



## SPECIFICATION

### Hot Cell for Synthesis of PET/SPECT Radiopharmaceuticals

#### 1. Scope

This specification describes the requirements for a Hot Cell (hereinafter referred as “the System”), for synthesis of gamma and beta emitting radiopharmaceuticals including [ $^{18}\text{F}$ ]-PSMA, [ $^{18}\text{F}$ ] AIF-FAPI-74, [ $^{18}\text{F}$ ]-NaF... etc. for production of GMP grade agents.

The system shall be installed and used in the Production Facilities of the Radioactive Isotope Centre (SISORA), Tunis, Tunisia (hereinafter referred as “the End-User”).

#### 2. Applicable Documents

The following documents shall be applicable for this Specification to the extent specified hereinafter:

- 2.1. EudraLex The Rules Governing Medicinal Products in the European Union Volume 4 EU Guidelines to Good Manufacturing Practice (GMP) Medicinal Products for Human and Veterinary Use Annex 1 Manufacture of Sterile Medicinal Products (corrected version)

In the event of conflict between the documents listed above and the content of this Specification, the content of this Specification shall take precedence to the extent of the conflict.

#### 3. Definitions, Acronyms, and Abbreviations

The following definitions, acronyms, and abbreviations shall apply throughout this Specification unless defined otherwise hereinafter:

- 3.1. GMP: Good Manufacturing Practice;
- 3.2. HEPA: High Efficiency Particulate Air;
- 3.3. DQ: Design Qualification;
- 3.4. IQ: Instrument Qualification;
- 3.5. OQ: Operations Qualification;
- 3.6. QC: Quality Control;
- 3.7. FAT: Factory Acceptance Test;
- 3.8. SAT: Site Acceptance Test.

#### 4. Requirements

##### 4.1. Functional, Performance and Technical Requirements

- 4.1.1. The System shall meet the following requirements:



- 4.1.1.1. The synthesis hot cell shall be designed to house most of the commercially available synthesis units that meet cGMP requirements. It shall provide a shielded compartment with 75mm (minimum) wide shielding in all directions.
- 4.1.1.2. An internal stainless-steel box with large radius corners for easy cleaning and a sliding tray for easy, ergonomic access to the module, making this a user-friendly synthesis box design.
- 4.1.1.3. The air inlet shall be HEPA filtered, the air is taken from the front and the outlet air is filtered via a carbon filter.
- 4.1.1.4. The Hot cell shall Have Front access through 2 doors, the primary hinged lead shielded door and a secondary (interior) hinged door shall be equipped with special seals to maintain airtight integrity. These doors shall be independent and open separately.
- 4.1.1.5. The Synthesis Hot cell shall be equipped with: shielded target line (from floor level to compartment bottom), power connections and basic gas connections.
- 4.1.1.6. Have air-tight passages for capillaries and technical gases and multi-diameter sealed pass-through system for cables.
- 4.1.1.7. Have a dose calibrator placed inside the shielded area, with automatic up/down lift for received radioactivity calculation.
- 4.1.1.8. Include the following:
- Removable sliding Tray for synthesis module (synthetizes chamber);
  - UV antibacterial lamp;
  - GM probe for radiation monitoring and interlock control system;
  - Sliding tray for laptop and dose calibrator read-out unit support;
  - A system for automatic leak tests.
- 4.1.1.9. Able to work with AC 110-220 V, 60 Hz.
- 4.1.1.10. Include an UPS due to the fluctuation of the electrical voltage in Tunisia.
- 4.1.1.11. As the system will be connected to the centralized ventilation-extraction system of the production area. Thus, the air leaving the containment enclosure shall pass through a HEPA and Active Carbon filter. Exhaust hose is needed to be connected to a standard air duct ending (Ø 100mm).
- 4.1.1.12. Be able to operate under the current environment in the laboratory: GMP Class B (temp = 22 °C) and no humidity control in the laboratory.



#### **4.1.2. Features of Synthesis Hot Cell:**

- 4.1.2.1. Approximate Outside dimensions:  $\pm 1200*1030*2800$  mm (W\*D\*H).
- 4.1.2.2. Approximate Working Chamber Internal dimensions:  $\pm 742*735*674$  mm (W\*D\*H).
- 4.1.2.3. Hinged door with special seals to maintain airtight integrity.
- 4.1.2.4. Door opening:  $\pm 970*800$  mm (W\*H)
- 4.1.2.5. 316L AISI stainless steel work chambers with Mirror- Bright internal surface finish, TIG (Tungsten Inert Gas) continuous welds, and widely rounded corners.
- 4.1.2.6. Shielded and hinged front doors.
- 4.1.2.7. 304 AISI stainless steel front coverings, easy to decontaminate, separates the laboratory area (front) from the technical cabinet (rear).
- 4.1.2.8. Shielded glass window (dimensions:  $\pm 150*150$  mm (W\*H)).
- 4.1.2.9. Shielding elements realised from primary ingots with Pb 98% + Sb 2% purity.
- 4.1.2.10. Air inlet filtration system made with HEPA absolute filtering cartridge with 99.995% efficiency.
- 4.1.2.11. Air outlet filtration system made with active carbon filtering cartridge.
- 4.1.2.12. Work chambers air quality complies with Class B "At rest" (EEC-cGMP).
- 4.1.2.13. Particle counter connection.
- 4.1.2.14. Basic gas connections: Three technical gasses and one compressed air.
- 4.1.2.15. 1/8" technical gas supply lines with shut-off valves, which can be controlled from the outside.
- 4.1.2.16. 6 mm technical gas supply line with shut-off valves, which can be controlled from the outside.
- 4.1.2.17. Touch-Screen HMI control panel for all controls to check and trace the critical parameters of the machine both in "at rest" or "in operation" mode.
- 4.1.2.18. Power connection in accordance with local requirements.
- 4.1.2.19. Exterior smooth finish, easy to decontaminate.
- 4.1.2.20. Geiger-Muller probe to detect radioactivity inside the cell and door interlock management.
- 4.1.2.21. Removable tray for synthesis module.
- 4.1.2.22. Lower technical cabinet.
- 4.1.2.23. Airtight connections for radioactive fluids.
- 4.1.2.24. Fluid supply lines made of AISI 316L stainless steel with ball shut-off valves.
- 4.1.2.25. Internal pressure automatic adjustment by modulating valves.

#### **4.2. the system shall:**

- 4.2.1. Have a PLC to control and modulate the various parameters and alarms: pressure difference, air flow, interlocking, opening and closing of doors, radiation within the hot cell.
- 4.2.2. Manage alarms and have access to different parameters.



4.2.3. Save the different data that can be exported or/and printed.

4.2.4. Have connection nozzles to any equipment for:

- Particle count control;
- qualification and verification of the pressure difference, integrity of the filters.

4.2.5. Have a Sliding tray for laptop (For synthesis units) and dose calibrator read-out unit support.

## 5. Marking

The System shall have all safety markings either in French or in English language.

## 6. Packing

The System, for the shipment by sea to the End-User, shall be packed in accordance with international standards that are applicable for the shipment by sea of this kind of equipment.

## 7. Quality Requirements

7.1. The System shall be manufactured, shipped and installed in accordance with the Contractor's ISO quality assurance system or an equivalent quality assurance system.

7.2. The Contractor shall document the compliance with this quality assurance system.

7.3. The System shall meet the local cGMP and GMP guidelines.

## 8. Testing and Acceptance

### 8.1. Factory Acceptance Test (FAT)

The System, prior to shipment, shall be tested for conformance of the System with manufacturer's performance specifications and the minimum requirements specified herein. FAT shall be performed in presence of a representative of the Contractor, End-User and the IAEA. The results of the testing of the System shall be documented in full detail by the Contractor in a FAT Report confirmed and signed by the end user and contractor and to be provided to the IAEA before shipment of the System to the End-User location.

### 8.2. Site Acceptance Test (SAT)

The System, after installation, shall be tested by the Contractor together with the End-User to demonstrate that the performance meets the manufacturer's performance specifications and the minimum requirements specified herein as determined by the IAEA and the End-User.

SAT shall be performed in presence of a representative of the contractor and the End-User. The results of the testing of the System shall be documented



in full detail by the Contractor in an SAT Report that shall be confirmed and signed by the End-User and the Contractor's representative to be provided to the IAEA. This document shall be dated and accepted as the start of the System's warranty period.

## 9. Installation and Training

9.1. The Contractor shall install the System at the End-User's location. The Contractor shall provide all necessary drawings and installation provisions, including photos and other useful information for site preparation. The installation will be accepted after commissioning (SAT), training and validation. The validation will consist of three (3) runs of the installation (without activity) to validate that the process allows to meet the design specifications and GMP requirements. The results of the installation and operation of the System shall be documented in full detail by the Contractor in the DQ, IQ and OQ documentation, to be provided to the IAEA.

9.2. The Contractor shall provide two (2) days full training for up to three (3) staff of the End-User in the operation and application of the System and its components at the End-User location immediately after the installation has been completed. The training shall be held in the English and/or French language.

## 10. Deliverable Data Items

The Contractor shall provide two (2) complete sets of operation and servicing manuals and technical drawings in either French or English language.

The Contractor shall provide all necessary drawings and documents relevant to the manufacturing and operation of the Hot Cell to the End-User. The documentation to be provided shall include, but it is not limited to the following:

- 10.1. Maintenance and User's manual in English;
- 10.2. Technical documentation
- 10.3. Technical drawings (electrical, mechanical, pneumatic & process schemes);
- 10.4. DQ, IQ and OQ documentation;
- 10.5. Certificates of stainless steel and filters and all used materials
- 10.6. Recommended spare parts list (included in the maintenance manual);
- 10.7. Main equipment data sheets;
- 10.8. Instruments calibration certificates
- 10.9. Welding Processes qualification.