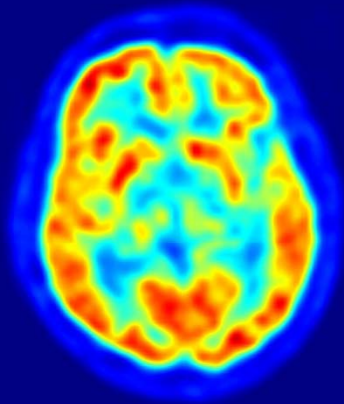




United States Nuclear Regulatory Commission

*Protecting People and the Environment*



# Radiopharmacy Inspection

# Inspection References

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- **The license and the licensee's application and/or amendment document(s).**
- **10 CFR 20, 30, 32, 71, etc regulations or State equivalents**
- **NUREG-1556, Vol. 13, Program-Specific Guidance About Commercial Radiopharmacy Licenses, Rev. 1, Nov. 2007**
- **NUREG-1556, Vol. 21, Program-Specific Guidance About Possession Licenses for Production of Radioactive Material Using an Accelerator, Oct. 2007**

# Inspection Procedures

- **Inspection Procedure (IP) 87127 Radiopharmacy Programs**
  - **Applies if the licensee operates as a radiopharmacy - work performed under supervision of pharmacists licensed by the State Board of Pharmacy**
- **Inspection Procedure (IP) 87125 Materials Processor/Manufacturer Programs**
  - **Applies if the licensee operates as a manufacturer – work performed using cGMPs (current Good Manufacturing Practices) approved by the FDA**

# Commonly Used Isotopes

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- **Molybdenum 99/Technetium 99m**
  - **approx. 80% of nuclear studies worldwide**
- **Thallium 201**
- **Iodine 123 & 131**
- **Fluorine 18**

# Less Commonly Used Isotopes

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- **Xenon 133**
- **Gallium 67**
- **Indium 111**
- **Cobalt 57**
- **Strontium 82/Rubidium 82 generators**
- **Other PET isotopes – Carbon 11, Nitrogen 13, Oxygen 15**

# Therapeutic Isotopes

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- **Samarium 153, Strontium 89 & Rhenium 186**
- **Palladium 103 & Iodine 125**
- **Iridium 192**
- **Yttrium 90**

# Small quantities, small volumes



# Production & Supply

- Production of Mo-99 (Tc-99m) has become a major issue worldwide.
- Over 90% is produced in only 5 reactors around the world (Canada, Netherlands, Belgium, South Africa & France)
- All 5 of those reactors are well over 40 years old.
- Recent shutdowns and maintenance problems have caused severe worldwide shortages at times over the last few years.
- This has created new interest in other and newer production sources and different technologies.



# **Inspection Procedure (IP)**

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**Inspection Procedure (IP) 87127**

**Radiopharmacy Programs**

# IP Focus Elements

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- 1. Security / Prevent Loss of Licensed Materials
- 2. Maintain Shielding of Licensed Materials
- 3. Comprehensive Safety Measures
- 4. Radiation Dosimetry Program
- 5. Radiation Instrumentation
- 6. Knowledgeable Workers
- 7. Management Systems & Oversight

# IP Focus Element 1

## Security/Prevent Loss of Licensed Materials

- **Access to facility, control of laboratories:** facility, lab, or both may be limited access (locked or attended and persons trained); who has keys?; training OK?
- **Storage and control of materials:** secured/attended
- **User responsibilities and knowledge:** appropriate for types and quantities of RAM
- **Receipt/transfer/inventory:** who/when/how receive material (i.e., new generators); records

# IP Focus Element 2

## Maintaining Shielding of Licensed Materials

- **Hot cells, mini-cells, glove boxes:** access; engineering controls; adequate number and size; properly maintained
- **Generator and waste storage areas**
- **Shielding appropriate for type of RAM:** lead for gamma; plastics/low-Z for betas; amounts of shielding adequate for max loads of cells or glove boxes; ALARA – transfer lines shielded, remote handling, etc.

# IP Focus Element 2

## Maintaining Shielding of Licensed Materials

- **Contamination controls depend on types, forms, quantities, and procedures performed:**
  - good housekeeping
  - lots of “in and out” – do they stick to personal surveys?
  - area surveys adequate
  - ALARA; time, distance, shielding

# IP Focus Element 3

## Comprehensive Safety Measures

These are “*measures to limit other hazards from compromising the safe use and storage of licensed material*”

- **Fire protection:** combustibles, flammables, up-to-date extinguishers, sprinklers, relationship with local fire dept.
- **Other industrial/chemical/biological/etc hazards considered:** lighting, noise, sharps controls, chemical storage, ergonomics

# IP Focus Element 3

## Comprehensive Safety Measures

### ➤ **Transportation**

- **IAW DOT regulations:** shipping containers, shipping papers, surveys, labeling, driver training includes HAZMAT, block and brace, emergency procedures
- **Transfers:** do they pick up waste? If so, do they become the shipper to relieve customer of shipping issues? How do they handle?

# IP Focus Element 4

## Radiation Dosimetry Program

- **External exposure:**
  - External dosimetry is a very important area to look at due to the safety significance – often close to limits
  - With the increased use of unit doses and newer materials with higher specific activity, dose from preparation has shifted from thousands of NMTs in thousands of hospitals and clinics to the pharmacy personnel in 100+ facilities



# IP Focus Element 4

## Radiation Dosimetry Program

- **External exposure:**
  - Look closely for proper use and storage of dosimeters (whole body, ring, others as needed)
  - Also look closely at exchange of dosimeters since doses often push near limits
  - Are dosimeters worn to receive highest doses? If not, why not, and are assessments made?
  - Look for wide differences or discrepancies

# External Dosimeters



# IP Focus Element 4

## Radiation Dosimetry Program

### ➤ Internal exposure:

- Internal dose assessment is typically only needed if they are compounding iodine or other volatiles
- If used, look for appropriate procedures and analysis depending on compound and radionuclide
- Beware of “GIGO” – poor sample collection won’t be improved by complex computer dose models
- Hood/cell flows checked and maintained

# IP Focus Element 4

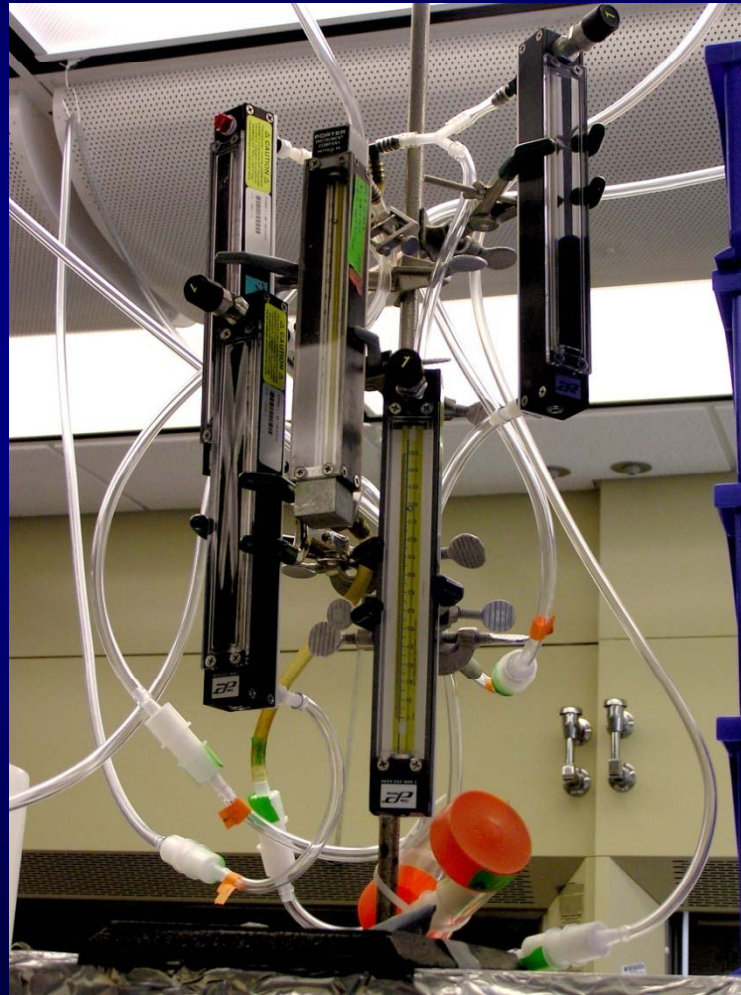
## Radiation Dosimetry Program

- **Internal exposure:**
  - What engineering controls are in place?
  - Look closely at ventilation systems
  - Are hood/cell flows and filters properly checked and maintained?
  - Have them demonstrate airflows where appropriate
  - Don't forget 20.1101(d) – EPA constraint on air emissions – must be below 10 mrem

# Thyroid Bioassay System



# Personnel Monitoring Area Air Sampler





# IP Focus Element 4

## Radiation Dosimetry Program

- **public dose assessment MUST be done and recorded**
  - **Dosimetry:** location of area monitors, assumptions for total/max public doses; and/or
  - **Effluent monitoring:** location of samplers, type of sample, collection time/volume/etc; and/or
  - **Calculations:** EPA Comply code, other; and/or
  - **Surveys:** appropriate instruments, locations, assumptions
  - **Emergency Plan:** review, if applicable

# IP Focus Element 5

## Radiation Instrumentation

- **Observe/check for sufficient number and types**
  - appropriate, available, operable, used (properly)
  - may be for detection and/or measurement
  - other equipment: air samplers, rotometers, liquid samplers, bioassay collection, etcetera
- **Test or have demonstrated**
  - Do comparative survey measurements



# IP Focus Element 5

## Radiation Instrumentation

- **Laboratory measurement instrumentation**
  - sufficiently sensitive: check MDA/LLD
  - calibrated for required geometries
  - QA/QC programs where applicable
- **Calibration**
  - Frequency, including maintenance of instruments
  - compare measurements
  - **Calibrated by licensee: check/observe their procedures, facilities, calculations and results**

# IP Focus Element 6

## Knowledgeable Workers

\*\*\*\*\* **OBSERVE, ASK, VERIFY** \*\*\*\*\*

### ➤ **General Training**

- Initial training scope, method(s), testing
- Refresher frequency, method(s)
- Driver training, including HAZMAT

### ➤ **Operating and Emergency Procedures**

- Real incidents (typically spills/contamination or driving accidents)
- Ask about hypothetical situations

# IP Focus Element 6

## Knowledgeable Workers

- **Preventive activities**
  - **Radiation/contamination control: surveys**  
Who, what , when, where, how
  - **Sealed source leak tests, inventory:** do a “scavenger hunt”; review licensee follow-up to any leaking sources or lost/missing sources
  - **Use of protective clothing:** routine lab safety (lab coats, gloves, safety glasses etc); occasional special needs (static-free safety shoes, clean-room dress-out, lead aprons/gloves, etc)

# IP Focus Element 6

## Knowledgeable Workers

### ➤ Preventive activities

- **Good housekeeping:** absorbent paper, washable trays, disposable pipette tips etc, regular cleaning, segregated RAM work areas and equipment
- **Respiratory protection program:** not typical; if used, do appropriate prep for inspection

# IP Focus Element 6

## Knowledgeable Workers

### ➤ Preventive activities

#### ➤ Waste management:

- decay-in-storage (DIS) for short-lived (120 days or less)
- sewerage disposal – must be soluble or biological dispersible
- Solid waste transfer to burial site – watch for compacting, crushing, and other treatments
- Other less typical – effluents, incineration, 20.2002 alternates

# IP Focus Element 6

## Knowledgeable Workers

### ➤ Preventive activities

#### ➤ Able to detect/assess radiation and contamination:

- good survey technique
- correctly read meter face
- Appropriate use of “cpm” versus “dpm”

#### ➤ Able to identify and investigate events:

review/discuss surveys/inspections/audits - do they identify events, how do they follow-up?

# IP Focus Element 6

## Management Systems and Oversight

- **The licensee is responsible for the radiation protection program; senior management delegates authority to RSO to implement**
- **Management focus should include: awareness of events; safety and compliance; providing adequate resources; human performance issues; communications with the NRC**

**\*\*\*INTERVIEW MANAGEMENT \*\*\***

# IP Focus Element 6

## Management Systems and Oversight

- **Annual Program Review and other audits**
  - Review/understand licensee's review program; may be internal or external, annual or segmented
- **RSO:** Interview "local" RSO (usually a pharmacist), if available. Call (at a reasonable hour!!) if necessary.
- **RSO:** Debrief the Corporate RSO after the inspection



# Performance Based Inspection

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- **Observe Licensed Operations**
- **Interview Licensee Personnel**
- **Make Independent Measurements**
- **Review Representative Records**

**STRIKE A GOOD BALANCE**

# Performance Based Inspection

- **Observe Licensed Operations**
  - **You can learn a lot in a short amount of time by observing**
  - **Must be at the pharmacy during peak operations , which means backshift, during the midnight to 6 am window. ☹️**
  - **Before inspection, you might want to find the location in daylight**
  - **Bring your I.D. so you can identify yourself to the staff when you arrive**

# Performance Based Inspection

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## Entrance with Local RSO or ANP

- **Be quick and informal – they're busy and both of you know why you are there!**
- **Discuss current scope of program:** number of doses/clients; number of runs; staff size
- **Ask about activities happening during the inspection**
- **State your inspection goals and set your inspection schedule:** observe, interview, review records – tell them how long you plan to be there

# Performance Based Inspection

- **Interview Licensee Personnel**
  - **Observe without getting in the way. Peak operations are VERY busy. Ask questions, but don't hound them (yet!) – let them get the work done**
  - **Interview as you follow the process: From orders to dose production to packing to surveying to loading to transporting**
  - **Talk to each type of personnel – pharmacists, techs, and drivers**
  - **LISTEN!!**

# Performance Based Inspection

- **Make Independent Measurements**
  - **Take measurements as you observe, but don't be alarmed if you find radiation! ☺**
  - **Are the levels you're seeing consistent with the operations?**
  - **Look more at their technique**
  - **Do some side-by-side comparisons, taking types of equipment, etc., into account**
  - **Follow their rules for personal surveys in and out of areas**

# Performance Based Inspection

- **Review Representative Records**
  - **Easier to look at records after major operations are completed for the night**
  - **Focus on most safety significant items:**
    - **Effluents**
    - **Dosimetry**
    - **Surveys**
  - **Look at enough to be satisfied – you don't need to see it all!!**

# Performing an Effective Exit

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## PREPARE for the exit

- **Take time to organize your presentation**
- **Be sure of your findings:** know your basis, have your data, review understanding with licensee staff
- **Use notes:** stay organized, use a logical order

# Performing an Effective Exit

- **Pre-brief the Local RSO/ANP (and staff):**
  - ensure they are aware of all your findings
  - allow the staff to ask questions/clarify issues
  - allow discussion of major and minor issues in technical detail, including issues that will not be discussed at the exit
- **Coordinate with Project Manager (NRC only)**



# Performing an Effective Exit

- **Exit with the highest possible level of management:**  
Probably be after the inspection, by phone, with corporate personnel. Corporate RSO may or may not be a pharmacist, so tailor your discussions to minimize unnecessary technical detail.
- **Explain the inspection process and any follow-up**
- **Discuss what you found**
  - opportunity to highlight positive findings
  - give perspective to negative findings
  - be open; accept comments; answer questions



**Questions???**



**THE END**