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Competency Based Hospital Radiopharmacy Training

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TRAINING COURSE SERIES 39

COMPETENCY BASED HOSPITAL RADIOPHARMACY TRAINING

TRAINING COURSE SERIES No. 39

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FOREWORD

Quality management systems in nuclear medicine are vital to a high level of nuclear medicine (NM) practice. Trained and competent staffs are essential for achieving high standards and growth in NM. One of the key bottlenecks for NM is the shortfall in human resources, especially of radiopharmacists. There is an acute shortage in most Member States and in some countries an absence of nationally registered pharmacists with radiopharmacy experience.

Most nuclear medicine facilities operate their radiopharmacies (commonly referred to as the hot laboratories) with the support of technologists and radiographers. Recent surveys have found the level of training amongst technologists to be extremely variable. Most had little or no training in hot laboratory practices. The survey also indicated the poor state of hot laboratories in many countries. Basic quality systems in the hot laboratory could be improved significantly with better training. This competency-based education manual is designed with those radiopharmacy practitioners in mind.

This competency-based trainer's manual provides trainers in each of the IAEA regions with the essentials of a training programme for all radiopharmacy practitioners. The competency-based training is a two week programme followed up with three months of practice achievements. The syllabus provides a standardized approach to lectures, practical sessions, and interactive workshops focusing on critical aspects of hot laboratory practices. The trainers, with the assistance of this manual, can deliver essential skills, competencies, and underpinning knowledge to operate safely and effectively in their hot laboratory. The course focuses on simple but practical steps that could be undertaken to improve staff performance. In addition, a basic framework of quality management principles related to radiopharmacy practices is also covered.

Further, the syllabus can be adapted to the particular needs and characteristics of any training centre, country or region. It can be translated and delivered in a local language, making it more accessible for the training of staff employed within the hot laboratory.

This trainer's manual will be of interest to nuclear medicine physicians, radiologists, radiopharmacists, medical physicists, medical technologists, radiographers, 'qualified persons', educationalists, diagnostic centre managers, and those engaged in quality systems in public health.

This training syllabus was drafted following a consultants meeting held in Vienna, Austria. The IAEA is grateful to the key authors, contributors, and reviewers. The IAEA officer responsible for this publication was K.K. Solanki, of the Division of Human Health.

EDITORIAL NOTE

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1. INTRODUCTION

1.1. Background

The IAEA has a long history (over 20 years) of providing assistance for nuclear medicine to its Member States. This includes establishment and operation of nuclear medicine centres for diagnosis and treatment using radiopharmaceuticals. Following recruitment of a specialist radiopharmacologist to the nuclear medicine section, with extensive expertise in the hospital radiopharmacy sector, the IAEA has accelerated its efforts to strengthen all aspects of quality programs related to clinical practice. This includes a new chapter in International Pharmacopoeia on Radiopharmaceutical [1], IAEA operational guidance on Hospital radiopharmacy [2] and a series of guidance documents on quality management in nuclear medicine [3]. The central objective is to strengthen practice by facilitating and empowering continuous quality improvement. One area that was found in serious need of attention was the deficiencies directly related to 'hot laboratory' practices. Many of the staff had simply learned from others whilst in employment. This competency based training manual is designed with these individuals in mind. Unlike other IAEA training courses this training program includes 1-2 weeks of standardized lectures, practical and interactive sessions followed by three months of follow-up, in which the individual has to apply and demonstrate learning. The net result is improvement in daily standards of practice and optimization of resources in the radiopharmacy.

1.2. Objective

To provide training that addresses the following requirements:

- Standardization of training for staff members that operate in hospital radiopharmacy practice;
- To improve performance and management of the radiopharmacy service;
- To encourage good radiopharmacy practices for the preparation and quality assurance;
- To establish a quality management system which encourages continuous update of core competencies in hot laboratory staff.
- encourages continuous update of core competencies in hot laboratory staff.

1.3. Scope

This IAEA syllabus provides essential education for staff working at operational guidance on Hospital radiopharmacy [2] 'operational levels 1 and 2'. It provides standardized training therefore it aims to deliver essential skills, competency and to underpinning knowledge to operate safely and effectively in hot laboratory. It is a minimally essential syllabus which can and should be adapted to the particular needs and characteristics of the training centre, country or region. It can be translated and used in a local language version for the training of staff employed within the hot laboratory.

1.4. Structure

The IAEA syllabus provides trainers with basic contents of an education course for staff working at IAEA hospital operational levels 1 and 2. The course delivery focuses on simple

but practical things that could be undertaken to improve performance of staff working in hot laboratories including better understanding of quality management related to radiopharmacy, documentation, and safer operating systems. Better operational safety is required as many of the radiopharmaceuticals are injections containing radioisotopes. The net result is an immediate improvement in standards of practice and optimization of resources in the radiopharmacy service.

There is essential training material for 1-2 weeks with key lectures in the morning and set practical reinforcing lectures with critical practices. The scope, learning objectives, subject headings and example lectures are provided for each of the key subject area. The local trainers should follow these parameters in order to deliver a standardized programme. Rather than a textbook approach the trainers should focus on actual experience and simple steps that could be undertaken to improve daily standards of performance of staff working in the nuclear medicine (NM) hot laboratories. The three months of follow-up, in which the individual has to apply and demonstrate learning should also reflect this. The training therefore should deliver key points of learning, essential skills and competency to operate safely and effectively in their hot laboratory.

1.5. Who is this training manual designed for?

This training manual targeting trainers who wish to train others in the following three broad categories:

- Pharmaceutical scientists, medical physicists, technologists, radiographers, basic scientists, chemists, employed in radiopharmacy;
- These could be individuals working in RP, and/or Individuals who rotate through RP;
- Individuals who provide oversight of radiopharmacy.

1.6. Why train this target audience?

One of the key bottlenecks for NM is a human resources shortfall, especially radiopharmacists. There is an acute shortage and in many countries absences of nationally registered pharmacists with radiopharmacy experience. Most of NM facilities operate at 'IAEA operational level 1 and 2' mainly with support of technologists and radiographers. The level of training amongst technologists was found in practice to be extremely variable. This document provides a minimally essential syllabus which can and should be adapted to the particular needs and characteristics of the training centre, country or region.

There is a global need for effective implementation of the 'IAEA operational guidance on hospital radiopharmacy-a safe and effective approach' [2]. Under these guidelines there is a strong recommendation to strengthen skills, competencies and professional qualifications of all staff involved in clinical radiopharmacy practice. They should be empowered to address the poor state of hot laboratories in many countries. They should be more aware of cost of radiopharmaceuticals. For safety of patient they should be aware of proper registration of radiopharmaceuticals and quality assessment required locally. At a time when there are difficulties with supply and relative high cost of routine radiopharmaceuticals, trained staff in hot laboratories could make the difference to NM.

1.7. IAEA Operational guidance on Hospital Radiopharmacy

The IAEA document 'Operational Guidance on Hospital radiopharmacy' [2] provides a safe and effective approach. It divides the radiopharmacy operational levels as follows:

- Operation level 1a ready to use Radiopharmaceuticals (RP);
- Operation level 1b Radioiodine dispensing;
- Operation level 2a Kits and generators;
- Operation level 2b Radiolabelled autologous products especially white cells (WBC);
- Operation level 3a Compounding;
- Operation level 3b preparation of radiolabelled therapeutics;
- Operation level 3c preparation of PET tracers.

This approach takes into account diversity and more importantly the levels of associated risks in radiopharmacy. This guidance document [2] aims to standardize practices at international level. Furthermore they take into consideration the skill mix, busy nature and limitations applicable at clinical practice level. It provides nuclear medicine physicians who take responsibility of routine service at operational levels 1, 2, and to some extend 3 with what is required in practice including training, facilities, equipment, operations and quality systems for safe operation. Those operating at level 3 i.e. larger nuclear medicine centres should have well qualified radiopharmacists or oversight by a pharmacist.

The IAEA syllabus provides the basic contents of an education course for staff working at Hospital operational levels 1 and 2. It therefore provides standardized training which results in a better understanding of quality management related to radiopharmacy, documentation, and safer operating systems. This training program includes 1-2 weeks of set training mainly lectures together with critical practices, followed by three months of follow-up, in which the individual has to apply and demonstrate learning. The training focuses on simple things to be undertaken in order to improve performance of staff working in the hot laboratories thus improving daily standards of practice in the nuclear medicine hot laboratories. It delivers key points of learning, essential skills and competency to staff to operate safely and effectively in their hot laboratory. Therefore, to improve the quality system means to encourage safer working practices and reduces the risk to patients as many of the radiopharmaceuticals come in the form of injections and/or formulations containing radioisotopes.

1.7.1. Radiopharmacy operation level 1a

1a - Dispensing radiopharmaceuticals purchased or supplied in their final form from recognised/authorised manufacturers or centralised radiopharmacies. This includes unit doses or multiple doses of prepared radiopharmaceuticals for which no compounding is required.

1.7.2. Elements of staff training at radiopharmacy operational level 1a.

The activity required at this level could be performed by any one staff member who received training in following areas:

- dose dispensing;
- dose calibration;
- dose labelling;
- quality control procedures;
- radiation safety;

- aseptic procedures;
- record keeping.

1.7.3. Radiopharmacy operation Level 1b

At IAEA operational 1b the activities include dispensing radioiodine and other ready-to-use radiopharmaceuticals for radionuclide therapy.

1.7.4. Elements of staff training at radiopharmacy operational level 1b

The procedures operated at this level can be performed by one assigned staff Member who has received training, in addition to that specified for level 1a, in the following areas:

- use and maintenance of fume hood;
- handling of beta-emitting radioisotopes;
- with special emphasis on shielding materials for beta radiation;
- on how to avoid contamination, cross contamination;
- inhalation, particularly important for volatile radioisotopes like ^{131}I.

1.7.5. Radiopharmacy operation Level 2a

At IAEA operational level 2a, the majority of activities include the preparation of radiopharmaceuticals from pre-prepared and approved reagent kits and radionuclides. In general the procedures are referred to as ‘closed procedure’.

1.7.6. Operational elements at radiopharmacy operational level 2a

The procedures operated at this level can be performed by one assigned staff member who has received training, in addition to what specified for level 1, in the following areas:

- Receipt and use of approved ^{99}Mo/^{99m}Tc Generator;
- Receipt of approved cold radiopharmaceutical kits;
- Radiolabelling of approved cold kits;
- Unit dose dispensing from reconstituted multi-dose vial;
- Receipt of the radiolabelled radiopharmaceutical kits.

1.7.7. Elements of staff and training at radiopharmacy operational level 2a.

To operate a radiopharmacy performing the procedures described at level 2a, at least 2 staff members are required. In particular, an assigned staff member is required who has received training, in addition to that specified for level 1a and 1b, in the following areas:

- maintenance and operating procedures of the radioactive 99mTc generator;
- radiolabelling of commercially available kits using generator eluate;
- quality control of generator performance quality control tests for radiopharmaceuticals;
- radiation monitoring;

- safety regulations and related documentation;
- training on aseptic procedure for generator elution, transfer of sterile solutions from one sealed vial to another;
- the use of biological containment devices (Biological safety cabinet, class II (BS EN12469:2000 Biotechnology – Performance criteria for microbiological safety cabinets);
- use of shielded water bath.

1.7.8. Radiopharmacy Operation Level 2b

IAEA operational level 2b procedures includes radiolabelling of autologous blood cell, namely red blood cells and white cells.

1.7.9. Elements of staff training at radiopharmacy operational level 2b

To operate a radiopharmacy performing the procedures described at level 2b, at least 2 staff members are required. In particular, an assigned staff member is required who received training, in addition to that specified for level 2a, comprehensive operator 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;
- operation and maintenance of centrifuge;
- use of microscope and haemocytometer;
- comprehensive cleaning procedures of equipment and facilities between successive patients to prevent any cross infections.

1.8. Why competency based training?

The competency based approach has been successfully piloted by the IAEA in Europe, Asia, Middle East, Latin America with very positive feedback together with results following such training. Many have noticed the marked improvement in daily practices. Many of the technologists and radiographers felt that this programme was more acceptable than the traditional IAEA three month fellowships. Part of the success related to the target group which in general had young families and would otherwise find it difficult to travel under the normal IAEA fellowship system. Many of them are of female gender and again, travel for some of them under the traditional fellowships is not always easy. More can be done to encourage gender balanced training using this competency based approach.

1.9. IAEA Technical cooperation projects

Recently, the Agency has supported the African Regional Co-operative Agreement (AFRA) missions, which carried out an assessment of the safety, clinical and managerial practices in nuclear medicine centres to identify deficiencies and weaknesses and to recommend practical change both technical and managerial. AFRA has agreed to support a new IAEA project,

RAF2008, ‘Strengthen practices in radiopharmacy in Africa’ which is a five year project specially aimed at improving the number of competent staff in hot laboratories. Another IAEA project, RAS2013, has also embraced this approach for training on hot laboratory in the Asia region which has the fastest growth in nuclear medicine facilities. In each of these regions regional professional bodies have taken ownership and provide the actual certificate of ‘competency in hot laboratory practices’.

In each IAEA region our approach has been to ‘train the trainers’ who then train many others. The trainers have to be carefully selected as it is important to have individuals that have broad radiopharmacy experience as well as being excellent communicators. Engagement of hospital based nationally registered radiopharmacists is essential, however, since there are very few of these in each region inter-regional support is essential. ‘Hot laboratory’ staff in Member states with less than 6 nuclear medicine facilities should be trained at regional level. The Member states with larger numbers of facilities usually coordinate their own training following the initial ‘train the trainers’ programme.

Following a decision to develop a training document for nuclear medicine, the Division of Human Health at the IAEA has been in active dialogue with nuclear medicine professional bodies, and other stakeholders i.e. nuclear medicine specialists, medical physicists and radiopharmacists around the world. There is general acceptance that this approach for training at IAEA operational levels 1 and 2 would be very beneficial for MS as actual numbers of specialist nationally registered pharmacists are not likely to be increased in the immediate or near future.

This course is mainly intended for individuals who are working in hospital radiopharmacy laboratories either as a radiopharmaceutical scientist, medical physicist, technologist, radiographer or basic scientist. The level of the radiopharmacy is aimed to be at IAEA operational levels 1 and 2 as defined in the ‘IAEA operational guidance on hospital radiopharmacy-a safe and effective approach’. The main purpose is to supply these professionals with knowledge about standards in all aspects of running a radiopharmacy and to help them improve their performance.

1.10. Entry requirements

All grade of staff, e.g. medical technologists (nuclear medicine), radiographers, biochemists or chemists, physicists working in a hot laboratory. Ideally they should have had some exposure to the procedures and practices in radiopharmacy. Understanding the terminology used in radiopharmacy and some radioisotope dispensing knowledge is essential. In general, the optimal training group size per training session is between 12 to 20.

1.11. Course content

Normally a two week course programme is required so that the pace and details of the course material can be delivered effectively. Since nuclear medicine technologists come from a variety of backgrounds, the first week is essential for ensuring the use of a common terminology, creation of a common level of understanding of e.g. essential radiation safety elements, and cohesive group activities. The second week is more effective at delivering a key understanding and sharing of practical experiences in the form of interactive sessions and practices. A typical 2 week time is as follows (Table 1).

TABLE 1. TYPICAL TWO WEEKS TRAINING PROGRAMME

Week 1.

	Tuesday 15 Aug.	Wednesday 16 Aug.	Thursday 17 Aug.	Friday 18 Aug.	Saturday 19 Aug.
Morning **(Break 11:00-11:30)** **Lunch 12:30-14:00**	**Lect. 1-** General introduction to RP* course. **TL+A** **09:00-10:00** **Lect. 2** Types of radiation, Radioactivity and Radionuclides. Instruments. **TL-M.Tuntawiron** **10:00-11:00** **Lect. 3** Radiation Safety(Radiation Protection Principles and Regulations) **TL-S.Komolsuk** **11:30-12:30**	**Lect.1-** Production of Radionuclides Radioactive component of RP Characteristics and the selection of radionuclides RP. **A** **Lect 2** Properties of Generator system Tc/Mo generators Wet and Dry generators Generator profile **A** **Lect. 3** Radiopharmacology and mechanism.-Basic principles. -Overview of different radiopharmaceutials used in NM. **A**	**Lect.1-** operation (Basic aspects, staff, design of facilities).**A** **Lect. 2** Safe handling of radioiodine. Fume hoods and safety cabinets. **TL-N.Sritongkul** **Lect. 3** Radioactive waste related to RP and safe practices. **TL-A.Patanasub**	**Lect. 1** &2 QA in Hospital RP QC in Hospital RP Radionuclide purity Radiochemical purity Chromatography pH Particles Temperature Shelf life **A** **Lect.3-** Basic radiation environmental monitoring in hospital RP **TL-O.Chaudakshetrin**	**Lect 1** *Mathematic in daily RP practice.* Radioactive decay calculation of common RP. Generator Calculation from Reference Dose and volume **A** **Lect. 2**. Radioactive packages (Categories, ordering, receiving, sending radioactive substances) **A** **Lect. 3**.Mathematics in QC Chromatogram calculation Rf, Particle counts Extraction values Sd and change analysis **A**
Afternoon **(14:00-16:00)**	Practical:-**M.Tuntawiron** Diff. types of radiation Radiation hygiene Calibrator geometry	Practical: **A** Generator experiments: Profile Eluation records Build up Al-breakthrough	Practical: **N.Sritongkul** Practice safe radioiodine handling and dispensing Practice **A.Patanasub** RP waste management and associated SOP and documentation	Practical: **A** QC Run chromatography pH Keeping Quality log sheets	Practical: A Look at RP mathematics in practice Examples and trial calculations. Look at package insert of different RP kits and establish working parameters.

Week 2.

	Monday 21 August	Tuesday 22 August	Wednesday 23 August	Thursday 24 August	Friday 25 August
Morning **(Break 11:00-11:30)** **Lunch 12:30-14:00**	**Lect. 1-** Microbiology In process testing Sterility test Pyrogen test LAL **A** **09:00-10:00** **Lect. 2** GMP In hospitals. Centralised –radio-pharmacy. **I** **10:00-11:00** **Lect. 3** Aseptic operations (Basic aspects, staff, design of facilities). Preparation and aseptic. Isolator technology **I** **11:30-12:30**	**Lect. 1-** Aseptic assessment Basic environmental monitoring Broth run Microbiology in practice. **I** **Lect. 2** RP licensing systems and role of Pharmacopoeia. Working a RP Monograph. **A** **Lect. 3** Purchasing and tender RP Practical in purchasing RP setting and working tenders. **I**	**Lect. 1-** Infection imaging. **A** **Lect. 2** Radiolabelling of white cells. **I** **Lect. 3** Radiolabelling RBC **A**	**Lect. 1-** Monoclonal and Peptides in RP **A** Practical: Dispensing Monoclonal antibody or peptide RP **Lect. 2-** PET radiopharmaceuticals Safe handling of PET products. Dose calculation of FDG. Dispensing dose **A** + **I** **Practical**: Monoclonal and Peptides in RP **A**	**Lect. 1-** Use of pharmaceuticals in NM e.g. Thyroid blockade, Adenosine etc.**I** **Lect. 2-** Drug and radiopharmaceutical interaction. **A** **Lect. 3** RP results Routine monitoring and trouble shooting in RP. QA in Hospital RP and QC Radiopharmaceuticals. **I**
Afternoon **(14:00-16:00)**	Practical: I Create ideal layout and state why. Documentation- worksheet IT, RP database, and electronic work sheet. Transportation of RP experiments	Practical: I Microbiology in practice: Aseptic practice – a) Generator b) Kit preparation Dispensing practices -VLFC -Isolator	Practical: A Radiolabelling of white blood cells Radiolabelled red blood cells	Practical: I Competencies of staff working in RP. Staff induction in RP practices Creating competencies list. Practical accreditation. Creating site file. QA policy Creating working SOPs	**Interactions and Discussions:** - Cover area of RP training specific to trainee request. - Assess training - Continuous development. - Journal reading and online support. Practical log-book keeping for at least 3 months. Trainee and tutor support. Method of final assessment and certification.

1.12. Logistics

It is essential for an organization or professional body to take ownership and provide logistical support . Varying from MS to MS this role has been taken up by either the National Atomic Commission, specialist hospitals or university departments. Since it is the main target for this programme the hospital sector has increasingly linked up with key stakeholders and managed successful training programmes.

1.12.1. Stakeholders

The engagement of key stakeholders is essential for this specialist training. These should include nuclear medicine physicians, medical physicists, Atomic commission, and whenever possible pharmacologists. Under most national regulations radiopharmaceuticals are medicines and pharmacy and health related legislation is applicable. The stake holders' committee is also responsible for the approval of business plans, announcements, participation selection and ensuring a transparent certification process.

1.12.2. Business plan and funding

A business plan is essential for the training course. There are operating costs which, although small, are associated with undertaking this training programme. Materials and other provisions have to be made for training groups the size of 12 to a maximum of 20 participants. In general, hospitals, Atomic commissions, Radiation protection Agencies, nuclear medicine professional bodies and industry are key sponsors. Some are happy to provide training funds, others offer facilities, operational costs, logistical costs for trainees or other payments in-kind.

1.12.3. Location

It is general advisable to arrange the training in larger cities as access can be easier and ideally within commuting distance for the trainees. Hospital facilities are good choices and some of the practical demonstrations can also be accommodated without additional licensing constraints.

1.12.4. Trainers

Regional and nationally based trainers are encouraged to participate, to provide a higher level of sustainability. Ideally trainers should be practitioners with significant practical experience rather than individuals with an exclusively theoretical knowledgebase. Knowledge, comprehension and application are equally important. However, the trainers must work within the framework of each of the lectures, practical sessions and/or interactive sessions as described in this training manual. Learning objectives and sub-topics should be covered within the allotted time frame. This can be in national or local languages. On occasions it might proof essential to invite external experts to the programme. However, they too should either have experience with training at IAEA operational levels 1 and 2 or conform to the framework of this training manual. Feedback on each of the sessions is useful for continual refinement of the training delivery.

1.12.5. Accreditation

Acceptance of this programme by local or national professional bodies or technical colleges/universities is essential. The certification process is provided nationally. The participants should feel real merit of undertaking this type of training. People do tend to travel to other parts of the country or region for employment. With national or regional recognition of these certificates, this approach could provide staff with more portable certifications meeting the demands for increased mobility in the world e.g. Certificate of hot laboratory training undertaken in Dubai would be accepted by the other Emirates.

1.13. Pre-course material (CDs)

Pre-course preparations are essential for a successful delivery of the training programme. A time table together with essential training material is useful. Many participants are highly motivated and would like to come prepared for the lectures, practical and interactive sessions.

In a digital age, a CD-ROM or web site containing key elements of training are useful and a good reference point.

1.14. Standardization of delivery

A standardized delivery is essential for many reasons – the time span of trainees' attention is a key factor. Broadening skills and a better understanding of a subject matter are not always achieved nor appreciated by listening alone. Therefore this training programme is trying to strike a balance between lectures, practical and interactive sessions. Clear objectives for each session are listed as well as key topics and sub headings to be covered. Model lectures are included in the material and are thought to provide some insight into the content and different delivery styles. The following points are essential:

- Each lecture session should be 45 minutes to an hour in duration;
- Practical sessions could be 1-1.5 hours per topic;
- Interactive sessions should last 45 minutes to an hour;
- Approximately 10-15 minutes for 'questions and answers' and discussion.

Sharing their practical experience is essential amongst course participants, so that the trainees should clearly understand and apply facts, rules and principles to the routine radiopharmacy practices. Specific attention should be drawn to a list of key operational responsibilities in hospital radiopharmacy. In addition illustrating implications of change and managing changes in radiopharmacy practices is important.

A template is provided for adaptation locally, however, it is strongly recommended to cover all the topic headings. Each lecture is designed to be delivered over a 45 minute period, therefore allowing time for question and answer sessions together with some discussion.

1.15. Format for each lecture and practical

Each session should be carefully planned which including the following elements:

- Scope;
- Learning objectives;
- Outline of the presentation;
- Topic sub-headings;
- Key points under each sub-headings (slide);
- Include some graphics, picture;
- Summary section;
- Key reference materials;
- Further reading.

In addition allow time for question and answer session together with some discussion.

1.16. Essential lectures

Format for essential lectures and sessions included in course are as follows:

1. General introduction to RP course;
2. Types of radiation; radioactivity, radio-nuclides and essential monitoring instruments;
3. Radiation safety;
4. RP operation;
5. Radiopharmacology and mechanisms;
6. Radioactive component;
7. Mathematics in daily RP practice;
8. Preparation and aseptic operations;
9. GMP in hospitals;
10. Isolator technology, centralized RP;
11. QA in hospital RP and QC in radiopharmaceuticals;
12. Basic environmental monitoring;
13. Production of radionuclides;
14. RP licensing systems and role of pharmacopoeia;
15. Radioactive packages;
16. Safe handling of radioiodine, fume hoods and safety cabinets;
17. Biological distribution of radiopharmaceuticals;
18. Purchasing and tender RP practices;
19. Radioactive waste related to RP and safe practices;
20. Competencies of staff working in RP; Staff induction in RP practices;
21. IT, RP database and electronic work sheet;
22. Routine monitoring and trouble shooting in RP;
23. Sterility test, pyrogen test LAL, aseptic assessment, QC results;
24. Infection imaging;
25. Radiolabelling of white blood cells;
26. Radiolabeling of red blood cells;

27. Biomolecules in RP;

28. Monoclonal antibodies in RP;

29. Peptides in RP;

30. Role of PET in NM together with essentials on QC of PET radiopharmaceuticals;

31. Safe handling of PET products;

32. Use of radiopharmaceuticals in NM e.g. thyroid blockade, adenosine etc.;

33. Drug pharmaceutical interactions.

1.17. Laboratory set-up and materials

Ideally a laboratory should be able to accommodate 12-15 students at any one time. The students can be in smaller sub-groups for effective demonstration or approach to practical.

1.18. Essential practical or interactive sessions

A balance of practical and interactive sessions is required between the series of lectures and these include:

1. Different types of radiation, Radiation hygiene, Calibrator geometry;

2. Generator experiments: Profile, Eluation records, Build up, Al-breakthrough;

3. Practical: QC, Run chromatography, pH;

4. Creating competencies list;

5. Creating documents and working SOPs;

6. Practical on QC, documentation, worksheet, quality log sheets, trend analysis, exceptional reporting;

7. Practical Working a RP monographs;

8. Shelf live experiments;

9. Practice safe radioiodine handling and dispensing;

10. Practice RP waste management and associated SOP and documentation;

11. Practical Blood labelling;

12. Practical accreditation.-creating site file.-SOPs-QA policy;

13. Microbiology in practice. Aseptic practice –a) generator b) Kit preparation;

14. Dispensing practices-VLFC-Isolator;

15. Practical: broth run, dispensing practices;

16. Clinical trial products (overview);

17. Practical: dispensing monoclonal antibodies, peptide RP;

18. Practical: dose calculation of FDG. dispensing PET dose;

19. Interactive session: .1- purchasing and tender RP practices; 2- RP licensing systems and role of Pharmacopoeia.; practical in purchasing RP setting and working tenders;

20. Interactive session: practical log-book keeping for at least 3 months; trainee and tutor support; method of final assessment and certification.

1.19. Internship and methods of follow-up

This training is designed to encourage local national and regional empowerment. In most cases local professional bodies create a framework for assessment and also hold responsibility for the follow up. The national or regional nuclear medicine professional bodies set standards and accordingly assess the achievements of the participants. Same bodies will also provide guidance for nuclear physicians as supervisors on standardized assessment requirements after 3 months. Three months on the job basis training and a practice diary under supervision of an accepted tutor is essential. Daily log-book entries and self assessments are an integral part of the IAEA training approach in radiopharmacy practice. Each trainee is expected to proof a minimum of competencies after completion of the training. In a few cases professional bodies have also taken note of trainees' performances immediately following the training with a series of open and carefully designed MCQ (multiply choice questions) assessments.

The key elements of a follow-up include the following:

- Practical log-book keeping for at least 3 months;
- Feedback from trainee and tutor support;
- Method of final assessment and certification.

Table 2 provides details of typical elements that are covered in the practical log book. Not all elements have to be completed, however, an honest assessment of application is essential. Regular dialogue between trainee and supervisor is essential to keep the process on track.

A periodical audit process of training should include reviews with trainees and progress reports following training. The trainees should be encouraged to provide feedback therefore helping in developing a sustainable culture of regular reviewing, updating and change. Through regional projects the IAEA can provide an external review process to further strengthen the system.

TABLE 2. TYPICAL LOG BOOK ASSESSMENT ELEMENTS.

Practical log-book keeping for at least 3 months

	Topic	**Date**	**Practice**	**Comment**	Supervisor s signature
1	Types of radiation, Radioactivity and Radionuclides. Instruments				
2	Radiation Safety (Radiation Protection Principles and Regulations) Diff. types of radiation Radiation hygiene Calibrator geometry				
3	Production of Radionuclides Radioactive component of RP Characteristics and the selection of radionuclides RP				
4	Properties of Generator system Tc/Mo generators Wet and Dry generators Generator profile . Profile				

	Eluation records Build up Al-breakthrough				
5	Radiopharmacology and localization mechanisms of radiopharmaceuticals- Basic principals				
6	RP operation (Basic aspects, staff, design of facilities).				
7	Mathematic in daily RP practice. Radioactive decay calculation of common RP. Generator Calculation from reference Dose and volume				
8	Look at package insert of different RP kits and establish working parameters.				
9	QA in Hospital RP QC in Hospital RP Radionuclide purity Radiochemical purity Chromatography pH Particles				

	Temperature Shelf life Keeping quality log sheets				
10	Basic radiation environmental monitoring in hospital RP				
11	Safe handling of radioiodine. Fume hoods and safety cabinets Practice safe radioiodine handling and dispensing				
12	Radioactive packages (Categories, ordering, receiving, sending radioactive substances) Transportation of RP experiments				
13	Radioactive waste related to RP and safe practices Practice RP waste management and associated SOP and documentation				
14	Microbiology In process testing Sterility test Pyrogen test LAL				
15	GMP In hospitals. Centralised –radio-pharmacy Create ideal layout and state why.				

	Documentation- worksheet IT, RP database, and electronic work sheet.				
16	Aseptic operations (Basic aspects, staff, design of facilities). Preparation and aseptic. Isolator technology				
17	Aseptic assessment Basic environmental monitoring Broth run Microbiology in practice Microbiology in practice: Aseptic practice – a) Generator b) Kit preparation Dispensing practices -VLFC -Isolator				
18	RP licensing systems and role of Pharmacopoeia. Working a RP Monograph				

19	Purchasing and tender RP Practical in purchasing RP setting and working tenders				
20	Infection imaging				
21	Radiolabelling of white cells.				
22	Radiolabelling RBC				
23	Monoclonal and Peptides in RP Practical: Dispensing Monoclonal antibody or peptide RP				
24	PET radiopharmaceuticals Safe handling of PET products. Dose calculation of FDG. Dispensing dose				
25	Competencies of staff working in RP. Staff induction in RP practices Creating competencies list. Practical accreditation. Creating site file. QA policy Creating working SOPs				
26	RP results Routine monitoring and trouble shooting in				

	RP. QA in Hospital RP and QC Radiopharmaceuticals				
27	Use of pharmaceuticals in NM e.g. Thyroid blockade, Adenosine etc.				
28	Drug and radiopharmaceutical interaction				
29	Continuous development. Journal reading and online support.				
30	Additional related activities				

2. TRAINING OBJECTIVES

It is essential for the trainers to clearly understand not only the objectives but what are the key competencies essential for all the technologists or radiographers involved with hot laboratory services at IAEA operational levels 1 and 2. Additional suggested topics have been stated under each of the objectives to assist the trainers. These series is based on training objectives for nuclear pharmacy technicians approved by American pharmaceutical association.

2.1. Objective 1

The nuclear pharmacy technician should have a working knowledge of the radiopharmaceutical terms, abbreviations, and symbols commonly used in prescribing, compounding and dispensing radiopharmaceuticals.

2.1.1. Competencies

The technician should be able to:

1. Transcribe and generate computer labels without error for any 25 radiopharmaceutical orders selected at random from at least four different institutions serviced by the radiopharmacy;

2. Demonstrate a working knowledge of the multiple ‘names’ and abbreviations of 10 radiopharmaceuticals (e.g. Cardiolite®, sestamibi, MIBI, C'lite, RP-30);

3. Define the terms of radioactiovity Bequerels (Bq), Curie (Ci), MBq, millicurie (mCi), using both decimals and scientific notation.

2.1.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Radiopharmaceutical-medical terminology;

2. Radiopharmaceutical abbreviations and symbols, radioisotope abbreviations.

2.2. Objective 2

The nuclear pharmacy technician should demonstrate an ability to perform the mathematical calculations required for the usual dosage determinations and solution preparations in the compounding and dispensing of radiopharmaceuticals.

2.2.1. Competencies

The technician should be able to:

1. Convert without error any given activity to pre and post calibration activity;

2. Perform the calculations necessary to prepare a standard cold kit from a generator elution;

3. Perform the calculations necessary to prepare a time-specific unit dose from a pre or post calibrated prepared radiopharmaceutical;

4. Perform the calculations necessary to prepare weight-in-volume and volume-in-volume solutions.

2.2.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Review of fractions, decimals, scientific notation, ratios, and percentages;

2. Review of the Decay Equation;

3. Dosage calculations;

4. Preparation of compounded solutions.

2.3. Objective 3

The nuclear pharmacy technician should have a working knowledge of the procedures and techniques relating to aseptic compounding and parenteral admixture operations.

2.3.1. Competencies

The technician should be able to:

1. List five different possibilities for contamination of an injectable solution during its preparation and for each possibility a precaution that would prevent the contamination;

2. Demonstrate the proper technique for using a syringe and needle for aseptic withdrawal of the contents of:

    a. A rubber-capped vial;

    b. A glass ampoule;

3. Demonstrate the proper technique for aseptic reconstitution of a cold kit;

4. Describe the occasions when hand washing is required and demonstrate the proper technique';

5. Demonstrate the correct technique and procedure for preparing at least three technetium radiopharmaceuticals, including the proper preparation of the label and completion of appropriate records;

6. Demonstrate the proper technique for cleaning a laminar air flow hood, including appropriate record keeping;

7. Identify the major components of a laminar air flow hood and state their functions;

8. Define or describe:

    a. Microbial growth and transmission;

    b. Simply assessment methods;

c. Origin, pharmacologic effect and prevention of pyrogens;

d. Sterility;

e. Heat sterilization;

f. ‘Cold’ sterilization;

9. Demonstrate the proper technique for visual inspection of parenteral solutions.

2.3.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Parenteral routes of administration common to nuclear pharmacy (rationale, precautions and problems);

2. Equipment and systems used in parenteral administration (needles and syringes, administration sets, containers, filters, and pumps);

3. Aseptic compounding techniques (specific to the system in use and including the prefilling of syringes);

4. Labelling and recordkeeping;

5. Quality control (microbiological and particulate matter inspections and monitoring of contamination).

2.4. Objective 4

The nuclear pharmacy technician should have working knowledge of the procedures and operations relating to the reconstitution, packaging and labeling of radiopharmaceuticals.

2.4.1. Competencies

The technician should be able to:

1. Repackage and label 25 unit doses from bulk prepared radiopharmaceuticals and correctly complete all necessary records;

2. Demonstrate for each of five technetium labelled radiopharmaceuticals the reconstitution and unit or multi dose packaging of specified radiopharmaceuticals;

a. Proper selection of each ingredient;

b. Correct selection of necessary equipment;

c. Proper assembly and use of the equipment;

d. Accurate calculation and measurement of each ingredient;

e. Proper completion of worksheet records and other required information;

f. Correct procedure for mixing and preparing radiopharmaceutical;

g. Correct procedure for quality control testing of the radiopharmaceutical;

h. Proper selection and preparation of dosage containers and closures;

i. Proper packaging technique for both unit and multi dose prescriptions;

j. Correct selection and preparation of labels.

3. Identify from the pharmacy reconstitution procedure those functions that must be performed by a pharmacist only;

4. Demonstrate proper completion of all record-keeping requirements for each formulation.

2.4.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Measurements of quantity (volume, weight, activity, and numbers);

2. Use, assembly, and maintenance of equipment and apparatus;

3. Control and recordkeeping procedures;

4. Packaging considerations;

5. Storage and inventory control;

6. Lot numbers and expiration dates and times;

7. Types of drug containers and packages;

8. Labelling of drug containers and packages.

2.5. Objective 5

The nuclear pharmacy technician should demonstrate the ability to perform the usual technician functions associated with a specific radiopharmacy.

2.5.1. Competencies

The technician should be able to:

1. Demonstrate the proper technique for technetium generator elution, including appropriate record keeping;

2. Describe the specific dispensing and record keeping procedures that apply to the dispensing of:

a. Compounded radiopharmaceuticals;

b. Adaptive compounded radiopharmaceuticals;

c. Therapeutic radiopharmaceuticals;

d. Non radioactive drugs;

e. Investigational radiopharmaceuticals;

3. List for each of 30 common radiopharmaceuticals;

a. The various trade-names;

b. The generic name;

c. The usual dose associated with a given procedure;

d. The manufacturers and their calibration date/time, and expiration time;

4. Describe for at least ten technetium radiopharmaceuticals, as appropriate:

a. Quality control testing for radiochemical purity;

b. Quality control testing for radionuclidic purity;

c. Quality control testing for chemical purity;

d. Procedural errors that result in substandard radiopharmaceuticals

2.5.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Setting up doses for patients;

2. Checking doses;

3. Equipment used to perform quality control testing;

4. Quality control techniques;

5. Review of prescription orders;

6. Manufacturer package inserts

2.6. Objective 6

The nuclear pharmacy technician should demonstrate the ability to perform the manipulative and record keeping functions associated with the compounding and dispensing of radiopharmaceuticals.

2.6.1. Competencies

The technician should be able to:

1. Carry out the following functions for any 10 randomly selected radiopharmaceuticals:

a. Correctly type the label;

b. Select the proper drug and lot from dispensing stock;

c. Compound the proper drug if not in dispensing stock;

d. Accurately measure the product and place in the proper container;

e. Properly label the dose container and exterior shielding;

f. Complete the necessary records and documents.

2. Correctly determine the availability of radiopharmaceuticals not in dispensing stock, including:

a. Manufacturer;

b. Calibration and expiration time;

c. Soonest availability;

d. Appropriate order quantity.

3. Designate from of a list of 10 steps involved in radiopharmaceutical dispensing those functions that only a pharmacist may carry out.

2.6.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Preparing prescription labels;

2. Manufacturer package inserts and information sheets;

3. Measuring and assaying drugs.

2.7. Objective 7

The nuclear pharmacy technician should demonstrate the manipulative and record keeping functions associated with quality control testing of radiopharmaceuticals.

2.7.1. Competencies

The technician should be able to:

1. Carry out the following functions for any ten randomly selected radiopharmaceuticals:

a. Select the appropriate solvents and media for the radiopharmaceutical chromatographic analysis;

b. Accurately perform the appropriate physical test;

c. Describe the species identified with the appropriate procedure;

d. Complete the necessary records and documents.

2. Correctly carry out the following functions for any generator elution:

a. Select the equipment necessary to perform radionuclide purity;

b. Accurately perform the purity test according to the equipment manufacturer's specification;

c. Determine the expiration time of the generator elution;

d. Complete the necessary records and documentation;

3. Correctly perform sterility testing of both radioactive and non radioactive products according to pharmacy protocols.

2.7.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Performing quality control testing;

2. Review of radiochemical and radionuclidic purity testing;

3. Review of sterility testing of radiopharmaceuticals;

4. Review of USP and pharmacy standards of quality.

2.8. Objective 8

The nuclear pharmacy technician should demonstrate a working knowledge of drug dosages by imaging procedure, routes of administration, dosage forms, and be able to distinguish therapeutic from diagnostic radiopharmaceutical utilization.

2.8.1. Competencies

The technician should be able to:

1. Distinguish unit-dose and multi-dose prescription amounts;

2. List the three most common routes of administration of radiopharmaceuticals;

3. Identify an appropriate radiopharmaceutical dosage for a specified imaging procedure for ten radiopharmaceuticals (e.g. Tc-99m dosage for thyroid scan, Meckel's diverticulum, red blood cell labelling, or testicular scan);

4. Distinguish the dosage appropriate for diagnostic or therapeutic use of a given radiopharmaceutical (e.g. I-131 for uptake and scan, whole body imaging, hyperthyroidism, or thyroid ablation).

2.8.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Sources of radioisotopes, radiopharmaceuticals and supplies;

2. Review of diagnostic procedures using radiopharmaceuticals;

3. Review of therapeutic procedures using radiopharmaceuticals;

4. Dosage forms (capsules, solutions, injectables, gases);

5. Review of radiopharmaceutical dosages for specific procedures.

2.9. Objective 9

The nuclear pharmacy technician should demonstrate the ability to perform the essential functions relating to drug purchasing and inventory control.

2.9.1. Competencies

The technician should be able to:

1. Prepare a written report of a physical inventory of pharmacy drugs and supplies using prepared forms and records;

2. Determine from existing reorder levels which inventoried items should be ordered and in what quantity;

3. Demonstrate an ability to check in a drug shipment by using the packing list or invoice and purchase order, completing the receiving report, and adding the items to the inventory;

4. Demonstrate the ability to appropriately store and retrieve from storage at least ten randomly designated items;

5. Describe the procedure for lost shipments and for shipments received short or over quantity ordered.

2.9.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Inventory and purchasing procedures and records;

2. Maintaining radioactive materials records;

3. Use of computer terminals.

2.10. Objective 10

The nuclear pharmacy technician should demonstrate appropriate knowledge and understanding of the specific nuclear pharmacy site with emphasis on the technician duties and responsibilities, including standards of ethics governing pharmacy practice.

2.10.1. Competencies

The nuclear pharmacy technician should be able to:

1. Interpret the pharmacy's organizational chart in terms of general responsibilities and job status of personnel with whom the technician will have contact in carrying out assigned duties;

2. State the general employee performance standards of the pharmacy including reasons for initiation of disciplinary actions;

3. State all of the nuclear pharmacy technician's primary job responsibilities, the duties falling under each, and how these differ from the primary responsibility of the nuclear pharmacist;

4. State the pharmacy policies applicable to each of the primary job responsibilities and describe the procedures for each;

5. Define what is meant by a ‘decision requiring a pharmacist's judgement’ and cite at least 10 examples;

6. Demonstrate the use of correct telephone communication technique and protocol in both receiving and in initiating calls;

7. Demonstrate the use of correct written skills by drafting a memorandum to the supervisor requesting a change in work schedule;

8. State the general requirements of any local, state, or federal laws that specifically affect any of the nuclear pharmacy technician's responsibilities;

9. Demonstrate appropriate working knowledge of any additional training or safety requirements mandated by the pharmacy or by any local, state, or federal agency by successful completion of any required program (e.g. Notice and Instruction to Workers Frequenting a Restricted Area, Blood Born Pathogens Instruction).

2.10.2. Additional topics

The following topics have been suggested in addition for inclusion:

1. Organization, functions, and responsibilities of the pharmacy;

2. Pharmacy policies and procedures, including employee handbook;

3. Orientation of nuclear pharmacy technician duties (job description);

4. Relationship of technicians to pharmacists and other staff;

5. Communication principles and techniques;

6. Legal aspects of technician functions, such as:

    a. Accountability and liability

    b. Pharmacy regulations

7. Other aspects of regulatory compliance, such as:

    a. Radiation Health regulations

    b. OSHA regulations

    c. Hazardous Materials management regulations

3. TYPES OF RADIATION, RADIOACTIVITY, INSTRUMENTS, RADIONUCLIDES, GENERATORS, MATHS, PACKAGES, WASTE AND RADIO-IODINE

3.1. Radioactive component

3.1.1. Scope

To introduce the types of radiation emission and radionuclides. In addition, what radioactivity is and how it can be optimally measured by choosing the correct instrument.

3.1.2. Learning objectives

The trainee must know the basis of the radioactive decay, the types of radiation emission and the mechanisms of radiation interaction. Types of radionuclides and their detection by instruments used in radiopharmacy.

3.1.3. Subject headings and key subject areas radiation and radioactivity

Subject headings	Key areas
Radiation Physics:	Basic Sciences: Nature of Radiation, Atom Structure, • Radiation Terminology, • Line of Stability, • Radioactivity, • Mode of Decays, • Radiation Interaction with Matter, Activity reference Time (ART) or Calibration Date. • Calculations of Radioactive Doses: $A = A_0e^{-\lambda t}$ • Instrumentation (Based on Ionization and Scintillation) Added
Radioactive Component	Definition, role of the radioactive component Detection/Damage
Radioactive Component	n/p ratio

	Range of stability Unstable Nuclide (Change, release energy to more stable range) Characteristics of Radiations Range, ionization
Selection of Radionuclides	Half-life Decay mode Radiations emitted
Requirements for Diagnostic Radionuclides	Radiations emitted Diagnostic benefit Radiation exposure to the patient
Requirements for Diagnostic Radionuclides	Arguments on gamma energies, abundance, monochromatic energy Sensitivity of detection Radiation exposure
Requirements for Therapeutic Radionuclides	Beta, Alpha, Electron Capture
Requirements for Therapeutic Radionuclides	Arguments on beta energies Ranges in tissue
Requirements for Therapeutic Radionuclides	Alpha radiation Comparison of alpha and beta radiation in cell killing
Auger Electrons	I-125, In-111, Ga-67 Internalization of low energy electrons Range of biological effectiveness

Model lecture 1- ‘Types of radiation’ is on CD at the back this trainer’s manual.

3.1.4. Subject headings and key subject areas Instrumentation

Subject headings	Key areas
Instrumentation:	Based on Ionization o Dose Calibrators o Survey Monitors o Personal Dosimetry • Based on Scintillation o Solid Scintillation Gamma Counter o Gamma Camera o SPECT o PET

Model lecture 2- 'Types of Instruments' is on CD at the back this trainer's manual.

3.2. Practical types of radiation

3.2.1. Part 1-To show the different types of radiation emission and radionuclides

3.2.1.1. Learning objectives

The trainees must be able to differentiate the types of radiation emission and the mechanisms of radiation interaction in order to understand the basis of radiation detection

3.2.1.2. Materials

- Gamma counter or gamma camera
- Ionization Chamber
- Well gamma counter (or thyroid probe)?
- Monitor
- ^{32}P source 37MBq (1 mCi)
- ^{99m}Tc source 37MBq (1 mCi)

3.2.1.3. Steps

1. Measure the ^{99m}Tc source in the Gamma counter or gamma camera. Record the counts rate.
2. Measure the ^{99m}Tc source in the Ionization Chamber. Record the activity.
3. Measure the ^{99m}Tc source in the Well gamma counter (or thyroid)? Record the counts rate.
4. Measure the ^{99m}Tc source with the Monitor. Record the counts rate.
5. Repeat steps 1.1.1 to 1.1.4 changing by a ^{32}P source. (If it is possible)

3.2.1.4. Results

For this part of the practical, the trainees should expected to learn that not all the radioisotopes can be measured in all the equipments and that each equipment displays different measure units, which can be correlated applying efficiency geometry factors.

3.2.1.5. Discussion

Discussion should be centralized in what kind of equipment is chosen for the measurement each radionuclide for a certain purpose and how he/she can be sure that the obtained result is the correct one.

3.2.2. Part 2- To demonstrate to the trainees the importance of shielding containers in RP operations

3.2.2.1. Learning objectives

To understand the importance of shielding for their daily practice and to understand the importance of distance for dose radiation diminishing

3.2.2.2. Materials

- Monitor
- ^{32}P source
- ^{99m}Tc source
- Lead Shielding containers of 3mm, 5mm and 6mm
- Lucite Shielding containers

3.2.2.3. Steps

1. Place the ^{99m}Tc source in a lucite container of 5 mm thickness. Place the monitor in contact with the shielding. Record the count rates.

2. Place the ^{99m}Tc source in a lead container of 3 mm thickness. Place the monitor in contact with the shielding. Record the count rates.

3. Place the ^{99m}Tc source in a lead container of 5 mm thickness. Place the monitor in contact with the shielding. Record the count rates.

4. Place the ^{99m}Tc source in a lead container of 6 mm thickness. Place the monitor in contact with the shielding. Record the count rates.

5. Repeat steps 1 to 4 changing by a ^{32}P source

3.2.2.4. Results

The trainees must learn the importance of the appropriate material for the shielding container and should be able to evaluate the importance of its thickness.

3.2.2.5. Discussion

Discussion should be centralized in the importance of a correct shielding in daily routinely radiopharmacy practices.

3.2.3. Part 3- To demonstrate the importance of distance in radiation interaction with matter

3.2.3.1. Learning objectives

To understand the importance of distance in radiation interaction with matter with the objective of dose radiation diminishing and correct measurements.

3.2.3.2. Materials

- Monitor
- ^{32}P source
- ^{99m}Tc source
- Lead Shielding containers of 6mm
- Lucite Shielding containers

3.2.3.3. Steps

1. Place the ^{99m}Tc source in a lead container of 6 mm thickness. Place the monitor in contact with the shielding. Record the count rates.

2. Place the ^{99m}Tc source in a lead container of 6 mm thickness. Place the monitor at 5 cm of the shielding. Record the count rates

3. Place the ^{99m}Tc source in a lead container of 6 mm thickness. Place the monitor at 10 cm of the shielding. Record the count rates

4. Place the ^{99m}Tc source in a lead container of 6 mm thickness. Place the monitor at 50 cm of the shielding. Record the count rates.

5. Repeat steps 1 to 4 changing by a ^{32}P source in a Lucite container.

3.2.3.4. Results

The trainees should be able to understand the importance of distance in radiation protection.

3.2.3.5. Discussion

Discussion should be centralized in the importance of an optimal distance maintenance in daily routinely radiopharmacy practices.

Discuss different types of radiation. Selecting the equipment according to the radionuclide, the purpose of the determination and the activity involved. Most important: Calibrated equipment to assure the data.

Discuss aspects of radiation shielding.

3.3. Radionuclide calibrators

Model lecture 3- 'Radionuclide calibrators' is on CD at the back this trainer's manual.

3.4. Practical calibrator

3.4.1.1. Scope

To demonstrate the importance of equipment calibration and geometry factors.

3.4.2. Learning objectives

To understand the significance of a well calibrated equipment and the knowledge of correction factors to arrived to correct measurements and dose calibrations.

3.4.2.1. Materials

- Dose Calibrator
- ^{99m}Tc source
- Lead Shielding containers of 6mm
- Vials
- Syringes
- Saline solution

3.4.2.2. Steps

3.4.3. Vial geometry

1.1 Draw 1 mL of Tc-99m 37MBq (1 mCi), inject into an empty glass vial
1.2 Assay in a dose calibrator, record activity (Ri)
1.3 Add 1 mL increments of saline to the vial up to a total of 10 mL and record the activity (Ri)
1.4 Using 5 mL as the reference volume (Rn) calculate the ratio for each volume. (R = Rn/Ri). Or graph.
If the reading varies more than ± 10%, of the reading obtained from the reference volume use a correction factor (C.F.) equal to R = Rn/Ri.
1.5 Repeat step 1.1 to 1.4, using a Tc-99m radioactivity of both 1 mCi and 10 mCi.

Volume (mL)	Activity MBq (mCi)	R = Rn/Ri

3.4.4. Syringe geometry

2.1 Draw 0.2 mL of Tc-99m MBq(1 mCi) into a 1 mL syringe
2.2 Assay in a dose calibrator, record activity (Ri)
2.3 Add 0.2 mL increments of saline to the syringe up to a total of 1 mL and record the activity (Ri)
2.4 Using 0.6 mL as the reference volume (Rn) calculate the ratio R for each volume (R=Rn/Ri). If the reading varies more than ± 10% of the reading from the reference volume use a correction factor (C.F.) equal to R=Rn/Ri Or graph.

2.5 Repeat step 1.1 to 1.4 using a 5 mL syringe (adding 1 mL increments) and 10 mL syringe (adding 2 mL increments). Repeat experiment using both 37MBq (1 mCi) and 370MBq (10 mCi0 Tc-99m

Volume (mL) Activity (mCi) R = Rn/Ri

3.4.5. Geometry independence evaluation between vial and syringe

3.1 Assay the vial activity (≈1mCi in 10 mL) and record (R1)
3.2 Using a 1 mL syringe draw 0.3 mL from the vial
3.3 Assay the vial (R2) and syringe (Rs) activity
3.4 Using a 1 mL syringe draw 0.6 mL from the vial
3.5 Assay the vial (R2) and syringe (Rs) activity
3.6 Calculate the ratio for each volume as the difference in vial activity divided the syringe activity, R=(R1-R2)/Rs
3.7 Repeat Step 3.1 to 3.6 using a 5 mL syringe (drawing 1 mL increments) and a 10 mL syringe (drawing 2 mL increments from 2mL to 8 mL)
Repeat experiment using 37MBq (1 mCi) and 370MBq(10 mCi) of Tc-99m.
3.8 If the syringe reading varies more than ±10% of the difference in vial activity before and after each volume is drawn use correction factor (C.F.) equals to R=(R1-R2)/Rs.
3.9 (Optional and if available) Repeat experiment using 37MBq (1 mCi) of In-111 activity. Explain why C.F. is needed when using In-111.
Vol. drawn (mL) Diff. in Vial Syringe (R1-R2)/Rs Activity (R1-R2) Activity(Rs)

3.4.5.1. Results

Results are recorded in a table.

3.4.5.2. Discussion

3.4.5.3. Conclusion

3.5. Radiation safety

3.5.1. Objective

To bring the basic knowledge in radiation protection and radiation safety.

3.5.2. Learning objectives

To become familiar with the types of sources used in nuclear medicine. To become aware of how the basic principles of ‘defence in depth’, safety of sources and optimization as applied to routine practice in radiopharmacy. To get basic information about shielding, distance and time analysis.

3.5.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Radiation Safety:	Basic Principles of Radiation Protection • Radiation Dose Control Parameters • Radiation Protection Regulations (Basics, Transportation and Radioactive Waste)
Magnitude and Units used in radiation protection	Units SI. Absorbed energy. Doses. Dose rate. Equivalent Dose.
Recommendations of the International Commission on Radiation Protection (ICRP).	Pondered Equivalent Dose. • Definitions, concepts and units. • Critical organ. • Internal and external sources. • Physical and biological half life. Accumulated Dose. • Internal Dosimetry Alpha, Beta and gamma sources • External Dosimetry Beta and gamma sources • Exposition. Exposition rate. Material Selection. • Biological Aspects of Radiation protection. • Biological Effects of ionizing radiations. Specific constants for gamma radiation (tau) • Dosimetry of internal sources. Risk and damage concepts. Determining and Stochastic Effects. • Principals of radiation protection practical justification protection optimization dose limitation. • ICRP Recommendations. Individual Protection: individual protection and limitation of the total impact of a source practical. • Exposure Types. Occupational exposure.

	Medical exposure. Public exposure • Occupational exposure Optimization Limitation. Control of the occupational exposure. • Medical exposure Justification Optimization. • Exposure in pregnant women. Radiation Protection in pregnancy and breast feeding. • Public exposure Controls. • Accidents and incidents. • Implementation of the ICRP recommendations. Competent Authority. Responsibilities. Practices Regulations. • Working Conditions. Working Areas. Operational Guide. Importance of the Practices Code. • External exposure and contamination restrictions. Aerosols. • Monitoring. Dosimetry of the occupational exposure. Dosimetry of medical practices. Dosimetry of public exposure. Emergency Plans. Intervention System of the National Nuclear Authority.
Introduction to MIRD methodology.	• Protection system for external radiation. • Shielding. Design and calculation for electromagnetic radiations Transmission Relation; influence of source geometry. • Shielding for Beta radiation.

Model lecture 4- ‘Radiation safety in radiopharmacy’ is on CD at the back this trainer’s manual.

3.6. Production of radionuclides

3.6.1. Objective

To give the overview knowledge in radionuclide production (reactor, cyclotron and generators), reaction mechanisms and what impurities are likely to be in the product.

3.6.2. Learning objectives

The trainee should be familiar with the mechanisms of radionuclide production with the aim of be able to understand the radionuclide purity in quality controls data sheets. The methods and equipment for its production and its limitations. In addition, be aware of the requirements of specific activity for labelling some RP.

3.6.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction Method of Production	Radioisotope Production and Processing Facilities Production of Radionuclides Change of n/p ratio (from range of stability to n-rich or n-poor) • Bombarding with sub-atomic particles Production of Radionuclides • During bombardment not all atoms become radioactive Neutron Induced Reactions Nuclear Reactor (Structure) Natural uranium, enriched uranium • Nuclear Reactor Fission reaction, fissionable elements, U-235 fission • Fission, Probability of Interaction Neutrons emitted with high energy (1.5 MeV) fast neutrons Neutrons emitted thermal energy (0.025 eV) slow neutrons • Nuclear Reactor Design Fuel elements (U-235)

	Moderator (water, heavy water, graphite) Control rods (Cd) Calculation of Radionuclide Production I do not agree to teach it at that level Equation for production • Neutron flux, cross section
Carrier and Carrier Free concepts	Carrier Radioisotopes containing some stable isotope(s) of the target element Carrier-free Radioisotopes without the presence of stable isotope(s) No carrier added • Specific Activity Calculation of specific activity Calculation of Radionuclide Production Equation for production Neutron flux, cross section • Properties of Fission Products • Properties of Neutron Bombardment Products • Charged Particle Reactions • Particle accelerators
Cyclotron	• Charge Particle Reactions Repulsive force due to positively charged nucleus (Coulomb Barrier) Particles with sufficient energy to overcome the Coulomb Barrier Excitation function • Cyclotron Design Two metal electrodes [Dee(s)]

	Two magnets High frequency electricity • Cyclotron Operation (mini) PET cyclotron, 30 MeV and greater cyclotrons • Cyclotron Products Specific activity, carrier-free Positron decay group, E.C. decay group • Cyclotron Products Limitations: beam intensity Yield, short half-lives • Cyclotron Products Challenges: Logistics, targets, difficult chemistry, exposure rates • PET Products (short-lived) C-11, N-13, O-15, F-18 Nuclear Reactions and yields • F-18 Synthesis Box • F-18 Radiopharmaceuticals FDG, DOPA, FLT, F-MISO • E.C. Decay Group Ga–67 production routes In-111 production routes Tl-201 production routes I-123 production routes I-123 I-124 free production Ph. Int. Direct link to radiopharmaceutical chapter http://www.who.int/medicines/publications/pharmacopoeia/radiopharm/en/index.html

Specific Weight and Specific Activity	
Radionuclide Charts, Characteristics of Radionuclides	http://hpschapters.org/northcarolina/nuclide_information_library.php3 http://www.nndc.bnl.gov/nudat2/

Model lecture 5- 'Radioisotope production' is on CD at the back this trainer's manual.

3.7. Tc-99m generator

3.7.1. Scope

This lecture will describe the mechanism and characteristics of a Tc-99m generator. The lecture will also provide information on how a Tc-99m generator should be operated in order to achieve maximum yield. The quality control of the Tc-99m eluate from a Tc-99m generator will also be covered.

3.7.2. Learning objective

At the end of this lecture, the trainee are expected to know how a Tc-99m generator functions, different types of Tc-99m generators, the equilibrium between Tc-99m and Mo-99, as well as the optimal time interval for elution of a Tc-99m generator. The trainee should be able to estimate the Tc-99m yield on different days of a week and should know the quality control tests (including the procedures, frequency, and acceptance limits) applicable to the Tc-99m eluate from a Tc-99m generators.

3.7.3. Subject headings and key subject areas

Subject headings	Key areas
Structure and mechanism of a Tc-99m generator Characteristics of an ideal generator	• Structure of a Tc-99m generator • Mechanism of aTc-99m generator • Column • Parent-daughter relationship • Properties of parents • Generator kinetics-intervals and yields between each elution

	• eluant • shelf life • Separation of parent and daughter • impurities-parent breakthrough
Different types of Tc-99m generator	• Different types of Tc-99m generators based on the origin of Mo-99 (fission Mo-99 and fusion Mo-99) • Different types of Tc-99m generator based on the mode of elution (wet type and dry type)
Tc-99m generator kinetics	• Transient equilibrium between of Mo-99 and Tc-99m • Time to reach equilibrium since last elution • Ratio of Tc-99m radioactivity to Mo-99 radioactivity at equilibrium • Amount of Tc-99m eluted from a Tc-99m generator on different day of a week • Multiple elution of a Tc-99m generator on the same day • Examples of calculations
Quality control of Tc-99m eluate	• Radionuclidic purity o Definition o What is the common radionuclidic impurity in Tc-99m eluate and its source o methods to test for radionuclidic purity (Mo-99 breakthrough test) o The Mo-99 breakthrough canister o Multichannel analyzer o Frequency of testing for radionuclidic purity o Acceptance limit o Radionuclidic purity increases with time • Chemical Purity

	○ Definition ○ What is the most common chemical impurity and its source ○ Methods to test for chemical purity (Al+++ breakthrough test) ○ Frequency of testing for chemical purity ○ Acceptance limit • pH ○ frequency of testing for pH ○ methods to test for pH ▪ pH meter ✓ daily calibration of pH meter ▪ pH paper ✓ validation of pH paper ○ acceptance limit • Screening of sterility ○ importance of screening for sterility ○ frequency ○ procedure ○ culture media –SCDM and FTM ○ culture time and temperature for aerobic and anaerobic bacteria ○ validation of sterility test with known strains of bacteria • Screening for bacterial endotoxins ○ What is endotoxin ○ importance of screening for bacterial endotoxin ○ frequency

	o procedure ▪ LAL test ✓ Turbimetic LAL test ✓ Chemogenic LAL test
Shelf life and storage of Tc-99m generator	• Shelf-life of Tc-99m generator • Storage in class A environment
Trouble-shooting	• Low yield • Fail to elute

3.8. Tc-99m generator -practical

3.8.1.1. Objective

The session aims at providing the trainee some experiences of eluting a Tc-99m generator, performing Mo-99 breakthrough test and Al+++ breakthrough test.

This session also provides an interactive discussion so that the trainee would know how to calculate the Tc-99m yield of a generator and to decide on the performance of a Tc-99m generator

3.8.1.2. Material

- Tc-99m generator
- Evacuated Tc-99m collection vials properly fitted inside a vial shield
- Normal saline eluent for elution (if required)
- moly-99 breakthrough canister
- Al+++ breakthrough kit
- Dose calibrator

3.8.1.3. Steps

3.8.2. Mo-99 breakthrough test

1. Place the Evacuated Tc-99m collection vial on the collection slot of the Tc-99m generator, if the generator requires introduction of normal saline, place the normal saline eluent vial on the normal saline slot.
2. After the elution is completed, remove the Tc-99m collection vial from the generator.
3. Change the setting of the dose calibrator to Mo-99, place the Mo-99 breakthrough canister into the dose calibrator to measure and record the Mo-99 background radioactivity
4. Remove the Tc-99m vial from its vial shield, place it into the, measure and record the Mo-99 radioactivity

5. Remove the Tc-99m vial from the Mo-99 breakthrough canister, place it back into the dose calibrator, change the calibrator setting to Tc-99m, measure and record the Tc-99m eluate radioactivity.
6. Mo-99 breakthrough = $\frac{\text{(Mo-99 radioactivity – Mo-99 background) x 2}}{\text{Tc-99m radioactivity – Tc-99m background}}$
7. Acceptance = 5.55 Kbq (0.15µCi) Mo-99 per 37 Mbq (1 mCi) Tc-99m

3.8.3. Al^{+++} breakthrough test

1. Place the Tc-99m vial back into its vial shield. Measure and record the Tc-99m background radioactivity
2. Place one drop of the Al^{+++} breakthrough test standard onto the Al^{+++} test paper
3. Use a properly shielded syringe, withdraw a small amount of Tc-99m from the Tc-99m vial above, and apply one drop onto the Al^{+++} test paper
4. Observe the different in color between the Al^{+++} breakthrough standard and the Tc-99m drops. The Al^{+++} standard drop should have a darker color

3.8.4. Perform pH test.

Using pH strips.

3.8.5. Results

3.8.5.1. Mo-99 breakthrough test

Mo-99 background radioactivity =

Mo-99 radioactivity =

Tc-99m background radioactivity =

Tc-99m radioactivity =

Mo-99 breakthrough = $\frac{\text{(Mo-99 radioactivity – Mo-99 background) x 2}}{\text{Tc-99m radioactivity – Tc-99m background}}$
=

Acceptance = 5.55 Kbq (0.15µCi) Mo-99 per 37 Mbq (1 mCi) Tc-99m

3.8.5.2. Al^{+++} breakthrough test

Al^{+++} standard colour (10 µg/mL) =

Tc-99m colour =

Al^{+++} concentration in the Tc-99m eluate is (higher/lower) than 10 µg/mL

Acceptance limit = Al^{+++} concentration in the Tc-99m eluate should be

lower than10 µg/mL, i.e. the Al^{+++} standard drop should have a darker colour

3.8.5.3. pH

pH = acceptance limit (4 to 8)

3.8.5.4. Record

Record on Tc-99m elution registry form; time of elution, activity, volume, radioactive concentration, Mo-99 (µCi), Mo-99 breakthrough (µCi/mCi), Al (µg/mL), pH information.

3.9. Interactive discussion on Tc-99m generator

Consider the following table

Tc-99m generator size 37Gbq (1Ci), calibration: Mon

Days of a week	Radioactivity of Tc-99m eluate	Expected Tc-99m radioactivity
Mon	1105 mCi	
Tue	702 mCi	
Wed	560 mCi	
Thu	450 mCi	
Fri	150 mCi	

1. Discuss with the trainee on the calculation of the expected Tc-99m radioactivity on each day?
2. Has the Tc-99m generator been functioning properly throughout the week?
3. If there was one day on which the generator had been eluted twice, this happened most likely on which day?
4. Why rdionuclidic impurity (Mo-99 breakthrough) increase with time?

3.9.1. Tc-99m generator (work sheet)

Place the elution vial in a properly shielded container

1. Elute the generator
2. Assay the radioactivity of the eluate in a dose calibrator
3. Record the following information, on the generator registry:

Elution:

Date/time, activity, volume, radioactivity concentration, Mo-99 breakthrough

The suppliers assay, calibration and expiration dates

4. Calculate the yield by the following steps

Mo-99 activity determination (decay)
Tc-99m activity determination as a fraction of Mo-99 activity
Calculate the elution yield of generator column

$$\frac{A2}{A1} = \frac{0.86\lambda_2 (e^{-\lambda_1 t} - e^{-\lambda_2 t})}{(\lambda_2 - \lambda_1)(e^{-\lambda_1 t})}$$

Mo-99 decay factors

Time (h)	Decay factor	Time post elution (h)	Amounts of 99mTc expressed as fraction of Mo-99 A2/A1
-48	1.65	2	0.179
-36	1.46	4	0.324
-24	1.28	8	0.537
-12	1.13	12	0.677
0	1	16	0.769
12	0.882	20	0.830
24	0.779	22	0.852
28	0.747	23	0.861
32	0.716	24	0.870
36	0.687	25	0.877
40	0.659	26	0.884
44	0.632	27	0.890
48	0.606	28	0.896
72	0.472	29	0.901
96	0.368	30	0.905
120	0.286	36	0.924
144	0.223	48	0.940
168	0.174	54	0.943
192	0.135	72	0.946
216	0.105		

3.10. Mathematics in radiopharmacy practice

3.10.1. Scope

To teach the trainees various calculations used in routine radiopharmacy practices.

3.10.2. Learning objectives

At the end of this lectures, the trainees should know the decay equations, how the use the decay equation to calculate radioactivity before and after a certain calibration time. The trainee should also know Tc-99m generator kinetics, how to estimate the amount of Tc-99m eluted from a Tc-99m generator, how to estimate the amount of radioactivity required to prepare a radiopharmaceutical, how to calculate the dosage of a radiopharmaceutical at different time after preparation, how to estimate the volume of the radiopharmaceutical dose to be drawn. In addition, the trainee should understand that radiation decay is a random process and there is a tolerance limit for each dose prepared.

3.10.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• Importance of correct calculation o More efficient o Minimize exposure o Minimize confusion o Minimize error
The decay equation	• Definition of each term in the decay equation • Use of decay equation • Calculation of radioactivity at different time after calibration • Calculation of radioactivity at different time before calibration • Calculation of half life • Examples of each calculation
Tc-99m generator kinetic	• Transient equilibrium between of Mo-99 and Tc-99m • Time to reach equilibrium since last elution

	• Ratio of Tc-99m radioactivity to Mo-99 radioactivity at equilibrium • Amount of Tc-99m eluted from a Tc-99m generator on different day of a week • Multiple elution of a Tc-99m generator on the same day • Examples
Estimation of the amount of Tc-99m required to prepare a radiopharmaceutical	• Different factors to be considered o Number of doses to be prepared o Amount of radioactivity for each doses o Time of preparation and time of calibration o Extra amount of Tc-99m to be added into each kit o Maximum level of radioactivity allowed for each kit • Total amount add to a kit = • # of doses x Tc-99m amount for each dose + extra Tc-99m required • Examples
Calculation the dosage of a radiopharmaceutical at different time after preparation	• Factors to be considered o Time in between calibration of dispensing of the doses o Radioactivity amount required for each dose • Calculation of dosage at different time after calibration • Calculation of dosage at different time before calibration
Estimate the volume of the radiopharmaceutical dose to be drawn	• Factor to be consider o Concentration of the radiopharmaceutical preparation o Radioactivity amount required for each dose

	o Time in between calibration of dispensing of the doses • Calculation of dosage volume at different time after calibration • Calculation of dosage volume at different time before calibration

3.11. Mathematics in hospital radiopharmacy-interactive discussion

3.11.1. Objective

To let the trainee be familiar with mathematics used in hospital radiopharmacy

Discuss with the trainee about the flowing calculations;

(1). Decay equation $A = A0e^{-\lambda t}$

A= final radioactivity (to be calculated)

A0 = initial radioactivity (100 mCi)

λ= decay constant (0.693/half life)(halflife=6hr)

t=time elapsed (3.5 h)

(2) Use of Tc-99m decay factor

Time elapsed	Decay factor
15 min	0.972
30 min	0.944
45 min	0.917
1 h	0.891
2 h	0.794
3 h	0.707
4 h	0.640
5 h	0.561
6 h	0.500

3.5 h = 0.707 x 0.944 = 0.6674

100 mCi will become 66.74 mCi in 3.5 h

(3)Example dose calculation in different cases

$A=A_0$ x decay factor

case 1:

at 8 am dose=20 mCi

at 9 am dose = 20 x 0.891 = 17.82

at 11:45 dose = 20 x 0.707 x 0.971 = 13.73

Case 2:

a hospital wants a dose of 20 mCi at 10:30 am

at 10 am the dose should be 20/0.944 = 21.18

at 9:30 the dose = 20/0.891 = 22.45

at 8:15 the dose = 20/0.794/0.972 =25.91

(4) At 8 am you elute the a generator, the total radioactivity in the vial =1200 mCi, you draw out 1 mL and measured the radioactivity = 120 mCi,

you are to label Tc-99m MDP and the order is

9:00 2 dose of 15 mCi

10:00 2 dose of 15 mCi

11:00 2 dose of 15 mCi

12:00 2 dose of 15 mCi, how much Tc-99m do you need?

at 8:00 am the concentration of Tc-99m is 120mCi/mL

the doses at 9:00 would require 2 x 15/0.891= 34 mCi at 8:00

the doses at 10:00 would require 2 x 15/0.791 = 38 mCi at 8:00

the doses at 11:00 would require 2 x 15/0.707 = 43 mCi at 8:00

the doses at 12:00 would require 2 x 15/0.64 = 47 mCi at 8:00

In theory the total radioactivity required at 8:00 = 34+38+43+47 = 162 mCi

the volume of Tc-99m required = 162/120 = 1.4 mL

add 1 extra dose and 20 % = (34+38+43+47+47) x 1.2 = 251 mCi

the volume require of Tc-99m required = 251/120 = 2.1 mL

Do not exceed the maximum amount of Tc-99m recommended by manufacturer !

(5) At 8:00 am you make a vial of Tc-99m MDP

you add 2 mL of TcO4 and 2 mL of normal saline

The final radioactivity of the vial is 120 mCi

now is 10:30, you need to draw a dose of Tc-99m MDP of 15 mCi, what would be the volume to be drawn?

The concentration at 8:00 am = $\frac{120 \text{ mCi}}{2+2 \text{ mL}}$ = 30 mCi/mL

at 10:30 the decay factor = 0.794 x 0.944 = 0.7495

the concentration of Tc-99m MDP at this time =

30 x 0.7495 = 22.5 mCi/mL

The volume to be drawn = $\frac{15 \text{ mCi}}{22.5 \text{ mCi/mL}}$ = 0.67 mL

(6) Calculation of half life using decay equation

Decay equation $A = A_0 e^{-\lambda t}$

A= final radioactivity

A_0 = initial radioactivity

λ= decay constant (0.693/half life)

t=time elapsed

if the radioactivity at the beginning is 10 mCi

at 2 hour later, the radioactivity is 7.9 mCi

then $7.94 = 10e^{-(0.693/\text{half-life})(2)}$

$2.0712 = 2.3026-(0.693/\text{half-life})(2)$

$-0.2314 = -(0.693/\text{half-life})(2)$

-0.1157 = -0.693/half life

half life = 5.99 h

(7) FDG dose calculation

Trainer can ask the trainee to work out the decay factor of FDG

$A=A_0$ x decay factor

Case 1:

at 8 am dose=100 mCi

at 9 am dose =?

at 11:45 dose =?

Case 2:

a hospital wants a 100mCi of FDG at t 10:30 am

at 10 am the dose should be =?

at 9:30 the dose =?

at 8:15 the dose =?

3.12. Radioactive packages

3.12.1. Scope

To supply information about safe receipt, handling and dispatching of radioactive packages.

3.12.2. Learning objectives

After this lecture the trainee should know what kinds of written documents and labels he/she should expect to receive with a radioactive package, what kinds of measurements and precautions he should take before/after opening the package and the registries he should keep for this radioactive shipment. The trainee should also know the need for regulatory practices to transport radioactive material.

3.12.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Types and categories of radioactive packages	Type A, Type B and Categories I,II,III Category White I Surface: 0.5 mrem/h

	Transport Index: None Category Yellow II Surface: 50 mrem/h Transport Index: 1 Category Yellow III Surface: 200 mrem/h Transport Index: 10 Shipping Packages Definition of Transport Index Receiving radioactive shipments
A) Before opening the package	Visual examination External measurement at 1m and at the surface Acceptable limits for the surface and 1m measurements Wipe test within three hours of receipt Wiping the external surface of the package Measuring the radioactivity of the wipe in a well scintillation counter * Acceptable limit of wipe counts according to NRC * What happens if limit is exceeded? * Log keeping
B) After opening the package	o Checking for leaks o Monitoring the package material o Removing radiation signs and symbols from package material before discarding o Check the label for Identity

	Radioactivity Calibration date Volume • Expiry date
Check the certificate for quality control results	Keeping o Receipt log o Inventory Storage o Monitoring storage conditions Keeping in a secure place Radiation safety considerations Temperature, humidity and light Despatching radioactive Packages Shipping license for the radioactive material Copy of the license from the receiving institution Bill of lading Radioactive labels for appropriate category UN Codes Radiation exposure at 1 meter and surface Wipe test Insert information on labels and bills Record on shipping log

3.13. Radioactive waste related to RP and safe practices

3.13.1. Scope

To teach the essential and safe practices of radioactive waste management in hospital radiopharmacy.

3.13.2. Learning objectives

After this lecture the trainee should know that radioactive waste should be handled differently from regular waste. He/she should know that radioactive waste from different half life radionuclides should be separately collected. How to operate efficiently to minimise radioactive waste from the radiopharmacy.

3.13.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction	Classification of radioactive waste according to half life • Lead lined waste storage boxes of different size for different purposes • Radioactive waste storage area • Labels on radioactive waste bags • What are the conditions of discarding a radioactive waste as a regular or (medical waste)

Model lecture 6- 'Radioactive waste' is on CD at the back this trainer's manual.

3.14. Safe handling of radioiodine, fume hoods and safety cabinets

3.14.1. Objective

To explain the internal and external radiation hazards of radioiodine (I-131) and strategies of safe handling. To instruct about the 131I administration systems and how to manage radioiodine contamination.

3.14.2. Learning objectives

The trainee must have the knowledge about the radioiodine hazards and how to protect themselves from the external and internal radiation hazards of I-131. They must know safe practices including the use of radioisotopes fume hoods with suitable types of filters. They must also know how to dispense and transport radioiodine internally (within the hospital) and what is the patient information needed. They must be familiar with the management of contamination.

3.14.3. Subject headings and key subject areas

Subject headings	**Key areas**
	• Iodine-131 Physical Data • External Radiation Hazard I-131

Introduction Radioiodine Hazards	• Internal Radiation Hazards • Recommendations for radioiodine users
Radioisotope fume hood	Charcoal filter or activated carbon filter • The TEDA (Tri-ethylene diamine) impregnated activated charcoal • Fume hood testing and maintenance • Equipment use in the fume hoods.
Practical Advices	Administration of I-131 Capsule • Administration of I-131 Solution: Closed system Dispense and Internal transport • Patient information needed
pillage	Causes of spillage • Decontamination kit • Management of Contamination Nature

Model lecture 7- 'Radioiodine' is on CD at the back this trainer's manual.

3.15. Practice safe radioiodine handling and dispensing

3.15.1.1. Objective

To show the trainees the whole circuit of radioiodine in the radiopharmacy, since the receipt to dispense. To instruct the trainees in the control and maintenance of the fume hoods.

3.15.1.2. Materials

- 37MBq (1 mCi) Iodine-131
- Lead shielding
- Dose calibrator
- Radioisotope fume hood
- Syringes and glasses
- I-131Capsule (if available)
- I-131Solution
- Administration systems: Closed system (if available)
- Decontamination kit (if available)

3.15.1.3. Steps

1. The trainers will show the trainees the correct circuit for radioiodine handling and dispensing (reception, inspection, measurement, calibration and dispensing) and how to record the data.
2. Trainers must demonstrate how to control, check, monitor and do the maintenance of the fume hoods (use and filters).
3. Interactive session: Meanwhile the demonstration goes through; the trainers will simulate situations and asking questions to the trainees in order to check the assimilation of some of the learned concepts: how to protect themselves from the external and internal radiation hazards of I-131, recommendations for its use, administration systems and how to manage radioiodine contamination. (make some questions)
   - Why do you must avoid direct contact with unshielded radioiodine?
   - Why do need lead to shield containers having radioiodine?
   - Why do you try to minimize the time near radioiodine sources?
   - What do you do with radioiodine waste?
   - Do you need to monitor the area after work? With what equipment?
   - Is radioiodine pH an important parameter to be checked?
   - At the reception of the material, what is important to check?
   - Where is the correct place to work with radioiodine (opening vials, dispensing, etc.)?.
   - What kind of maintenance must you do to the fume hoods?
   - How do you proceed in case of radioiodine spillage?
   - What kind of personal cares must you follow for working with radioiodine?

3.15.1.4. Results

3.15.1.5. Discussion

At the end of the practical, answers are put in common. Where there are some discrepancies in the answers, discussion will take place.

3.15.1.6. Conclusion

Clear idea on how to manage ^{131}I.

4. OPERATION, STAFFING AND DESIGN OF FACILITIES

4.1. Radiopharmacy operations

4.1.1. Scope

To give an overview of conditions of good practice in hospital radiopharmacy.

4.1.2. Learning objectives

After this lecture the trainee should be able to understand that good practices pertaining to medicine hold for radiopharmaceuticals in addition of radiation safety. Should also be able to differentiate between manufacturing and compounding and understand IAEA operational standards. He/she should know that good practice is necessary in all operations performed in hospital radiopharmacy from the starting materials to the point of final dispensing with of assurance of product safety, quality and purity.

4.1.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• Overview of IAEA operational guidance on hospital radiopharmacy
Essentials	Operation level 1a -Ready to use approved products. Operation level 1b -Dispensing Radioiodine Operation level 2a -Approved generators and kits Operation level 2b -Radiolabelled white blood cells Operation level 3a -Compounding and 'in-house' Operation level 3b -Compounding therapeutic products Operation level 3c –Compounding PET and long lived generator
Practice notes	• training, • facilities, • equipment, • operations and • quality systems for application at clinical practice level.
Staff training and quality systems	• Staff training and quality systems at each operational level.
Radiopharmacy audits	• Audit at operational level one and two.

Model lecture 8- 'operational guide to hospital radiopharmacy' is on CD at the back this trainer's manual.

4.2. Good radiopharmacy practice in hospital radiopharmacies

4.2.1. Scope

To give an overview of conditions of good practice in hospital radiopharmacy.

4.2.2. Learning Objectives

After this lecture the trainee should be able to understand that good practices pertaining to medicine hold for radiopharmaceuticals in addition of radiation safety. The trainee should also be able to differentiate between manufacturing and compounding. He/she should know that good practice is necessary in all operations performed in hospital radiopharmacy from the starting materials to the point of final dispensing.(to ensure product safety, quality and purity.)

4.2.3. Subject headings and key subject areas

Subject headings	**Key areas**
Basic operations performed in hospital radiopharmacy	• Procurement • Compounding • Quality assurance • Dispensing • Documentation • Research and development • Training and consultation
Personnel	
Premises and equipment	
Self inspection	

Model lecture 9- 'QA in radiopharmacy' is on CD at the back this trainer's manual.

4.3. Design of facilities

4.3.1. Scope

To understand operations and design elements in an ideal radiopharmacy.

4.3.2. Learning objectives

After this lecture the trainee should know the essential steps in the design of an ideal laboratory. In addition, they should be able to assess and audit radiopharmacy laboratory with the standards together with tools given in this lecture. He should be able to define various operations that can be carried out in a radiopharmacy laboratory and the needs.

4.3.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction Ideal design of hot lab	Consider: Brick and mortar Security Radiation safety Pharmaceutical considerations Key operations performed Work flow Air flow Equipment Transportation
Basic operations carried out in a hospital radiopharmacy	• Procurement • Ordering • Receiving • Storage • Record keeping • Compounding • Radiopharmaceuticals used in hospital radiopharmacies: • Ready- to - use radiopharmaceuticals • Radiopharmaceuticals prepared from radionuclide generators and kits • Autologous labelled products • Quality assurance control of RP • Physical • Radionuclidic

	• Radiochemical • Chemical • Biological • Instruments • Dose calibrator • LAF • Area monitors • Centrifuge • Well counter • Balance • PH meter • Water bath • Radiochromatogram scanner • Dispensing • Drawing of patient doses based on • Age • Weight • Indication • Patient history and characteristics • Documentation • Orders • Deliveries • Inventory • Standard Operation Procedures • Elution profile of generators • Preparation

	• Patient doses • Quality assurance • Radiation safety registries • Waste • Radiation safety considerations • Work flow • Air flow • Equipment

Model lecture 10 - 'Radiopharmacy design' is on CD at the back this trainer's manual.

4.4. Staff training and competence in hospital radiopharmacy

4.4.1. Scope.

To teach the trainee of suitable training methods and how to provide systematic and standardized training to staff in radiopharmacy

4.4.2. Learning objective

At the end of this lecture, the trainees should know what is the most important mission of a radiopharmacy, what training should a new staff in a hospital radiopharmacy should receive and how to access the competency of a staff in a hospital radiopharmacy

4.4.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• Nature of the works in hospital radiopharmacy o Predominately IV injections o Involve radioactivity • Patients diagnosis and management may depends on the quality of radiopharmaceuticals
Most important mission of a hospital radiopharmacy	• Provide o the correct dose o at the correct time o to the correct patient

	• ensure the radiopharmaceutical is safe (from medical and radiation safety point of view)
Areas of training for a new staff in hospital radiopharmacy	• Aseptic technique • Quality assurance • Characteristics of different kinds of radiation • Radiation safety • Basic nuclear medicine • Mathematics in hospital radiopharmacy • Tc-99m generators • Labelling and preparation of radiopharmaceuticals • Quality control of radiopharmaceuticals • Radiopharmaceuticals used in different nuclear medicine procedures • Pharmaceuticals used in nuclear medicine • Side effects, precautions, and contraindication of radiopharmaceuticals • Paediatric doses • Documentations
Assessment of staff	• Most important- Aseptic technique • Pass media fill simulation test • Radiation safety • Competency in mathematics in hospital radiopharmacy • Preparation and dispensing of doses without spills • Able to perform quality control tests • Familiar with documentation.

4.4.4. Staff training - Interactive practical

4.4.4.1. Objective

To stimulate the trainee to consider what kind of training they can give to their new staff and how they would consider a certain staff is competent in their works

Discuss with the trainee:

- What are the most important skills they would require from a new staff and why?
- What are the training they would give to their new staff?
- If a certain staff is not competence in their job, what would they do?
- Trainer and trainee share their experiences in access competency of their staff.

4.5. Standard operating procedures (SOP)

4.5.1. Scope

This lecture is to provide information on creating and management of standard operating procedures.

4.5.2. Learning objectives

At the end of this lecture, the trainee should know about writing of SOP, different sections to be included in an SOP, control of SOP, revision of SOP, and management of expired SOP.

4.5.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction	• What is an SOP • Why is SOP important • Rationale of having SOP • How should SOP be used
Different sections of an SOP	• Identification # • version # • Revision history • Name of author and the date the SOP is written • Name of person who review and approve the SOP • Date of approval and effective date

	• Date of next revision • Introduction-why this SOP is written • Objective and scope- this SOP is written for what procedure • Who should follow this SOP • Procedures- the actual steps of carrying out the task • Results (if application) • Interpretation of the results (if applicable)-gives instructions on how the results should be interpreted • References (if applicable)-provides a list of the articles or books based on which the sections of 'procedures' and 'interpretation of results ' are formulated • Affiliated documents –this allows the staff to cross reference to other SOP when necessary
Master copy and photocopied copy	• Definition of master copy • Master copy not to be used routinely, photocopies of the master copy should be used • Photocopying the master copy – the copies should be clearly marked photocopies, there should be a record of how many photocopies have been made
Distribution of SOP	• SOP normally distributed to staff involved • If not distributed, it should be located in a common but secured place where staff can have access to it • Only the controlled photocopy are to be distributed or located in common but secured area • Master copy are to be kept in department office
SOP as controlled documents	• SOP is internal document and should not be circulated outside of the radiopharmacy • Master list of SOP – a list of all SOP with correct version #, creation date and expiry date • Record of SOP distribution – a record to show

	which SOP is distributed to which staff or where the SOP is located (if the SOP is not distributed to individual staff) • Staff responsibility of the security of SOP
Revision of SOP	• Change process- who does the change, who does the review . • Update of version # • Update of revision history • Approval and effective date • Update of the master list of SOP • Distribution of SOP with newer version- update the distribution list, take back the replaced version
Storage of replaced version	• replaced version should be clearly marked and keep in secure place/locker/drawer etc.

Model SOP 11 - 'SOP-Eluation' is on CD at the back this trainer's manual.

Model lecture 12- 'Chromatography' is on CD at the back this trainer's manual.

Model lecture 13- 'Quality Control of Radiopharmaceutical kits' is on CD at the back this trainer's manual.

Model SOP 14- 'Waste' is on CD at the back this trainer's manual.

4.5.4. Computer practice creating working SOPs

4.5.4.1. Objective

To create and to enact working SOPs.

4.5.4.2. Materials

- Computers
- Pen
- Paper
- Bibliography

4.5.4.3. Steps

1. Trainees will separate in groups (2-3 persons per group)
2. The trainers will underline the essentials for creating a SOP.
3. Each group must create the SOP that the trainer has assigned.

4.5.4.4. Suggested SOPs

- Receipt and storage of radioactive materials;
- Preparation and Calibration of doses;
- Use and maintenance of measurement equipments;
- Quality control of measurement equipments;
- Quality control for 99Mo/99mTc generators;
- Labeling of RP;
- Labeling blood cells;
- Quality control of RP;
- Radioiodine handling and dispensing;
- Use and maintenance of fume hoods;
- Use and maintenance of isolators;
- Aseptic Practices;
- Environmental monitoring.

4.5.4.5. Results

Examine written SOPs.

4.5.4.6. Discussion

At the end of the practical, each group share with the others, troubleshooting in the documents creation.

4.5.4.7. Conclusion

Trainee feedback and summary of session. Trainee should be able to create their own working SOPs for their institutions.

4.6. Environmental check list

Monitoring	**Daily**	**Weekly**	**Monthly**	**Annually**
Daily monitoring of the laboratory surfaces.	X			
Calibration of monitors (Ideally 3monthly)				X

Room differentials	X			
Isolator/VLFC manufacture check				X
Isolator/VLFC operational check (airflow, pressure between filter)	X			
Calibrator check on all used isotopes	X			
Full calibrator check				X
Generator Mo-breakthrough	X			
Generator Al-check		X		
Generator Radiochemical check	X	X		
Generator pH		X		
Generator performance check		X		
Operator broth run initially 3 clear runs than every 3 months			3monthly	
Agar plates during dispensing	X			
Finger dabs	X			
Agar plates in working spaces		X		
Contact plates		X		
Sterility sample of generator start and end sample		X		
Sterility sample from one kits each day	X			
Clearing log	X			
Cleaning of surround areas		X		
High level clean			X	
Refrigerator check	X			

4.7. Information technology and database in hospital radiopharmacy

4.7.1. Scope

Documentation system - To teach the trainees importance of keeping various records, what record to be kept and how to use simple computer programme for record keeping

4.7.2. Learning objective

At the end of this lecture, the trainees should know the objectives of record keeping, the importance of traceability in record keeping, and what kind of records to be kept.

An example of using Word, Excel and Access for record keeping will be shown to the trainee so that they can write their records with minimal computer skills.

The trainee should also know about real-time and duration of records and backing up of records

4.7.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• Why do we need to keep record • What would happen without records
Main objectives of record keeping	• Future reference • Learning • Prevention of mistakes
Most important element in record keeping	• Traceability o Lot # o Which raw material, from which company, when received, how it is stored o How the radiopharmaceutical is made o When it is made o Who made it o Who dispense it o Who perform the QC o others • There should be a mean to cross-reference all documents

What records to be kept	Cold kit inventory Tc-99m generator and radiopharmaceutical receiving record Tc-99m elution record Radiopharmaceutical preparation record Radiopharmaceutical quality control record Radiopharmaceutical dispensing record Dose calibrator daily check record MCA calibration record (if any) Radiopharmacy daily monitoring record Radioactive material disposal record radiopharmaceutical Sterility and endotoxin test record settle plate and contact plate monitoring record

Means of record keeping	• By paper • Digital o Commercially available computer programme ▪ Advantage ▪ Disadvantage o In-house programme ▪ Excel and Access ▪ Advantage ▪ Disadvantage ▪ Example

4.8. Information technology and database in hospital radiopharmacy - Interactive practical

4.8.1.1. Objective

To let the trainee understand how to write records with traceability and understand that digital records can be created with simple computer skills

4.8.1.2. Discuss with the trainee

(1) What do you see the most important element of record keeping

(2) How would you design a record to keep track of the doses prepared (or doses received from centralized pharmacy) and dose dispensed? i.e. what are the parameters to be recorded in order to establish traceability

(3) Trainer prepare a record and discuss with the trainee if the record is good in term of traceability

Trainer may use the following as an example:

Dose Calibrator QA Test

(ver 1, 19 May 2005)

Department of Nuclear Medicine & PET

	STATION 1 S/N 1073052						STATION 2 S/N 155211						
	Cs-137			Co-57			Cs-137			Co-57			
Date	theorectical value/ uCi	Measured value/ uCi	% error	theorectical value/ mCi	Measured value/ mCi	% error	theorectical value/ uCi	Measured value/ uCi	% error	theorectical value/ mCi	Measured value/ mCi	% error	Performed by
09-Jul-07	220.9997	215.000	*-2.71*	1.4688	1.458	*-0.74*	220.9997	217.000	*-1.81*	1.4688	1.460	*-0.60*	CWW
10-Jul-07	220.9857	214.000	*-3.16*	1.4651	1.458	*-0.48*	220.9857	217.000	*-1.80*	1.4651	1.460	*-0.35*	CWW
11-Jul-07	220.9717	214.000	*-3.16*	1.4614	1.440	*-1.47*	220.9717	216.000	*-2.25*	1.4614	1.450	*-0.78*	LSL
12-Jul-07	220.9577	215.000	*-2.70*	1.4577	1.453	*-0.33*	220.9577	215.000	*-2.70*	1.4577	1.450	*-0.53*	CWW
13-Jul-07	220.9438	213.000	*-3.60*	1.4541	1.449	*-0.35*	220.9438	217.000	*-1.78*	1.4541	1.450	*-0.28*	CWW

Radiopharmaceutical Preparation Record

(ver 1, 19 May 2005)

Department of Nuclear Medicine,

Date 13-Jul-07

1	2		Rx kit used					SKH	Rx					Tc-99m			Normal Saline				Prepared
scan	dose ordered adult	pediatric & age	Name	source	lot #	Exp	Physical check of kit	lot #	Tc-99m activity	volume	time prepare	time exp	QC	Vol used	Tc Lot#	Generator Lot#	Vol used	Lot #	source	exp	by
Bone	15		MDP	Amersham	666	16Sep08	no abnormality	md130707a	358	6	709	1309	92	6	tc130707a tc130707d	5342a 5334ab	0	7103E1	BBraun	Aug 10	CWW
MIBI Stress	8		Myoview	Amersham	1462	13Sep07	no abnormality	my130707a	208	6	717	1517	94.7	5.3	tc130707b tc130707d	5342c 4334ab	0.7	7103E1	BBraun	Aug 10	CWW
MIBI Rest (pm)	6		same	as	above			my130707c	255	6	1222	2022	93.2	3.4	tc130707c tc130707f	5342d 5342b	2.6	7103E1	BBraun	Aug 10	CWW
Gastric Emptying	1		Hepatate	Amersham	208	27Dec07	no abnormality	he130707a	13	4	806	1406	99.5	0.9	tc130707e	5334cd	3.1	7103E1	BBraun	Aug 10	LSZ
Lung Ventilation	2		DTPA	Mallinckrodt	263761	19Sep07	no abnormality	dt130707a	150.1	8	1228	1828	98.7	3.2	tc130707g	5342cd	4.8	7103E1	BBraun	Aug 10	CWW
Lung Perfusion	2		MAA	Mallinckrodt	269430	14Jun08	no abnormality	ma130707a	41.7	4	1230	1830	99.8	0.9	tc130707g	5342cd	3.1	7103E1	BBraun	Aug 10	CWW
MIBI Thyroid	1		Myoview	Amersham	1462	13Sep07	no abnormality	my130707a	208	6	717	1517	94.7	5.3	tc130707b tc130707d	5342c 4334ab	0.7	7103E1	BBraun	Aug 10	CWW
Parathyroid	1		Cardolite	Dupont	3913	1Jun08	no abnormality	cd130707a	72.9	2	726	1526	97.2	0.8	tc130707c	5342d	1.2	7103E1	BBraun	Aug 10	CWW

Department of Nuclear Medicine and PET

RADIOPHARMACEUTICAL QC SHEET

13-Jul-07

Name	Lot #	Solvent 1			Solvent 2			Final % RCP	Acceptable Limit	Solvent 1	Solvent 2	Done By
		origin cts	front cts	%	origin cts	front cts	%					
Medronate	md130707a	157653	27	0.02	4740	54272	8.03	92.0	*90.00*	Acetone	0.9%Nacl	LSL
Medronate	md130707b	80778	30	0.04	1353	93056	1.43	98.5	*90.00*	Acetone	0.9%Nacl	LSL
Myoview	my130707a			#DIV/0!	1148	20456	5.31	94.7	*90.00*		ethyl acetate	LSL
Myoview	my130707b			#DIV/0!	2526	31386	7.45	92.6	*90.00*		ethyl acetate	LSL
Myoview	my130707c			#DIV/0!	616	8438	6.80	93.2	*90.00*		ethyl acetate	CWW
Myoview	my130707d			#DIV/0!	1412	19488	6.76	93.2	*90.00*		ethyl acetate	LSZ
Cardiolite	cd130707a			#DIV/0!	512	17477	2.85	97.2	*90.00*		ethyl acetate	LSL
DMSA	dm130707a	53152	1550	2.83			#DIV/0!	97.2	*85.00*	Acetone		LSL
DTPA	dt130707a	36597	27	0.07	398	31306	1.26	98.7	*90.00*	Acetone	0.9%Nacl	CWW
MAA	ma130707a	22496	47	0.21			#DIV/0!	99.8	*90.00*	Acetone		CWW
Sulfur Colloid	sc130707a	11997	185	1.52			#DIV/0!	98.5	*90.00*	Acetone		LSL

Room Monitoring Record (ver 1, 19 May 2005)

Radiopharmacy lab, Department of Nuclear Medicine & PET,

Date		Back ground	GM Counter	Water bath	Sharp Bin	drawing station 1	drawing station 2	Generato r	waste Box	FDG	QC station	bench	performed by
09-Jul-07	*mR/hr (am)*	0.1	9.0	0.1	0.1	0.1	0.1	0.2	0.3	0.1	0.1	0.1	LSL
	mR/hr(pm)	0.1	9.0	0.1	0.2	0.1	0.3	0.3	0.4	0.2	0.1	0.1	LSZ
10-Jul-07	*mR/hr (am)*	0.1	9.0	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.1	LSL
	mR/hr(pm)	0.1	9.0	0.1	0.1	0.1	0.1	0.1	0.3	0.1	0.1	0.1	LSZ
11-Jul-07	*mR/hr (am)*	0.1	9.0	0.1	0.1	0.1	0.1	0.1	0.3	0.1	0.1	0.1	QLH
	mR/hr(pm)	0.1	9.0	0.1	0.2	0.1	0.2	0.2	0.3	0.1	0.1	0.1	LSL
12-Jul-07	*mR/hr (am)*	0.1	9.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	LSZ
	mR/hr(pm)	0.1	9.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	LSZ
13-Jul-07	*mR/hr (am)*	0.1	9.0	0.1	0.1	0.1	0.1	0.1	0.3.	0.1	0.1	0.1	LSZ
	mR/hr(pm)	0.1	9.0	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.1	LSZ

4.9. Isolator technology

4.9.1. Scope

To give a general idea of isolator technology and essentials points of working with them

4.9.2. Learning objectives

After this lecture the trainee should know the differences between fume hoods, laminar flow cabinets and glove boxes and he/she should also acquire knowledge proper way of working with these equipment.

4.9.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction	Overview • Horizontal LAF o Drawing the air through a pre-filter o Pressurizing the air o Blowing the air across the work surface towards the operator o Good for product protection • Vertical LAF o Drawing air through a pre-filter o Pressurizing the air o Blowing the air down from the top of the workstation onto the work surface o Good for radiopharmacy and advantages and disadvantages of isolator technologies. Types of isolators 1. Laminar Flow Cabinets (LAF) 2. Horizontal flow 3. Vertical flow

	4. Converging flow 5. Containment cabinets 6. Glove boxes
Operations	• Daily leak testing • Loading isolators and transfers in and out • Cleaning
Maintenance	• Daily • Weekly • Quarterly

Model lecture 14- 'Isolator technology' is on CD at the back this trainer's manual.

4.10. Centralized radiopharmacy

4.10.1. Scope

To introduce to the trainees the concept and operation of centralized radiopharmacy

4.10.2. Learning objective

At the end of the lecture, the trainees should know the concept of centralized radiopharmacy, the difference between hospital radiopharmacy and centralized radiopharmacy, advantage of and disadvantage of centralized radiopharmacy

4.10.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• History of centralized radiopharmacy • Current status of centralized radiopharmacy • Concept of centralized radiopharmacy
Operation of radiopharmacy	• Receiving of others from hospitals • Preparation and quality control of doses • Delivery of doses • Consultation to hospitals o Radiopharmaceutical related o Radiation safety related • Radioactive waste management

Difference between hospital radiopharmacy and centralized radiopharmacy	• Staff- more strict requirements and training in centralized radiopharmacy • # of doses prepared • Delivery of doses • Quality assurance program- much more complicated, in some cases, GMP is required • Licensing- a centralized pharmacy is a registered a pharmacy or in some countries as drug manufacturers • Regulations: subject to more strict regulations including auditing from pharmacy regulatory authorities, radiation safety authorities, drug manufacturer regulatory authorities
Advantage of a centralized radiopharmacy	Lower cost – especially for expensive radiopharmaceuticals Hospitals who do not have enough or adequate staff can still operate Better equipments and facilities, more strict regulations Radiopharmaceuticals requiring special skills to prepare can also be available to hospital radio-pharmacies operating at level 1 and level 2A Convenient to hospitals Consultation to level1 and level 2 A hospital radiopharmacies
Disadvantage of a centralized radiopharmacy	For staff – less patient contact Higher risk in the case of any faulty products as doses are provided to many hospitals

Model lecture 15- ‘Centralized radiopharmacy’ is on CD at the back this trainer’s manual.

5. RADIOPHARMACEUTICALS AND QUALITY CONTROL

5.1. Quality control of radiopharmaceuticals

5.1.1. Scope

To provide trainees with essentials on quality assurance system and various quality control tests in hospital radiopharmacy

5.1.2. Learning objective

At the end of this lecture, the trainees are expected to understand the importance of a quality management and assurance systems, the difference components of a quality assurance system and how to develop a quality assurance system.

The trainees should also know the importance of quality control tests in hospital radiopharmacy, how and when to perform various quality control tests in hospital radiopharmacy, recording, trouble-shooting, decisions related to test results and follow-up (trend analysis)as well as follow-up and outcome of abnormal/defective radiopharmaceuticals.

5.1.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• Why quality assurance • Why quality control • How dos quality assurance and quality control affect patient safety and scan quality
Definition of quality assurance	• A system with all the components built in to ensure o safety o efficacy o purity
Difference between quality assurance and quality control	• Quality assurance is not the same as quality control • Quality control is trying to detect any faults in the final product by random sampling • Quality assurance is a system with safety control measures built in
Various components of quality assurance system in hospital radiopharmacy	• A quality assurance system should include o Staff- enough number of staff and adequate training of each staff

	○ Facility-good planning and monitoring ○ Equipments –adequate equipment, proper calibration and maintenance ○ Documentation- proper SOP and records with good tracking ability ○ Quality control – proper quality controls tests to be carried out
Implementation of a quality assurance system	• Long process • Quality assurance is a culture • Requires efforts and dedications
Various quality control tests	• Radionuclidic purity ○ Definition ○ What is the common radionuclidic impurity for Tc-99m radiopharmceuticals and its source ○ methods to test for radionuclidic purity ○ The Mo-99 breakthrough canister ▪ Multichannel analyzer ▪ When to test for radionuclidic purity ○ Acceptance limit ○ What to do if a product fails radionuclic purity ○ Radionuclidic purity increases with time • Radiochemical purity ○ Definition ○ Impurities inside a radiopharmaceutical preparation ○ method to test for radiochemical purity ○ ITLC technique-mobile phase, stationary phase ○ Pitfalls in running ITLC

	○ When to test for radiochemical purity ○ Calculations of radiochemical impurities ○ Commonly used stationary phase and mobile phase (ITLC-SG, normal saline, acetone) ○ Acceptance limit ○ What to do if a product fails radiochemical purity • Chemical purity ○ Definition ○ What is the most common chemical impurity and its source ○ Methods to test for chemical purity (Al+++ test kit) ○ When to test for chemical purity ○ Acceptance limit ○ What to do if a product fails chemical purity • pH ○ methods to test for pH ▪ pH meter ✓ daily calibration of pH meter ▪ pH paper ✓ validation of pH paper • particle size ○ Radiopharmaceuticals that requires particle size measurement ○ Method of measuring particle size ○ Use of hemocytometer ○ Acceptance limit • sterility screening ○ importance of sterility screening ○ screening for sterility after final labelling ○ how to perform sterility test ○ culture media –SCDM and FTM

	○ culture time and temperature for aerobic and anaerobic bacteria ○ validation of sterility test with known strains of bacteria • endotoxin screening ○ What is endotoxin ○ importance of endotoxin test ○ when to perform endotoxin test ○ how to perform endotoxin test ○ LAL test- Turbimetic and Chemogenic LAL test
Shelf life and stability of radiopharmaceutical	• factors affecting: • time – Mo-99 breakthrough- radionuclidic impurity increases with time • Moisture - increase rate of breakdown • Air –Increase rate of breakdown • pH
Follow up of abnormal outcome of radiopharmaceutical	• Abnormal uptake in thyroid, stomach, liver • Medical point of view – Abnormal uptake in non-target organs/tissue - poor scan quality, wrong diagnosis, • improper pH - severe pain during injection • non-sterile product can be life threatening • pyogen-fever • Radiation safety point of view- Abnormal uptake in non-target/tissues leads to unnecessary exposure to patients • Recording –what drug, what procedure, when happened, investigations carried out, results of the investigation, report to proper regulatory uthourities (if required)

Model lecture 16 - ‘QC in radiopharmacy’ is on CD at the back this trainer’s manual.

5.1.4. Quality Control- Practical

5.1.4.1. Objective

To let the trainees acquire experiences in performing radiochemical purity test of radiopharmaceuticals

5.1.4.2. Materials required

- Tc-99m DTPA or Tc-99m MDP
- Two ITLC-SG paper (1cm x 8 cm)
- Two Small 10mL or 20 mL vials with cover
- Normal saline
- acetone
- pencil
- Scissor
- Counting tubes
- 1mL with 27 G needle or TB syringe
- forceps
- Gamma counter (if not available, can be replaced by thyroid probe or gamma camera).

5.1.4.3. Steps

1. On the ITLC-paper, very gently draw a line at about 1 cm from one end, mark it as origin, another line at 1 cm from the other end, mark it as solvent front, and a line in the middle

2. Add normal saline to one of the vials (to about 0.8 cm from the bottom)and acetone to another one. Make sure to put the cover on.

3. Draw no more than 0.1 mL of the Tc-99m MDP(or Tc-99m DTPA) provided using then 1mL syringe or the TB syringe

4. Apply a small drop at the origin of both ITLC-SG paper

5. Allow the spot to dry in air for about 2 to 3 min.

6. Place one of the ITLC paper into the normal saline vial and the other into the acetone vial. Make sure that the radiopharmaceutical spots are above the solvent level. Close the cap .

7. Allow the solvent to migrate up the ITLC-paper. When the solvent has reached the ‘solvent front line’, remove the ITLC-paper using the forceps.

8. Allow the ITLC paper to dry in air for about 2 to 3 min

9. Cut the ITLC paper along the middle line. Place each section into separate counting tubes

10. Place the counting tube into the gamma counter or thyroid probe for counting at Tc-99m window (140KeV $\pm$ 20%)

11. If gamma counter or thyroid probe are not available, it is possible to use gamma camera for counting

12. Turn the camera so that the collimator is facing upward, place a pierce absorbent paper on it, then place the ITLCSG segments on it. Acquire 1 min counts at 140KeV $\pm$ 20% window.

13. Draw a region of interest around the radioactive spots and record the counts.

14. Draw a region of interest of the same pixel size at a region away from the radioactive spots and record the counts as ‘background’

from the acetone strip:

$$\% \text{ of free Tc-99m} = \frac{\text{radioactivity of the upper half} \times 100\%}{\text{radioactivity of the upper half + radioactivity of the lower half}}$$

from the normal saline strip

$$\% \text{ of RH-Tc-99m} = \frac{\text{radioactivity of the lower half} \times 100\%}{\text{radioactivity of the upper half + radioactivity of the lower half}}$$

% of the radiopharmaceutical = 100% - % of free Tc-99m - % of RH-Tc-99m

5.1.4.4. Results and calculation

Counts of Solvent front section of normal saline strip=	Background counts =	Net counts=
Counts of origin section of normal saline strip=	Background counts=	Net counts=
Counts of Solvent front section of acetone strip=	Background counts=	Net counts=
Counts of origin section of normal saline strip=	Background counts=	Net counts=

from the acetone strip:

$$\% \text{ of free Tc-99m} = \frac{\text{radioactivity of the upper half} \times 100\%}{\text{radioactivity of the upper half + radioactivity of the lower half}}$$

$$= \_\_\_\_\_$$

$$= \_\_\_\_\_\%$$

from the normal saline strip

$$\% \text{ of RH-Tc-99m} = \frac{\text{radioactivity of the lower half} \times 100\%}{\text{radioactivity of the upper half + radioactivity of the lower half}}$$

$$= \_\_\_\_\_$$

$$= \_\_\_\_\_\%$$

Radiochemical = 100% - % of free Tc-99m - % of RH-Tc-99m

= 100% -_____% -_____%

=_____%

5.1.5. Shelf life practical

5.1.5.1. Objective

To allow the trainee understand that radiochemical purity decreases during the duration of storage after labelling. Hence it is important that radiopharmaceutical should not be used after its shelf life

The experiment also allows the trainee to understand the importance of storage condition. If radiopharmaceuticals are not stored properly, their radiochemical purity can decrease quickly.

5.1.5.2. Material

- Tc-99m MDP
- Six ITLC-SG paper (1cm x 8 cm)
- Two Small 10mL or 20 mL vials with cover
- Two evaluated vial
- Normal saline
- acetone
- pencil
- Scissor
- Counting tubes
- 1 mL with 27 G needle or TB syringe
- forceps
- Gamma counter (if not available, can be replaced by thyroid probe or gamma camera)

5.1.5.3. Steps

Perform radiochemical purity test on the Tc-99m-MDP provided as described above

Divide the Tc-99m MDP into 2 portions into the 2 evacuated vial

Open the cap of one of the evacuated vial so that air can enter the vial and then close the cap, but do not remove any air

The other evacuated vial with Tc-99m MDP will remain in evacuated condition

Place both vial in proper vial shield and store at room temperature for 7 hour

Perform radiochemical purity test on both Tc-99m MDP from both vial at he end of storage

5.1.5.4. Results

Radiochemical of the Tc-99m MDP before splitting into 2 portion	
Radiochemical purity of the Tc-99m MDP stored in vial with air after 7 h	
Radiochemical purity of the TC-99m MDP stored in evacuated condition after 7 h	

5.1.5.5. Discussion and conclusion

5.2. RP Licensing systems and role of pharmacopoeia

5.2.1. Scope

To give information on regulations related to general pharmaceuticals and radiopharmaceuticals.

5.2.2. Learning objectives

After this lecture the student should be informed about various regulations related to radiopharmaceuticals in terms of related chapters in pharmacopoeias and also be aware that all people must have a way of licensing the radiopharmaceuticals to be used in their country.

5.2.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Radiopharmaceuticals as medicines	Radiopharmaceuticals are drugs in spite of the arguments about being radioactive • Short stay in body • No pharmacological effect expected • Little amount of material bound to the radionuclide • Low volume • Used at the time and place of preparation • Mostly given once to a patient

Regulations related to radiation safety	ICRP 60: Recommendations by International Commission on Radiological Protection Directive 97/43 Euratom: Patient Safety Directive 96/29 Euratom: Worker Safety
Regulation related to the pharmaceutical nature of radiopharmaceuticals	Declaration of Helsinki: Studies involving human subjects Directive 2001/83/EC: Medicinal products for human use Directive 2004/27/EC: amending 2001/83/EC Directive 2001/20/EC: Clinical trials on medicinal products for human use Directive 2005/28/EC: Good Clinical Practice Directive 2003/94/EC: Good Manufacturing Practice National regulations on medicines or specifically on radiopharmaceuticals • ICH
Pharmacopoeias	*General Chapters and Monographs on individual radiopharmaceuticals • International Pharmacopoeia (Ph.Int) • United States Pharmacopoeia (USP) • European Pharmacopoeia (EP) • National Pharmacopoeias
Good radiopharmacy guides	IAEA operational guidance of hospital radiopharmacy – safe and effective approach. Guidelines for classical and PET radiopharmaceuticals (EANM) Current Good Manufacturing Practice for Positron Emission Tomography Drugs: proposed rule (FDA)

Model lecture 17 - ‘RP licensing monographs’ is on CD at the back this trainer’s manual.

5.2.4. Practical working a RP monograph

5.2.4.1. Objective

To understand how to meet Pharmacopoeia requirements for RP at different radiopharmacy levels.

5.2.4.2. Materials

- Computers
- Pen
- Paper
- International Pharmacopoeia monographs for:
    - ^{131}I capsules
    - ^{153}Sm-EDTMP
    - ^{99m}Tc-MDP
    - ^{111}In-labelled leukocytes

Web link: http://www.who.int/medicines/publications/pharmacopoeia/radiopharm/en/index.html

5.2.4.3. Steps

1. The trainers will explain to the trainees that each RP must meet the Pharmacopoeia requirements previous to their release.
2. The trainers will ask this single question: How can you assure that your RP meets all the requirements?
3. Each trainee must answer the question for each RP considering each part of the monograph (radiochemical and radionucleidic purities, physicochemical aspects, sterility, etc.)
4. Which are the QC that are needed to be done, and which ones are taken from data sheets?
5. How do you record the results?

5.2.4.4. Results

Trainees will obtain a check list of the parameters to test for each RP as well as the ones that they must guarantee in other way.

5.2.4.5. Discussion

At the end of the practical, all the answers are share with the others, comparing the answers and evacuating doubts.

5.2.4.6. Conclusion

All the RP released must meet Pharmacopoeia or other chosen standards

5.2.5. Sterility test, pyrogen test LAL in RP results

5.2.5.1. Objective

To explain the principles of sterility in the formulation of injections and the differing role of sterility and bacterial endotoxin testing.

5.2.5.2. Learning objectives

At the end of the lecture, the trainee must understand the concept of sterility. The difference between concepts of sterility and apyrogenicity and the methods used. They must also know how to control RP sterility and apyrogenicity and when to perform each test. Refer to pharmacopoeias.

5.2.5.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Methods of Sterilization	Methods of Sterilization Autoclave (120°C at 18 psi for 30 minutes) Dry heat oven (250°C for 30 minutes) Gamma irradiation Ethylene dioxide gas (older method) (Heat sensitive supplies, disposables) Membrane filtration(Sieving, common pore size 0.22µm).
Sterility Tests for Radiopharmaceuticals	Medias for aerobic and anaerobic microorganisms Fluid thioglycolate (30 – 35°C for 7-14 days) Sterility Tests for Radiopharmaceuticals Medias for fungus and mold Soybean casein (25°C for 7-14 days)
Bacterial endotoxin testing	Apyrogenicity Pyrogens: (Filterable, soluble, heat resistant) Endotoxin

	(End-product gram negative bacteria) Apyrogenicity (methods)
	Sterilization does not destroy pyrogens • Apyrogenicity Tests Rabbits (3) 0.6°C temperature rise in any one 1.2 ° C in all three rabbits (8) Rabbits (if positive) 0.6°C rise in any three each 3.7°C rise in the sum of eight rabbits • Apyrogenicity (Tests) Limulus Amebocyte Lysate (LAL) Horse Shoe Crab LAL test • LAL Test Incubation at 37°C for 60 minutes Formation of a gel (+) • Pyrogen Reactions 30-120 minutes following the administration Fever, chills, flushes, sweating, headache, pain in joints

5.3. Procurement of radiopharmaceuticals

5.3.1. Scope

To provide an overview of procurement mechanism including regulatory framework for purchase of radiopharmaceuticals as medicines through a tender process.

5.3.2. Learning objectives

To give the trainee information about how to buy the material needed in radiopharmacy practice. The points to be considered for different type of materials like radioactive material, kits, equipment, sterile products, chemicals, gases and quality control supplies should be emphasized .

5.3.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction- Procurement	I- Ordering • Materials essential for the radiopharmacy laboratory *Radioactive material • Ready –to -use radiopharmaceuticals • Radiopharmaceuticals which needs compounding • Radionuclide generators Points to be taken into consideration when ordering radioactive material • Manufacturer or centralized radiopharmacy (Licensed?) • Activity and concentration • Calibration and expiry dates • Lead time • Special delivery and stock conditions (cold chain?) • Regulatory issues *** Nonradioactive Materials** • Kits (DTPA,MIBI ..) • Drugs (Captopril,diprydamole,bicarbonate) • Chemicals (Decontamination solutions, disinfectants..) • Tests (Sterility test media, pyrogen tests)

	• Gases (Oxygen,nitrogen..) • Chromatography supplies (Columns, strips, solvents..) • Sterile material (Syringes, needles, filters, tubes, gloves, vials, disinfectants) • Other supplies II- Receiving What kinds of checks to be made upon receipt? 1. Points to be considered for radioactive packages (Chapter….) 2. Package inserts and certificates (Sterility, analysis..) 3. Expiry dates 4. Transport conditions (Cold chain, etc.) III-Storage All material to be storaged according to the conditions given for that material in package inserts and SOPs. IV-Record keeping • Orders • Deliveries • Inventory (Stocks and consumptions) • Alert/alarm limits according to the lead times and amounts used daily, weekly, monthly and yearly • Record keeping o Centralized radiopharmacy o Cold chain.

Tender	Usually made yearly Usually made by 'Tender Committees' of hospitals. These people may not be aware of the needs of radiopharmacy practices Person in charge of radiopharmacy should define the amount and quality of material to be bought according to o Previous consumption records o Previous suppliers o List of certified suppliers At the time of tender the offers must be evaluated by someone from the radiopharmacy to get the best quality at the cheapest price by considering o Certification of the producer o License of the product o Calibration and delivery dates of radioactive material o Price per unit dose o Lead times o Ease of use

Model interactive session 18 - 'Monographs' is on CD at the back this trainer's manual.
Discuss the chapter on Radiopharmaceuticals in the Ph. Int. and the monographs.
Web link:: http://www.who.int/medicines/publications/pharmacopoeia/radiopharm/en/index.html

5.3.4. Practical – Package inserts

1. Review the package inserts for all Tc-99m radiopharmaceuticals

1.1 Make a list for each Tc-99m radiopharmaceutical indicating:

1.2 Injected dose (recommended dose)

1.3 Maximum amount of Tc-99m radioactivity to be used for reconstitution

1.4 Recommended final volume of Tc-99m for reconstitution

1.5 Expiration period after reconstruction

2. Determine the optimal radioactive concentration of the Tc-99m radiopharmaceutical (MBq/mL or mCi/mL), based on the recommended dose (MBq or mCi) and the volume to be drawn (mL)

2.1 Determine optimal (and maximum) radioactivity for preparation

2.2 Determine optimal volume for reconstruction

2.3 Make a list of optimal parameters for the preparation of each kit

3. Determine the optimal number of particles to be injected for radiopharmaceuticals such as Tc-99m-MAA

3.1 Determine the optimal radioactive concentration (MBq/mL or mCi/mL), based on the recommended dose (MBq or mCi) and number of particles and the volume to be drawn (mL)

3.2 Determine the optimal radioactivity for preparation to provide the required number of particles

3.3 Determine the optimal radioactivity for preparation for a patient with pulmonary hypertension to provide the required number of particles

4. Determine storage conditions for each radiopharmaceutical before and after reconstitution

5. Record all information

5.3.5. Tender – interactive session

5.3.5.1. Objective

To make the trainees find out about the needs of a simulated radiopharmacy laboratory and determine the terms of a yearly tender for this laboratory. The final aim is to let them also evaluate the offers coming from companies for this tender.

Simulating a case of a tender where the yearly need of Tl-201 Chloride will be bought for a radiopharmacy:

5.3.5.2. Questions

1. How many myocardial perfusion studies they have performed with Tl-201 last year?
2. What is the maximum number of Tl-201 scans they can perform in a week?
3. How many MBq (or millicuries) per week should he order?

Offers coming from the companies:

i. Company A: 370MBq (10 mCi) vials, delivery day:tuesday and calibration day:thursday, price 100 Euros per vial

ii. Company B: 925MBq (25 mCi) vials,delivery day:Tuesday and calibration day:Tuesday, price (….to be thought) Euros

- What kind of documentation you would want to see?
- Which one would you choose if everything is OK on paper.

6. BASIC ASEPTIC PRACTICES AND MICROBIOLOGICAL ASSESSMENT

6.1. Basic aseptic practices

6.1.1. Scope

To teach the trainees importance of aseptic technique and how to carry out aseptic operation in a hospital radiopharmacy

6.1.2. Learning objective

At the end of this lecture, the trainees should know what is aseptic technique, what are the components of an aseptic operation, what are the facilities and equipment required for aseptic operations what staff training required for aseptic operations

The trainee should also know the aseptic technique to be observed during radiopharmaceutical preparation and dispensing, environment monitoring (particle counts, settle plates counts, contact plate counts, finger prints monitoring), Tests (sterility test, pyrogen test, media fill simulation), method of sterilizations.

The trainee should also be aware of the important references regarding aseptic operations.

6.1.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• What is aseptic technique • Why is aseptic technique so important in radiopharmacy • Problems with sterility tests and endotoxin tests in radiopharmacy • Aseptic technique and quality assurance • Aseptic technique and safety of radiopharmaceutical preparations
Responsibility	• Who is responsible for the safety of the doses • Who should observe aseptic technique
Various components of aseptic technique	• Staff • Facilities

	• Equipment • Monitoring • Test • Practices
Staff and staff training in aseptic technique	• Adequate number of staff • Staff must understand the importance of aseptic technique • Staff must be aware of the risk involved in IV injections • Staff must shown competence before preparing and dispensing radiopharmaceuticals through • Staff must have basic knowledge of aseptic technique • Staff must be able to master the practical technique in aseptic preparation and dispensing of radiopharmaceuticals • Staff should pass finger print counts and media fill simulations
Facilities required for aseptic operation	• Definition of clean room • Different classification of clean room and activity allowed o PIC/S, BP, EU (Class A, Class B, Class C, Class D) o FDA (Class 100, Class 1,000 Class 10,000 Class 100,000) o ISO (Grade 3, Grade 4, Grade 5, Grade 6) • Clean room cascade design • Activity allowed in each clean room class • Particle counts and microbial counts limit of each clean room class • Lamina flow Cabinet o Vertical lamina flow Vs horizontal lamina flow cabinet

	○ Location of lamina flow cabinet ○ Activities allowed in lamina flow cabinet • Validation of clean room and lamina flow cabinet ○ Frequency of validation ○ Who does the validation ○ Parameters to be validated ▪ Air flow speed ▪ Air flow direction ▪ HEPA Filter leakage ▪ Pressure differential with respect to adjacent area ▪ Particle counts at rest and at operation ▪ Microbial counts at rest and at operation
Aseptic environment monitoring	• Particle counts monitoring ○ Frequency of monitoring ○ Particle counters • Microbial counts ○ Frequency of monitoring ○ Settle plate monitoring ○ Contact plate monitoring
Finger print counts and media fill simulation	• Objectives of finger print counts • Objective of media fill simulation • How to perform finger print counts and media fill simulation
Alert level and action level	• How to set alert level and action level • What to do when exceeding alert level and action level
Sterility test and endotoxins test	• Objective of sterility and endotoxins test

	• How to carry out sterility test • Aerobic bacteria – culture media, temperature, duration • Anaerobic bacteria – culture media, temperature, duration • LAL tests- Turbimetric and Chemogenic LAL test • Problems (low sensitivity, late results) with sterility test and endotoins test
Sterilization method used in hospital radiopharmacy	• Autoclave: temperature, duration, advantage and disadvantage • Millipore membrane filtration: advantage and disadvantage
aseptic practice in hospital radiopharmacy	• use, cleaning, maintenance and validation of lamina flow cabinet • assembling and use of syringe and needle in aseptic manner • arrangement of items inside lamina flow cabinet • segregation of sterile and non sterile items • settle plate and contact plate monitoring during preparation and dispensing • media fill simulation of operator
Some constraining factors to aseptic practices in hospital radiopharmacy	• lead shields • syringe shields
Important references	• USP chapter 797 • USP chapter 1116 • USP chapter 85 • Aseptic technique BP, EP

Model lecture 19 - ‘Aseptic practices’ is on CD at the back this trainer’s manual.

6.1.4. Aseptic practice – Practical & interactive

6.1.4.1. Objective

To reinforce the importance of aseptic operation and to demonstrate aseptic technique.

6.1.5. Interactive

Trainer to show video clip of how settle plate, contact plate, finger print counts to be done.

Trainer to show video on how lamina flow hood should be cleansed before and after use.

Trainer discuss with trainee on the arrangement of items within lamina flow so that air flow will not be blocked.

6.1.5.1. Material required

- Unopened syringe and needle
- Two Sterile evacuated vial, one filled with normal saline, anther empty
- Sterile glove
- Lamina flow hood

6.1.5.2. Steps

1. Wear sterile glove
2. Trainer demonstrate aseptically assembling of syringe and needle
3. Trainer demonstrate aseptically drawing normal saline from a vial and transfer to the empty vial
4. Trainer demonstrate aseptically drawing a dose (normal saline)
5. Trainee aseptically assembling of syringe and needle
6. Trainee aseptically draw normal saline from a vial and transfer to the empty vial
7. Trainer aseptically e draw a dose (normal saline)

6.1.5.3. Discussion

Trainer and trainee discuss the constraints of observing aseptic technique in hospital radiopharmacy

6.1.6. Basic environmental monitoring

6.1.6.1. Scope

Aseptic environmental monitor:

To give basic aseptic environmental monitoring issues in radiopharmacy laboratories for product safety.

6.1.6.2. Learning Objectives

After this lecture the trainee should be aware of main sources of product contamination, the importance of aseptic technique and related monitoring during radiopharmacy dispensing. The dispensing should be carried out in a controlled environment and essential parameters should be monitored. He/she should be aware of 'alert and action' limits and how they relate to contamination and cleanliness together with strategies of preventing them.

6.1.6.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Sources of contamination in a laboratory	Design of Controlled Environments Laminar airflow work bench Buffer zone Ante area • Environmental Validation Levels of particulates in controlled areas Alerts and action levels • Environmental Validation Determination of microorganisms, in-process Gowning, gloving Cleaning Facilities Material handling Design of Controlled Environments Low and medium risk products High risk products Process control indicator Environmental Monitoring of Air and Surface Viable air: CFU/volume Non-viable air: Counter Passive air: CFU/time

	Surface: Contact plates on table tops, walls, floors, gowns, gloves, and garments: CFU/time
LAF cabins suitable for radiopharmaceutical compounding and Parameters to be monitored for a LAF cabin	• Particle counts • Microorganism counts • Air flow • Pressure differential • others Definition of cleanliness levels according to ISO, US and Europe same in 'isolator technology ' and also' aseptic processing' this will be a repetition
Routine monitoring, trouble shooting and follow up	Settle plates, contact plates, finger prints included in 'aseptic processing' Media fill simulation runs included in 'aseptic processing' this will be a repetition Definition of cleanliness levels according to ISO, US and Europe Standards. Clean room standards Air particulate control Temperature control Humidity control Air Exchange Bioburden Settle plates, contact plates, finger prints Media fill simulation runs

Model interactive session 20 - 'Aseptic practices' is on CD at the back this trainer's manual.

7. RADIOPHARMACOLOGY AND LOCALIZATION MECHANISMS, BASIC PRINCIPLES

7.1.1. Scope

To understand essential mechanisms of action of radiopharmaceuticals and the basis of its biological distribution together with radiopharmacology in order to understand their applications in nuclear medicine.

7.1.2. Learning objectives

To be familiar with the mechanism of action of the most common RP used to be able to understand rationale of the imaging acquisition protocols, the preparation of the patient, and the post-diagnosis/treatment cares. At the end of the class, the students will be able to understand the basis of the biological distribution in humans (images) and appreciate that changes to normal could be due to patients, or quality of the RP.

7.1.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Sufficient Contrast and Localization	X rays and radioactive drugs • Sufficient Contrast and Localization Delineation, nuclear image • Nuclear Image Detection Visualization • Nature of Nuclear Image
Physiology, biochemistry, function	Perfusion, metabolism, In vivo chemistry • Localization Physicochemical aspects: Molecular weight, solubility, polarity, protein binding and pH • Localization Pharmacokinetic aspects: Blood, plasma clearance Mode and rate of excretion

	• Time Course of Localization Image at the time of greatest lesion to BG ratio • Requirements for Lesion Detection Target to non-target ratio Target to BG ratio Lesion size
Localization Mechanisms	Active Transport: Cellular metabolic process Energy, carrier • Active Transport Examples: Radioiodine, glucose metabolism • Simple Diffusion Membrane transport of substances Concentration gradient Pressure gradient Electrical gradient • Blood Brain Barrier (BBB) Limiting free exchange of substances to the brain Description of BBB • Blood Brain Barrier Diffusion of small, lipophilic and non-polar molecules
Pathologic conditions	• Simple Diffusion Examples: o Brain perfusion o Heart perfusion o Capillary Blockade

	Particles larger than 7µm Trapping of particles in the first capillary bed they encounter • Capillary Blockade Lung perfusion: How it works, what it means • Capillary Blockade Example: Lung perfusion, localization • Phagocytosis Particles smaller than 1µm Removal by the reticuloendothellial cells • Phagocytosis Example: Liver-spleen localization • Cell Sequestration Slightly damaged RBC(s) Removal by spleen • Cell Sequestration Spleen localization without liver interference • Compartmental Localization A nondiffusable substance Retaining in a well defined space Vascular system, CSF kinetics, lung air space, GI emptying
Compartmental Localization	Examples: o Lung ventilation o Blood pool localization • Specific Localization Mechanisms Antibodies: Binding to associated antigens Receptors: Specific binding proteins

	• Receptor Based Localization Surface receptors, intracellular receptors • Receptor Based Localization Tumour receptors Somatostatin Hormones: Estradiol Bombesin, Choline • Receptor Based Localization Brain Receptors Dopamine, Opioid • Receptor Based Localization Examples: o Pancreatic, prostate, breast tumour localization o Parkinson disease o Brain function responses

Model lecture 21- 'Radiopharmacology' is on CD at the back this trainer's manual.

7.2. Infection and inflammation imaging

7.2.1. Scope

To understand pathology of infection and inflammation and how radiopharmaceuticals are used for investigating these process.

7.2.2. Learning objectives

After this lecture the trainee should know changes occurring in the target tissue during infection and inflammation. Understand ideal properties of an infection radiopharmaceutical and the names and methods of localization of some common infection imaging agents.

7.2.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Definition of infection and inflammation	Increased blood supply, permeability and protein/leukocyte influx • The properties of an ideal infection radiopharmaceutical o No side effect o Specific to infection o Low non-target uptake o Rapid blood clearance o Simply to prepare and perform radiolabelled WBC o Long shelf life o Low radiation dose o Reasonable cost
Radiopharmaceuticals	Ga-67 Binding to transferrin Lactoferrin Siderophores • Avidin/Biotin Avidin: 60,000 D protein Biotin: Vitamin H Increased permeability • Avidin/Biotin Pretargeting with avidin Injecting In-111-biotin 3 hours later Improved T/NT ratios • Colloids

	Localization at endothelial damage site Positive in 1 hour • Polyclonal IgG In-111 and Tc-99 forms Vascular permeability • Leukoscan Anti-CD66 Fab Fragment Fast clearance, less immunogenic High T/NT, positive at 1 hour Intestinal uptake • Tc-99m Infecton Qinolone antibiotic Binds to DNA gyrase enzyme in dividing bacteria Rapid detection of bacterial infection • FDG Granulocytes and macrophages use glucose When activated by infection, uptake increases FDG Measures glycolitic activity Does not discriminate infection • FDG and FDG-labelled-WBC FDG-WBC shows higher uptake compared to FDG alone FDG is retained in WBC(s) as FDG-6-phosphate

Model lecture 22 - ‘Infection imaging’ is on CD at the back this trainer’s manual.

7.2.4. Radiolabelling of white blood cells (WBC)

7.2.4.1. Scope

To give the important consideration in handing and radio-labelling of autologous white blood cells.

7.2.4.2. Learning objective

After this lecture the trainee should know the use of radiolabelled white blood cells. Which radionuclides could be used and points to be taken into consideration. Critical steps of radio-labelling from blood withdrawal to imaging of the patient. The trainee should also get the necessary information about safe handling of blood components in addition to radioactive products.

7.2.4.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction	Minimum conditions necessary for the facility (Separate room and LAF?) o Related GMP Chapters o Sterile products o Aseptic products o Radiopharmaceuticals Product derived from human blood or plasma • Possible sources of hazard o For the product 1. Particle and microbes 2. Radiation damage to cells 3. Damage to cells due to operator handling o For the operator 1. Radiation 2. Biological (bacterial,fungal,viral)
Key steps of procedure	• Collection of blood • Separation of WBC from RBC

	• Labelling of the WBC • Separation of unbound radioactivity • Quality control • Injection back to the patient • Imaging Criteria for good labelling Factors that effect the efficiency of labelling • Plasma concentration • Cell concentration • Ligand quality and concentration • incubation time and temperature • pH • Cell damage • Medication • Operator experience.
QA	• Check system and protocol • Confirm quality of aseptic environment • Confirm correctness of equipment • Confirm skill of operator • QC radiolabel before addition • Check labelling efficiency • QC final radio-labelled product • Cells integrity check • Reconfirm identity check before re-injection • Clean-up and decontamination • Check outcome of the scan.

Model lecture 23 - ‘Radiolabelled white cells’ is on CD at the back this trainer’s manual.

7.2.5. Practical on radiolabelling of WBC(s)

7.2.5.1. Objective

To let the student judge his/her facilities for suitability of blood cell labelling and to show the main points to be considered in the practice of white blood cell labelling

7.2.5.2. Material

- Sterile centrifuge tubes 50mL
- Syringes 20-50 mL
- Sterile Pasteur Pipettes
- Tc-99m pertechnetate
- HMPAO kit
- Acid Citrate Dextrose (ACD)
- 6% Hetastarch

7.2.5.3. Steps

1. Tc-99m-labelled WBC(s)

1.1 Draw a 7 mL of Acid Citrate Dextrose (ACD) in a 60 mL syringe

1.2 Using a 20 g needle withdraw 50 mL of blood from the patient

1.3 Transfer the syringe into a laminar airflow work bench (LAWB)

1.4 Dispense the whole blood and ACD mixture in two 50 mL sterile centrifuge tubes

1.5 Add 5 mL of 6% Hetastarch into each tube

2. Incubate the mixture for 30 minutes in the LAWB at 45° angle for sedimentation of RBC(s)

2.1 Using a sterile disposable pipette transfer the supernatant (leukocyte rich plasma) into an empty sterile tube

3. Centrifuge leukocyte rich plasma at 180 g for 10 minutes

3.1 Using a sterile pipette transfer the supernatant (leukocyte poor plasma) into an empty sterile tube and save

3.2 Add 10 mL of saline (0.9% NaCl) onto the WBC pellet and resuspend

3.3 Centrifuge at 180 g for 5 minutes

3.4 Discard the supernatant

4. Add freshly prepared 1 mL of Tc-99m-HMPAO (10 mCi) no later than 10 minutes after reconstitution of the HMPAO kit using 30 mCi Tc-99m pertechnetate in 3 mL

4.1 Incubate the mixture for 10 minutes

4.2 Add 10 mL of saline and centrifuge the mixture at 180 g for 5 minutes

4.3 Discard supernatant in an empty tube save for calculation of labelling yield

5. Add 5 mL saline (or 5 mL leukocyte poor plasma if the reinjection can not be made within the next 30 minutes) onto the Tc-99m-WBC pellet.

5.1 Resuspend and withdraw into a 10 mL syringe using a 20 g blunt needle

5.2 Measure the radioactivity of the syringe containing Tc-99m-WBC(s)

5.3 Measure the radioactivity of discarded supernatant (4.3)

5.4 Calculate the Tc-99m-WBC labelling efficiency by the ratio of radioactivity of the final syringe (5.2) divided by the sum of radioactivities from the final syringe and discarded supernatant (5.2 + 4.3).

Labelling yield=5.2/(5.2+4.3).

5.5 Determine cell viability using trypan-blue test (optional)

7.2.6. Radiolabelling of red blood cells

7.2.6.1. Objective

To explain the medical indications for RBC labelling and the available radioisotopes and techniques for in-vivo, in-vitro and in-vivo/in-vitro labelling. Advantages and disadvantages of each techniques for radiolabelling.

7.2.6.2. Learning objectives

The trainee should know the techniques of RBC labelling and the precautions that must be taken in each method.

7.2.6.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction Radiolabelling of Cellular Blood Elements	Prerequisite for labelling Labelled cells should behave as normal cells Radiotracer should remain in the cell. • Radiolabelled RBC(s) Compartmental Localization Vascular System o Myocardial blood pool o Gastrointestinal bleeding

	Hemangioma Venography RBC survival
Methods of Labelling	(Other stannous kits can be used, must they know, how to calculate the stannous dose for in vivo studies?) Tc04, Tc (7+) oxidation state Required reduction Most common reducing agent: Sn (2+) • Tc-99m-RBC labelling Principal RBC(s) are mixed with Sn (2+) ions Sn ions penetrate into RBC(s) Subsequently Tc-99m diffuses into RBC • Tc-99m-RBC Labelling Principal Tc-99m (7+) reduces by Sn (2+) 80% of which binds to beta chain of hemoglobin, 20% to heme • Tc-99m-RBC Labelling In Vivo Tc-Sn-PYP is reconstituted with saline and injected into patients 20 mCi of Tc-99m is injected after 30 minutes of waiting • Tc-99m-RBC Labelling In Vivo Limitation: 80% labelling yield Extravascular distribution • Tc-99m-RBC-Labelling

	In Vi-Vitro Tc-Sn-PYP is reconstituted and injected into patient 3mL patient blood is withdrawn after 30 minutes Incubated with 20 mCi of Tc-99m for 10 minutes • Tc-99m-RBC Labelling In Vi-Vitro Tc-99m-RBC is injected Labelling efficiency is 95% • Tc-99m-RBC Labelling In Vitro Principal Blood is drawn and incubated with Sn (2+) Tinned RBC(s) are then incubated with 20 mCi of Tc-99m Labelling efficiency is 95% • Tc-99m-RBC (ULTRATAG-RBC) Vial: Stannous citrate Syringe 1: Sodium hypochlorite Syringe 2: Citric acid, ACD • Tc-99m-ULTRATAG-RBC Procedure Blood is incubated with stannous citrate for 5 minutes Syringe 1 is added to remove excess Sn (2+) Syringe 2 is added to remove plasma bound tin Tc-99m is added and incubated for 15 minutes

	Labelling efficiency is 97% • Cr-51 Labelled RBC(s) Principal Cr-51 (Cr 6+) incubated with blood Cr (6+) binds globin Reduction to Cr (3+) with ascorbic acid stops reaction • Cr-51-RBC Procedure 50 µCi Cr-51 Cr (6+) is incubated with 30 mL of blood and 10 mL of ACD After 20 minutes, ascorbic acid added to reduce unbound Cr-51 to Cr (3+) Cr (3+) is excreted in the urine • Cr-51-RBC Survival Actual RBC half-life is 50-60 days Normal Cr-51-RBC half life is 25-30 days due to elution of Cr-51.

7.2.7. Practical radiolabelling of RBC(s)

7.2.7.1. Objective

The trainee should learn the different techniques of RBC labeling and the precautions that must be taken in each method.

7.2.7.2. Materials

- Sn-PYP kit
- Sterile Saline
- XXX mCi of Tc-99m (pertechnetate)
- Sterile syringes
- sterile vials
- ULTRATAG-RBC kit
- Acid Citrate Dextrose (ACD)
- Disposable tubes
- ITLC-SG

7.2.7.3. Steps

1. In Vivo Method

1.1 Reconstitute a Sn-PYP kit with 2-3 mL of saline (0.9% NaCl)
1.2 Incubate at room temperature for 10 minutes
1.3 Withdraw the solution and inject into the vein of the patient to give 10-20 µg/kg of Sn (2+)
1.4 Wait 30 minutes
1.5 Inject 20 mCi of Tc-99m (pertechnetate)

2. In Vi-Vitro Method

2.1 Reconstitute a Sn-PYP kit with 2-3 mL of saline (0.9% NaCl)
2.2 Incubate at room temperature for 10 minutes
2.3 Withdraw the solution and inject into the vein of the patient to give 10-20 µg/kg of Sn (2+)
2.4 Wait 30 minutes
2.5 Draw 3 mL of patient blood
2.6 Incubate the patient blood with 20 mCi of Tc-99m (pertechnetate) in a sterile vial for 10 minutes
2.7 Reinject the Tc-99m-RBC(s) into the patient

3. In Vitro Method, ULTRATAG-RBC

3.1 Draw 1-3 mL blood from the patient into a syringe previously rinsed with Acid Citrate Dextrose (ACD)
3.2 Inject anticoagulated blood into the kit vial containing stannous citrate
3.3 Incubate at room temperature for 5 minutes
3.4 Inject syringe 1 (Na-hypochlorite) and syringe 2 (ACD solution)
3.5 Inject 30 mCi of Tc-99m (pertechnetate) immediately after adding syringe 1 and 2
3.6 Incubate the vial at room temperature for 15 minutes
3.7 Inject the required activity of Tc-99m-labelled RBC back into the patient

4. Labelling efficiency

4.1 Perform chromatographic evaluation of a sample from 3.7 using a disposable tube and ITLC-SG and saline as developing solvent
4.2 Determine Tc-99m-RBC labelling efficiency.

7.2.7.4. Results

Labelling efficiency must be higher than ……%

7.2.7.5. Discussion

The trainees should discuss the advantages and disadvantages of each methodology, according to the intended use.

7.2.7.6. Conclusion

7.3. Monoclonal antibodies in radiopharmacy

7.3.1. Scope

To introduce to trainees some of the commonly used peptides and monoclonal antibodies used in nuclear medicine.

7.3.2. Learning objectives

At the end of this lecture, the trainees should know the properties and characteristics of biological, the precautions of handling radiolabelled peptides and monoclonal antibodies and currently available peptides and monoclonal antibodies in clinical nuclear medicine including their indications, dosage, storage

7.3.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction	• What are bio-molecules?
Properties of bio-molecules (antibodies, peptides and fragments)	• What are the difference between bio-molecules radiopharmaceuticals and other radiopharmaceuticals • Essential chemistry and radiolabelling • Biological activity • Stability • Sensitive to environment, eg temperature, pH, concentration, level of radioactivity
Radioisotopes used in labelling bio-molecules Precautions in handling bio-molecules	In-111, I-131,Y-90, Tc-99m • Storage condition • Labelling condition • pH • concentration • physical shaking • maximum amount of radioactivity allowed
Currently commonly used bio-molecules in clinical hospital radiopharmacy	• Octreotide • Zevalin • Bexxar

	• Indication • radioisotope • Dosage • Storage condition before labelling • Storage condition after labelling

Model lecture 24- 'Radiolabelled antibodies' is on CD at the back this trainer's manual.

7.4. Pharmacological intervention in nuclear medicine.

7.4.1. Scope

To inform the trainees on the use of pharmaceuticals in conjunction with radiopharmaceuticals in nuclear medicine

7.4.2. Learning objective

At the end of the lecture, the trainees should know what is the purpose of using pharmaceuticals in conjunction with radiopharmaceuticals in nuclear medicine, what are the pharmaceuticals commonly used, the rationale, dosage, route of administration, side-effects/precautions and contraindications of these pharmaceuticals

7.4.3. Subject headings and key subject areas

Subject headings	**Key areas**
Purpose of using pharmaceuticals in conjunction with radiopharmaceuticals in nuclear medicine	• Better scan quality • To mimic a certain physiological condition • To protect the patients
Pharmaceuticals commonly used	• Lasix (Furoxemide) • Dipyridamole • Adensoine • Cholecyskinin • Amosfostin • rationale • Dosage

	• Route of administration • Procedure • Precaution/side –effects • contraindications

7.4.4. Drug pharmaceutical interactions

7.4.4.1. Scope

To explain the fundamentals of drug interactions and the most frequent mechanisms of interaction (positive and negative). To provide a rapid reference for Nuclear Pharmacy staff to look for such interactions.

7.4.4.2. Learning objectives

To introduce particular RP interactions, in this lecture, it is necessary to recover some of the concepts learned in Lecture of mechanism of action-localization (excretion, clearance, etc.). At the end of the lecture, the trainee should know the basis of RP-drug interaction, where they can take the information, and mechanisms to inform the Health Authorities of each country, in case they found a new RP-drug interaction. In this case I suggest bringing a table containing the drug-RP interactions to the students.

7.4.4.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction Mechanisms of drug interaction:	Poor or delayed extraction of RP and increased intravascular activity • Poor elimination of RP • Delayed clearance of RP • Decreased target tissue uptake • Localization of RP in non desire tissues • Increased renal retention of RP • Decreased renal excretion • Increased hepatic uptake • Failure of RP to leave vascular space; Increased blood pool activity • Extra care with new products.

Other routes - not i.v. administration:	• Decreased absorption of RP • Delayed absorption of RP • Accelerated absorption of RP
Interactions for the most common RP	• Tc-99m Labelled Colloids • Tc-99m Labelled Iminodiacetic Acid Derivatives • Tc-99m Labelled Phosphates & Phosphonates • Tc-99m Dimercaptosuccinic Acid (DMSA) • Tc-99m Dietilen triamino pentaacetic acid (DTPA) • Tc-99m Labelled radioaerosols • Tc-99m Labelled Macroaggregated Albumin & Albumin Microspheres • Tc-99m Pertechnetate • Tc-99m Sestamibi • Tc-99m Radioantibiotics • Tc-99m Labelled Red Blood Cells • In-111 Labelled White Blood Cells • I-131 & I-123 • I-131 Iodobenzylguanidine (MIBG) • Tl-201 Thallium Chloride • Ga-67 Gallium Citrate • F-18 Fluor deoxiglucose (FDG) • Sm-153, Sr-89 Labelled compounds for pain palliation

8. ROLE OF PET IN NUCLEAR MEDICINE COMBINED WITH PET RADIOPHARMACEUTICALS

8.1. Introduction to PET tracers

8.1.1. Objective

To give information about the Positron Emission Tomography (PET) technique and FDG as the most common PET Radiopharmaceutical

8.1.2. Learning objective

After this lecture the trainee should be able to know the difference between SPECT and PET modalities and the importance of positron emitting radioisotopes of the main elements of body composition, namely, carbon, oxygen and nitrogen. Comprehensive knowledge on FDG as the main clinically used PET radiopharmaceutical including the need for automation in the production of PET radiopharmaceuticals.

8.1.3. Subject headings and key subject areas

Subject headings	Key areas
Introduction	• FDA approved PET radiopharmaceuticals • PET in the Ph Int., EP and USP, • Positron Emission and production of positron emitters o Generators o Cyclotron • Detection of 511 KeV gamma radiations • The most important positron emitters and their use in terms body chemistry
Production of FDG	• Cyclotron • Chemical synthesis o Why automation? Nucleophilic substitution reaction
Quality control of FDG	• pH • Identity

	• Chemical • Radiochemical • Pyrogen • Sterility • Parametric release

8.2. Safe handling of PET products

8.2.1. Scope

To supply the necessary information in terms of safe handling of PET radiopharmaceuticals where the radiopharmaceutical is supplied from an outside manufacturer. It doesn't include the case of an on-site cyclotron.

8.2.2. Learning objectives

After this lecture the trainee should be able judge the design of his/her laboratory in terms suitability for PET radiopharmaceuticals handling and should realize that more stringent radiation shielding is required for positron emitters. He/she should be aware of possible radiation exposure during handling and dispensing. The shielding capacity of material like tungsten, lead and concrete for positron emitters compared to regular gamma emitters will be given in addition to receiving, dispensing and waste of PET products.

8.2.3. Subject headings and key subject areas

Subject headings	**Key areas**
Introduction	• Difference of positron emitters and other radionuclides in terms of the radiation they emit • Major considerations for facility design o Space availability o Power o Building strength o Radiation shielding requirements • Radiation shielding requirements o Location of the department in the hospital building

	○ The usage of surrounding rooms (adjacent, below and above) ○ Position of the rooms in relation to each other ○ Waiting/injection rooms and toilets ○ Number of patients imaged ○ Activity given to each patient for imaging ○ Time spent for imaging a patient • Possible sources of personnel exposure • Patient dose withdrawal (if not unit-dose) ○ Patient injection ○ Patient positioning ○ Patient scanning
Hot Lab design	• L – shaped table top shields • Sufficient ventilation • Shielded sharps disposal • Dose calibrator with additional shielding • Benchwork solidly built • Extra wall shielding • Protection from 511 gamma rays • HVL of lead and concrete for PET and SPECT radionuclides • Suggestions (Tungsten syringe shields • Automatic dose dispensing units

	• Automatic injection units • Syringe carriers and sharp containers with extra shield • Unit doses when possible • Patient veni-puncture by butterfly infusion sets • Transportation of vials and syringes by a card • Informing the patient before injection • Minimizing time spent with patient after injection • Arranging the hot lab in a way not to spend too much time in dose handling/withdrawal and assaying activity steps)

Model lecture 26- 'PET' is on CD at the back this trainer's manual.

Model lecture 27- 'FDG QC' is on CD at the back this trainer's manual.

8.2.4. Practical: Calculation of FDG dispensing doses

8.2.4.1. Objective

To practice the dose dispensing with short half life radiopharmaceuticals

8.2.4.2. Scenario

The FDG arrived to the department at 08:30 am and the label says it is 300 mCi?? Bq at 9:00 am in 3.5 mL. If the patient is ready for injection at 8:30 and if this department uses 15 mCi/patient;

What would be the initial volume you should withdraw for the first patient?

How many patients can this hospital scan with 30 minute intervals?

8.2.4.3. FDG dose calculation

Trainer can ask the trainee to work out the decay factor of FDG

$A=A_0$ x decay factor

Case 1:

at 8 am dose=100 mCi

at 9 am dose =?

at 11:45 dose =?

Case 2:

a hospital wants a 100mCi of FDG at t 10:30 am

at 10 am the dose should be =?

at 9:30 the dose =?

at 8:15 the dose =?

Model interactive 28- ‘Troubleshooting in radiopahrmacy’ is on CD at the back this trainer’s manual.

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ANNEX I. RADIOPHARMACY SELF ASSESSMENT AND AUDIT

Model lecture 29- 'RP Audit' is on CD at the back this trainer's manual.

I-1. Audit excel

Staffing

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.1	Is there a professional responsible for the radiopharmacy? Provide details.	A				
1.2	Is the radiopharmacy unit operated under the direction of a person with appropriate training as defined by local or national regulations?	A				
1.3	Are there written staff training manuals for all grades of staff?	B				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
2.1	Have all staff working at operational level 2 received specific staff training on the following:	A				
2.1a	Calibration of equipment- please provide details and training records	A				
2.1b	Working practices in the radiopharmacy - please provide details and training records	A				

2.1c	Preparation of individual doses - please provide details and training records	**A**				
2.1d	Quality control and analytical techniques - please provide details and training records	**A**				
2.1e	Dose release - please provide details and training details	**A**				
2.1f	Record keeping - please provide details and training records	**A**				
2.1g	Cleaning - please provide details and training records	**A**				
2.2	Is there a system for formal approvals of all documentations including radiopharmaceutical (RP) preparation, QC and formal release to patient?	**B**				
2.3	What training is provided to staff performing final checks on all products prepared before release for patient use?	**A**				
2.4	Are there training records for all staff performing cell labelling, e.g. RBC, WBC?	**B**				
2.5	Is there an annual performance review to check the competencies of radiopharmacy staff?	**B**				

Facilities

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.4	Does the unit have appropriately finished rooms (including adequate lighting, appropriate finishes to walls, floors, ceilings and ventilation) and a shielded dispensing station?	A				
1.5	Is there a shielded dispensing station available?	A				
1.6 a	For operational level 1b is there a shielded dispensing station and/or a fume hood available? [Is there a fume cupboard with suitable filters for volatile radioactive materials such as 131I solutions?]	A				
1.6 b	[If only radioiodine capsules are handled is the package opened in a well ventilated area?]	A				
1.7	Is there a validated (annual check on air flow, safety and challenge testing) fume hood with suitable filters for handling radioiodine solutions?	A				
1.8	Are there records and logs kept for all equipment irrespective of whether maintenance and calibration is performed 'in-house' or by external contractors?	B				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
2.6	For operational level 2: Are there regular checks on validated Class II type B microbiological safety cabinets located in a dedicated room?	A				
2.7	Are monometer readings of pressure differentials across HEPA filters recorded daily?	B				
2.8	Are there periodic records of air velocities determination for LAF cabinets or isolators?	B				
2.9	Is challenge testing of the HEPA filters in LAFs and isolators carried out annually?	B				
2. 10	For negative pressure isolators: Before preparation takes place, are gloves or gauntlets visually inspected and integrity tests carried out and recorded?	B				
2.11	Is there a system and record of planned preventative maintenance for all equipment in the radiopharmacy including the refrigerator?	B				
2.12	When clean rooms are used, are the over-pressures gauges monitored and recorded daily?	B				

Puchase of materials

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.9	Are there suitable protocols and trained staff for the purchase of approved or Marketing Authorized radiopharmaceuticals?	A				
1. 10	Are all goods received checked and recorded against the order for correctness of delivery?	B				
1.11	Are records kept for batch numbers and quantities received?	B				
1.12	Are visual inspections and label checks carried out prior to acceptance?	B				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.

2.13	Do all products, kits and generators have product approval, marketing authorisation, or bear a product licence number?	**A**				
2.14	How many unlicensed or unapproved products are used each year and is there a record of them?	A				
2.15	For all unlicensed kits, radiopharmaceuticals or radio-chemicals are the prescribers or responsible medical doctors made aware of his/her responsibilities?	**A**				
2.16	Do the suppliers or reagents and unapproved products provide a "Certificate of Analysis"?	B				

Dispensing protocols

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: that units operating at Operational Level 1, using pre-prepared pharmaceutical products, should complete the first checklist- Self Assessment for Operational Level 1 & 2.
Units operating at Operational Level 2 and preparing own pharmaceuticals should also complete the checklist with regards to dispensing protocols - Self Assessment for Operational Level 1 & 2.

Self Assessment for Operational Level 1 & 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.13	Are there specific written radiopharmacy procedures for dispensing operations undertaken in the radiopharmacy?	B				
1.14	Under operational level 1a: Are there written procedures for the aseptic dispensing and labelling of unit doses of ready-to-use radiopharmaceuticals?	B				
1.15	Is there a system for labels which assesses quality, number produced and number applied to dispensed doses?	A				

1.16	For operational level 1b: Do the written procedures contain clear safety and monitoring instruction for dispensing radioiodine solutions or capsules?	**A**				
1.17	Under operational level 1b are there written procedures for calibration assay, preparation and dispensing of individual patient radionuclide therapy?	**A**				
1.18	Can the audit and documentation for each RP batch be traced from the prescription to the actual administration of individual patient doses?	**A**				

Preparation Protocols

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

All units operating at Operational Level 2 and preparing own pharmaceuticals must also complete the checklist below with regards to preparation protocols (Self Assessment for Operational Level 1 & 2).

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
2.17	Are there written and approved procedures for the use of generators and reconstitution of each radiopharmaceutical kit used?	A				
2.18	Are SOPs independently reviewed and approved at specified intervals?	B				
2.19	Is the preparation of 99mTc radiopharmaceuticals from kits and generators carried out in a LAF cabinet?	A				
2. 20	Are there set criteria before release for preparation for patients use? Is this undertaken by the same operator or a different individual?	B				
2.21	Can each individual patient dose be traced to a specific generator and kit batch number?	A				

2.22	Under operational level 2b: Do the written procedures for any autologous preparation, e.g. red and white blood cells, include a clear instructions on safety, cleaning and decontamination?	**A**				
2.23	Are there written procedures for the preparation and dispensing of approved kit formulations of radio-labelled biological e.g. monoclonal antibodies, peptides?	**A**				

QA & QC

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.19	Are daily QC checks performed on radionuclide calibrators?	A				
1. 20	What quality checks are undertaken on a supplier before purchase?	B				
1.21	Are periodic quality checks on radiopharmaceuticals (RP) performed?	B				
1.22	Is there a written procedure for dealing with product/s failing to meet the required standard?	B				
1.23	Is there a record of complaint/s and any associated follow-up and investigation?	B				
1.24	Are there written procedures and records for regular contamination surveys of the radiopharmacy unit?	A				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.

2.24	For operational level 2 are there records for the following:	B				
2.24 a	Purchase of radioactive products and ingredients					
2.24 b	Generator elution, yield, [^{99}Mo] molybdenum breakthrough and aluminium ion breakthrough					
2.24 c	Product preparation, QC and release					
2.24 d	Environmental and microbiological monitoring					
2.24 e	Aseptic process, aseptic operator validation and trend analysis					
2.24 f	Laboratory cleaning and maintenance					
2.24 g	Equipment and plant calibration and maintenance					
2.24 h	Radioactive contamination monitoring and radioactive waste disposal					
2.24 i	Product defects and SOPs non-conformance, i.e. when a procedure is performed in a manner other than that described in the relevant SOP					
2.24 j	Independent inspection and audit					

2.25	In line with the IAEA "Operational guidance on Hospital Radiopharmacy" document, are there records of routine microbiological monitoring of the preparation area in the radiopharmacy?	**A**				
2.26	Are there calibration and linearity checks of the dose calibrator response over the complete range of activities measured at least annually?	A				
2.27	Is there set programme for checking the quality of radiopharmaceuticals (RP)?	**B**				
2.28	Considering patient safety, are certain simple checks performed on prepared radiopharmaceutical, e.g. mini-chromatography?	**A**				
2.29	For operational level 2 is a [^{99}Mo] Molybdenum breakthrough measurement performed on the first eluate from each [^{99m}Tc] Technetium generator and repeated when the generator is moved?	**A**				
2. 30	Is aluminium ion breakthrough checked on the first eluate from a [^{99m}Tc] Technetium generator?	A				
2.31	Are changes in the source of any kits, diluents or vehicle used, needles, syringes, swabs and sterile containers used within radiopharmacy recorded?	**B**				

2.32	On first use of a new batch or first new delivery of RP kits is radiochemical purity performed?	B				
2.33	Are rapid alternative methods employed for swift prospective QC for critical RP e.g. the determination of RCP for [^{99m}Tc] HMPAO)?	**A**				
2.34	Is there regular pH testing of RP carried out?	**B**				
2.35	Prior to release for patients is each individual radioactivity dose checked?	A				
2.36	Is there a record of the formal approval/release by an authorized person before a product is administered to a patient?	**A**				
2.37	Are there written procedures for the recall of defective products?	**A**				
2.38	Is there a record of complaints and any associated follow-up and investigation?	**B**				
2.39	Is there a system of recorded self-inspection and reports evaluation?	B				
2. 40	Is there a system for external audit or peer review process?	**B**				

Waste

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist - Self Assessment for Operational Level 1.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.25	Are there written procedures for the disposal of radioactive and non-active waste specific to the radiopharmacy?	A				
1.26	Is there a periodic review/audit of arrival, use and disposal of all radioactive materials?	A				
1.27	Are there written logs for each solid sources that indicate usage, transfer, disposal of solid sources?	A				

Audit Summary

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

The audit summary below should be completed by all units in order to prioritise needs.
Critical priorities have the highest importance.
Major priorities are second to critical priorities however they should still be addressed in a timely manner
Minor priorities are areas which need addressing but do not require such urgent attention as the above two categories.

Critical priority

No:	Class	Comment/action	Time frame	Date achieved

Major priority

No:	Class	Comment/action	Time frame	Date achieved

Minor priority

No:	Class	Comment/action	Time frame	Date achieved

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