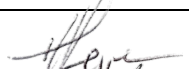
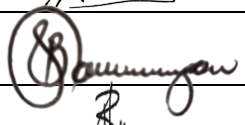
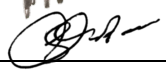
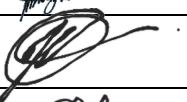
1. PURPOSE

The purpose of this document is to outline the design, regulatory, and performance requirements for the proposed upgrade of the existing NovaTec-P Production Area and associated HVAC system. It is intended for distribution to the market to solicit proposals for the provision of engineering design and project management services aligned with the ECSA Professional Services Framework (Stages 1–6).

This document includes reference to NECSA and NTP requirements as well as compliance with current Good Manufacturing Practice (cGMP) and Good Engineering Practice (GEP) where relevant.

ACTION	NAME & EXPERTISE	SIGNATURE	DATE
Originated	M van Vuuren *Process Engineering*		2025/11/15
Checked	I Ferreira *Quality Control Review*		2025/11/17
Checked	T More *HVAC Engineering review*		2025/11/19
Checked	T Mailula *Industrial Review*		2025/11/19
Checked	M Moloisi *Production Review*		2025/11/19
Checked	S van Niekerk *Maintenance Review*		2025/11/19
Checked	B Tlou *Waste Management Review*		2025/11/24
Checked	B Nolte *Safety Review*		2025/11/24
Checked	T Chuene *Regulatory Review*		2025/11/24
Checked	G Wortmann *Regulatory Compliance review*		2025/11/25
QA Approved	L Montjane *Quality Assurance Review*		2025/12/08
Approved	V Legoabe *Engineering Review*		2025/12/09
Approved	J Selome *Project Senior User Review*		2025/12/09
		Implementation Date:	2025/12/09

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The URS is compiled to facilitate prospective service providers in understanding the needs, identifying further requirements, and proposing a suitable design. This document is not intended as an exclusive approach, the identification or omissions of alternative suggestions by prospective suppliers/service providers and/or design engineers are welcome. 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 will be used as input into the basis of design and as a point of reference throughout the validation life cycle of the facility 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 NovaTec-P Production Area and associated HVAC System located in Building P3000 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].

This document specifies the requirements associated with the design, development, and qualification of the upgrade of the existing NovaTec-P Production Area and HVAC System and all its associated systems and support services.

The existing NovaTec-P Production Area and HVAC System is used to produce sterile NovaTec-P (Mo-99/ Tc-99m) generators. 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.

The hot cell production line, i.e. the hot cells and the associated in-cell processes do not form part of the scope of this document.

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 are mandatory and remain the sole responsibility of the service providers. NTP has an expectation of a compliant facility from the prospective 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 providers on the existing NovaTec-P Production Area and HVAC System to determine the scope of the upgrade required in order to align the NovaTec-P Production Area and HVAC System to this document.

The following is not covered by this URS, but will be specified in separate requirement documents as needed:

- The detailed requirements of the utilities and supporting systems.
- Statutory construction requirements - considered the responsibility of the builder and their sub-contractors.
- Architectural or engineering functional or detailed design - considered the responsibility of the contracted designers.

3. REFERENCES

This document complies with the requirements of:

ISO 9001: 2015	:	Quality Management System – Requirements, Fifth edition, 2015.
SAHPGL-INSP-02_v9	:	SAHPRA Guideline on Good Manufacturing Practice for Medicines, Version 9, August 2025
ISPE Baseline Guide	:	Commissioning and Qualification, Volume 5, 2nd Edition, 2019
NTP-PRG-0300	:	Control of Documented Information and Forms

The following documents are referenced in this document:

Act 15 of 1973	:	Hazardous Substances Act 15 of 1973
Act 45 of 1965	:	National Environmental Management: Atmospheric Pollution Prevention Act 45 of 1965
Act 59 of 2008	:	National Environmental Management: Waste Act 59 of 2008
Act 85 of 1993	:	The Occupational Health and Safety Act 85 of 1993
Act 103 of 1977	:	National Building regulations and building standards Act 103 of 1977
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: 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
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 7240-16:2008	:	Fire Detection and Alarm Systems Part 16: Sound System Control and Indication
SANS 7240-19:2008	:	Fire detection and alarm systems Part 19: Design, installation, commissioning, and service of sound systems for emergency purposes
SANS 10114-1: 2020	:	Interior Lighting Part 1: Artificial Lighting of Interiors, 4th Ed.
SANS 10139:2007	:	Fire Detection and Alarm Systems for buildings – System design, installation and servicing, Edition 3.1.
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-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
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
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
NECSA	:	Nuclear Energy Corporation of South Africa
OHSA	:	Occupational Health and Safety Act
OQ	:	Operational Qualification
Pa	:	Pascal
PA	:	Public Address
PAL	:	Personnel Airlock
PIC/S	:	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PPE	:	Personal Protective Equipment

PQ	:	Performance Qualification
QC	:	Quality Control
QRM	:	Quality Risk Management
QMS	:	Quality Management System
RH	:	Relative Humidity
SAHPRA	:	South African Health Product Regulatory Authority
SANS	:	South African National Standards
SAQCC	:	South African Qualification and Certification Committee
UPS		Uninterrupted Power Supply
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 the air and 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.
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 together, 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 actually 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.
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.

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 NovaTec-P generators Production Area is located in Building P3000 on the NECSA complex and is used to produce sterile NovaTec-P (Mo-99/ Tc-99m) generators (hereinafter referred to as the "generators"). The generators are compact units, used to deliver sterile, pyrogen-free radiopharmaceutical elutes, containing Sodium Pertechnetate (Tc-99m), for parenteral (intravenous) administration or for the aseptic production of Tc-99m labelled radiopharmaceutical preparations. The generators are manufactured and loaded aseptically with final filtration of the loading solution through a sterilizing grade filter.

The generator components are prepared under the required air cleanliness in the Preparation Area, sterilized and aseptically assembled in the Sterile Area before column loading.

The radioactive Active Pharmaceutical Ingredient (API) is brought into the facility via a shielded transfer container, introduced into the hot cells where the bulk solution is formulated.

The sterile inactive generator is assembled under aseptic conditions and connected to the column loading system in the Sterile Area, after which the generator is loaded with the formulated bulk solution.

The loaded generator is then identified, labelled, stored for predetermined period, eluted and closed under aseptic conditions in the QC Elution Area.

The generator is then removed from the aseptic processing area, radiologically decontaminated, and cleared in the Decon and Clearance Area before packaging and dispatch.
Refer to Appendix A for the overall process flow diagram of the NovaTec-P production process.

The upgraded NovaTec-P Production Area will consist of the following areas:

- Preparation Area,
- Sterile Area
- QC Elution Area,
- Decon and Clearance Area
- Hot Cells Area
- Emergency Shower Area
- Personnel Change Rooms
- Material Transfer Areas

Refer to Appendix C for the concept layout and section 7.2 below for the detailed requirements.

5.2. System Classification and Risk Assessment

The NovaTec-P Production Area and 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 upgraded NovaTec-P Production Area and HVAC 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. N/A

7. PROCESS

The user requirements for the proposed upgrade of the existing NovaTec-P Production Area and associated 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 in order to meet its intended purpose.

7.1. Compliance Requirements

The NovaTec-P Production Area and HVAC System shall be design, constructed, commissioned, and qualified in accordance with Good Engineering Practice (GEP), current Good Manufacturing Practice (cGMP) and hazardous (chemical/radiological safety) material requirements and key focus area stipulated herein:

ID No.	Description
7.1.1.	Act 15 of 1973: Hazardous Substances Act 15 of 1973
7.1.2.	Act 45 of 1965: National Environmental Management: Atmospheric Pollution Prevention Act 45 of 1965
7.1.3.	Act 59 of 2008: National Environmental Management: Waste Act 59 of 2008
7.1.4.	Act 85 of 1993: The Occupational Health and Safety Act 85 of 1993

ID No.	Description
7.1.5.	Act 103 of 1977: National Building regulations and building standards Act 103 of 1977
7.1.6.	ISO14644-1:2015 - Cleanrooms and Associated Control Environments, Part 1: Classification of Air Cleanliness by Particle Concentration
7.1.7.	ISO14644-3:2019 - Cleanrooms and Associated Control Environments, Part 3: Test Methods
7.1.8.	ISO14644-4:2022 - Cleanrooms and Associated Control Environments, Part 4: Design, Construction and Start-up.
7.1.9.	ISO 17873-2004: Nuclear facilities — Criteria for the design and operation of ventilation systems for nuclear installations other than nuclear reactors
7.1.10.	ISPE Baseline Guide: Commissioning and Qualification, Volume 5, 2nd Edition, 2019
7.1.11.	ISPE Good Practice Guide, Heating Ventilation and Air Conditioning (HVAC), 2009
7.1.12.	PE-009-17 (Part I): PIC/S Guide to Good Manufacturing Practice for Medicinal Products Part I, August 2023.
7.1.13.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 1: Manufacture of Sterile Medicinal Products, August 2023.
7.1.14.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 3: Manufacture of Radiopharmaceuticals, August 2023
7.1.15.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 15: Qualification and Validation, August 2023.
7.1.16.	SAHPGL-INSP-02_v9: SAHPRA Guideline on Good Manufacturing Practice for Medicines, Version 9, August 2025
7.1.17.	SANS 7240-16:2008 Fire Detection and Alarm Systems Part 16: Sound System Control and Indication
7.1.18.	SANS 7240-19:2008 Fire detection and alarm systems Part 19: Design, installation, commissioning, and service of sound systems for emergency purposes
7.1.19.	SANS 10114-1: 2020: Interior Lighting Part 1: Artificial Lighting of Interiors, 4th Ed.
7.1.20.	SANS 10139:2007 Fire Detection and Alarm Systems for buildings – System design, installation and servicing, Edition 3.1.
7.1.21.	SANS 10400: Application of the National Building Regulations
7.1.22.	SANS 10142: The Wiring of Premises
7.1.23.	SHEQ-INS-0234: NECSA QMS Requirement for External Design Organisations
7.1.24.	SHEQ-INS-1110: Housekeeping and Demarcation
7.1.25.	SHEQ-INS-1120: Lighting (Natural and Artificial)
7.1.26.	SHEQ-INS-7010: Zoning of facilities with hazardous chemical substances
7.1.27.	SHEQ-INS-7030: Surveillance programme for workplaces containing hazardous chemical substances
7.1.28.	SHEQ-INS-7140: Management of hazardous chemical waste
7.1.29.	SHEQ-INS-8030: System for the classification and demarcation of radiological areas
7.1.30.	SHEQ-INS-8050: Radiological surveillance programme for workplaces
7.1.31.	SHEQ-INS-8180: ALARA programme
7.1.32.	SHEQ-INS-8310: Requirements in respect of ventilation systems for nuclear facilities

ID No.	Description
7.1.33.	SHEQ-INS-8920: Access Control to NECSA Sites and Its Facilities
7.1.34.	WHO Technical Report Series (TRS) No. 957, Annex 3: WHO Good Manufacturing Practices for Pharmaceutical Products Containing Hazardous Substances, 2010.
7.1.35.	WHO Technical Report Series (TRS) No. 1010, Annex 8, Guidelines on Heating, Ventilation and Air-Conditioning Systems for Non-sterile Pharmaceutical Products, 2018
7.1.36.	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
7.1.37.	WHO Technical Report Series (TRS) No. 1019, Annex 3, Good Manufacturing Practices: Guidelines on Validation, 2019
7.1.38.	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.
7.1.39.	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 NovaTec-P Production Area layout shall include the existing and following additional areas: • Preparation Area (incl. Weighing Booth) • Sterile Area • QC Elution Area • Decon and Clearance Area • Street Clothes Change Room, • Change Rooms 1,2 and 3 (i.e. Grade D, C and B) • Emergency Shower Area • Hot Cells Area • Hot Cell Change Room Refer to Appendix C for the concept layout of the upgraded NovaTec-P Production Area.
7.2.2.	The new areas shall be designed to suit the operations to be carried out in them and adequately sized for the orderly placement of equipment and materials to avoid mix-ups and cross-contamination.
7.2.3.	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.
7.2.4.	Sufficient bench space shall be provided in all areas to place bench-top equipment and performing the required activities.
7.2.5.	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.

ID No.	Requirement
7.2.6.	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 (incl. Weighing Booth)	
7.2.7.	The Preparation Area shall provide adequate space for the segregation of the following radiological and non-radiological processes to avoid mix-ups and cross-contamination: • Washing and sterilization of glassware • Weighing, preparation and sterilization of generator columns • Preparation and sterilization of components (tubes, needles etc.) • Preparation and sterilization generator bodies (casing, lid, base) • Preparation and sterilization of lead pots. • Preparation and sterilization of reagents.
7.2.8.	The Preparation area shall be equipped with a GMP compliant conveyor or roller system to enable the safe and ergonomic handling of the lead pots.
QC Elution Area	
7.2.9.	The QC Elution Area shall provide adequate space for the segregation of the following radiological processes to avoid mix-ups and cross-contamination: • Introduction of elution vials • Storage of radioactive generators for decay • Elution of radioactive generators • Storage of elution samples
7.2.10.	The QC Elution area shall be equipped with a GMP compliant conveyor or roller system to enable the safe and ergonomic handling of the radioactive generators.
Decon and Clearance Area	
7.2.11.	The Decon and Clearance Area shall provide adequate space for the segregation of the following radiological processes to avoid mix-ups and cross-contamination: • Contamination monitoring of radioactive generators • Decontamination of radioactive generators
7.2.12.	The Decon and Clearance area shall be equipped with a GMP compliant conveyor or roller system to enable the safe and ergonomic handling of the radioactive generators.
Change Rooms (incl. Street Clothes and Grade D, C and B Change Room)	
7.2.13.	The Street Clothes Change Room 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.

7.3. Process Requirements – Product Physical Properties

ID No.	Requirement
7.3.1.	The NovaTec-P generator has the following physical properties: • Sodium Pertechnetate (^{99m}TC) Injection • Clear, colourless solution

ID No.	Requirement
	• Sterile **radiopharmaceutical** injectable • **Radiological** • Aseptic preparation with final filtration of the API (before loading) through a sterilizing grade filter.

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

ID No.	Requirement
7.4.1.	The NovaTec-P Production areas shall consist of the following air cleanliness classifications in the "at-rest" state: • Street Clothes Change Room: Controlled Not Classified (CNC) • Change Room 1: GMP Grade D [ISO 14644 Class 8] • Change Room 2: GMP Grade C [ISO 14644 Class 7] • Change Room 3: GMP Grade B [ISO 14644 Class 5] • Hot Cells Change Room: GMP Grade D [ISO 14644 Class 8] • Emergency Shower Area: GMP Grade C [ISO 14644 Class 7] • Preparation Area: GMP Grade C [ISO 14644 Class 7] • Weighing Booth: GMP Grade C [ISO 14644 Class 7] • Sterile Area: GMP Grade B [ISO 14644 Class 5] • Sterile Area Conveyers/Roller System: GMP Grade A UDAF [ISO 14644 Class 5 UDAF] • QC Elution: GMP Grade B [ISO 14644 Class 5] • QC Elution Conveyers/Roller System: GMP Grade A UDAF [ISO 14644 Class 5 UDAF] • Decon and Clearance: GMP Grade C [ISO 14644 Class 7] • Hot Cells Area: GMP Grade D [ISO 14644 Class 8] • PTH-1: GMP Grade C [ISO 14644 Class 7] • PTH-2: GMP Grade B [ISO 14644 Class 5] • PTH-3: GMP Grade B [ISO 14644 Class 5] • PTH-4: GMP Grade B [ISO 14644 Class 5] • PTH-5: GMP Grade B [ISO 14644 Class 5] • PTH-6: GMP Grade C [ISO 14644 Class 7] • CLAF-1: GMP Grade D [ISO 14644 Class 8] • CLAF-2: GMP Grade C [ISO 14644 Class 7] • CLAF-3: GMP Grade D [ISO 14644 Class 8] Refer to Appendix C for the concept GMP area classifications.
7.4.2.	The GMP classified areas shall comply to the requirements of PIC/S Annex 1, par. 4.27 (total particle concentration) and 4.31 (microbial contamination levels) in the "at-rest" and "in operation" occupancy states, to ensure that the required environmental cleanliness level is achieved and maintained.
7.4.3.	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. Refer to Appendix C for the concept area classifications.

ID No.	Requirement
7.4.4.	Unidirectional airflow (UDAF) systems shall provide a homogeneous air speed in the range of 0.36 – 0.54 m/s at the working position as per PIC/S Annex 1, par. 4.30.
7.4.5.	The maximum leakage / penetration through HEPA filter surface, seals, and framework shall be < 0.01% as per ISO 14644 Part 3.
7.4.6.	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.
7.4.7.	The pressure cascade for the facility shall comply with both GMP and radiological requirements in order 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. GMP classified area must be at a positive pressure to the atmosphere and radiological area must be at a negative pressure to the atmosphere. Refer to Appendix B for the existing pressure cascade of the NovaTec-P Production Area and Appendix E for the concept pressure cascade.
7.4.8.	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.
7.4.9.	Adjacent rooms of different GMP classifications shall have air pressure differentials between 10 and 15 Pa as per PIC/S Annex 1, par. 4.14. The alert limits shall be ±3 and action limits of ±5 of the design/operating limit.
7.4.10.	The radiological areas shall comply with the area requirements specified in SHEQ-INS-8030.

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 must 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. Refer to Appendix D for the concept material and personnel flows.
7.6.2.	Facility layout shall allow for the safe and easy removal and storage of the waste.
7.6.3.	Transfer of materials between different area classifications must be via appropriate actively ventilated transfer chambers (pass through hatches) or Material Airlocks (MAL).

ID No.	Requirement
7.6.4.	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.
7.6.5.	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.
7.6.6.	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.
7.6.7.	Entry of unauthorised personnel shall be prevented.
7.6.8.	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.
7.6.9.	Actively ventilated change rooms must be provided for movement of personnel between different GMP and radiological area classifications.
Surface Finishes	
7.6.10.	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 in order to minimize shedding or accumulation of particles, micro-organisms or radiological contamination on the surfaces.
7.6.11.	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, cupboards, and equipment shall be kept to a minimum.
7.6.12.	Crevices shall be avoided where possible. Alternatively, they shall be sealed.
7.6.13.	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.
7.6.14.	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.
7.6.15.	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).
7.6.16.	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.
7.6.17.	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.
7.6.18.	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.

ID No.	Requirement
7.6.19.	The facility shall be a well-sealed structure with no air leakage through ceilings, cracks or service areas.
Ceilings and Walls	
7.6.20.	Ceilings and walls shall be designed and sealed to prevent contamination from above and the adjacent areas.
7.6.21.	Walls and ceilings shall be of modular sandwich panel type construction with a high aesthetic appearance.
7.6.22.	Cleanroom panel fill material shall be constructed of non-combustible material.
7.6.23.	All wall to floor, ceiling to wall and wall to wall junctions (incl. between panels) shall be suitably coved and sealed.
7.6.24.	All walls of radiological areas shall be constructed to provide adequate shielding of the radiological operations within the room.
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 high 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.
7.6.29.	Door handles, where required, shall be smooth, non-snagging and easy to clean.
7.6.30.	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.
7.6.31.	All doors of radiological areas shall be constructed to provide adequate shielding of the radiological operations within the room.
Windows	
7.6.32.	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.
7.6.33.	Windows are to be flush and sealed with the wall/ door surfaces.
Floors	
7.6.34.	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.
7.6.35.	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.
7.6.36.	Floor surfaces should be slip-proof.
Sinks and Drains	

ID No.	Requirement
7.6.37.	Sinks and drains (incl. floor drains) are not permitted in GMP Grade A and B “at-rest” [ISO 14644 Class 5] areas.
7.6.38.	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.
7.6.39.	Floor drains in GMP Grade C and D “at-rest” [ISO 14644 Class 7 and 8] and radiological areas must be fitted with traps or water seals designed to prevent back flow and should be flush sealed with the floor.
7.6.40.	Sinks shall be made of a durable material, without overflow and be adequately spaced away from walls to avoid uncleanable joints and crevices.
7.6.41.	Sinks and drains shall be acid, solvent and stain resistant.
Pipe Work, Light Fittings, Ventilation Points and Other Services	
7.6.42.	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.
7.6.43.	Pipe work, light fittings, ventilation points and other services shall be fully sealed against the ceiling panels in order to ensure an airtight fitting to prevent air leakage and possible ingress of dirt and dust.
7.6.44.	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, in order to reduce the risk of contamination.
7.6.45.	Exposed piping, tubing and cable runs shall be minimized in the cleanrooms.
7.6.46.	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.
7.6.47.	Pipe work, light fittings, ventilation points and other services shall be labelled with name of service as well as flow direction where appropriate.
7.6.48.	Pipes shall be adequately sloped for drainage and constructed without ‘dead-legs’.
Personnel Airlock (PAL) or Change Rooms	
7.6.49.	The area classification of the final 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).
7.6.50.	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.
7.6.51.	The entry and exit doors of personnel airlocks shall not be opened simultaneously. For airlocks leading to the GMP Grade A and B areas, an interlocking system should be used. For airlocks leading to GMP Grade C and D “at-rest” areas [ISO 14644 Class 7 and 8], a visual and/or audible warning system should be operated as a minimum.

ID No.	Requirement
7.6.52.	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.
7.6.53.	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.
7.6.54.	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.
7.6.55.	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.
7.6.56.	Actively ventilated change rooms must 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.
7.6.57.	Decontamination showers and hand wash basins must be provided in the radiological change rooms going from one radiological classification to another.
Material/Waste Airlocks (MAL) or Transfer Chambers	
7.6.58.	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).
7.6.59.	The entry and exit doors, for material/waste airlock or transfer chambers shall not be opened simultaneously. For material/waste airlock or transfer chambers leading to the GMP Grade A and B areas, an interlocking system shall be used. For airlocks leading to GMP Grade C and D "at-rest" areas [ISO 14644 Class 7 and 8], a visual and/or audible warning system shall be operated as a minimum. Where required to maintain area segregation, a time delay between the closing and opening of interlocked doors shall be considered.
7.6.60.	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. Consideration should be given to having a timing device on the door interlock to allow sufficient time for the decontamination process to be effective.
7.6.61.	Adequate space shall be provided around the material/waste airlock or transfer chambers for the introduction and removal of materials.
7.6.62.	Clear windows shall be provided on all the doors of the material/waste airlock or transfer chambers to allow a line-of-sight view.
Furniture	
7.6.63.	Fittings and furniture shall present as few horizontal surfaces as possible. Furniture shall be kept to a minimum.
7.6.64.	Laboratory furniture shall be fit for purpose. Open spaces between and under benches, cabinets and equipment shall be accessible for cleaning.
7.6.65.	Furniture shall not include any fabric surfaces which may absorb and hold contaminants.

ID No.	Requirement
7.6.66.	Bench tops shall have curved edges wherever possible for easy cleaning.
Weighing Areas	
7.6.67.	Weighing areas shall be appropriately designed to provide the required levels of containment, operator protection and product protection.
7.6.68.	Weighing shall be performed under the same environmental conditions as specified in the areas for the next stage of use.
7.6.69.	Vibration damping measures shall be considered in all the weighing areas in the facility.
7.6.70.	In cases where dust is generated (e.g. weighing) specific provisions shall be taken to avoid cross-contamination and facilitate cleaning.

7.7. Equipment

ID No.	Requirement
7.7.1.	Facility layout and design shall provide adequate space for the installation, use and effective maintenance of the existing and new equipment. All equipment will be provided by NTP.
7.7.2.	Equipment integrated into the HVAC system, which has an impact on the balance of the airflow of the facility, must be provided as part of the facility design and layout.

7.8. Utilities and Support Systems

ID No.	Requirement
7.8.1.	The upgraded facility and HVAC system shall be integrated with the following existing utilities and support systems: • Heating Ventilation and Air Conditioning (HVAC) System • Lighting • Compressed Air • Potable/Drinking Water • Process Water (Purified Water System) • Electricity Supply • Emergency Power Back-up Supply (Generator and UPS) • Information and Communication Technology (ICT) System • Fire Detection and Protection System • Safety Systems • Plumbing and Drainage • Access Control • CCTV • Public Address • Intercom • Building Management System (BMS)
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 temperature in all storage and processing laboratories shall be controlled and continually maintained between 18 - 25 °C.
7.8.4.	Relative humidity (RH) is not required to be controlled to ensure material and/or product storage conditions are met, however, humidity control for purposes of operator comfort shall be provided at ≤ 60% RH.
7.8.5.	The performance of the HVAC shall be 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.
7.8.6.	Differential rooms pressure of the new areas shall be monitored and locally displayed by pressure differential measuring devices and the BMS. Differential pressures shall be measured directly (room-to-room) and indicated on the local display and the BMS. 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 preferred. Refer to ID No. 7.4.9 for the differential pressure limits.
7.8.7.	All instrumentation related to the monitoring of the HVAC system shall be calibrated. Calibration of the instrumentation shall be valid at the time of system handover.
7.8.8.	Air supplied to the GMP classified areas shall be adequately filtered to ensure that there is no risk of cross-contamination and to provide the required level of area cleanliness.
7.8.9.	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.
7.8.10.	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.
7.8.11.	Air supply and return grilles in the new areas shall be appropriately located to facilitate appropriate airflow direction in an area, provide effective room flushing and prevent zones of stagnant air.
7.8.12.	In areas where weighing is performed, unidirectional airflow shall be provided. The airflow shall not disrupt the accuracy of balances.
7.8.13.	The HVAC upgrade shall consider the operation of the extraction systems in the design, where applicable, to avoid any risk or any impact on pressure cascade imbalances.

ID No.	Requirement
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/wall panels in order 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.
Lighting	
7.8.18.	Lighting to be LED type with suitable ingress protection. Lights shall be energy efficient.
7.8.19.	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.
7.8.20.	Lighting levels of 450-500 lux are required at bench level.
7.8.21.	Facility shall be provided with a sufficient number of emergency lights, located adequately to ensure the safe evacuation of staff during power failures as per OSHACT and SHEQ-INS-1120.
Compressed Air	
7.8.22.	Compressed air must be provided to the following areas from the existing compressed air system: • Preparation Area. The compressed air is primarily used for the pneumatic operation of equipment and instrumentation (non-product contact).
Potable / Drinking Water	
7.8.23.	Potable water shall be provided at basins for hand washing, in the GMP and radiological change rooms. Hot and cold water shall be provided, where possible.
7.8.24.	Potable water shall be provided as the in-feed to the Water Purification Systems located in the Preparation Area.
7.8.25.	Potable water shall be supplied to the emergency showers.
Process Water (Purified Water System)	
7.8.26.	Purified water shall be provided to the Preparation Area through a water purification system. Space shall be provided in the Preparation Area for the installation of the water purification system. The water purification system shall be provided by NTP.
Electricity Supply	
7.8.27.	Single and three-phase electrical supply shall be provided to the facility. Adequate number of wall sockets shall be provided in the all the areas.
7.8.28.	Power cabling shall be located in dedicated cable tray or in conduits.
7.8.29.	A Certificate of Compliance shall be furnished for the electrical installation.
Emergency Power Back-up Supply (Generator and UPS)	

ID No.	Requirement
7.8.30.	Emergency back-up supply connection points (Generator and UPS) shall be provided in the following areas from the existing systems: • Preparation Area • Weighing Booth • Sterile Area • Decon and Clearance • Hot Cells Area • Change Room 2 and 3 • Emergency Shower Area
7.8.31.	The existing systems shall be assessed to ensure sufficient capacity is available to meet the requirement specified in URS ID No. 7.8.30.
Information and Communication Technology (ICT) System	
7.8.32.	Sufficient ethernet points shall be provided in the following areas to support the related equipment in the rooms to be connected to the network. • Preparation Area • Weighing Booth • Decon and Clearance • Hot Cells Area
7.8.33.	An assessment shall be performed to determine what is required regarding network connectivity.
Fire Detection and Protection	
7.8.34.	The appropriate regulatory body and NECSA ECC shall approve the fire protection design and installation.
7.8.35.	The facility shall be fitted with a fire detection system connected to a fire panel and audible alarming system.
7.8.36.	Fire escape routes shall be identified and, where required, specific fire exit doors shall be fitted.
7.8.37.	Emergency exit doors shall be easily accessible.
7.8.38.	Design of the facility shall allow for sufficient emergency assembly points for emergency preparedness.
Safety System	
7.8.39.	Appropriate safety signage shall be provided throughout the facility, in accordance with relevant regulations.
7.8.40.	Adequate number of emergency safety showers, eye wash stations and eye wash bottles shall be provided within the facility and appropriately located.
7.8.41.	When designing storage arrangements, consideration shall be given to the hazards associated with handling of hazardous chemical substance in line with safety requirements.
Plumbing and Drainage	
7.8.42.	Washbasin and drains shall be provided in the following areas: • Preparation Area • Change Room 1 • Emergency Shower Area

ID No.	Requirement
	• Hot Cells Change Room
7.8.43.	The facility shall be equipped with adequate plumbing system for the drainage of Low Active (LA) effluent to the existing LA effluent system.
7.8.44.	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	
7.8.45.	Access to production areas shall be restricted to authorised personnel only.
7.8.46.	The Access Control system shall be connected to the existing system.
CCTV	
7.8.47.	The facility shall be equipped with a CCTV system in accordance with safety and security requirements.
7.8.48.	The CCTV system shall be connected to the existing system.
Public Address	
7.8.49.	The facility shall be equipped with a PA system in accordance with safety standards.
7.8.50.	The PA system shall be connected to the existing PA system.
Intercom	
7.8.51.	Facility shall be equipped with an intercom system to ease communication between the areas.
Building Management System (BMS)	
7.8.52.	The critical parameters (i.e. temperature, Relative Humidity and pressure) of the following areas shall be monitored via a new BMS system. • Preparation Area (incl. Weighing Booth) • Sterile Area • QC Elution Area • Decon and Clearance Area • Street Clothes Change Room, • Change Rooms 1,2 and 3 (i.e. Grade D, C and B) • Emergency Shower Area • Hot Cells Area • Hot Cell Change Room
Radiation Protection (RP) and Monitoring Systems	
7.8.53.	Radiation Protection (RP) and monitoring systems must be provided in the following radiological change rooms: • Change Room 2 • Change Room 3 • Emergency Shower Area. The RP equipment will be provided by NTP. Adequate space and power supply must be provided in the respective areas.
7.8.54.	Barrier radioactive contamination monitors shall be adequately shielded by the wall material where they are mounted to facilitate their effectiveness and accuracy.
7.8.55.	Dedicated storage area such as shelves for storage of personal dosimetry and ease of retrieval by the Radiation Protection Officer (RPO).

ID No.	Requirement
Radioactive Gaseous Waste Management System	
7.8.56.	The radioactive gaseous waste management system for the control and monitoring of radioactive gas emissions of the upgraded facility shall be integrated with the existing system, in accordance with nuclear requirements.

7.9. Operations and Maintenance

ID No.	Requirement
7.9.1.	The NovaTec-P consumables, components, intermediates, columns etc. should be sterilized and passed into the Sterile Area through a pass-through autoclave (double-ended) from the Preparation area. The pass-through autoclave will be provided by NTP, adequate space, purified water connection and a drain point must be provided for the autoclave.
7.9.2.	Removal panels must be provided for the introduction and removal of equipment that are too big to fit through a normal size door.
7.9.3.	Maintenance access panels must be easily removable and re-sealable.
7.9.4.	All equipment must be installed to allow effective maintenance of the equipment.
7.9.5.	Maintenance of all utilities and systems must 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 NovaTec-P Production area shall be included as part of the facility upgrade. The additional areas required shall be constructed within the allocated footprint provided. Refer to the Appendix B for the existing NovaTec-P Production area layout and Appendix C for the concept layout for the upgraded facility.
7.10.2.	The additional areas of the facility shall be integrated with the utilities and support systems provided to the existing facility.
7.10.3.	An assessment shall be performed by the prospective service provider on the existing NovaTec-P Production area and HVAC system to determine the scope of the upgrade required in order to align the NovaTec-P 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 must be involved with the Design review meetings. The outcomes of these meetings will be recorded and compiled as the design review.

ID No.	Requirement
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, utilities 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 must be involved with the commissioning activities and must review and approve the commissioning plans/protocols, acceptance criteria and reports.
7.11.4.	All commissioning protocols must be completed in accordance with Good Documentation Practices as per GMP requirements.
7.11.5.	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.
7.11.6.	The service provider shall supply documented evidence that the requirements of this URS have been met where appropriate.
7.11.7.	Certificates of compliance with relevant national standards shall be supplied where applicable.
Qualification Requirements	
7.11.8.	At the completion of the construction of the facility and commissioning activities, the quality critical facility, utilities and support systems (where applicable) shall be qualified by the service provider, prior to handover to NTP. The qualification activities shall include Design, Installation and Operational Qualification. NTP must be involved with the qualification activities and must review and approve the qualification plans/protocols, acceptance criteria and reports.
7.11.9.	All qualification protocols (DQ, IQ and OQ) must be completed in accordance with Good Documentation Practices as per GMP requirements.
7.11.10.	Performance Qualification (PQ) shall be performed by NTP.
7.11.11.	Qualifications shall be completed prior to hand-over to NTP and routine use of the facility, utilities, and systems.
7.11.12.	The following tests shall be included as part of the qualification tests of the upgraded NovaTec-P Production Area and HVAC system as per PIC/S Annex 1, par. 4.25: • Installed filter system leakage and integrity testing • Airflow tests – volume and velocity • Air pressure difference test • Airflow direction test and visualisation • Microbial airborne and surface contamination • Temperature measurement • Relative humidity • Recovery test The tests shall be performed as per the test methods prescribed in ISO 14644.
Handover Documentation	

ID No.	Requirement
7.11.13.	The service provider shall supply the following documentation as a minimum (for all systems, utilities, services, structure, and components): • Commissioning documentation and completed records. • Qualification/validation 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, pneumatic, mechanical, and process and instrumentation diagrams (P&ID's)]; • Design Codes and Standards used; • Material data sheets; • Material certificates for Direct Impact Systems (i.e. components in direct contact with the product); • Control strategies/ philosophies (where applicable) • Contact details for suppliers and maintenance contractor(s) • Preventative maintenance task list with recommended frequencies
Maintenance and Service Level Agreement	
7.11.14.	The systems, utilities, services, structure, and components shall be installed and maintained by the service provider.
7.11.15.	A Service Level Agreement must be established for 3 consecutive years between the service providers and NTP. The Service level Agreement must include the following as a minimum: • Spare parts • Preventative maintenance requirements • Ad-hoc/corrective maintenance requirements • Call-out requirements
7.11.16.	The routine preventative maintenance schedule for the systems, utilities, services, structure, and components, shall be included in NTP's preventative maintenance and calibration schedule.
Life-cycle Testing	
7.11.17.	All controlling and monitoring sensors/displays and measuring instruments shall be added to NTP's preventative maintenance and calibration schedule and calibrated in accordance with the frequency determined for each item.
Training	
7.11.18.	Training must be provided to NTP personnel (production and maintenance) by the service provider of the systems, utilities, services, structure, and components prior to handover to NTP. Training must cover operation, monitoring, cleaning, safety, calibration, and maintenance. Training shall be documented and maintained.

ID No.	Requirement
QMS Documentation	
7.11.19.	NTP shall ensure that the following SOPs have been created and/or updated for the facility, systems, utilities, services, structure, and components: • Operation • Monitoring • Calibration • Maintenance • Cleaning
Change Management	
7.11.20.	All changes to the user requirement specification and equipment/ system design after approval must be performed as per the service provider's quality / engineering management system requirements.
7.11.21.	Adequate change management must be performed by the service provider during the design phase as per the service provider's quality / engineering management system requirements.
7.11.22.	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 requirements.

8. RECORDS

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

9. TASK HAZARD ASSESSMENT

No task hazard assessment is associated with this document.

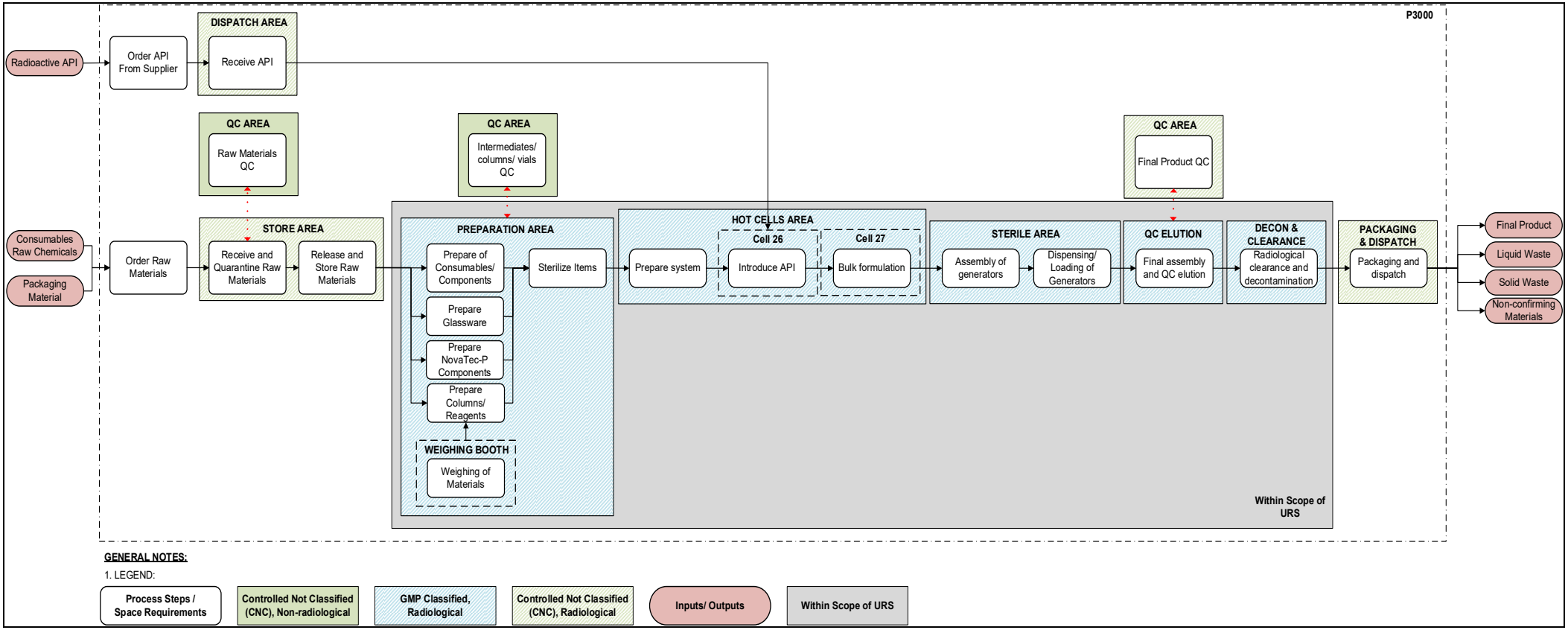
10. LIST OF FORMS

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

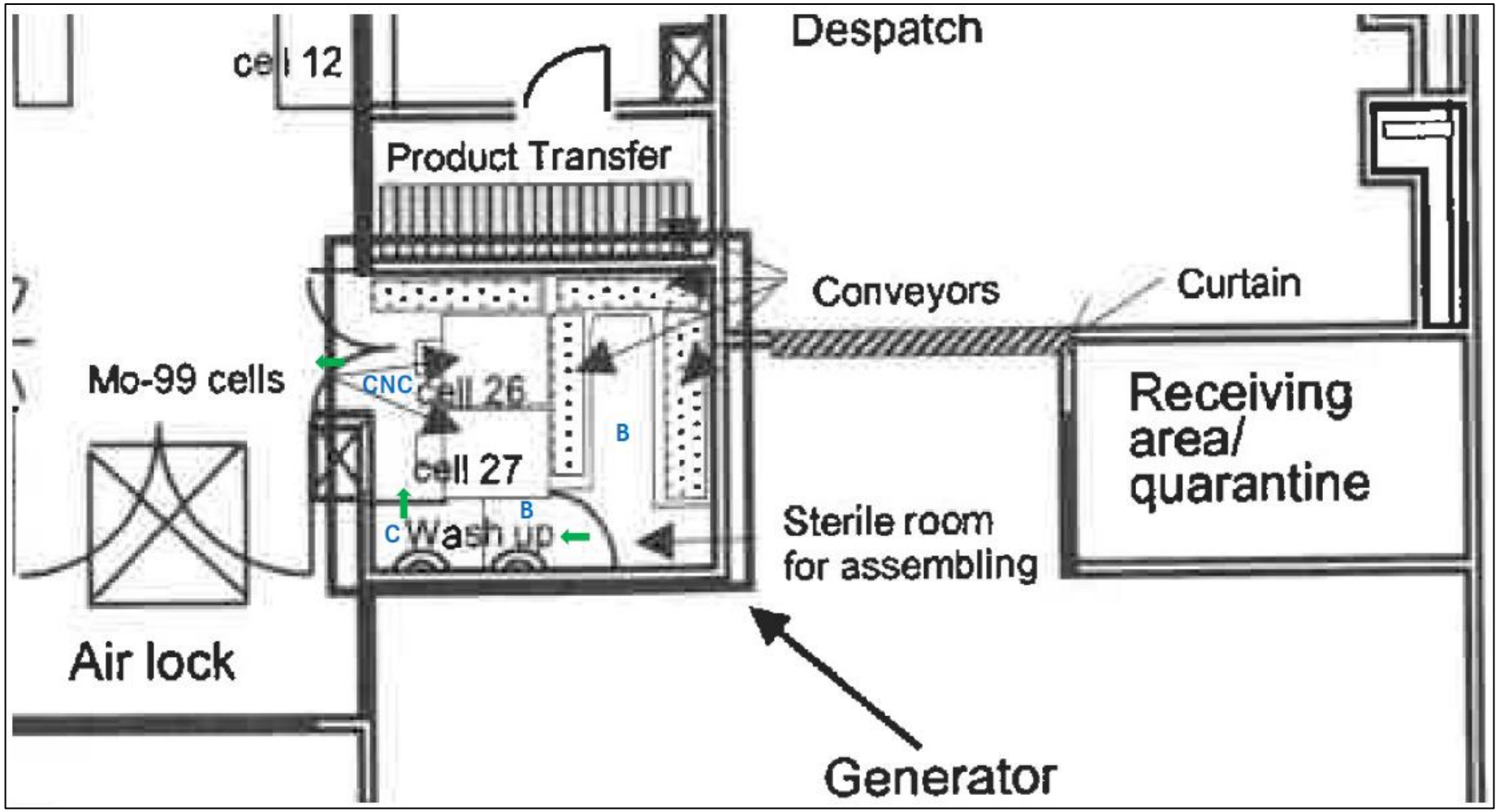
11. REVISION HISTORY

Rev.	Date Approved	Nature of Revision	Originated by
1	See title page	First issue	MM van Vuuren

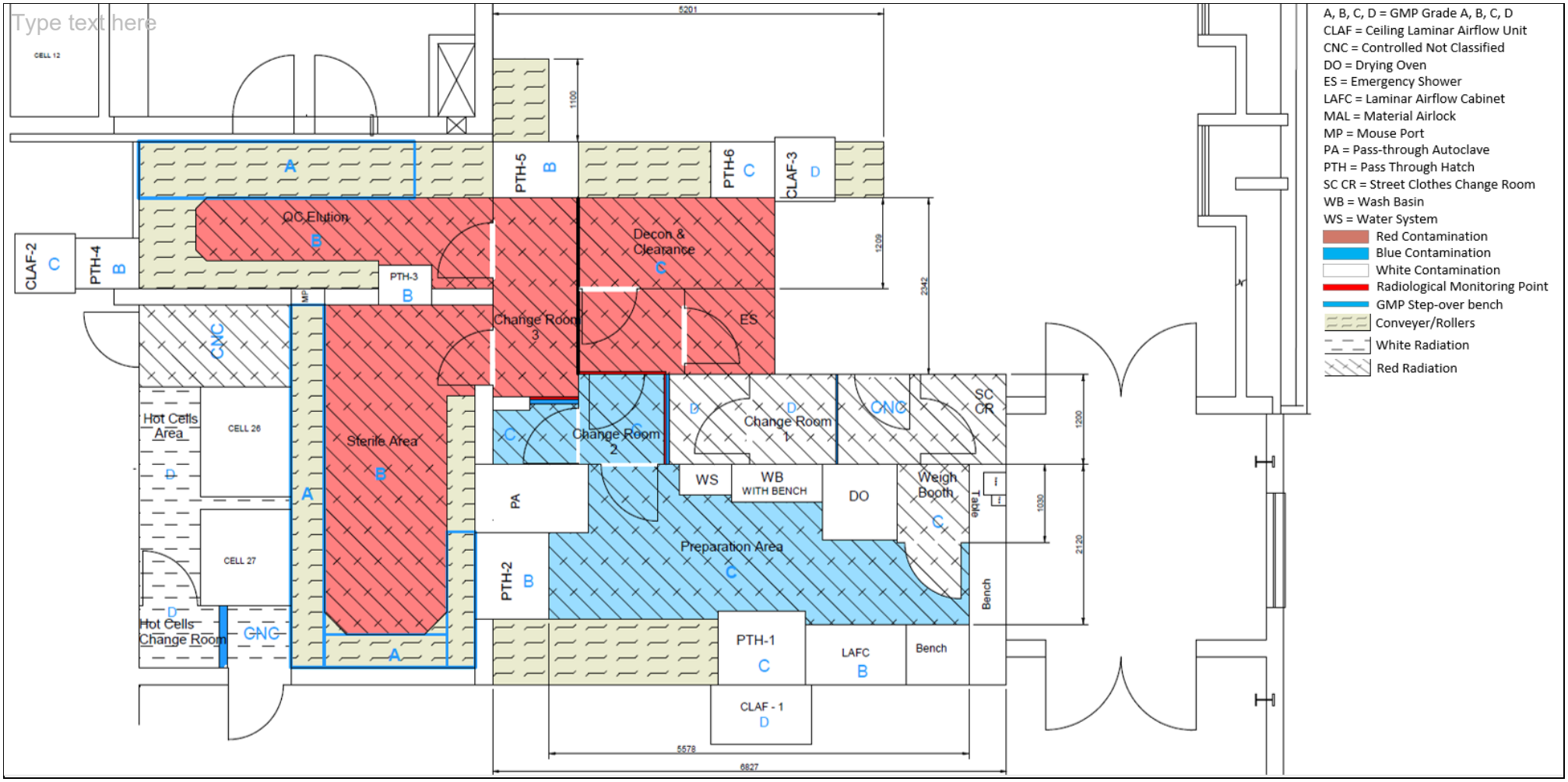
APPENDIX A:
OVERALL NOVATEC-P PROCESS FLOW DIAGRAM



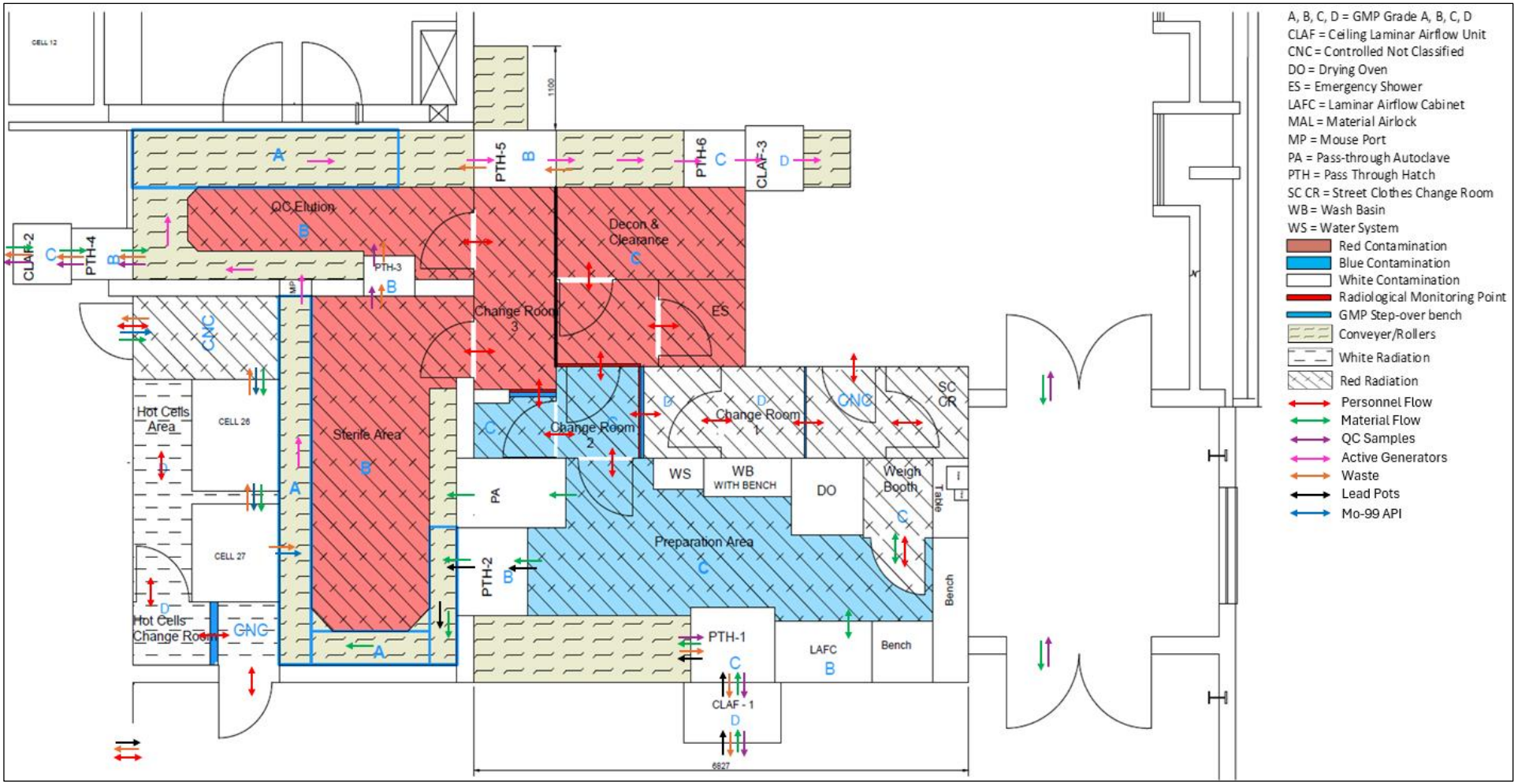
APPENDIX B:
P3000 NOVATEC-P PRODUCTION AREA EXISTING LAYOUT AND PRESSURE CASCADE



APPENDIX C:
P3000 NOVATEC-P PRODUCTION AREA CONCEPT LAYOUT AND AREA CLASSIFICATIONS



APPENDIX D:
P3000 NOVATEC-P PRODUCTION AREA CONCEPT PERSONNEL AND MATERIAL FLOWS



APPENDIX E:
P3000 NOVATEC-P PRODUCTION AREA CONCEPT PRESSURE CASCADE