, continually maintained and monitored between 30 – 60 % RH.
7.4.3.	The critical processing areas shall consist of the following air cleanliness classifications in the "at-rest" state: • Preparation Area: GMP Grade C [ISO 14644 Class 7] • Radiochemistry Room (i.e. Hot Cell Operation Area): GMP Grade B [ISO 14644 Class 5] • The air cleanliness of all other areas in the "at-rest" state shall be determined based on the facility layout, ensuring correct GMP area classification and proper cascade sequence.
7.4.4.	The GMP classified areas shall comply to the requirements of PIC/S Annex 1, par. 4.27 [Table 1] (total particle concentration) and 4.31 [Table 2] (microbial contamination levels) in the "at-rest" and "in operation" occupancy states, to ensure that the required environmental cleanliness level is achieved and maintained.
7.4.5.	cGMP classified areas shall be classified for total particle concentration in accordance with ISO 14644 Part 1 in the "at rest" and "in operation" states.
7.4.6.	The maximum leakage / penetration through HEPA filter surface, seals, and framework during filter integrity testing shall comply to the acceptance criteria specified in ISO 14644 Part 3.
7.4.7.	The air change rate per hour (ACPH) of each cGMP classified area shall be adequate to provide a "clean up" period of less than 20 minutes (guidance value) from the "in operation" to the "at rest" state as per PIC/S Annex 1, par. 4.29iii.
7.4.8.	The pressure cascade for the facility shall comply with both GMP and radiological requirements to minimize the risk of product contamination and to protect personnel from the risks of radiological material exposure. Appropriate controls should be put in place to promote the containment of radiological material and radioactivate gases and vapours. The design of the pressure cascade shall be based on scientific justification and shall be a rational design.
7.4.9.	The limits for the pressure differential between adjacent areas shall be of sufficient magnitude to prevent an overlap and thus reverse flow when tolerances are at opposite extremities but shall not be so high as to create turbulence problems.

ID No.	Requirement
7.4.10.	Adjacent rooms of different GMP classifications shall have air pressure differentials of at least 10 Pa as per PIC/S Annex 1, par. 4.14.
7.4.11.	The radiological areas shall comply with the area requirements specified in SHEQ-INS-8030 and ISO 17873

7.5. Automation and Records

Not applicable to this User Requirement Specification. The automation and records requirements for the equipment and utilities and support system will be included the respective requirements document.

7.6. Design and Consideration

ID No.	Requirement
General	
7.6.1.	The facility layout shall ensure effective and logical material and personnel flow, to avoid cross flows and minimize any risk of error, mix-up and contamination of the materials, products, and adjacent areas.
7.6.2.	The facility layout shall separate material and personnel flows as far as possible.
7.6.3.	Facility layout shall allow for the safe and easy removal and storage of the solid and liquid waste.
7.6.4.	Transfer of materials between different area classifications shall be via appropriate actively ventilated transfer chambers (pass through hatches) or Material Airlocks (MAL).
7.6.5.	The transfer of materials, equipment, and components into the critical zones (i.e. Grade A and B areas) shall be carried out via a unidirectional process.
7.6.6.	Facility design shall prevent the entry and accumulation of dust and other airborne materials, and the entry of insects, birds, rodents, vermin and other animals.
7.6.7.	Equipment, laboratory furniture, containers, personnel and other related components shall be appropriately located or placed in areas so as not to obstruct airflow and the effectiveness of the HVAC system.
7.6.8.	Entry of unauthorised personnel shall be prohibited.
7.6.9.	Areas for the handling of radioactive materials shall be appropriately designed. Consideration shall be given to radiation protection, ALARA compliance, a high level of cleanliness and the appropriate controls to minimize possible microbial contamination.
7.6.10.	Actively ventilated change rooms shall be provided for movement of personnel between different GMP and radiological area classifications.
Surface Finishes	
7.6.11.	All interior and/or exposed surfaces/finishes (incl. walls, floors, ceilings, furniture and chairs) in GMP cleanrooms, critical zones and radiological areas shall be smooth, impermeable, non-porous, unbroken, and free from open joints to minimize shedding or accumulation of particles, micro-organisms or radiological contamination on the surfaces.

ID No.	Requirement
7.6.12.	All interior surfaces/finishes (incl. walls, floors, ceilings, furniture and chairs) shall be designed to reduce accumulation of dust and dirt and allow effective and easy cleaning and disinfection. There shall be no recesses that are difficult to clean effectively, therefore projecting ledges, shelves and cupboards shall be kept to a minimum.
7.6.13.	Crevices shall be avoided where possible. Alternatively, they shall be sealed.
7.6.14.	Wood or wood-based material shall not be used (forbidden) as a material of construction or support for equipment or materials in cleanrooms and critical zones (GMP Grade D and up). Stainless Steel is the preferred material of construction.
7.6.15.	Materials used in cleanrooms and radiological areas, both in the construction of the room and for items used within the room (incl. furniture and chairs), shall minimize generation of particles, and permit the repeated application of cleaning, disinfectant, and sporicidal agents.
7.6.16.	All exposed surfaces/finishes (incl. walls, floors, ceilings, furniture and chairs) shall be resistant to cleaning, disinfectant, and sporicidal agents and process materials (chemicals and solvents).
7.6.17.	All exposed surfaces/finishes shall be able to withstand potential impact by trolleys or other equipment; alternatively, floor mounted bump rails / wall protection (kick plates) shall be considered.
7.6.18.	No finishes (incl. walls, floors, ceilings, furniture and chairs) shall present as a source of contamination and finishes shall be durable and not degrade over time.
7.6.19.	Penetration through wall, floors or ceiling into the room space shall be sealed with a suitable sealant to prevent contamination between areas and the introduction of dust and dirt.
7.6.20.	The facility shall be a well-sealed structure with no air leakage through ceilings, cracks or service areas.
Ceilings and Walls	
7.6.21.	Ceilings and walls shall be designed and sealed to prevent contamination from above and the adjacent areas.
7.6.22.	Walls and ceilings shall be of modular sandwich panel type construction with a good aesthetic appearance.
7.6.23.	Cleanroom panel fill material shall be constructed of non-combustible material.
7.6.24.	All wall to floor, ceiling to wall and wall to wall junctions (incl. between panels) shall be suitably coved and sealed.
Doors	
7.6.25.	Doors shall be designed to avoid recesses that cannot be cleaned. Sliding doors are not acceptable.
7.6.26.	Door frames shall be constructed from a durable material with a good aesthetic appearance. Sharp edges shall be avoided.
7.6.27.	All doors shall be fitted with flush mounted viewing panels.
7.6.28.	Self-closing mechanisms shall be fitted on all doors. Door closers shall be selected with minimal ledges and no uncleanable crevices or ledges.

ID No.	Requirement
7.6.29.	Doors shall be designed to open to the high-pressure side to assist in keeping doors closed, unless the door is deemed an emergency door, in which case the door will open in line with the exit route.
Windows	
7.6.30.	Architectural design to allow for an adequate number of windows to ensure optimal visibility into and within the facility. Windows opening to the exterior of the building are not permitted.
7.6.31.	Windows are to be flush and sealed with the door surfaces.
Floors	
7.6.32.	Floor surfaces shall be smooth, cleanable, non-porous and chemical resistant. Any joints or seams where microbial growth or accumulation of radiological contamination may occur shall be fully sealed. Acceptable material is epoxy coatings, polyurethane, or Vinyl flooring system.
7.6.33.	Floor surfaces shall be flush with the coving edge if the floor type is a compound and shall continue a minimum of 5 cm above the floor level up the walls if it is a vinyl finish.
7.6.34.	Floor surfaces shall be slip-proof.
Sinks and Drains	
7.6.35.	Sinks and drains (incl. floor drains) are not permitted in GMP Grade A and B “at-rest” [ISO 14644 Class 5] areas.
7.6.36.	Sinks and drains in GMP Grade C and D “at-rest” [ISO 14644 Class 7 and 8] areas shall be fitted with easily cleanable traps and air-breaks between the equipment/sink and the drains to prevent back flow.
7.6.37.	Sinks shall be made of a durable impervious corrosion resistant material, without overflow and be adequately spaced away from walls to avoid uncleanable joints and crevices.
7.6.38.	Floor drains in GMP and radiological areas shall be fitted with traps or water seals designed to prevent back flow and should be flush sealed with the floor.
7.6.39.	Sinks and drains shall be acid, solvent and stain resistant.
Pipe Work, Light Fittings, Ventilation Points and Other Services	
7.6.40.	Pipe work, light fittings, ventilation points and other services shall create minimal recesses that may allow accumulation of dust and dirt and shall be easy to clean.
7.6.41.	Pipe work, light fittings, ventilation points and other services shall be fully sealed against the ceiling panels to ensure an airtight fitting to prevent air leakage and possible ingress of dirt and dust.
7.6.42.	Pipe work, light fittings, ventilation points and other services shall be designed and positioned so that they allow effective cleaning and disinfection. Pipework, ducting and services shall be accessible from outside production areas, where possible, to reduce the risk of contamination.
7.6.43.	Exposed piping, tubing and cable runs shall be minimized in the cleanrooms.
7.6.44.	Power take-off points, data access point, taps and connections shall be designed and installed to facilitate regular cleaning, and to avoid the build-up of contamination in or behind blanking covers.

ID No.	Requirement
7.6.45.	Pipe work, light fittings, ventilation points and other services shall be labelled with name of service as well as flow direction where appropriate.
7.6.46.	Pipes shall be adequately sloped for drainage and constructed without 'dead-legs'.
Personnel Change Rooms (GMP [Grade D, C and B] and Radiological)	
7.6.47.	The GMP area classification of the change room, in the "at rest" state, shall be of the same cleanliness grade (viable and total particle) as the cleanroom into which it leads (highest classification).
7.6.48.	Change rooms shall be designed as airlocks and provide physical separation of the different stages of changing to minimise microbial and particulate contamination of operators and protective clothing.
7.6.49.	Separate change rooms for entering and exiting the Grade B areas shall be provided where feasible, subject to available space.
7.6.50.	The entry and exit doors of personnel airlocks shall not be opened simultaneously, an interlocking system shall be used.
7.6.51.	Handwash basins shall be provided only in the first stage of the GMP classified change rooms (GMP Grade D "at-rest" [ISO 14644 Class 8] change rooms) and hand sanitizing/disinfection systems in the next stage of change rooms.
7.6.52.	Full length mirrors shall be provided in all GMP classified change rooms. Mirrors shall be sealed to reduce the accumulation of dust and dirt and allow effective and easy cleaning and disinfection.
7.6.53.	Step-over benches or other clear demarcation systems shall be provided in all GMP classified change rooms. The design of the step over benches shall incorporate all required fixtures and shall be of sturdy construction to accommodate persons sitting on the benches as part of the gowning procedure.
7.6.54.	Storage of garments in the personnel change rooms shall be provided. Consideration shall be given to the use of hanging rails and perforated shelves rather than closed lockers.
7.6.55.	Actively ventilated change rooms shall be provided for movement of personnel between different radiological area classifications. The radiological classification of the change room must be of the same radiological classification as the area into which it leads.
7.6.56.	Decontamination showers and hand wash basins shall be provided in the radiological change rooms going from one radiological classification to another.
Material/Waste Dynamic Airlocks (MAL) or Transfer Chambers	
7.6.57.	The area classification of the material/waste airlock or transfer chambers, in the "at rest" state, shall be of the same cleanliness grade (viable and total particle) as the cleanroom into which it leads (highest area classification).
7.6.58.	The entry and exit doors, for material/waste airlock or transfer chambers shall not be opened simultaneously. Where required to maintain area segregation, a time delay between the closing and opening of interlocked doors shall be established.
7.6.59.	The material transfer chambers, or Material Airlock (MAL) should be of a size that enables the effective transfer and surface decontamination of materials being passed through it.

ID No.	Requirement
7.6.60.	Adequate space shall be provided around the material/waste airlock or transfer chambers for the introduction and removal of materials.
7.6.61.	Clear windows shall be provided on all the doors of the material/waste airlock or transfer chambers to allow a line-of-sight view inside the airlock, and/or the next room.
Furniture	
7.6.62.	Bench tops shall have curved edges wherever possible for easy cleaning.
7.6.63.	Laboratory furniture shall be fit for purpose. Open spaces between and under benches, cabinets and equipment shall be accessible for cleaning.
7.6.64.	Furniture shall not include any fabric surfaces which may absorb and hold contaminants.

7.7. Equipment

ID No.	Requirement
7.7.1.	Facility design shall allow the integration of the process equipment (i.e. hot cells etc.) to the structure, utilities and services. All process equipment will be provided by NTP.
7.7.2.	Facility layout and design shall provide adequate space for the installation, use and effective maintenance of the existing and new equipment.

7.8. Services and Support Systems

ID No.	Requirement
7.8.1.	The upgraded Facility and HVAC system shall be integrated with the following existing services and support systems: • Heating Ventilation and Air Conditioning (HVAC) System • Lighting (incl. Emergency Lights) • Compressed Air • Process Gases (Nitrogen, Hydrogen, Helium) • Potable/Drinking Water • Electricity Supply • Information and Communication Technology (ICT) System • Fire Detection and Protection • Safety Systems • Plumbing and Drainage • Access Control and Security Systems • Intercom • Building Management System (BMS) • Radiation Protection (RP) and Monitoring Systems • Low Active (LA) Effluent Management System • Hazardous Chemical Substances (HCS) Effluent Management System • Solid Radioactive Waste Management System
Heating Ventilation and Air Conditioning (HVAC) System	

ID No.	Requirement
7.8.2.	The upgraded facility shall be provided with an HVAC system capable of achieving the requirements listed in section 7.4. The prospective service provider shall review/assess the design details, performance and capacity of the current HVAC system to establish the condition of the system and whether the current system can provide the required air cleanliness to the existing and additional areas. The prospective service provider shall assume responsibility for the performance of the entire system, so the performance/condition of the current system must be very carefully reviewed/assessed. ***NOTE:*** *The existing HVAC design and performance documents will be provided upon signing of an NDA.*
7.8.3.	The performance of the HVAC system shall be capable of being controlled and monitored by the existing Building Management System (BMS) to ensure continuous compliance within the defined limits for parameters such as temperature, relative humidity, airflow and pressure differential.
7.8.4.	Differential room pressures of the classified areas shall be monitored and locally displayed by pressure differential measuring devices and be capable of being read by a BMS. Differential pressures shall be measured directly (room-to-room) and indicated on the local display. The operating range, alert and action limits shall be defined and displayed at the point of indication. The use of colour coding on the pressure gauge face is required.
7.8.5.	The pressure differential measuring device shall be of the analogue type, with a positive and negative range. The range of the device shall be suitable to the application.
7.8.6.	All instrumentation related to the HVAC and/or other systems shall be calibrated. Calibration of the instrumentation shall be valid at the time of system handover.
7.8.7.	Air supplied to the GMP classified areas shall be adequately filtered to ensure that there is no risk of cross-contamination with terminal filtration and to provide the required level of area cleanliness.
7.8.8.	The final filter shall be terminally located the GMP classified areas. The final filter used shall have an EN 1822 classification of at least H13 or equivalent. Each final filter shall be provided with individual serial numbers and test certificate.
7.8.9.	The HEPA or ULPA filters shall be installed in such a way to allow the in-situ testing for leakages, integrity and differential pressure across the filter.
7.8.10.	The design of the HVAC system shall allow the integrity testing of the HEPA or ULPA filters in accordance with ISO 14644 Part 3. Refer to URS ID No. 7.4.6 for the integrity testing acceptance criteria.
7.8.11.	The differential pressures across all individual filters or filter banks shall be monitored and displayed locally.
7.8.12.	Air supply and return grilles shall be appropriately located to facilitate appropriate airflow direction in an area, provide effective room flushing and prevent zones of stagnant air.

ID No.	Requirement
7.8.13.	The HVAC design shall consider the operation of the extraction systems in the design, where applicable, to avoid any risk or any impact on pressure cascade imbalances.
7.8.14.	The material of construction of the HVAC systems, components and ducting must be durable and non-shedding and not be a source of contamination.
7.8.15.	Ventilation points shall create minimal recesses that may allow accumulation of dust and dirt and shall facilitate cleaning and maintenance.
7.8.16.	Ventilation points shall be fully sealed against the ceiling panels to ensure an airtight fitting to prevent air leakage and possible ingress of dirt and dust.
7.8.17.	Where possible, ducting, piping, fittings, sensors, differential pressure measuring devices and other components shall be clearly marked or labelled for ease of identification, indicating location and direction of flow as appropriate.
7.8.18.	The radiological HVAC design shall comply with the requirements specified in SHEQ-INS-8030 and ISO 17873.
Lighting (Incl. Emergency Lights)	
7.8.19.	Lighting to be LED type with suitable ingress protection. Lights shall be energy efficient.
7.8.20.	Light fittings shall be selected to ensure longevity of lux levels. Sufficient lux levels shall be provided for the required activities in all the areas as per SHEQ-INS-1120 and SANS 10114-1.
7.8.21.	Lighting levels of 450-500 lux are required at bench level.
7.8.22.	Facility shall be provided with enough emergency lights, located adequately to ensure the safe evacuation of staff during power failures as per the Occupational Health and Safety Act and SHEQ-INS-1120.
Compressed Air	
7.8.23.	Compressed air is currently supplied via the existing compressed air system. The facility finishes shall ensure integration with the existing compressed air supply points.
Process Gases (Nitrogen, Hydrogen, Helium)	
7.8.24.	The process gases (Nitrogen, Hydrogen and Helium) are currently supplied via the existing gas systems. The facility finishes shall ensure integration with the existing gas system supply points.
Potable / Drinking Water	
7.8.25.	Potable water is already provided to the facility and shall be provided at basins for hand washing, in the change rooms. Cold water shall be provided as a minimum with hot water where possible.
7.8.26.	Potable water shall be supplied to the emergency showers.
Electricity Supply	
7.8.27.	400 V, 3-phase, 50 Hz electrical supply shall be provided to the facility.
7.8.28.	Adequate number of wall sockets and isolators shall be provided in the all the areas. The location of these shall be coordinated with equipment positions. Provision shall be made for at least 30% extra wall sockets.
7.8.29.	Power cabling shall be located in dedicated cable tray or in conduits.

ID No.	Requirement
7.8.30.	The electricity supply system design shall comply to SANS 10142 and is subject to Necsa approval.
7.8.31.	The facility electrical equipment shall be compatible with the South African national electrical grid (i.e. voltages, frequency and applicable tolerances).
7.8.32.	Only suppliers and equipment approved by Necsa shall be used.
7.8.33.	A Certificate of Compliance (CoC) shall be furnished for the electrical installation and shall be subject to sign-off by a Necsa responsible person.
Information and Communication Technology (ICT) System	
7.8.34.	Sufficient ethernet points shall be provided in the following areas to support the related equipment in the rooms to be connected to the network. • Hot Cell Operation Area • Decontamination and Clearance Area
Fire Detection and Protection	
7.8.35.	NECSA shall approve the fire protection design and installation. It is the responsibility of the service provider to obtain the approval and signature from Necsa.
7.8.36.	The facility fire design and signage shall comply to SANS 10400-T and SANS 7240.
7.8.37.	Fire escape routes shall be identified and, where required, specific fire exit doors shall be fitted.
7.8.38.	Emergency exit doors shall be easily accessible.
7.8.39.	Design of the facility shall allow for sufficient emergency assembly points for emergency preparedness.
Safety System	
7.8.40.	Appropriate safety signage shall be provided throughout the facility, in accordance with SHEQ-INS-2500 and SANS 1186-1.
7.8.41.	Adequate number of emergency safety showers, eye wash stations and eye wash bottles shall be provided within the facility as per SHEQ-INS-5150 and the OHS Act. The location shall be determined during the design phase.
7.8.42.	When designing storage arrangements, consideration shall be given to the hazards associated with handling of hazardous chemical substance in line with SHEQ-INS-7010.
Plumbing and Drainage	
7.8.43.	The plumbing and drainage system shall be designed and constructed as per SANS 10400-P.
7.8.44.	Washbasin and drains shall be provided in the following areas: • Change Rooms (GMP [Grade D, C and B] and Radiological) • Emergency Shower Area
7.8.45.	Washbasins and drains shall be acid and solvent resistant.
7.8.46.	The facility shall be equipped with adequate plumbing system for the drainage of Low Active (LA) effluent to the existing LA effluent system.
7.8.47.	Washbasins and drains located in the areas must be directly connected to the Low Active (LA) effluent management system for the direct transfer of the LA effluent.
Access Control and Security Systems	
7.8.48.	Access to production areas shall be restricted to authorised personnel only.

ID No.	Requirement
7.8.49.	The access control and security systems system shall be designed and installed by NTP.
7.8.50.	The prospective service provider shall ensure integration of the access control and security system requirements into the facility design.
Intercom	
7.8.51.	Facility shall be equipped with an intercom system to ease communication between the areas. The location shall be determined during the design phase.
Building Management System (BMS)	
7.8.52.	NTP shall provide the BMS. The supplier shall install the monitoring instrumentation and ensure that all installed instruments are equipped with communication interfaces as agreed between NTP and the supplier.
7.8.53.	The critical parameters (i.e. temperature, Relative Humidity and pressure) of the following areas shall be monitored via the BMS system as a minimum. • Preparation Area • Radiochemistry Room (i.e. Hot Cell Operation Area) • Street Clothes Change Rooms • Change Rooms (GMP [Grade D, C and B] and Radiological)
7.8.54.	The prospective service provider shall ensure integration of the BMS system requirements into the facility design.
Radiation Protection (RP) and Monitoring Systems	
7.8.55.	Radiation Protection (RP) and monitoring systems shall be provided in the radiological change rooms going from one area classification to another. The RP equipment will be provided by NTP. Adequate space and power supply shall be provided in the respective areas.
7.8.56.	Dedicated storage area such as shelves for storage of personal dosimetry and ease of retrieval by the Radiation Protection Officer (RPO).
Low Active (LA) Effluent Management System	
7.8.57.	The LA effluent system is existing. The existing facility connections to the Low Active (LA) effluent management system shall be maintained for the direct transfer of the LA effluent from the washbasin and drains to the system. LA effluent shall mostly consist of floor washing water.
Hazardous Chemical Substances (HCS) Effluent Management System	
7.8.58.	The facility layout shall provide a dedicated area for the interim storage of HCS effluent in its original container or similar prior to removal via a waste contractor.
7.8.59.	The facility layout shall ensure the safe and easy removal of the effluent from the facility.
Solid Radioactive Waste Management System	
7.8.60.	The solid radioactive waste is collected in drums and stored for an interim period in the facility until decay. The facility layout shall provide dedicated space for the interim storage of 2 x drums with the following size and weight (filled) per drum: • Size: ø 609 mm, H = 884 mm • Weight: 70 kg
7.8.61.	The facility layout shall ensure the safe and easy removal of the drums from the facility.

7.9. Operations and Maintenance

ID No.	Requirement
7.9.1.	Maintenance access panels shall be easily removable and re-sealable.
7.9.2.	All equipment shall be installed to allow effective maintenance of the equipment.
7.9.3.	Maintenance of all services and systems shall be performed from outside the cleanroom areas where possible, with good access for routine maintenance.

7.10. Constraints

ID No.	Requirement
7.10.1.	The existing areas of the P2000 Production Facility shall be included as part of the facility upgrade. The additional areas required shall be constructed within the allocated footprint. Refer to Appendix A for the existing layout of P2000 Production Facility.
7.10.2.	The upgraded facility shall be integrated with the existing services and support systems.
7.10.3.	An assessment shall be performed by the prospective service provider on the existing Cyclotron Production Facility and HVAC system to determine the scope of the upgrade required to align the production area and HVAC system to this user requirement specification document.

7.11. Life-cycle Requirements

ID No.	Requirement
Design Review	
7.11.1.	During the design phase, and as part of final design approval, design review meetings will be conducted. NTP shall be involved with the Design review meetings. The outcomes of these meetings will be recorded and compiled as the design review.
7.11.2.	The design review shall demonstrate that the design meets all relevant user, functional, design, regulatory and compliance requirements.
Commissioning Requirements	
7.11.3.	The facility, services and support systems (where applicable) shall be commissioned by the service provider and/or subcontractors to the service provider, prior to handover to NTP. NTP shall be involved with the commissioning activities and shall review and accept the commissioning plans/protocols, acceptance criteria and reports.
7.11.4.	All personnel of the service provider performing commissioning testing shall supply evidence of accreditation by a relevant testing authority or qualification to perform the commissioning.
7.11.5.	The service provider shall supply documented evidence that the requirements of this URS have been met where appropriate.
7.11.6.	Certificates of compliance with relevant national standards shall be supplied where applicable.

ID No.	Requirement
Handover Documentation	
7.11.7.	The service provider shall supply the following documentation as a minimum (for all systems, services, structure, and components): • Commissioning documentation and completed records. • Datasheets and specifications • User and maintenance manuals • Recommended spare parts lists. • Certificate of Compliance • Certificates (filters and instrument calibrations) • As built technical drawings [Layout, Electrical, HVAC, pneumatic, mechanical, and process and instrumentation diagrams (P&ID's)]. • Design Codes and Standards used. • Material data sheets. • Control strategies/ philosophies (where applicable) • Contact details for service providers and maintenance contractor(s) • Preventative maintenance task list with recommended frequencies
Warranty Agreement	
7.11.8.	The systems, services, structure, and components shall be installed with a warranty period of no less than 12 months on all parts and labour, from date of handover.
7.11.9.	The routine preventative maintenance schedule for the systems, services, structure, and components, shall be included into NTP's In-service Inspection and Maintenance Plan (ISI&MP).
Life-cycle Testing (NTP)	
7.11.10.	All controlling and monitoring sensors/displays and measuring instruments shall be added to NTP's In-service Inspection and Maintenance Plan (ISI&MP) and calibrated in accordance with the frequency determined for each item.
Training	
7.11.11.	Training shall be provided to NTP personnel (production and maintenance) by the service provider of the systems, services, structure, and components prior to handover to NTP. Training shall cover operation, monitoring, cleaning, safety, calibration, and maintenance. Training shall be documented and maintained.
QMS Documentation	
7.11.12.	NTP shall ensure that the following SOPs have been created and/or updated for the facility, systems, services, structure, and components: • Operation • Monitoring • Calibration • Maintenance • Cleaning • Quality

ID No.	Requirement
	• Safety • Regulatory
Change Management	
7.11.13.	All changes to the user requirement specification and equipment/ system design after approval shall be performed as per the service provider's quality / engineering management system. Change records shall be maintained and provided to NTP.
7.11.14.	Adequate change management must be performed by the service provider during the design phase as per the service provider's quality / engineering management system. Change records shall be maintained and provided to NTP.
7.11.15.	All changes to the user requirement specification and the facility, equipment, utilities and support system after approval and qualification, shall be performed as per the NTP's quality management system.

8. RECORDS

Record	Retention Period	By Whom
None	N/A	N/A

9. TASK HAZARD ASSESSMENT

N/A

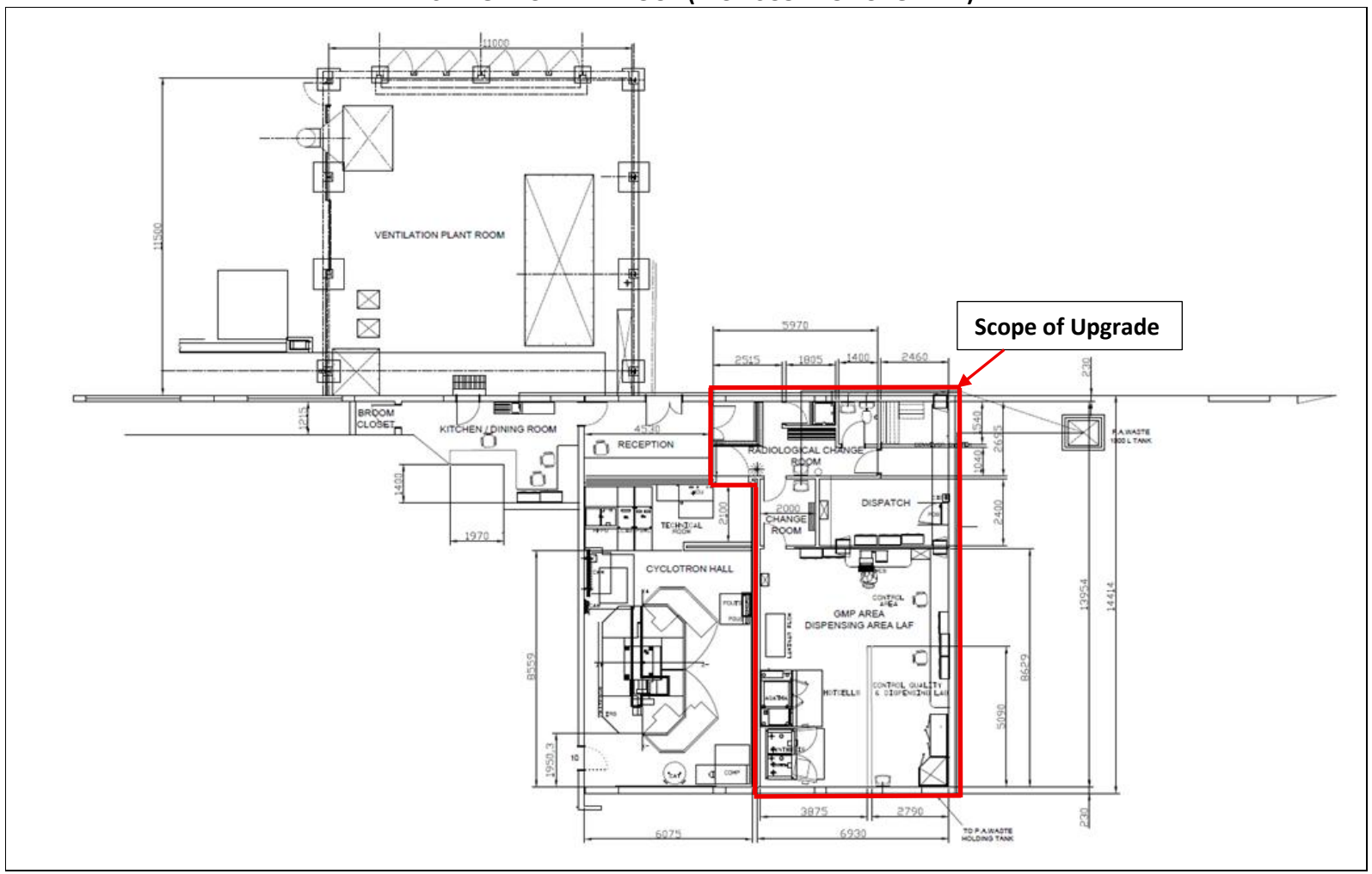
10. LIST OF FORMS

Form Title	Form Number	Exhibit Number
None	N/A	N/A

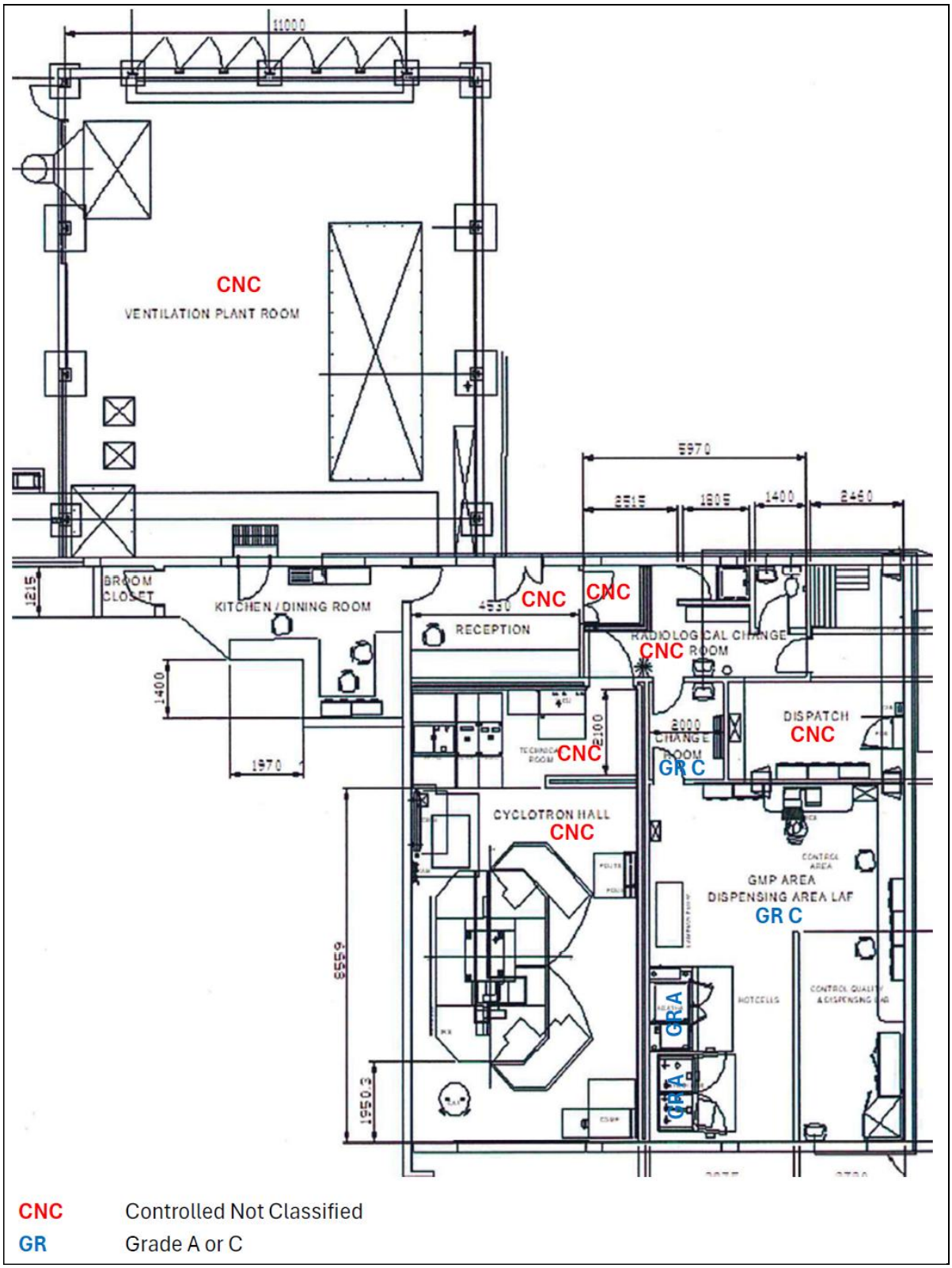
11. REVISION HISTORY

Rev.	Date Approved	Nature of Revision	Originated by
1	See title page	First issue	T Makate

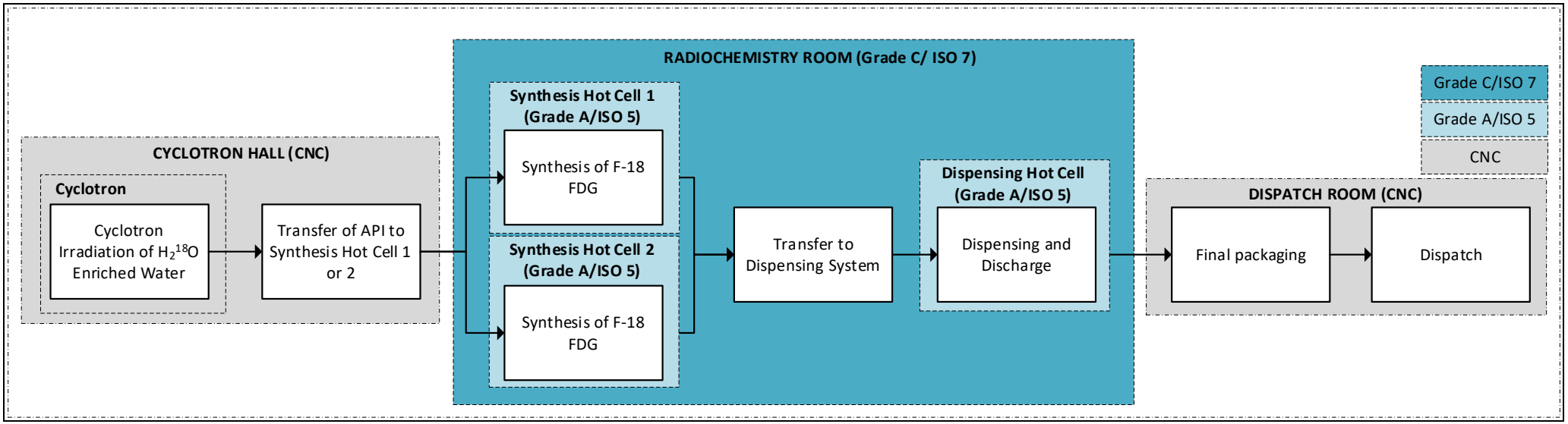
APPENDIX A:
EXISTING FACILITY LAYOUT (INCL. SCOPE OF UPGRADE)



APPENDIX B:
EXISTING FACILITY AREA CLASSIFICATIONS



APPENDIX C:
MANUFACTURING PROCESS FLOW DIAGRAM IN P2000 PRODUCTION FACILITY



APPENDIX D:
A POSSIBLE EXAMPLE OF THE PROPOSED NEW LAYOUT OF THE P2000 PRODUCTION FACILITY