Aim of this Guidance

To provide practical assistance to Nuclear Medicine Centres in setting-up and running a Hospital Radiopharmacy Service.

The advice provided in this publication gathers for simple dose dispensing to complex compounding of therapeutic radiopharmaceuticals.
International Atomic Energy Agency
- Division of Physical and Chemical Sciences
- Division of Human Health - Section Nuclear Medicine

PRACTICE OF RADIOPHARMACY
Requirements:
- Expertise of radiopharmaceutical preparation
- Skills to handle radioactive substances

Radiopharmaceuticals in clinical use
- Quality assurance
- Safe and effective procedures: operator and patient (radioprotection issues)
- Radiopharmaceutical quality control
  - Chemical purity
  - Radiochemical purity
  - Microbiological (sterily, pyrogens)

GUIDANCE CONTENTS
- Definitions
- Operational levels
- Staff and training
- Facilities
- Documentation
- QA and QC
DEFINITIONS

- Radiopharmaceutical
- Nuclear Pharmacy - Radiopharmacy
- Nuclear Pharmacist - Radiopharmacist
- Compounding

Compounding

Compounding includes formulation of cold kits from raw ingredients for radiopharmaceuticals preparation, adding reagents to commercial kits to modify or enhance performance of radiopharmaceuticals (shelf life extension, fractionation) and synthesis from raw materials.

OPERATION LEVELS

The procedures performed in a Nuclear Pharmacy can vary considerably in different parts of the world.

Can be classified:
- Levels 1 (a, b), 2 (a, b) and 3 (a, b and c)
- Scope
- Staff and training
- Facilities
- Operations
- Record keeping
- Quality control

OPERATIONAL LEVEL 1a

- Dispensing radiopharmaceuticals purchased or supplied in their final from recognised-authorised manufacturer or centralised radiopharmacy.
- Radiopharmaceuticals are supplied in single or multiple doses.
Operational level 1 b
Dispensing radiiodine and other ready-to-use radiopharmaceuticals for radionuclide therapy

Thyroid uptake of $^{131}$I

$^{131}$I is given in capsules or in solution

131-I-MIBG for pheochromocytoma and neuroblastoma diagnosis

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Operation level 2 a
Preparation of radiopharmaceuticals from prepared and approved reagent kits and radionuclide (closed procedure).

Operation level 2 b
Radiolabelling of autologous blood

Training
In addition to what specified for level 2a, training procedures for safe operations such as:
- aseptic cell manipulation
- radiolabelling of autologous blood cells
- transfer of sterile solutions from one open container to another
- handling of biological materials
- operator protection methods from biohazard material
- comprehensive cleaning procedures of equipment and facilities between successive patients to prevent any cross infections.
**Operation level 3 a**

- Compounding radiopharmaceuticals from ingredients and radionuclides for diagnostic application (open procedure): in house production of reagent kits from ingredients. Related research and development (R&D).
- **Training of all staff members in:**
  - GMP and GCP
  - Experimental design and interpretation of experimental results
  - Preparation of scientific reports (internal use, external assessment and publications)
  - Costing of research projects

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**Radiosinovectomy**

188Re-Sn colloid

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**Results in haemophilic patients**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Pre - RSO</th>
<th>Post - RSO</th>
<th>Follow Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bleeding Episode</td>
<td>Frequency</td>
<td>Bleeding Episode</td>
</tr>
<tr>
<td>HAG 12yr.</td>
<td>2 BE/month</td>
<td>Last 3 months</td>
<td>No more BE in treated Artic.</td>
</tr>
<tr>
<td>JGR 17yr.</td>
<td>1 BE / 20 days - Last 4 months</td>
<td>No more BE in treated Artic.</td>
<td>20 months</td>
</tr>
<tr>
<td>FL 27yr.</td>
<td>1 BE/week</td>
<td>Last month before 2BE/month</td>
<td>No more BE in treated Artic.</td>
</tr>
<tr>
<td>VS 14yr.</td>
<td>1BE/week</td>
<td>Last 3 months, before 2BE/month</td>
<td>No BE for 36 days, Knee Trauma 1BE/3M</td>
</tr>
</tbody>
</table>

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**Operation level 3 b**

- Compounding of radiopharmaceuticals from ingredients and radionuclides for therapeutic application (open procedure).
- **R&D**
  - **Staff and training**
    - Particular emphasis on
      - Radiation protection
      - Compounding
      - Dispensing
      - Internal dosimetry
      - Use of therapeutic radionuclides in clinical settings
**Operation level 3c**

- Synthesis of PET radiopharmaceuticals
- Compounding of radiopharmaceuticals produced from long-lived generators such as Gallium-68 or Rhenium-188. R&D.

**PERSONNEL AND TRAINING**

- In accordance with local regulations
- Present situation: nuclear technologist, physicians, chemist, biologist, nurses and pharmacist
- Basic training programme in:
  - Radiation physics and instrumentation
  - Radiactivity use and measurement
  - Radiation protection and biology
  - Radiopharmaceutical chemistry
  - Clinical use of radiopharmaceutical

**FACILITIES**

- Administrative area
  - Standard operational procedures
  - Records keeping (radiopharmaceuticals and patients)
  - QA/QC
- Dispensing area
  - Radiactive and biological waste storage area

**NSAD INTAKE**

- 78% less or higher
- 17% without changes
- 5% increased intake

**PAIN EVALUATION**

- 78% improved, higher than 60%
- 11% increased pain
- 11% without changes

**DECREASED INTAKE OF OPIOIDS DRUGS**

- 57% decreased dosage - 43% stop administration
- Facilities
  - Administrative area
  - Dispensing area
    - Centralised nuclear pharmacy (Level 1a)
    - Kit labelling (Level 2a)
  - Radiactive and biological waste storage area

- Equipment
  - The radiopharmaceutical labelling should be performed in a Class II Type safety cabinet.
  - $^{99m}$Tc generator should be well shielded and stored in a Class II Type safety cabinet.
  - There should be radionuclide calibrator with appropriate lead shielding for the re-entrant ionisation chamber.

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**Table 3. Model recording system.**

<table>
<thead>
<tr>
<th>Item</th>
<th>Details</th>
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</thead>
<tbody>
<tr>
<td>Labeling on the bench</td>
<td><img src="image-url" alt="Image" /></td>
</tr>
</tbody>
</table>
Labelling in a Class II Type Safety Cabinet

Radioprotection safety: appropriate lead shielding to protect the operator.

- Ideally Class II Type cabinets should be located in a grade C background environment. If the cabinet cannot be placed in a grade C background environment then stringent microbiological area monitoring and overall process control should be established in advance and monitored continuously to assure final product safety.
- In a situation where grade C background environment exists the microbiological area monitoring should be performed at least once a week basis to verify acceptable operational procedures.

Radiactive and biological waste storage area

Used disposable syringes, needles, cannula and other sharp items should be placed in hospital-approved puncture-resistant containers, which should be located as close as practicable to the point of use. They must be disposed of in accordance with hospital policy.
Adverse reactions and defective radiopharmaceuticals

- Uncommon, usually transient and minor in severity.
- But when it happens it causes alarming experiences in patient and staff with possibility of complaints.
- Staffs should familiarize with the type of reactions and recognize such events when they do occur.
- Defective radiopharmaceutical kits problems are seldom encountered especially those with near expiry date and whenever manufacturer changes formulation.
- But generator problems are not so infrequent.

Paediatric Use of radiopharmaceuticals

- Although radiopharmaceuticals are routinely used in paediatrics, in general few are licensed for this group of patients (where a system of licensing is present).
- Responsibility is on the clinician.
- Doses given to children should be reduced either according to weight or surface area. Refer to local guidance, if none available use the following table.

<table>
<thead>
<tr>
<th>Weight (Kg)</th>
<th>Fraction of Adult Dose</th>
<th>Fraction of Adult Dose</th>
<th>Fraction of Adult Dose</th>
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<tbody>
<tr>
<td>3</td>
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<td>26</td>
<td>0.30</td>
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<tr>
<td>4</td>
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<tr>
<td>6</td>
<td>0.19</td>
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<td>0.62</td>
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<tr>
<td>8</td>
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<tr>
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<td>0.68</td>
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<tr>
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<tr>
<td>22</td>
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<tr>
<td>24</td>
<td>0.53</td>
<td>48</td>
<td>0.85</td>
</tr>
</tbody>
</table>
Institute of Chemistry
School of Pharmacy (1915)
Faculty of Chemistry (1930)

Nuclear Medicine
Department -
University Hospital -
Faculty of Medicine