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Checked By:	M Sekgodi *Operations Review*		2026/05/18
Checked By:	JR Zeevaart *Scientific Review*		2026/05/18
Checked By:	T Ntuli *Maintenance Review*		2026/05/20
Checked By:	B Tlou *Waste Management Review*		2026/05/22
Checked By:	B Nolte *Safety Review*		2026/05/27
Checked By:	Z Steynberg *Nuclear Safety Review*		2026/05/27
Checked By:	G Wortmann *Regulatory Compliance review*		2026/06/03
QA Approved By:	L Baloyi *Quality Assurance Review*		2026/06/10
Approved By:	V Legoabe *Engineering Review*		2026/06/10
Approved By:	J Selome *Project Sponsor Review*		2026/06/10
		Implementation Date:	2026/06/17

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Title	Requirements Specification for the Activation I-131 Manufacturing Facility				
CMS Unique ID	N/A				
Project Number	NTP-PRJ-22/001				

TABLE OF CONTENTS

1. PURPOSE

The purpose of this document is to define the high-level proposed manufacturing facility requirements for the production of non-sterile activation Iodine-131 Active Pharmaceutical Ingredient (API).

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. This document is compiled to facilitate prospective suppliers/service providers and/or design engineers 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.

This requirements document is a key document 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 document applies to the Activation Iodine-131 API Manufacturing Facility to be located in Building P1900 on the Necsa site [Located at R104, Pelindaba, Brits Magisterial District]. This document specifies the requirements associated with the design, development, and qualification of the Activation Iodine-131 API Manufacturing Facility and all its associated systems and support services.

The Activation Iodine-131 API Manufacturing Facility will be used to produce non-sterile Iodine-131 API. 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 and will be supplied by a third-party specialist supplier.

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 consulting engineers are mandatory and remain the sole responsibility of the consulting engineers. 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.

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:

ICH Q7	:	Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Step 4 Version, Nov 2000
ISO 9001: 2015	:	Quality Management System – Requirements, Fifth edition, 2015.
ISPE Baseline Guide	:	Commissioning and Qualification, Volume 5, 2nd Edition, 2019
PE-009-17 (Parts I & II)	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products Part I & II, August 2023
SAHPGL-INSP-02_v9	:	SAHPRA Guideline on Good Manufacturing Practice for Medicines, Version 9, November 2025
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
ICH Q7	:	Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Step 4 Version, Nov 2000
ISO 8573-1:2010	:	Compressed Air – Part 1: Contaminants and Purity Classes
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
NTP-SPE-4168	:	Activation Iodine-131 API Manufacturing Facility Building Management System User Requirements Specification
PE-009-17 (Part I & II)	:	PIC/S Guide to Good Manufacturing Practice for Medicinal Products Part I & II, 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, November 2025
SAHPGL-INSP-GMP-02_v1	:	Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Version 1, October 2025
SAHPGL-RDN-RN-13_v2	:	SAHPRA Guideline for Management and Disposal of Non-nuclear Radioactive Waste, Version 2, December 2022
SANS 1186-1: 2022	:	Symbolic Safety Signs, Part 1: Standard Signs and General Requirements, Edition 3.8

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 10400	:	Application of the National Building Regulations
SANS 10140	:	Identification of Colour Marking
SANS 10142	:	The Wiring of Premises
SHEQ-INS-0233	:	Design Control
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-1250	:	Colour Codes
SHEQ-INS-2500	:	Affixing of Notices and Signs and Labelling of Electrical and Other Critical Equipment
SHEQ-INS-5150	:	First Aid Officer and Facilities
SHEQ-INS-7010	:	Zoning of facilities with 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-8150	:	Access and Egress Control to Radiological Areas
SHEQ-INS-8180	:	ALARA programme
SHEQ-INS-8230	:	Management of Radioactive Discharges to the Atmosphere at the Pelindaba Site
SHEQ-INS-8260	:	Management of Radioactive Effluent and Discharge at the Pelindaba Site
SHEQ-INS-8920	:	Access Control to Necsa Sites and Facilities
SHEQ-INS-8310	:	Requirements in respect of ventilation systems for nuclear facilities
SHEQ-INS-8360	:	Necsa Solid Radioactive Waste Management System
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:

ACPH	:	Air Changes Per Hour
API	:	Active Pharmaceutical Ingredient
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
I-131	:	Iodine 131
LAF	:	Laminar Airflow System
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
POU	:	Point of Use
PPE	:	Personal Protective Equipment
PQ	:	Performance Qualification

QC	:	Quality Control
QRM	:	Quality Risk Management
QMS	:	Quality Management System
RH	:	Relative Humidity
RTM	:	Requirements Traceability Matrix
SAHPRA	:	South African Health Product Regulatory Authority
SANS	:	South African National Standards
SAQCC	:	South African Qualification and Certification Committee
UDAF	:	Unidirectional Airflow System
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.
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.
Plant Equipment	:	Plant equipment often referred to as utility plant equipment or support equipment, consists of tangible, long-term capital assets that provide essential infrastructure—such as energy, water, climate control, and compressed air—required to operate production machinery and maintain a functional, safe environment, without directly creating the final product.
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.
Process Equipment	:	Process equipment refers to the machinery, apparatus, and devices used in industrial settings to physically or chemically transform raw materials into finished products.
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.
Services	:	Services are the conditioned, transformed, and distributed forms of utilities that are generated and utilized within the manufacturing facility to support production and operational processes.
Utilities	:	Utilities are considered as externally supplied sources of energy or media provided to the facility at or up to its boundary, in raw or bulk form, for the purpose of distribution within the facility to enable operations.
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.
Unidirectional Airflow	:	A rectified airflow over the entire cross-sectional area of a clean zone with a steady velocity and approximately parallel streamlines. (Previously also known as laminar flow, although modern standards no longer refer to laminar flow, but have adopted the term unidirectional airflow as per WHO TRS No. 1010, Annex 8, 2018).

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. NTP would like to establish a manufacturing facility to produce activation I-131 API in Building P1900 located on the Necsa site [R104, Pelindaba, Brits Magisterial District].

The Activation I-131 Manufacturing Facility will house the activation I-131 production process together with its support functions and infrastructure to enable continuous and sustainable manufacturing of the activation I-131 API product. A process flow diagram indicating the overall process flows of the activation I-131 API production process and the scope of the facility is provided in Appendix A.

The irradiated targets (radioactive material) will be received in the facility via a shielded transfer container, from the SAFARI-1 research reactor.

Once in the Activation I-131 Manufacturing Facility, the irradiated targets are introduced into the hot cell for the production, dispensing and packaging of the activation I-131 API product into a shielded container.

The shielded containers are cleared from any radiological contamination by the safety department before packaging and dispatch.

Activation I-131 Manufacturing Facility will consist of the following areas:

- Storeroom (incl. non-radiological receiving)
- Sampling and Preparation Area (incl. Weighing Booth),
- Target Welding Area,
- Production Area,
- Packaging Area,
- Receiving and Dispatch area,
- Maintenance Area
- Waste Storage Area (Radiological and Chemical/Industrial Effluent)
- Ancillary Areas

Refer to Appendix B for the proposed facility layout and section 7.2 below for the detailed requirements.

The activation I-131 production line (i.e. hot cells) shall be operated from the front and accessed from the back for process and maintenance purposes. The front of the hot cells shall be located in a controlled and GMP classified area and the back of the hot cells in a controlled area, but not GMP classified area. The Activation I-131 Manufacturing Facility shall be designed to ensure compliance with cGMP and radiological requirements.

5.2. System Classification and Risk Assessment

The Activation I-131 Manufacturing Facility 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 Activation I-131 Manufacturing Facility 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. It is the responsibility of NTP to ensure:

6.1.1. This document is up to date.

6.1.2. Liaise with the consulting engineers and provide access to the NTP facilities and end users.

6.1.3. Make .pdf layout drawings (not fully dimensioned and not to scale) available.

6.2. It is the responsibility of the consulting engineers to:

6.2.1. Develop a facility, services and systems design based on the requirements prescribed in this document.

7. PROCESS

The user requirements for the Activation I-131 Manufacturing Facility 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 completed Activation I-131 Manufacturing Facility shall be designed, 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 (OHS Act)
7.1.5.	Act 103 of 1977: National Building regulations and building standards Act 103 of 1977
7.1.6.	ICH Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Step 4 Version, Nov 2000
7.1.7.	ISO 8573-1:2010: Compressed Air – Part 1: Contaminants and Purity Classes
7.1.8.	ISO14644-1:2015: Cleanrooms and Associated Control Environments, Part 1: Classification of Air Cleanliness by Particle Concentration
7.1.9.	ISO14644-3:2019: Cleanrooms and Associated Control Environments, Part 3: Test Methods
7.1.10.	ISO14644-4:2022: Cleanrooms and Associated Control Environments, Part 4: Design, Construction and Start-up.
7.1.11.	ISO 17873-2004: Nuclear facilities — Criteria for the design and operation of ventilation systems for nuclear installations other than nuclear reactors
7.1.12.	ISPE Baseline Guide: Commissioning and Qualification, Volume 5, 2nd Edition, 2019
7.1.13.	ISPE Good Practice Guide, Heating Ventilation and Air Conditioning (HVAC), 2009
7.1.14.	PE-009-17 (Part I & II): PIC/S Guide to Good Manufacturing Practice for Medicinal Products Part I & II, August 2023.

ID No.	Description
7.1.15.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 1: Manufacture of Sterile Medicinal Products, August 2023.
7.1.16.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 3: Manufacture of Radiopharmaceuticals, August 2023
7.1.17.	PE-009-17 (Annexes): PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Annex 15: Qualification and Validation, August 2023.
7.1.18.	SAHPGL-INSP-02_v9: SAHPRA Guideline on Good Manufacturing Practice for Medicines, Version 9, August 2025
7.1.19.	SAHPGL-INSP-GMP-02_v1: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Version 1, October 2025
7.1.20.	SAHPGL-RDN-RN-13_v2: SAHPRA Guideline for Management and Disposal of Non-nuclear Radioactive Waste, Version 2, December 2022
7.1.21.	SANS 1186-1: 2022: Symbolic Safety Signs, Part 1: Standard Signs and General Requirements, Edition 3.8
7.1.22.	SANS 7240-16:2008 Fire Detection and Alarm Systems Part 16: Sound System Control and Indication
7.1.23.	SANS 7240-19:2008 Fire detection and alarm systems Part 19: Design, installation, commissioning, and service of sound systems for emergency purposes
7.1.24.	SANS 10114-1: 2020: Interior Lighting Part 1: Artificial Lighting of Interiors, 4th Ed.
7.1.25.	SANS 10400: Application of the National Building Regulations
7.1.26.	SANS 10142: The Wiring of Premises
7.1.27.	SHEQ-INS-0233: Design Control
7.1.28.	SHEQ-INS-0234: NECSA QMS Requirement for External Design Organisations
7.1.29.	SHEQ-INS-1110: Housekeeping and Demarcation
7.1.30.	SHEQ-INS-1120: Lighting (Natural and Artificial)
7.1.31.	SHEQ-INS-1250: Colour Codes
7.1.32.	SHEQ-INS-2500: Affixing of Notices and Signs and Labelling of Electrical and Other Critical Equipment
7.1.33.	SHEQ-INS-5150: First Aid Officer and Facilities
7.1.34.	SHEQ-INS-7010: Zoning of facilities with hazardous chemical substances
7.1.35.	SHEQ-INS-7132: Necsa Ventilation Design Specification
7.1.36.	SHEQ-INS-7140: Management of hazardous chemical waste
7.1.37.	SHEQ-INS-8030: System for the classification and demarcation of radiological areas
7.1.38.	SHEQ-INS-8050: Radiological surveillance programme for workplaces
7.1.39.	SHEQ-INS-8150: Access and Egress Control to Radiological Areas
7.1.40.	SHEQ-INS-8180: ALARA programme
7.1.41.	SHEQ-INS-8230: Management of Radioactive Discharges to the Atmosphere at the Pelindaba Site
7.1.42.	SHEQ-INS-8260: Management of Radioactive Effluent and Discharge at the Pelindaba Site

ID No.	Description
7.1.43.	SHEQ-INS-8920: Access Control to Necsa Sites and Facilities.
7.1.44.	SHEQ-INS-8310: Requirements in respect of ventilation systems for nuclear facilities
7.1.45.	SHEQ-INS-8360: Necsa Solid Radioactive Waste Management System
7.1.46.	SHEQ-INS-8920: Access Control to NECSA Sites and Its Facilities
7.1.47.	WHO Technical Report Series (TRS) No. 957, Annex 3: WHO Good Manufacturing Practices for Pharmaceutical Products Containing Hazardous Substances, 2010.
7.1.48.	WHO Technical Report Series (TRS) No. 1010, Annex 8, Guidelines on Heating, Ventilation and Air-Conditioning Systems for Non-sterile Pharmaceutical Products, 2018
7.1.49.	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
7.1.50.	WHO Technical Report Series (TRS) No. 1019, Annex 3, Good Manufacturing Practices: Guidelines on Validation, 2019
7.1.51.	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.
7.1.52.	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 Activation I-131 Manufacturing Facility layout shall cater for the following areas and provide adequate segregation between the areas: • Storeroom • Sampling and Preparation Area (incl. Weighing Booth) • Target Welding Area • Production Area • Hot Cell Maintenance/Service Area • Packaging Area • Receiving and Dispatch Area • Radiological Effluent Area • Chemical/Industrial Effluent Area • Manufacturing Facility Ancillary Areas Refer to Appendix B for the proposed layout of the Activation I-131 Manufacturing Facility.

ID No.	Requirement
7.2.2.	The facility shall be zoned based on radiological and Hazardous Chemical Substances (HCS) areas requirements. The Hazardous Chemical Substances (HCS) areas shall be zoned and classified as per SHEQ-INS-7010.
7.2.3.	The radiological areas shall be separated from the non-radiological areas. The radiological areas shall be zoned and classifications as per SHEQ-INS-8030.
7.2.4.	Facility layout shall be able to accommodate ad-hoc maintenance activities and movement of large and heavy equipment (i.e. replacement of hot cell components, telemanipulators etc.) using portable lifting equipment and/or gantry crane.
7.2.5.	Facility floor loading capacity and surface finish durability must be able to handle the movement of portable lifting equipment.
7.2.6.	The 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.
7.2.7.	Appropriate storage cabinets shall be provided in the areas for storage of small quantities of chemicals, flammable solvents, and other consumables that are currently in use.
7.2.8.	Sufficient bench space shall be provided in all areas to place bench-top equipment and performing the required activities.
7.2.9.	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.
7.2.10.	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.
7.2.11.	The facility shall provide a dedicated area for the collection and interim storage of Hazardous Chemical Substances (HCS) solid and liquid waste with ease of access to the waste contractor.
Storeroom	
7.2.12.	The Storeroom layout must provide adequate space for the segregation of the following operations and processes to avoid mix-ups and cross-contamination: • Receiving of all materials (chemicals, consumables, primary packaging materials, cleaning/ disinfecting equipment and materials, gowning etc.) • Quarantine and storage of all materials • Sampling of consumables, primary packaging materials, gowning, cleaning agents • Visual inspection of all materials • Release/reject of all materials according to a specification. • Status labelling of all materials (quarantine, sampled, released, rejected) • Storage of released materials • Storage of rejected/expired materials
7.2.13.	Storage areas shall be of sufficient capacity and storage space/ shelves to allow orderly storage and segregation of the various categories of materials: raw materials (solid and

ID No.	Requirement
	liquids), primary packaging materials, consumables, cleaning/ disinfecting equipment and materials, gowning, corrosive and flammable chemicals etc.
7.2.14.	Segregated areas shall be provided for the storage of quarantined, released, expired or rejected materials.
7.2.15.	Physical quarantine storage areas shall be provided with access control to restrict access to authorised personnel only.
7.2.16.	Physical storage areas shall be provided for expired or rejected materials with access control to restrict access to authorised personnel only.
7.2.17.	Storage of materials shall allow cleaning and inspection. Materials shall be stored off the floor and suitably spaced (from each other and the wall) to permit cleaning and inspection.
Sampling and Preparation Area (incl. Weighing Booth)	
7.2.18.	The Sampling and Preparation Area (incl. weighing booth) shall provide adequate space for the segregation of the following operations and processes to avoid mix-ups and cross-contamination: • Sampling of starting and raw materials (solid and liquids). • Washing and drying of laboratory and process glassware, consumables and primary packaging materials. • Preparation of Al canister and targets. • Drying, weighing and preparation of chemicals, buffers and reagents. • Storage of prepared glassware, buffers and reagents. • Printing of primary and secondary packaging labels.
7.2.19.	Sampling of starting and raw materials (solid and liquids) must be performed under appropriate conditions in a separate sampling/weighing area designed for such use.
7.2.20.	The weighing of materials must be performed under appropriate conditions in a separate weighing room designed for such use.
Target Welding Area	
7.2.21.	The Target Welding area shall provide adequate space for the segregation of the following operations and processes to avoid mix-ups and cross-contamination: • Welding of prepared targets • Inspection of the prepared targets • Leak testing of prepared targets • Storage of the prepared targets
Production Area	
7.2.22.	The Production area shall provide adequate space for the following operations and processes: • Primary control interface (incl. manipulations) with the hot cells. • Removal and replacement of the hot cell manipulators. • Administrative activities (lab bench etc.)
7.2.23.	The floor in the radiological production areas shall provide adequate loading capacity to be able to hold 4 hot cells, weighing a total of 170 ton.

ID No.	Requirement
Hot Cell Maintenance/Service Area	
7.2.24.	The Hot Cell Maintenance/Service Area shall provide adequate space for the segregation of the following operations and processes to avoid mix-ups and cross-contamination: • Receiving of irradiated targets. • Introduction of irradiated targets into hot cells, • Discharge and secondary packaging of QC samples and product vials, • Maintenance of hot cells and components, • Storage of maintenance critical spare parts, • Leak testing of Type B packaging. • Storage of radioactive solid waste (low and medium active waste). • Removal of radioactive solid waste containers.
7.2.25.	The Hot Cell Maintenance/Service Area design shall not compromise the functionality of the existing gantry crane system, located in the building.
7.2.26.	The Hot Cell Maintenance/Service Area shall be adequately sized to allow the preparation of the concrete drums, the filling of the concrete drums with medium radioactive solid waste and the storage of a maximum of 6 concrete drums for a maximum of 90 days.
7.2.27.	The floor Hot Cell Maintenance/Service Area shall provide adequate loading capacity to be able to store a maximum of 6 concrete drums, each weighing up to 3 ton.
7.2.28.	The layout and design of the Hot Cell Maintenance/Service Area shall allow the concrete drums to be moved into and out of the facility using the existing gantry crane system.
7.2.29.	The Hot Cell Maintenance/Service Area shall provide adequate space for the entry and parking of a 4-ton truck for the receiving of the radioactive targets and the removal of the concrete drums. The door to the area shall be able to accommodate the height of the 4-ton truck. An airlock type of system shall be used for the entry of the truck.
7.2.30.	The Hot Cell Maintenance/Service Area shall be adequately sized to allow the interim storage of ± 6 low radioactive solid waste drums, with the following size and weight (filled) per drum: • Size: ø 609 mm, H = 884 mm • Weight: 70 kg
7.2.31.	The layout, design and size of the Hot Cell Maintenance/Service Area shall allow the storage and manoeuvring of the pallet trolley or drum trolley for the transfer of the low radioactive solid waste drums.
Packaging Area	
7.2.32.	The Packaging Area shall provide adequate space for the segregation of the following operations and processes to avoid mix-ups and cross-contamination: • Storage of already assembled and released packaging materials, • Final packaging of final products.

ID No.	Requirement
Receiving and Dispatch Area	
7.2.33.	The Radiological Receiving and Dispatch Area shall provide adequate space for the segregation of the following operations and processes to avoid mix-ups and cross-contamination: • Receiving of radiological materials/targets. • Release (RPO, QA and Shipment) and dispatch of final products. • Loading of radiological products into the dispatch vehicle.
7.2.34.	The dispatch area must provide adequate space for the entry and parking of a 4-ton truck for the dispatch of products. The door to the dispatch area must be able to accommodate the height of the 4-ton truck.
Radiological Effluent Area	
7.2.35.	The Radiological Effluent Area shall provide adequate space for the installation of the Low Active (LA) effluent management system and shall include: • Space for the placement of the effluent tanks inclusive of a bund. • An effluent transfer station for the parking of a road tanker. Refer to section 7.8 for the Radiological Effluent area requirements.
Chemical/Industrial Effluent Area	
7.2.36.	The Chemical/Industrial Effluent area shall provide adequate space for the installation of Chemical/Industrial effluent management system and shall include: • Space for the placement of the effluent tanks inclusive of a bund. • An effluent transfer station for the parking of a road tanker. Refer to section 7.8 for the Chemical/Industrial Effluent area requirements.
Manufacturing Facility Ancillary Areas	
7.2.37.	The facility layout shall cater for the following manufacturing facility ancillary areas: • Utilities and services. • Amenities and change rooms. • Storage space for cleaning equipment and materials. • Material and personnel transfer systems.
7.2.38.	Separate male and female change rooms shall be provided for the entry and exit to the manufacturing facility.
7.2.39.	Facilities for washing and toilet purposes shall not directly communicate with manufacturing facility.
7.2.40.	Adequate storage facilities shall be provided in the facility change rooms for the storage of street clothes, personnel belongings, and protective clothing and shoes.
7.2.41.	Adequate storage facilities shall be provided in the GMP and radiological change rooms for the storage of cleanroom gowning and protective clothing and shoes.
7.2.42.	Rest and refreshment rooms shall be separate from manufacturing facility.
7.2.43.	Material entry and exit points to and from the facility shall be adequately sized to allow the transfer of the required material and product containers.

ID No.	Requirement
7.2.44.	The material transfer chambers, or Material Airlock (MAL) shall be of a size that enables the effective transfer and surface decontamination of materials being passed through it.

7.3. Process Requirements – Product Physical Properties

ID No.	Requirement
7.3.1.	The Activation I-131 API has the following characteristics: • Chemical Form: Sodium Iodide (I-131) Solution • Non-sterile API solution (oral dosage) • Radiological

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

ID No.	Requirement
7.4.1.	Temperature in the following areas shall be controlled, continually maintained and monitored between 18 - 25 °C: • Storeroom • Sampling and Preparation Area • Weighing Booth • Production Room • Grade D Change Room
7.4.2.	Relative humidity (RH) in the following areas shall be controlled, continually maintained and monitored between 30 – 60%: • Storeroom • Sampling and Preparation Area • Weighing Booth
7.4.3.	The Activation I-131 Manufacturing Facility areas shall consist of the following air cleanliness classifications in the "at-rest" state: • Grade D Change Room: GMP Grade D [ISO 14644 Class 8] • Sampling and Preparation Area: GMP Grade D [ISO 14644 Class 8] • Production Area: GMP Grade D [ISO 14644 Class 8] • All other areas shall be Controlled Not Classified. Refer to Appendix B for the proposed GMP area classifications.
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.

ID No.	Requirement
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. Refer to Appendix B for the concept area classifications.
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 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. 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.
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

ID No.	Requirement
7.5.1.	Equipment that requires control shall be equipped with a localised controller.
7.5.2.	Each localised controller shall have an interface with the Building Management System (BMS). The BMS shall serve as the human interface with the controllers for the input of settings and the output of parameter measurements. The communication protocols shall include: • BACNET over IP. • ETHERNET/IP. Refer to NTP-SPE-4168 for the BMS requirements.

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. Refer to Appendix C for the proposed material and personnel flows.
7.6.2.	Facility layout shall allow for the safe and easy removal and storage of the solid and liquid waste (all types) minimizing any risk of error, mix-up and contamination of the materials, products, and adjacent areas.
7.6.3.	Receiving and dispatch bays shall protect materials and products from the weather.
7.6.4.	Receiving areas shall be designed and equipped to allow containers of incoming materials to be cleaned where necessary before storage.
7.6.5.	Transfer of materials between different area classifications shall be via appropriate actively ventilated transfer chambers (pass through hatches) or Material Airlocks (MAL).
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 prevented.
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 in order to minimize shedding or accumulation of particles, micro-organisms or radiological contamination on the surfaces.
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.

ID No.	Requirement
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).
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.
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.

ID No.	Requirement
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 wall/ 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 should be slip-proof.
Sinks and Drains	
7.6.35.	Sinks and drains in GMP Grade D “at-rest” [ISO 14644 Class 8] and radiological areas shall be fitted with easily cleanable traps and air-breaks between the equipment/sink and the drains to prevent back flow.
7.6.36.	Floor drains in GMP Grade D “at-rest” [ISO 14644 Class 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.
7.6.37.	Sinks shall be made of a durable material, without overflow and be adequately spaced away from walls to avoid uncleanable joints and crevices.
7.6.38.	Sinks and drains shall be acid, solvent and stain resistant.
Pipe Work, Light Fittings, Ventilation Points and Other Services	
7.6.39.	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.
7.6.40.	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.
7.6.41.	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.
7.6.42.	Exposed piping, tubing and cable runs shall be minimized in the cleanrooms.
7.6.43.	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.
7.6.44.	Pipe work, light fittings, ventilation points and other services shall be labelled with name of service as well as flow direction where appropriate as per SHEQ-INS-1250 and SANS 10140.

ID No.	Requirement
7.6.45.	Pipes shall be adequately sloped for drainage and constructed without 'dead-legs'.
Personnel Airlock (PAL) or Change Rooms	
7.6.46.	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).
7.6.47.	Change rooms shall be designed as airlocks and provide physical separation of the different stages of changing to minimise microbial, particulate, and radiological contamination of operators and protective clothing.
7.6.48.	The entry and exit doors of personnel airlocks shall not be opened simultaneously.
7.6.49.	Handwash basins and hand sanitizing/disinfection systems shall be provided in the GMP classified change room (GMP Grade D "at-rest" [ISO 14644 Class 8] change rooms).
7.6.50.	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.
7.6.51.	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.
7.6.52.	Storage of garments in all the personnel change rooms shall be provided. Consideration shall be given to the use of hanging rails and perforated shelves rather than closed lockers.
7.6.53.	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.
7.6.54.	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	
7.6.55.	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).
7.6.56.	The entry and exit doors, for material/waste airlock or transfer chambers shall not be opened simultaneously.
7.6.57.	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.
7.6.58.	Adequate space shall be provided around the material/waste airlock or transfer chambers for the introduction and removal of materials.
7.6.59.	Clear windows shall be provided on all the doors of the material/waste airlock or transfer chambers to allow a line-of-sight view.

ID No.	Requirement
Furniture	
7.6.60.	Laboratory furniture shall be fit for purpose. Open spaces between and under benches, cabinets and equipment shall be accessible for cleaning.
7.6.61.	Furniture shall not include any fabric surfaces which may absorb and hold contaminants.
7.6.62.	Bench tops shall have curved edges wherever possible for easy cleaning.
Weighing Areas	
7.6.63.	Weighing areas shall be appropriately designed to provide the required levels of containment, operator protection and product protection.
7.6.64.	Weighing shall be performed under the same environmental conditions as specified in the areas for the next stage of use.
7.6.65.	Vibration damping measures shall be considered in all the weighing areas in the facility.
7.6.66.	In cases where dust (chemical powders) is generated (e.g. weighing) specific provisions shall be taken to avoid cross-contamination and facilitate cleaning.
7.6.67.	In the case where dust (chemical powders) is generated, they shall be removed at source. The HVAC system shall not be used as the primary mechanism of control.

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 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 process equipment (i.e. hot cells etc.).
7.7.3.	Extraction systems integrated into the HVAC system, which has an impact on the balance of the airflow of the facility, shall be provided as part of the facility design and layout.

7.8. Services and Support Systems

ID No.	Requirement
7.8.1.	The Activation I-131 Manufacturing Facility shall be provided with the following services and support systems: • Heating Ventilation and Air Conditioning (HVAC) System • Lighting (incl. Emergency Lighting) • Compressed Air • Potable/Drinking Water • Process Water (Purified Water System) • N_2 Process Gas • Electricity Supply • Back-up Power Supply (Generator) and Emergency Supply (UPS)

ID No.	Requirement
	• Information and Communication Technology (ICT) System • Fire Detection and Protection System • Safety Systems • Plumbing and Drainage • Access Control and Security Systems • CCTV • Public Address • Intercom • Building Management System (BMS) • Radiation Protection (RP) and Monitoring Systems • Low Active (LA) Effluent Management System • Chemical/Industrial Effluent Management System
7.8.2.	The service provider shall advise on the requirements (i.e. quality, capacity, condition etc.) of the utilities required to provide the required services to the facility.
Heating Ventilation and Air Conditioning (HVAC) System	
7.8.3.	The prospective service provider shall: • Review the list of relevant references listed in section 7.1 of this document for sufficiency (i.e. completeness). • Finalise a list a HVAC system design requirements, inclusive of the requirements listed in this document. • Identify potential conflicting design requirements. All conflicting design requirements shall be resolved through engagement between NTP and the service provider.
7.8.4.	The facility shall be provided with an HVAC system capable of achieving the requirements listed in section 7.4.
7.8.5.	The HVAC system shall be designed for a reliable operation at 100% duty cycle.
7.8.6.	The HVAC system shall be designed to be durable, with an expected service life of no less than 15 years.
7.8.7.	The HVAC system shall not generate excessive noise during normal operation. Normally occupied spaces shall not experience noise levels above ANSI NC 50 due to the function of the HVAC system.
7.8.8.	The HVAC system shall be controlled via a dedicated HVAC control system to ensure continuous compliance within the defined limits for parameters e.g. temperature, relative humidity, airflow and pressure differential. (Refer to section 7.5 for automation requirements)
7.8.9.	The performance of the HVAC system (incl. the CPPs in section 7.4) shall be monitored, recorded and alarmed by a Building Management System (BMS). Refer to section 7.5 for the BMS requirements.

ID No.	Requirement
7.8.10.	Differential pressures between rooms of the classified 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 differential pressures shall also be recorded and alarmed by 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 required.
7.8.11.	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.
7.8.12.	All instrumentation related to the monitoring of the HVAC system shall be calibrated. Calibration of the instrumentation shall be valid at the time of facility handover.
7.8.13.	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.
7.8.14.	The final filter used shall have an EN 1822 classification of at least H14. Each final filter shall be provided with individual serial numbers and test certificates.
7.8.15.	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.
7.8.16.	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.
7.8.17.	The differential pressures across all individual filters or filter banks shall be monitored and displayed locally and on the BMS. The pressures shall be recorded by the BMS.
7.8.18.	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.
7.8.19.	In areas where weighing is performed, unidirectional airflow (UDAF) (also known as LAF) shall be provided. The airflow shall not disrupt the accuracy of balances.
7.8.20.	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.
7.8.21.	In the areas where Hazardous Chemical Substances (HCS) are handled and stored, compatible extraction systems shall be installed for the removal of the HCS fumes. The HCS HVAC systems shall be designed as per SHEQ-INS-7132.
7.8.22.	In the areas where dust is generated, dust extraction systems shall be installed for the removal of the dust.
7.8.23.	The extraction systems shall be appropriately designed and installed. Dust/fumes shall not be able to flow back in the opposite direction in the case of component failure or airflow failure. The transfer velocity shall be sufficient to ensure that dust/fumes are carried away and does not settle in the ducting.
7.8.24.	The extraction points shall be positioned in such a way as to prevent particles dropping down from the extract point causing contamination or cross-contamination.

ID No.	Requirement
7.8.25.	The material of construction of the HVAC systems (incl. extraction systems), components and ducting shall be durable, non-shedding, not be a source of contamination and shall be resistant to HCS (acids and solvents) (where applicable)
7.8.26.	Insulated ducting shall be double skinned. No internally insulated ducting shall be used to provide clean and conditioned air to the GMP classified and controlled areas.
7.8.27.	Supply, return and exhaust grilles shall be appropriate, and their design shall facilitate cleaning and maintenance.
7.8.28.	Ventilation points shall create minimal recesses that may allow accumulation of dust and dirt and shall facilitate cleaning and maintenance.
7.8.29.	Ventilation points 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.
7.8.30.	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.
7.8.31.	Cross-contamination from room to room in the event of a system or fan failure shall be prevented.
7.8.32.	The design of the HVAC systems shall prevent back-flow of contaminated air to the areas in the event of failure.
7.8.33.	Where humidification or dehumidification is required, this shall be achieved by appropriate means that will not become a source of contamination.
7.8.34.	Dehumidification and cooling systems shall be well drained. Condensate shall not accumulate in air-handling systems and shall not become a source of contamination.
7.8.35.	The radiological HVAC exhaust or return systems shall be equipped with activated impregnated carbon filtration for the purposes of I-131 adsorption.
7.8.36.	HEPA and activated impregnated carbon filters installed on the radiological HVAC exhaust or return systems shall be of the Bag-in-Bag-out (BIBO) type.
7.8.37.	The radiological HVAC design shall comply with the requirements specified in SHEQ-INS-8310 and ISO 17873. Refer to Appendix D for a HVAC concept.
7.8.38.	The radiological HVAC design shall include a radiological monitoring and alarm system on the exhaust or return. The system shall be installed by NTP. The interface requirements of the system shall be coordinated with NTP's Safety Department.
7.8.39.	A central HVAC release point shall be required above the roof with monitoring. The requirements of the central HVAC release point and monitoring shall be coordinated with the Necsa Licensing Department.
7.8.40.	The HVAC system design, installation and commissioning shall be signed off by an ECSA registered Professional Engineer, Professional Technologist or Professional Technician competent in the field of radiopharmaceutical HVAC systems design.

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7.8.41.	All equipment supplied during the construction of the HVAC system (incl. filters) shall bear one of the following marks of quality: • The South African Bureau of Standard (SABS) mark • The Conformitè Europëenne (CE) mark • The Eurovent Certified Performance mark. • Or equal and approved.
Lighting (incl. Emergency Lights)	
7.8.42.	Lighting shall be LED type with suitable ingress protection. Lights shall be energy efficient.
7.8.43.	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.
7.8.44.	Lighting levels of ≥ 500 lux are required at bench level.
7.8.45.	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	
7.8.46.	Clean oil and moisture free compressed air shall be provided to the following areas as a minimum but not limited to: • Target Welding Area • Sampling and Preparation Area • Production Area • Hot Cell Maintenance/Service Area
7.8.47.	Compressed air with a purity of Class 3 as per ISO 8573-1 shall be provided at pressure of at least 8 bar.
7.8.48.	A duty standby compressed air system configuration shall be provided.
7.8.49.	The system shall provide a continuous supply of compressed air at a consistent pressure and flow at all POUs.
7.8.50.	Materials of construction shall be non-reactive, non-shedding and suitable for pharmaceutical use. Stainless steel 316L or similar is acceptable.
7.8.51.	The system shall be provided with sampling points, that are clearly and uniquely identified and easily accessible, to allow the sampling of the gas throughout the system.
7.8.52.	Compressed air system shall be tested and certified according to ISO 8573 and certificates shall be provided.
7.8.53.	The system pressure shall be monitored using calibrated instruments.
7.8.54.	The system pressure and status shall be continuously monitored, recorded and alarmed.
7.8.55.	The system shall interface with the BMS.
Potable / Drinking Water	
7.8.56.	Potable water shall be provided at basins for hand washing, in the GMP and radiological change rooms. Cold water shall be provided as a minimum with hot water where possible.

ID No.	Requirement
7.8.57.	Potable water shall be provided as the in-feed to the Water Purification Systems located in the Sampling and Preparation Area.
7.8.58.	Potable water shall be supplied to the emergency showers.
7.8.59.	Potable /drinking water shall be provided by NTP to a single point on the building boundary line. Distribution within the facility boundary shall be performed by the service provider.
Process Water (Purified Water System)	
7.8.60.	Purified water shall be provided via a Water Purification system provided by NTP.
7.8.61.	Space and a potable water connection point shall be provided in the Sampling and Preparation Area for the installation of the Water Purification system provided by NTP.
Nitrogen (N_2) Process Gas	
7.8.62.	Nitrogen gas shall be used in the hot cells as part of the production process. N_2 shall be provided to the Hot Cell Maintenance/Service Area in order feed into the hot cells. The final connection to the hot cells shall be performed by NTP.
7.8.63.	Nitrogen (N_2) with a purity of ≥ 99.999% (Purity N5.0) or higher (as per the European Pharmacopiea) shall be provided to the facility at pressure of at least 8 bar.
7.8.64.	A duty standby configuration with an automatic/semi-automatic change-over manifold shall be provided.
7.8.65.	The system shall provide a continuous supply of N_2 at a consistent pressure and flow at all POUs.
7.8.66.	The system shall consist of a capacity equal to 4 cylinders on each side of the bank (8 cylinders in total – 19 kg per cylinder).
7.8.67.	Materials of construction shall be non-reactive, non-shedding and suitable for pharmaceutical use. Stainless steel 316L or similar is acceptable.
7.8.68.	The N_2 system shall be equipped with adequate filtration to remove particles and ensure clean gas (as per URS ID No. 7.8.63) is supplied to the hot cells.
7.8.69.	The filters shall be integrity testable.
7.8.70.	Filter housing shall allow safe, easy and clean replacement of the filters.
7.8.71.	The Nitrogen system shall be located in a well-ventilated area.
7.8.72.	The system pressure shall be monitored using calibrated instruments.
7.8.73.	The system pressure and status shall be continuously monitored, recorded and alarmed.
7.8.74.	The system shall interface with the BMS.
7.8.75.	The system shall be tested as per the applicable standards and certificates provided.
7.8.76.	Gas installations shall be performed by SAQCC registered and authorised Gas Practitioners.
Electricity Supply	
7.8.77.	400 V, 3-phase, 50 Hz electrical supply shall be provided to the facility (incl. the effluent areas). Adequate number of wall sockets and isolators shall be provided in the all the

ID No.	Requirement
	areas (incl. the effluent areas). The location of these shall be coordinated with equipment positions. Provision shall be made for at least 30% extra wall sockets.
7.8.78.	Power cabling shall be located in dedicated cable tray or in conduits.
7.8.79.	The electricity supply system design shall comply to SANS 10142 and is subject to Necsa approval.
7.8.80.	All facility equipment shall be compatible with the South African national electrical grid (i.e. voltages, frequency and applicable tolerances).
7.8.81.	Only suppliers and equipment approved by Necsa shall be used.
7.8.82.	A Certificate of Compliance (CoC) shall be furnished for the electrical installation and shall be subject to sign-off by a Necsa responsible person.
7.8.83.	Electricity supply shall be provided by NTP to a single point on the building boundary line. Distribution within the facility boundary shall be performed by the service provider.
Back-up Power Supply (Generator) and Emergency Supply (UPS)	
7.8.84.	Back-up power supply (generator system) shall be provided to the critical equipment. The critical equipment that must be connected to the generator will be determined during the design phase.
7.8.85.	The Back-up power supply (generator system) shall be provided with a 999 L fuel capacity.
7.8.86.	Emergency supply (UPS system) shall be provided to the critical equipment. The critical equipment that must be connected to the UPS will be determined during the design phase.
7.8.87.	The emergency supply (UPS system) shall be provided with a 20-minute autonomous operating capacity at full load.
7.8.88.	The status of the UPS and Generator shall be monitored, recorded and alarmed by the BMS.
Information and Communication Technology (ICT) System	
7.8.89.	Sufficient ethernet points shall be provided in the areas to support the related equipment in the rooms to be connected to the network.
7.8.90.	The ICT system shall be designed and installed by Necsa/NTP. The requirements and installation of the ICT systems shall be coordinated with Necsa/NTP.
Fire Detection and Protection	
7.8.91.	The facility fire detection and protection design and signage shall comply to SANS 10400-T and SANS 7240.
7.8.92.	NECSA shall approve the fire detection and protection design and installation. It is the responsibility of the service provider to obtain the approval and signature from Necsa.
Safety Systems	
7.8.93.	Appropriate safety signage shall be provided throughout the facility, in accordance with SHEQ-INS-2500 and SANS 1186-1.

ID No.	Requirement
7.8.94.	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.
7.8.95.	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	
7.8.96.	The plumbing and drainage system shall be designed and constructed as per SANS 10400-P.
7.8.97.	Washbasin and drains shall be provided in the following areas: • Sampling and Preparation Area • All change rooms
7.8.98.	Washbasins and drains shall be acid and solvent resistant.
7.8.99.	The facility shall be equipped with adequate plumbing system for the drainage of household, industrial (i.e. chemical) and Low Active (LA) effluent. Effluents of different classifications shall be segregated.
7.8.100.	Washbasins and drains located in the radiological areas shall be directly connected to the Low Active (LA) effluent management system for the direct transfer of the LA effluent.
7.8.101.	Washbasins and drains located in the areas where HCS are handled (i.e. Sampling and Preparation Area) shall be directly connected to the Chemical/Industrial effluent management system for the direct transfer of the HCS effluent.
7.8.102.	Plumbing and drainage shall be provided by NTP to a single point on the building boundary line. Distribution within the facility boundary shall be performed by the service provider.
Access Control and Security Systems (Alarms, CCTV etc.)	
7.8.103.	Access to processing areas shall be restricted to authorised personnel only.
7.8.104.	The access control and security systems shall be designed and installed by Necsa Security Services. The requirements and installation of the access control and security systems shall be coordinated with Necsa Security Services as per SHEQ-INS-8920.
Public Address	
7.8.105.	The facility shall be equipped with a PA system in accordance with safety standards.
7.8.106.	The PA system shall be integrated with the existing PA system onsite.
7.8.107.	The PA system shall be designed and installed by Necsa ECC (Emergency Control Centre). The requirements and installation of the PA system shall be coordinated with Necsa ECC.
Intercom	
7.8.108.	Facility shall be equipped with an intercom system to ease communication between the areas.
Building Management System (BMS)	
7.8.109.	The facility shall be equipped with a BMS in compliance with NTP-SPE-4168.

ID No.	Requirement
Radiation Protection (RP) and Monitoring Systems	
7.8.110.	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.
7.8.111.	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	
7.8.112.	The Low Active (LA) effluent management system shall be designed and installed by NTP.
7.8.113.	The Low Active (LA) effluent management system shall be located in an enclosed radiological area with access control.
7.8.114.	The area shall be protected from weather conditions and vermin proof.
7.8.115.	Storm water/ rainwater shall be prevented from entering the area to avoid increasing the radiological effluent volumes.
7.8.116.	A bund shall be provided at the effluent transfer station and at the location of the effluent tanks. The materials of construction of the bund shall not be absorptive.
7.8.117.	The liquid effluent management system control system shall interface with the BMS.
7.8.118.	The area shall be provided with adequate ventilation, which is integrated into the facility radiological HVAC system.
Chemical/Industrial Effluent Management System	
7.8.119.	The Chemical/Industrial effluent management system shall be designed and installed by NTP.
7.8.120.	The Chemical/Industrial effluent management system shall be located in an enclosed HCS area with access control.
7.8.121.	The area shall be protected from weather conditions and vermin proof.
7.8.122.	Storm water/ rainwater shall be prevented from entering the area to avoid increasing the HCS effluent volumes.
7.8.123.	A bund shall be provided at the effluent transfer station and at the location of the effluent tanks.
7.8.124.	The liquid effluent management system control system shall interface with the BMS.
7.8.125.	The area shall be provided with adequate ventilation, which is integrated into the facility HCS HVAC system.

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.

ID No.	Requirement
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.
7.9.4.	There shall be good access to the HVAC system and components for routine maintenance.

7.10. Constraints

ID No.	Requirement
7.10.1.	The manufacturing facility shall be constructed within the allocated footprint provided. Refer to the Appendix B for the proposed layout for the facility.
7.10.2.	The design of the HVAC system shall consider the applicable altitude above sea level, ambient temperature and ambient humidity, atmospheric conditions and insolation loads to render a functional HVAC system.

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 successfully commissioned by the service provider and/or subcontractors to the service provider, prior to handover to NTP.
7.11.4.	NTP shall be involved with the commissioning activities and shall review and accept the commissioning plans/protocols, acceptance criteria and reports.
7.11.5.	All commissioning protocols shall be completed in accordance with Good Documentation Practices as per GMP requirements.
7.11.6.	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.
7.11.7.	The service provider shall supply documented evidence that the requirements of this URS have been met.
7.11.8.	Certificates of compliance with relevant national standards shall be supplied where applicable.

ID No.	Requirement
Qualification Requirements	
7.11.9.	At the completion of the construction of the facility and commissioning activities, the quality critical facility, services, support and computerised systems (incl. BMS) (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 shall be involved with the qualification activities and shall review and accept the qualification plans/protocols, acceptance criteria and reports.
7.11.10.	All qualification protocols (DQ, IQ and OQ) shall be completed in accordance with Good Documentation Practices as per GMP requirements.
7.11.11.	Performance Qualification (PQ) shall be performed by NTP.
7.11.12.	Qualifications shall be completed prior to hand-over to NTP and routine use of the facility, services and systems.
Handover Documentation	
7.11.13.	The service provider shall supply the following documentation as a minimum (for all systems, 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/service providers and maintenance contractor(s) • Preventative maintenance task list with recommended frequencies
Maintenance and Service Level Agreement	
7.11.14.	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.
7.11.15.	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).

ID No.	Requirement
Life-cycle Testing	
7.11.16.	All controlling and monitoring sensors/displays and measuring instruments shall be added to NTP's In-service Inspection and Maintenance Plan (ISI&MP) in accordance with the frequency determined for each item.
Training	
7.11.17.	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 requirements. Training shall be documented and maintained.
QMS Documentation	
7.11.18.	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
Change and Requirements Management	
7.11.19.	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.
7.11.20.	Adequate change management shall 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.
7.11.21.	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.
7.11.22.	The service provider shall provide a Requirements Traceability Matrix (RTM), inclusive of the relevant evidence and sign off each item in the matrix. Any deviation from the RTM shall be approved by NTP before execution.

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.

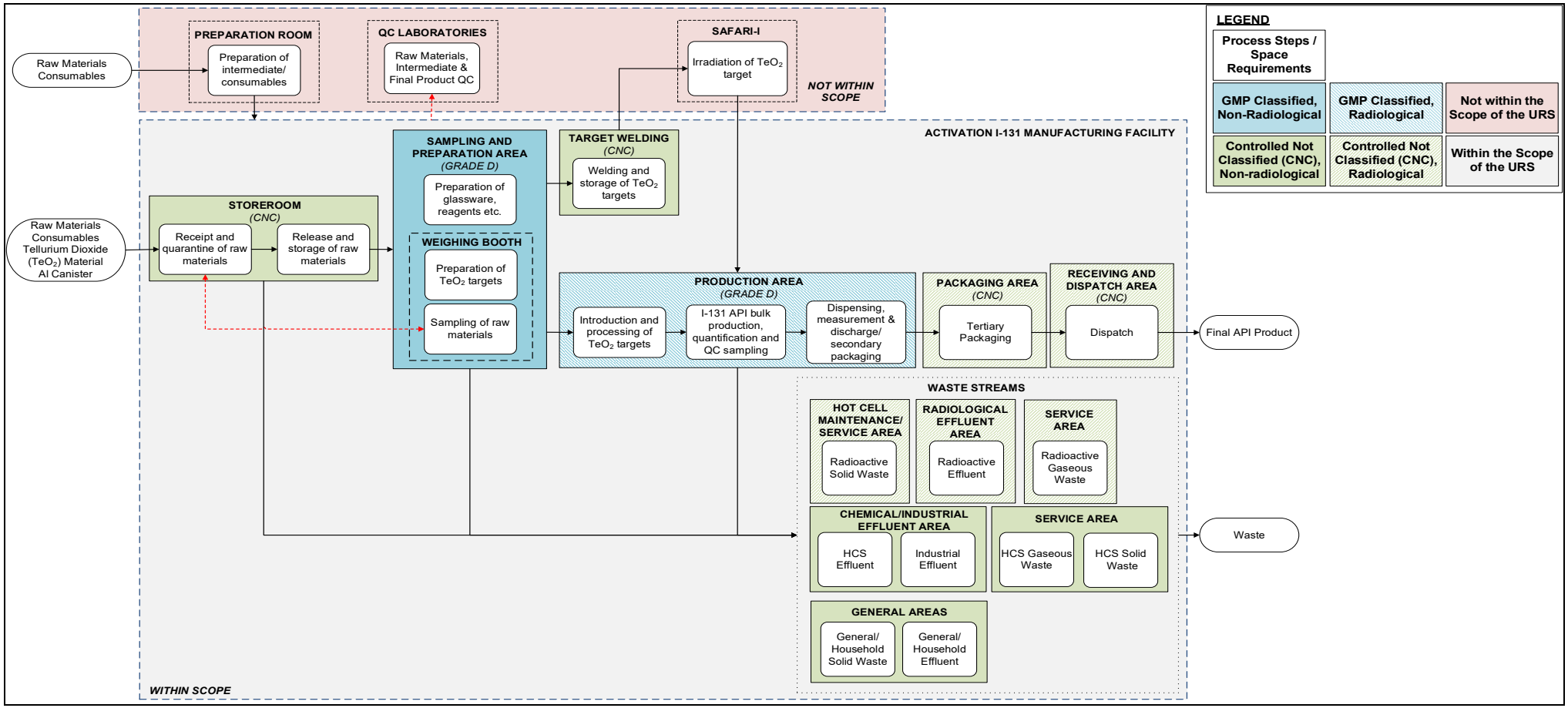
10. LIST OF FORMS

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

11. REVISION HISTORY

Rev.	Date Approved	Nature of Revision	Originated by
1	2024/06/03	First issue	M Mukwevho
2	See title page	Added more requirements to the document - Replaced section 7.1 with sections 7.2 to 7.11. Updated the diagram in Appendix A. Added Appendix B to D.	MM van Vuuren

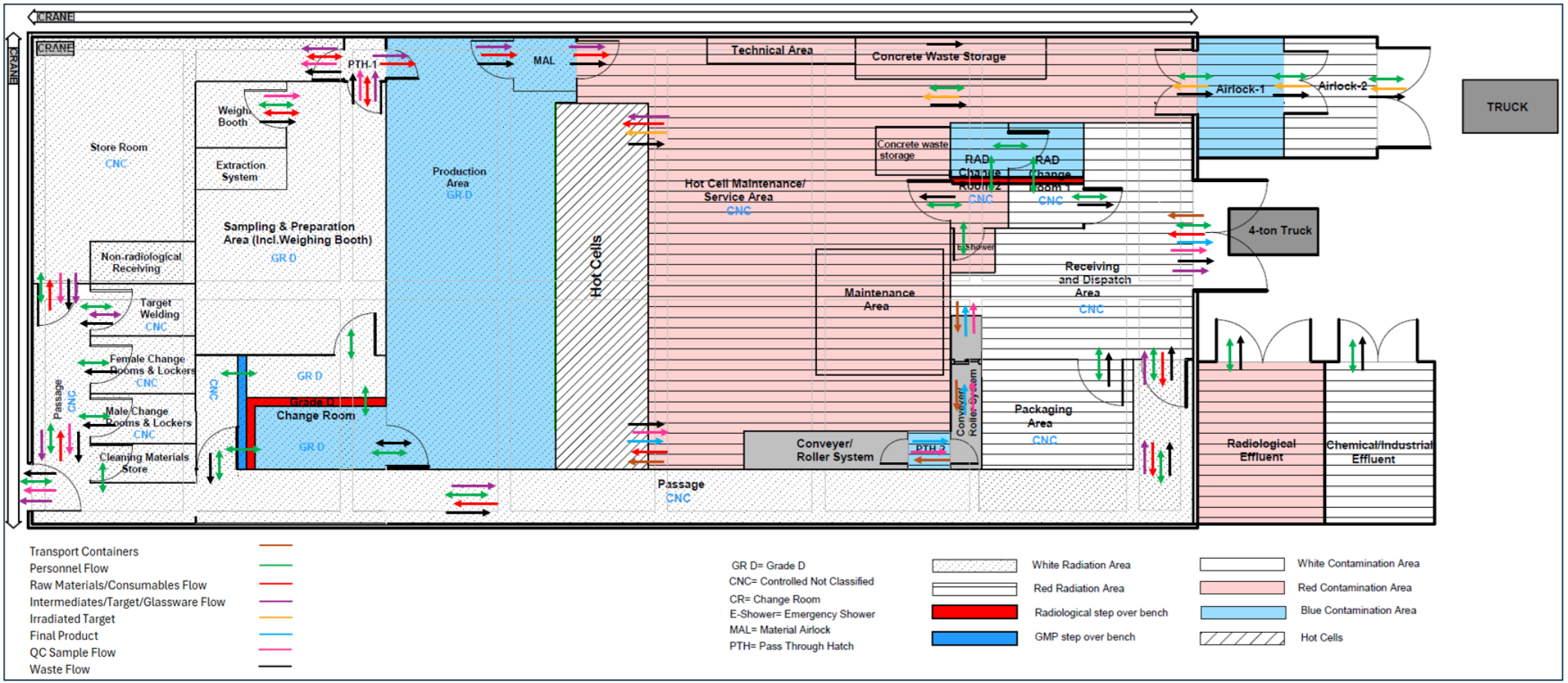
APPENDIX A:
OVERALL PROCESS FLOW DIAGRAM



APPENDIX B:
PROPOSED LAYOUT AND AREA CLASSIFICATIONS

Refer to Drawing No.: I5381-00-00: Facility Proposed Layout, Rev. 1

APPENDIX C:
PROPOSED PERSONNEL, MATERIAL AND WASTE FLOWS



APPENDIX D:
PROPOSED HVAC SCHEMATIC DIAGRAM