INSPECTION AGENDA – RADIOPHARMACEUTICALS

Inspection Activity

Opening Meeting
● Introductions, Attendance record, Inspection standard and scope
● Major Changes
● Key personnel
● Brief description of the company
● Buildings and facilities overview (for initial; if applicable)
  o Floor plan / Lay-out plan
  o Product and personnel flows
 	
On-site inspection
● Plant Tour
  o Warehouse (starting materials, packaging materials and finished goods)
  o Production
  ▪ Reactor/Cyclotron Production** - Non-GMP
  ▪ Chemical synthesis
  ▪ Purification
  ▪ Processing, formulation and dispensing
  ▪ Aseptic or final sterilization
  ▪ Packaging
  o Quality Control Laboratory
  o Utilities
  ▪ Water
  ▪ HVAC
  ▪ Gases
 	
Document Inspection

- *Establishment Records:*
  - License to Operate
  - List of Products Manufactured
  - Site Master File
  - Necessary licenses from PNRI
    - License to Construct
    - License to Operate for commissioning
    - Radioactive material license
    - LTO for controlled facility

- *Registered Pharmacist's Records:*
  - PRC ID, PTR

- *Pharmaceutical Quality System:*
  - Quality Manual
  - Quality Risk Management
    - Determine the extent of qualification/validation, focusing on a combination of Good Manufacturing Practice and Radiation Protection
    - Usage of closed or open equipment
    - Parametric Release
    - Pressure differences, air flow direction and air quality
  - Finished Product Release procedure
    - Assessment by a designated person of batch processing records
    - Assessment of the final analytical data
    - Radionuclides with long half-lives
  - Product Quality Review
  - Supplier Qualification including audits
  - Validation Master Plan including protocols and reports
    - Prospective Process Validation
    - Disinfectant Validation
    - Cleaning Validation

        - Computer Validation
    - Procedure, Records and logs:
        - Deviation
        - Change control
        - Corrective Action and Preventive Action (CAPA)

- *Personnel:*
    - Organizational Chart
    - Duties and Responsibilities / Job Description
    - Training:
        - Training program
        - Training records & traceability of training history
        - Assessment of effectiveness of training
        - Training on radiation safety and cleaning and maintenance of radiopharmaceuticals
    - QA / Plant manager / Key personnel
        - Training on Radiation protection
        - Training on radiopharmaceutical specific aspects of the quality management system
    - Medical and Health Examinations including eye check-ups
    - Personnel monitoring
        - Radiation activity
        - Equipment used
        - Disinfection / Decontamination of personnel

- *Premises and Equipment:*
    - General
        - Controlled (environmental and radioactive) areas
            - Self-contained facilities for radiopharmaceuticals
            - Thickness of wall and non-straight line building walls for facilities with reactor / cyclotron production
        - Detection of radioactivity contamination
        - Prevention of cross-contamination from personnel, materials, radionuclides
            - Closed or contained equipment
            - Open equipment

- Gowning area
  - Procedure
  - Appropriate gown / suits
  - Personnel protective equipment such as ring badge, pendosimeter
  - Log of entry and exit
- Warehouse (Starting Materials (excipients), Packaging Materials)
  - Receipt, handling & storage
  - Storage areas – quarantine, release, reject
  - Approval for use (materials)
  - Temperature & humidity monitoring
  - Dispatch
  - Inventory control
- Production areas
  - Surfaces and finishes
  - Lighting and Ventilation
  - Dedicated premises / areas
  - Air locks
  - Environmental monitoring
    - Radioactivity
    - Particle
    - Microbiological quality
- Equipment
  - Storage
  - Cleaning
  - Qualification
    - Hot cells – filtered feed air
    - Isolator / Laminar
  - Repair and Maintenance
  - Calibration and reading of radiation monitor devices
- Engineering and Services:
  - Pest Control

- Housekeeping
- Back-up system
- Radioactive waste disposal
- Drainage system

  - Water
    - Lay-out
    - Qualification
    - Monitoring and Testing (method, specifications and results including trending)
    - Maintenance
  - HVAC
    - Lay-out
      - One-pass air
      - Exhaust filter (Carbon filters)
    - Alarm system
    - Qualification – Classification should be the same with sterile production
    - Environmental Monitoring and Testing (method, specifications and results including trending)
    - Maintenance

- *Documentation:*
  - Batch Record Review
  - Document control (history, issuing, superseded, obsolete)
  - Specifications for starting materials
  - Specifications of packaging materials
  - Specifications of bulk product
  - SOPs
  - Delivery documents
  - Lot Numbering System
  - Records of equipment
    - Usage
    - Cleaning
    - Sanitization / Sterilization
  - Specifications

- Starting materials
- Packaging materials
- Critical items (such as process aids, gaskets, sterile filtering kits)

- Distribution records
- Acceptance criteria
  - Criteria for release
  - Shelf-life (chemical identity of the isotope, radioactive concentration, purity, and specific activity)

- *Production:*
  - Process Flow
    - Gowning procedures
    - Preparation
    - Processing
      - Assembly of sterilized equipment under aseptic conditions
      - Formulation
      - Filter sterilization (aseptic)
        - Integrity testing with radiation protection and maintenance of filter sterility
      - Process simulation (Media fill)
      - Batch processing documentation
      - Sterilization processes
      - Labelling
      - In-process and Line clearance checks
    - Packaging
      - Control of labels & pre-printed packaging materials
      - In-process controls
      - Line clearance checks
      - Reconciliation
      - Batch packaging documentation
      - Storage of packed product
  - Control of materials (starting, in-process, finished and returned materials)

- *Quality Control:*
  - Sample receipt
  - Equipment Calibration and Maintenance
  - Handling of OOS
  - Test Methods & References (i.e. official pharmacopeia) and Specifications
    - Radioactivity decay
    - Identification of radionuclide
    - Identification of radiopharmaceutical
  - Reference Standards and reagents
    - Special storage and directions
    - Traceability of primary and secondary standards
  - Analysts work books/records & test results (if available)
  - Training & assessment
  - Period of validity (finished product)
  - Stability program
  - Identification test procedure and specifications of starting materials
  - Microbiology Laboratory testing
    - Sterility tests
    - Bacterial Endotoxin test
    - Equipment / Laminar Flow hood
    - Testing procedure, references and results
    - Media preparation
    - Growth Promotion Testing
    - Storage of Reagents
    - Strains
      - Receipt
      - Certificate of Analysis
      - Identification tests
      - Passage (procedure and records)
      - Storage

- *Outsourced Activities*: Contract Manufacturing Agreement, Testing laboratories agreement, others

- *Complaints and Product Recall* (procedure and records)
- *Self-inspection* (procedure and records)

Report Writing
Exit Meeting