ACPSEM
Australasian College of Physical Scientists & Engineers in Medicine

TRAINING EDUCATION & ASSESSMENT PROGRAM (TEAP) CURRICULUM FRAMEWORK

RADIOPHARMACEUTICAL SCIENCE (RPS)

INTRODUCTION

The purpose of the curriculum framework is to provide stakeholders with a clear understanding of what registrars should be learning throughout their training. It also provides the opportunity to align learning activities to the curriculum for the purposes of programmatic assessment. Hence, the curriculum framework is intended to be used in conjunction with the training handbook.

The curriculum framework divides learning into Key Areas and Topics, which are content focused. They are specified in the Table of Contents. Key Areas are brief, high-level descriptions of content in the RPS TEAP. The Topics are similar to Key Areas, in that they specify content but with finer granularity. Each Topic has Learning Outcomes.

Learning Outcomes are statements of what a learner is expected to know, understand and/or be able to demonstrate after completing a process of learning. This means that each Learning Outcome in the RPS TEAP is a statement about what the registrar knows, understands, or is able to do at the completion of training. They provide a distinction between a description of the attainment of learning, and learning activities, which are described in the training handbook. Learning activities can be aligned with the Learning Outcomes in the curriculum framework.

Elements are contained within Learning Outcomes. Elements are similarly worded in such a way that they complete the sentence, “The registrar is able to…”. Elements provide a finer level of granularity, and group together to form the attainment of a Learning Outcome.

Competence in Learning Outcomes is demonstrated through forms of assessment evidence specified in the RPS Programmatic Assessment Evidentiary Framework. Assessors use expert judgement, and the form of assessment evidence specified for each Learning Outcome, to determine attainment. The form of assessment evidence for each Learning Outcome is specified in the training handbook. The forms of assessment evidence are routine evidence, written assessment, oral assessment, practical activity, and entrustment activity.

Overall, the purpose of Key Areas and their corresponding Topics is to specify the content that is important to the RPS TEAP. Learning Outcomes and their corresponding Elements describe what the registrar needs to be able to know or be able to do for each Topic and Key Area to demonstrate competence. The curriculum provides a robust and defensible framework such that progression throughout the RPS TEAP can be underpinned by the principles of programmatic assessment.

RPS CURRICULUM FRAMEWORK STRUCTURE

KA 1 - A KEY AREA (KA) IS AN AREA OF STUDY ACROSS THE PROGRAM.

Topic 1.1 - A Topic within the Key Area

LO 1.1.1 - A Learning Outcome (LO) is a statement contained within the Topic. An LO is a statement about what the registrar knows, understands, or can do by the end of the program. Assessment evidence is used to determine attainment of a LO.

E 1.1.1a - An Element (E) is a granular statement contained within a LO.

E 1.1.1b - Each Element is a distinct and specific description of a component of the LO.

LO 1.1.2 - Another LO contained within the Topic. Each LO can be thought of as the completion of the sentence, ‘At the completion of training, the registrar is able to…’

E 1.1.2a - Another Element (E) contained within the LO.

E 1.1.2b - An LO usually has several Elements.

E 1.1.2c - A registrar should be able to demonstrate competence in each of the Elements to demonstrate attainment of the related LO.

TABLE OF CONTENTS

KA 1 - INDUCTION TO CLINICAL RADIOPHARMACEUTICAL SCIENCE

Topic 1.1 - Education

LO 1.1.1 - Complete relevant undergraduate and postgraduate education

E 1.1.1a - Submit evidence of undergraduate and postgraduate academic transcript(s).

Topic 1.2 - TEAP

LO 1.2.1 - Enroll in TEAP

E 1.2.1a - Submit TEAP application and approval to enrol.

E 1.2.1b - Submit a training plan prepared in consultation with nominated supervisor.

Topic 1.3 - Induction activities

LO 1.3.1 - Complete relevant inductions (department, radiation safety, hospital induction)

E 1.3.1a - Submit evidence of completing a radiation safety induction.

E 1.3.1b - Submit evidence of completing relevant inductions for the department and the hospital.

E 1.3.1c - Choose a historical topic on the early use of radiation in medicine and reflect on the changes imposed by legislation and safe work practices.

LO 1.3.2 - Explain the tracer principle

E 1.3.2a – Consider the history of the use of radiopharmaceuticals in medicine to probe pathological conditions. Include the history and principles of targeted radionuclide therapy (TRNT).

E 1.3.2b - Explain and give an example of how TRNT may be able to deliver a very specific treatment and the impact this can have on therapy and quality of life.

LO 1.3.3 - Reflect on the importance of SPECT imaging

E 1.3.3a - Describe how the gamma camera functions.

E 1.3.3b - Attend several SPECT reporting sessions covering a minimum of 3 different studies. Reflect on the role of SPECT and/or planar imaging in patient management.

LO 1.3.4 - Reflect on the importance of PET imaging

E 1.3.4a – Describe how the PET camera functions.

E 1.3.4b - Attend several PET reporting sessions covering a minimum of 3 different studies. Reflect on the role of PET in patient management.

Topic 2.1 - Nuclear physics and instrumentation

LO 2.1.1 - Describe the nature of radioactivity

E 2.1.1a - Provide evidence of understanding the nature of radioactivity by completing the supplied short answer questions(SAQ).

E 2.1.1b - Define each term relating to atomic structure, including atomic number, mass number.

E 2.1.1c - Differentiate between an isotope and a radionuclide. Give examples of each.

E 2.1.1d - Explain the Line of Stability and the information it represents. Explain how the Neutron to Proton (N/Z) ratio and binding energy determines whether an isotope will be stable or unstable - hence radioactive.

E 2.1.1e - Explain atomic structure and the fundamental properties that lead to unstable atoms and hence radioactive decay.

E 2.1.1f - Describe and differentiate between alpha, beta, positron, gamma and x-rays, electron-capture, isomeric transition, internal conversion and Auger electrons.

E 2.1.1g - Explain a decay scheme for a radionuclide. Include an example.

E 2.1.1h - Explain the 'parent/daughter' concept.

LO 2.1.2 - Explain the principles and demonstrate skill in the operation of radiation detectors

E 2.1.2a - Describe the types, uses and principles of operation of a range of radiation detectors used to detect α, β, Υ, x-ray radiation and neutrons using examples of different detectors and their use for a specific radiation measurement e.g. NaI, BGO.

E 2.1.2b - Compare the basic components of an ionisation chamber to solid-state detectors.

E 2.1.2c - Explain the effects of pressure and gas on the ionisation process, and how geometry and the type of container used will affect the measurement.

E 2.1.2d - Explain the functions, advantages and limitations of an automated dose delivery system. List radionuclides able to be used in the system. Explain reasons for limitations.

E 2.1.2e - Explain expected limits of uncertainty e.g. changing range may affect linearity of measurement, dose rate affects precision, time of measurement vs activity.

E 2.1.2f - Select the correct equipment to detect and monitor the area of a spill, and subsequent clean up.

E 2.1.2g - Perform the procedures in place for maintenance and calibration of dose calibrators, Υ-counters and any other radiation detection equipment used in the laboratory.

E 2.1.2h - Select the correct measurement parameter for a specific application (e.g. dosimetry, radioactivity measurement and detection) and use the correct units in each application (e.g. GBq, cpm, mSv).

E 2.1.2i - Calculate the limit of detection for different radiation detection equipment.

E 2.1.2j - Calculate the maximum activity that can be detected without dead-time affecting the measurement.

E 2.1.2k - Ability to correlate the measurement (e.g. cpm to Bq).

LO 2.1.3 - Explain and apply the concept of radioactive decay

E 2.1.3a - Apply decay corrections to measurements.

E 2.1.3b - Interpret a decay series, identifying any emissions relevant to radiation safety and use of the radionuclide in medicine.

E 2.1.3c - Understand the effect of half-life in the manufacturing process.

E 2.1.3d - Understand the management of radioactive waste based on the half-life of a radionuclide.

E 2.1.3e - Demonstrate awareness of the clinical application of a radiopharmaceutical as a function of its half-life.

Topic 2.2 - Biological effects of ionising radiation

LO 2.2.1 - Explain the models applicable to radiation effects

E 2.2.1a - Describe and explain the Linear No-Threshold Hypothesis and alternative models.

LO 2.2.2 - Describe how exposure to ionising radiation is quantified

E 2.2.2a - Differentiate between the different types of radiation dose: effective dose, absorbed dose, and equivalent dose.

LO 2.2.3 - Explain how exposure to ionising radiation can induce biological effects

E 2.2.3a - Identify the major sources of radiation exposure.

E 2.2.3b - Place occupational and medical exposure into context relative to natural background radiation levels.

E 2.2.3c - Explain why biological effects of radiation exposure differ depending on the type and energy of emission, the half-life of the radionuclide and the dose rate.

E 2.2.3d - Explain the delay in the appearance of the biological effects of radiation exposure and that these effects do not usually manifest for many years.

E 2.2.3e - Explain the difference between stochastic and deterministic effects.

E 2.2.3f - Explain the mechanisms for interaction including direct damage (cleavage of chemical bonds, gene and chromosome damage) and indirect damage (via the production of free radicals or intermediate reactive species).

E 2.2.3g - Describe, with diagrams, the molecular processes associated with radiation-induced chemical ionisation, the creation of ion pairs and reactive oxygen species (radicals) and their subsequent chemical reactions in the body.

E 2.2.3h - Explain the increased effect of radiation damage in utero because cells are dividing rapidly.

E 2.2.3i - Describe, briefly, the mechanisms of repair.

E 2.2.3j - Identify and differentiate between sensitive and insensitive tissues, giving examples of the respective radiation factors (WT's).

Topic 2.3 - Regulatory framework governing the use of radiation in medicine

LO 2.3.1 - Explain the principles behind the international system of radiation protection and how it is applied in the workplace

E 2.3.1a - Identify the units of measurement used to describe absorbed, effective and equivalent dose in radiation safety and protection.

E 2.3.1b - Explain the phrase 'Time, Distance, Shielding'.

E 2.3.1c - Define and explain the acronym ALARA.

E 2.3.1d - Describe personal protective equipment (PPE) used in radiation protection and when it is used.

E 2.3.1e - Describe equipment and techniques, other than PPE, used to protect staff and the public from radiation exposure.

E 2.3.1f - Interpret the concept of 'risk vs benefit'. Identify differences in 'appropriate' dosing for diagnostic and therapeutic applications.

E 2.3.1g - Explain the purpose of radiation dose limits (RDLs) set for different organs, procedures and population groups based on the different tissue and organ responses to radiation.

E 2.3.1h - Explain how RDLs are set, implemented and regulated locally.

E 2.3.1i - Define 'Allowable Dose Rates' - occupational and general population.

LO 2.3.2 - Demonstrate understanding of local Radiation Management Plan

E 2.3.2a - Identify governing bodies, laws and regulations relevant to Radiation Safety.

E 2.3.2b - Explain the content and the associated legislation behind the institutional radiation management plan.

LO 2.3.3 - Demonstrate knowledge of codes of practice governing the packaging and transport of RP

E 2.3.3a – Describe the Transport index and the regulations, equipment, signage, and documentation required whenever a radioactive material is transported from one area to another.

E 2.3.3b - Submit a Certificate of attainment if a course in the transport of radioactive materials has been completed.

KA 2 - RADIATION & CHEMICAL SAFETY

Topic 2.4 - Management of radiation safety

LO 2.4.1 - Competent to handle radioactive materials in the workplace

E 2.4.1a - Maintain a current radiation (and other requisite) license(s) relevant to the state in which employed.

E 2.4.1b - Show competence to manage spills of different levels of radioactive materials.

E 2.4.1c - Consistently demonstrate the application of good practice in radiation safety.

Topic 2.5 - Management of chemical safety

LO 2.5.1 - Demonstrate competence in chemical safety

E 2.5.1a - Identify chemical hazard handling precautions based on the risk associated with the chemical and solvent.

E 2.5.1b - Interpret relevant Safety Data Sheet (SDS) for chemicals and solvents used in the laboratory. Demonstrate knowledge and use of PPE and associated safety equipment - how and when it is used.

E 2.5.1c - Identify the appropriate method of disposal for a range of chemicals and solvents used in the laboratory.

E 2.5.1d - Consistently demonstrate the application of good practice in chemical safety.

Topic 2.6 - Evaluation of chemical and radiation safety

LO 2.6.1 - Ability to evaluate risk in the radiopharmaceutical science laboratory

E 2.6.1a - Submit a risk assessment relevant to either chemical or radiation safety.

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Topic 3.1 - Basic laboratory practice

LO 3.1.1 - Identify basic laboratory equipment and processes used in the RPS laboratory

E 3.1.1a - Identify processes and analytical techniques used in the radiopharmaceutical laboratory.

E 3.1.1b - Explain how buffers work, their role in chemistry, where commonly used buffers are best applied and any limitations they might have.

E 3.1.1c - Explain how the acidic groups on a chelator affect the pKa and how we ensure they will be de-protonated at the reaction pH while still maintaining the solubility of the metal ions.

E 3.1.1d - Describe the principle of the different methods used for the separation of analytes (ITLC, HPLC, GC, ion exchange chromatography, preparative LC, filtration).

E 3.1.1e - Describe the principle for each of the different methods of analyte detection and quantification (UV Absorbance, Infra-red, Radiometric, Colourimetric, ELSD, Refractive Index, NMR, Mass Spectrometry). Describe how other analyte detection and separation methods may be relevant in non-radioactive chemical synthesis e.g. NMR, HPLC and Mass Spectrometry.

E 3.1.1f - Differentiate between types of column separation using as examples two types of HPLC columns and two solid phase extraction (SPE) cartridges. Explain how to apply correctly.

Topic 3.2 - Laboratory skills relevant to the radiopharmaceutical laboratory

LO 3.2.1 - Use and apply simple laboratory and analytical techniques

E 3.2.1a - Prepare a buffer solution, utilising the Henderson-Hasselbalch equation.

E 3.2.1b - Perform calibration checks on equipment and assist with maintenance including pipettes, pH meter, absorbance spectrometer, analytical balance, and water purification system.

E 3.2.1c - Consistently apply Good Laboratory Practice (GLP) to laboratory activities.

E 3.2.1d - Maintain the laboratory workplace as fit for purpose.

E 3.2.1e - Operate test equipment and instruments and make appropriate adjustments to controls.

E 3.2.1f - Process data, recognise trends and out-of-control conditions. Monitor the quality of test results and data.

LO 3.2.2 - Describe sterility and bacterial endotoxin laboratory and analytical techniques

E 3.2.2a - Define a sterile, apyrogenic solution.

E 3.2.2b - Describe the steps and controls necessary to achieving a sterile, endotoxin- free environment in the radiopharmaceutical laboratory.

E 3.2.2c - Explain the sterility and endotoxin testing measurement in radiopharmaceutical products, and the principles of the testing process.

E 3.2.2d - Describe the steps in sample collection and transport that minimise the potential for error in sterility and endotoxin testing.

E 3.2.2e - Describe pyrogen (endotoxin) decontamination conditions.

E 3.2.2f - Describe sampling techniques required to minimise contamination; that 'pooling' of samples is permitted but is conditional on retaining individual test samples to be used in the event of contamination in the pooled sample.

LO 3.2.3 - Use and apply advanced laboratory and analytical techniques

E 3.2.3a - Apply the principles of techniques used in the RPS laboratory, including TLC, ITLC, HPLC, GC, GCMS, and gamma spectroscopy.

E 3.2.3b - Explain 1-2 limitations of each of these analytical equipment considering the ways they are usually applied in RPS.

E 3.2.3c - Operate the analytical equipment used in routine quality control of radiopharmaceutical preparations.

E 3.2.3d - Perform periodic routine maintenance of analytical equipment in your own laboratory, and demonstrate awareness of maintenance procedures typically performed by professional maintenance personnel e.g. HPLC annual service or preventative maintenance.

E 3.2.3e - Calibrate equipment, prepare standards and standard curves (as applicable).

E 3.2.3f - Demonstrate the ability to identify and troubleshoot problems with analytical equipment (e.g. lack of backpressure on a HPLC system) using trend data, final report, and quality of test results and identify the problem.

E 3.2.3g - Perform routine analytical tasks to a high technical standard.

E 3.2.3h - Operate analytical equipment with competence.

E 3.2.3i - Display care in the use and maintenance of the analytical equipment.

E 3.2.3j - Interpret analytical data - analyse and interpret results.

E 3.2.3k - Communicate with professional maintenance personnel when required.

E 3.2.3l - Provide advice to other scientists, develop and write protocols, and mentor and train junior scientists on equipment functions, troubleshooting and adjusting modifying equipment.

LO 3.2.4 - Evaluate experimental results of chemical analysis

E 3.2.4a - Present a portfolio of acquired and processed quality control data from 5-10 batches of the same radiopharmaceutical. The quality control data from each batch must include data from at least 3 types of analytical equipment,
and at least one of these must be HPLC or TLC.

E 3.2.4b - Evaluate a selection of data from the portfolio. Comment on the data consistency, identify any trends and what a trend in that data may indicate. Draw some conclusions and recommendations based on any trend identified in this data.

E 3.2.4c - Apply quantitative analysis using standard curves, dose measurements, preparation of standards.

E 3.2.4d - Interpret potential causes of abnormal biodistribution, uptake or clearance of a radiopharmaceutical that may correlate with potential out-of-specification quality control results.

E 3.2.4e - Identify some limitations of quality control analysis to evaluate the identification, purity and safety of a radiopharmaceutical.

Topic 3.3 - Method development/improvement

LO 3.3.1 - Establish a new analytical method, or evaluate an existing analytical method used in the quality control testing of a radiopharmaceutical

E 3.3.1a - Discuss the suitability of the method for the intended purpose, accuracy, precision, specificity, linearity, range, stability, limit of detection and limit of quantification.

E 3.3.1b - Identify analytical instrumentation used and include brand/model, service frequency and calibration date and data.

E 3.3.1c - Submit records detailing methods and results for the analytical method development parameters.

Topic 4.1 - Methods of radionuclide production

LO 4.1.1 - Describe each of the methods of radionuclide production and explain how they are applied in radiopharmaceutical science

E 4.1.1a - Describe the process to produce radionuclides in a reactor.

E 4.1.1b - Describe the process to produce radionuclides in a cyclotron.

E 4.1.1c - Create a table that identifies the method of production, starting element (target), reaction, irradiation conditions, extraction and purification, production yields, and half-life for the following radionuclides: Mo-99, I-131, Cu-64, Y-90, Lu-177, C-11, F-18, N-13, O-15, Cu-64, I-123, I-124, Zr-89, Ac-225; As-21.

LO 4.1.2 - Explain the principles of the ^{99}Mo/^{99m}Tc and ^{68}Ge/^{68}Ga generators. Supply evidence of experience and competence in the use of the generators.

E 4.1.2a - Explain how the physical and chemical properties of the parent vs the daughter enables the function of a generator.

E 4.1.2b - Identify the elution process and medium, and the adsorbent or retaining medium for the parent, for each of the following generator systems: ^{99}Mo/^{99m}Tc and ^{68}Ge/^{68}Ga, plus one emerging generator.

E 4.1.2c - Explain the terms:

- 'Carrier-free' and 'carrier added' in relation to radionuclide production, and the effect on radiolabelling and the resultant radiopharmaceutical.
- Transient equilibrium.
- Radionuclidic purity.
- Breakthrough.

E 4.1.2d - Describe potential problems that may be encountered during the elution process and what impact these may have on subsequent radiochemistry and the radiopharmaceutical produced.

E 4.1.2e - Submit evidence on successful elution of a ^{99}Mo/^{99m}Tc and/or ^{68}Ge/^{68}Ga generator.

E 4.1.2f - Submit evidence of testing the eluant of both ^{99}Mo/^{99m}Tc and ^{68}Ge/^{68}Ga generators for radionuclidic purity, radioactive concentration and potential contaminants.

E 4.1.2g - Evaluate the effect of concentration, volume and pH on the eluate from a ^{68}Ge/^{68}Ga generator on subsequent radiolabelling chemistry.

E 4.1.2h - Elute a generator and assess suitability for use by relevant quality control methodology.

LO 4.1.3 - Experience in cyclotron operations

E 4.1.3a - Submit logs of cyclotron production processes, whether observed or undertaken.

E 4.1.3b - Reflect on how the direct experience has enhanced your understanding of cyclotron operations.

E 4.1.3c - Interpret production run information, 'sign-off' points, critical steps, and trends to assess.

E 4.1.3d - Use problem solving skills to solve problems related to cyclotron operations.

KA 5 - ASEPTIC PREPARATION & QUALITY RISK MANAGEMENT

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Topic 5.1 - Regulations, Codes, Standards and Guidelines that apply to the practice of radiopharmaceutical science

LO 5.1.1 - Has knowledge of the Legislation, Codes and Regulations by which the Radiopharmaceutical Scientist (RPS) must abide by

E 5.1.1a - Create a table, listing each of the guides, codes (GLP, ISO Standards, GMP, ICH, PIC/S), standards (BP, USP, Ph.Eur and Monographs) and regulatory authorities (TGA, Food & Drug Administration (FDA), European Medicines Agency (EMA)). Describe the origin, purpose and how or why it is relevant to the practice of RPS in Australia.

E 5.1.1b - Differentiate between GLP, GMP and cGMP.

E 5.1.1c - Describe the function of the ARTG (Australian Register of Therapeutic Goods).

E 5.1.1d - Describe a registered product and explain how this may impact RPS.

E 5.1.1e - Describe exempt persons, exempt products, and how this is implemented in Australian departments which are manufacturing radiopharmaceuticals.

LO 5.1.2 - Apply and interpret resources to ensure product quality and safety

E 5.1.2a - Submit examples of documentation, identifying, by annotation, the resources from which the components of the document were derived.

Topic 5.2 - The PQS - Quality management in the practice of radiopharmaceutical science

LO 5.2.1 - Design and implement a Pharmaceutical Quality System (PQS) suitable for use in a hospital-based radiopharmaceutical production facility

E 5.2.1a - Identify the elements of a PQS and explain the objectives of each.

E 5.2.1b - Examine methodically and in detail the constitution or structure of the PQS system in your workplace laboratory and submit evidence of procedures and templates supporting the PQS.

E 5.2.1c – Conduct a review that identifies any gaps.

E 5.2.1d – Where a decision is made to exclude a recommended component of the PQS from the local interpretation, an assessment of the risk is to be submitted (see 5.4.1d)

E 5.2.1e – Comment on how procedures aim for best achievable outcome in circumstances where the department does not have facilities that allow best practice.

E 5.2.1f – Utilise knowledge of best practice and mitigate shortfalls that may be due to available facilities and work to realise 'best achievable' outcomes.

E 5.2.1g – Exhibit a commitment to ongoing improvement, and improve or evaluate alternatives to established procedures where appropriate.

Topic 5.3 - The facilities, equipment and processes employed to create a manufacturing environment

LO 5.3.1 - Identify the facilities, equipment and processes used in sterile manufacture

E 5.3.1a - Identify (list) facility, infrastructure and equipment resources used to ensure product quality and safety, including controls, procedures and processes.

E 5.3.1b - Explain the role of each identified resource in maintaining product quality and safety.

E 5.3.1c - Explain how a Grade A environment is achieved using positive pressure airflow and grading of adjacent areas in dispensing cell or laminar flow unit and clean rooms.

E 5.3.1d - Identify testing procedures and frequency required by GMP for plate testing of environment, gowning technique, air quality and microbial control.

E 5.3.1e - Describe requirements for acquisition and testing of starting materials.

E 5.3.1f - Explain the limitations of end-stage filtration to remove contamination; how limitations are mitigated by minimising the introduction of microbial contamination at every step of the process.

E 5.3.1g - Identify the potential consequences of microbial contamination.

E 5.3.1h - Identify the processes used in aseptic dispensing that require validation and/or operator qualification.

LO 5.3.2 - Validate competency in performing tasks in a clean room environment

E 5.3.2a - Provide evidence of validation of competency through training and competency testing for the skills used in preparation of aseptic products.

E 5.3.2b - Provide evidence of receipt and management of starting materials.

E 5.3.2c - Provide evidence of documentation required by regulatory bodies as it applies to aseptic preparation.

E 5.3.2d - Submit the supervisor's report confirming competence in the appropriate use and maintenance of a dispensing hot cell.

E 5.3.2e - Submit the supervisor's report to confirm compliance with expected practice standards in a clean room environment.

Topic 5.4 - Application of Quality Risk Management (QRM) in a radiopharmaceutical manufacturing environment

LO 5.4.1 - Explain the processes used in the management of risk (QRM) within a pharmaceutical production laboratory

E 5.4.1a - Identify the components of a risk assessment.

E 5.4.1b - Explain how QRM principles are integrated into the PQS to ensure patient safety.

E 5.4.1c - Describe the methods and tools available for QRM (e.g FMEA, HACCP, CC, PD, CAPA).

E 5.4.1d - Submit a completed risk assessment. Provide an example of proactively managing a risk e.g. conduct an internal audit of aseptic processes, review the quality of a sterile injectable product, review equipment and infrastructure available or change control. Identify mitigation strategies or make recommendations for improvement where applicable. Note: see 5.2.1d.

LO 5.4.2 - Conduct an investigation into a manufacturing deviation or incident

E 5.4.2a - Investigate a manufacturing deviation or incident.

LO 5.4.3 - Apply the Change Control process to manufacturing situations

E 5.4.3a - Submit an example of a change control process covering the justification of the proposed change, the risk assessment of the change, the effect of implementation and the final review.

LO 5.4.4 - Display skill and judgement in application of QRM to the radiopharmaceutical manufacturing environment

E 5.4.4a - Display application of QRM principles to radiopharmaceutical preparation.

KA 6 - PREPARATION OF DIAGNOSTIC & THERAPEUTIC RADIOPHARMACEUTICALS

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Topic 6.1 - The use of radiopharmaceuticals in medicine

LO 6.1.1 - Describe the application of radiochemistry to medicine

E 6.1.1a - Identify and explain how the physical properties (e.g. T1/2, energy of emission, availability) make the radionuclides suitable for use in diagnostic or therapeutic medicine.

E 6.1.1b - Create a table of radionuclides commonly used in diagnostic or therapeutic medicine. Identify the physical characteristics, use and examples of radiopharmaceuticals containing the radionuclide.

E 6.1.1c - Describe the different mechanisms of uptake that can be utilised to create a functional diagnostic or therapeutic radiopharmaceutical e.g. tracer, receptor-ligand, physiological mimic, therapeutic mimic.

E 6.1.1d - Identify factors that contribute to the biological behaviour (biodistribution) of a range of radiopharmaceuticals. Include the targeted tissue or organ, the biological uptake mechanism and potential causes of abnormal biodistribution that may be encountered.

E 6.1.1e - Identify potential causes of abnormal biodistribution that may be encountered.

LO 6.1.2 - Explain the application of radiochemistry to therapy (TRNT)

E 6.1.2a - Explain how the physical properties, emissions, and energies of a therapeutic radiopharmaceutical induce the biological /therapeutic effects and influence the choice of radionuclide used.

E 6.1.2b - Explain how optimising uptake, retention at the target and clearance of the radiopharmaceutical improve the safety and efficacy of TRNT.

E 6.1.2c - Identify the agent(s)/mechanism of damage in TRNT.

E 6.1.2d - Compare the relative biological effectiveness of different radionuclides used in TRNT. Explain how this might be applied to create the most effective therapeutic agent.

E 6.1.2e - Describe free radical processes, including formation, types of radicals formed, conditions under which they are formed and the interactions free radicals are likely to engage in with water, biological molecules, and radiopharmaceuticals.

E 6.1.2f - Compare the relative likelihood of free radical interactions with SPECT, PET and therapeutic radionuclides. Identify factors which contribute to vulnerability to free radical reactions and damage.

Topic 6.2 - The chemical basis for the incorporation of a radionuclide into a molecule

LO 6.2.1 - Describe the chemistry of radiolabelling with Carbon-11

E 6.2.1a - Describe methods that allow the direct incorporation (insertion) of C-11 onto the molecule of interest using synthons.

E 6.2.1b - Identify the different synthons used for the incorporation of ^{11}C-carbon on to molecules. Include ^{11}C-methyl iodide, ^{11}C-methyl triflate, ^{11}C-Carbon monoxide and ^{11}C-carbon dioxide synthons, and other ^{11}C-synthons, such as ^{11}C-cyanide, ^{11}C-formaldehyde.

E 6.2.1c - Describe the laboratory process and procedures associated with Carbon-11 radiolabelling including any precautions.

E 6.2.1d - Describe the practical issues associated with C-11 radiolabelling including time factors, quality control and specific activity.

E 6.2.1e - Identify the advantages and limitations of C-11 radiolabelling.

LO 6.2.2 - Describe the chemistry of radiolabelling with the halogens

E 6.2.2a - Describe the general physical and chemical properties of halogens in terms of their elemental structures and reactivity with an emphasis on fluorine and iodine.

E 6.2.2b - Describe the nucleophilic and electrophilic methods of radiohalogen incorporation.

E 6.2.2c - Compare the type of precursor required, labeling conditions and the radiolabelling outcomes.

E 6.2.2d - Compare the reaction yield, radiochemical purity and specific activity achieved by the different methods.

E 6.2.2e - Describe the advantages, disadvantages and limitations of each method.

LO 6.2.3 - Describe the chemistry of radiolabelling with radiometals

E 6.2.3a - Explain the use of chelating agents to complex radionuclide metal ion and their significance in the biological/clinical application.

E 6.2.3b - Describe, with examples, the chelation chemistry of a range of diagnostic and therapeutic radionuclides. Include at least six (6) different radionuclides.

E 6.2.3c - Differentiate between the different types of chelators, e.g., acyclic, macrocyclic bifunctional chelators, and for each, the preferred donor atoms used, the coordination number, and the stability of the Metal-Ligand complex (ML).

E 6.2.3d - Discuss metal-ligand selectivity, trans-chelation and potential loss of the metal ions in the body, and the effect of charge/oxidation state (where relevant) on complex radiopharmaceutical formation.

E 6.2.3e - Describe the species that is obtained post $^{99}Mo/^{99m}Tc$ generator elution and how this is made available for radiolabelling the diversity of radiotracers required in nuclear medicine for SPECT imaging.

E 6.2.3f - Explain the reduction process and reducing agent, the various oxidation states, and the overall charge of nominated ^{99m}Tc-radiopharmaceuticals.

E 6.2.3g - Explain the level of importance of molar activity (specific activity) for radiopharmaceuticals incorporating alpha or beta-emitters.

E 6.2.3h - Discuss properties important to the effectiveness of alpha or beta-emitters, including in vivo stability, radiochemical stability, premature fragmentation of the radiopharmaceutical entity due to radiolysis, and loss of the metal ion in solution or in vivo due to trans-chelation.

E 6.2.3i - Compare the relative robustness and risks associated with the different radiolabelling schema.

Topic 6.3 - Preparation of radiopharmaceuticals

LO 6.3.1 - Describe synthetic processes

E 6.3.1a - Describe the range of synthetic processes available. Include a simple cold kit preparation, a complex, multi-step synthesis performed on an automated module and a formulation of a product containing large activities, supplying multi-patient doses.

LO 6.3.2 - Explain radiopharmaceutical formulation and its purpose

E 6.3.2a - Explain how post radiosynthesis formulation assists to deliver a safe, efficacious and injectable radiopharmaceutical at an appropriate concentration (dose/ml) at the time of administration.

E 6.3.2b - Articulate the role and need for additional constituents in the formulation including buffers, acid/base for pH adjustment, and isotonicity adjustments.

E 6.3.2c - Identify and describe the role of a range of protective constituents (e.g. stabilisers) to maintain integrity of radiopharmaceutical formulation.

Topic 6.4 - Specific examples of radiopharmaceutical preparation

LO 6.4.1 - Prepare SPECT radiopharmaceuticals

E 6.4.1a - Create a table of SPECT radiopharmaceuticals commonly in use, describe the method of preparation and any special considerations specific to each.

LO 6.4.2 - Prepare PET radiopharmaceuticals

E 6.4.2a - Create a table of PET radiopharmaceuticals commonly in use, describe the method of preparation and any special considerations specific to each.

LO 6.4.3 - Prepare Therapeutic radiopharmaceuticals

E 6.4.3a - Create a table of therapeutic radiopharmaceuticals commonly in use, describe the method of preparation and any special considerations specific to each.

LO 6.4.4 - Utilise an automated module for the synthesis of a radiopharmaceutical

E 6.4.4a - Identify 2 different types of the automated synthesis module (i.e. commercially available or otherwise).

E 6.4.4b - Explain the advantages and disadvantages of each type of module.

E 6.4.4c - Describe the process of installation and acceptance for an automated synthesis module.

E 6.4.4d - Discuss how a synthesis module provides data integrity in the manufacture of a radiopharmaceutical.

E 6.4.4e - Provide a synthesis report and explain/interpret the data associated with this report.

LO 6.4.5 - Describe the specific requirements or conditions required when radiolabelling proteins and peptides, cells/blood components, other biological entities

E 6.4.5a - Describe the effect pH, temperature and the buffer (i.e. isotonicity) may have on molecules of biological origin (e.g. including but not limited to proteins, cells, antibodies).

E 6.4.5b - Provide at least 2 examples of how handling and processing of biological entities (cells, proteins and most peptides) may impact their viability as a radiopharmaceutical.

E 6.4.5c - Explain how activation of various cellular pathways (e.g. the clotting cascade, induction of inflammatory pathway cascades) could impact the effectiveness of the radiolabelled biomolecule.

LO 6.4.6 - Independently prepare a range of radiopharmaceuticals

E 6.4.6a - Exhibit the ability to follow a written and validated SOP that describes the preparation/ manufacture of the radiopharmaceutical.

E 6.4.6b - Perform routine radiopharmaceutical preparation to a high standard.

E 6.4.6c - Submit batch preparation records for a range of radiopharmaceutical preparations.

Topic 6.5 - Quality control/analysis of radiopharmaceuticals preparation

LO 6.5.1 - Describe the parameters used to define radiopharmaceutical quality

E 6.5.1a - Identify the source(s) of information available which determine quality expectations.

E 6.5.1b - Explain the role of the release criteria of radiopharmaceuticals and how they are applied.

E 6.5.1c - Identify the parameters which define the quality or examine the integrity of a radiopharmaceutical. This should include routine testing of the batch preparation, formulation and those parameters which may be established during validation.

E 6.5.1d - Explain why each parameter is important for product quality.

LO 6.5.2 - Explain how radiopharmaceutical quality is assessed

E 6.5.2a - Identify the analytical methods and processes used to measure the quality of the product.

E 6.5.2b - Identify the potential limitations of each analytical technique used to measure the quality of a radiopharmaceutical.

E 6.5.2c - Explain the risks of quality control results that lack integrity, or adequate interpretation, pose to safety, efficacy and patient care.

Topic 6.6 - Management of radiopharmaceutical quality in line with the PQS

LO 6.6.1 - Management of radiopharmaceutical quality in line with the PQS.

E 6.6.1a - Differentiate between the terms - conditional release, non-conformance, product recall.

E 6.6.1b - Submit a report that illustrates the ability to utilise at least one of the following processes - Process Deviation, CPP, CQA, OOS, CAPA.

E 6.6.1c - Submit evidence of ability to conduct batch release of radiopharmaceuticals, comment on any potential deviations in the production processes, utilise trend data and recommend any actions/changes required.

E 6.6.1d - Demonstrate high level ability to assess data, undertake detailed and well-planned investigations, make logical deductions of root causes of OOS's and provide solutions.

KA 7 - RADIOPHARMACEUTICAL DEVELOPMENT

Topic 7.1 - Use molecular imaging to probe metabolic processes

LO 7.1.1 - Probe biochemical and metabolic processes using radiopharmaceuticals

E 7.1.1a - Describe how the nominated biochemical and/or metabolic processes are probed using specific radiopharmaceuticals.

Topic 7.2 - Designing a radiopharmaceutical for clinical use

LO 7.2.1 - Undertake preliminary design of a new radiopharmaceutical, including establishing quality criteria.

E 7.2.1a - Use and correctly interpret resources such as pharmacopoeia, monographs and Pic/s code, to establish quality criteria for a new radiopharmaceutical.

E 7.2.1b - Justify the choice of radionuclide, based on intended use, using literature and/or by suppling an experimental justification.

E 7.2.1c - Discuss the pharmacokinetic implications (absorption, distribution, metabolism and excretion, or ADME) and potential target interaction modifications.

E 7.2.1d - Define the proposed release criteria, and describe briefly the importance of each in terms of the radiopharmaceutical's quality, efficacy and safety.

E 7.2.1e - Justify the measurement of certain parameters during the development of a radiopharmaceutical.

E 7.2.1f - Explain product stability in terms of the mechanisms of degradation and the impurities formed.

E 7.2.1g - Differentiate between radiopharmaceutical degradation as part of formulation and degradation in vivo through metabolic processes.

Topic 7.3 – Validation of a new radiopharmaceutical

LO 7.3.1 - Validate all the processes involved in the synthesis of a new radiopharmaceutical

E 7.3.1a - Discuss the key elements or components of a process validation.

E 7.3.1b – Submit a proposed process validation, for validation of both the production procedures and quality control procedures for a new radiopharmaceutical.

E 7.3.1c - Submit evidence of carrying out the proposed **process validation** described in E 7.3.1b.

E 7.3.1d - Submit batch production records as evidence of production and quality control testing of the new radiopharmaceutical - **using the processes validated** in E 7.3.1c. Distinguish between process validation and product batch records.

KA 8 - RESEARCH CAPABILITY

Topic 8.1 - Research Capability

LO 8.1.1 - Undertake independent research

E 8.1.1a - Propose a topic of research to address a specific problem. Review the available literature on the topic of research, identifying the aspects of the topic the project will address.

E 8.1.1b - Generate a hypothesis to create a framework for the research project.

E 8.1.1c - Design an experimental plan to be undertaken with an explicit description of the suitability of the techniques and methodologies to be applied.

E 8.1.1d - Provide examples of preliminary data, or other results, obtained. Comment on validity of the data.

E 8.1.1e - Discuss how the data corroborates (or doesn't) the hypothesis.

E 8.1.1f - Select a target journal and write a scientific report of work in a format suitable for publication. Cite references according to the style used in the selected journal.

ACPSEM
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KA 9 - THE PROFESSIONAL RADIOPHARMACEUTICAL SCIENTIST

Topic 9.1 - Apply professionalism to clinical practice of radiopharmaceutical science

LO 9.1.1 - Define professionalism and its application to radiopharmaceutical science practice

E 9.1.1a - Define professionalism.

E 9.1.1b - Explain how the concept of professionalism can be applied to radiopharmaceutical science.

E 9.1.1c - Recognise the importance of ongoing learning.

LO 9.1.2 - Practice Patient Centred Radiopharmaceutical Science Practice

E 9.1.2a - Explain the meaning of Patient Centred Practice.

LO 9.1.3 - Communicate as a professional Radiopharmaceutical Science Specialist

E 9.1.3a - Communicate as a radiopharmaceutical science specialist through presentations and other methods.

LO 9.1.4 - Participate in Radiopharmaceutical Science Communities of Practice

E 9.1.4a - Contribute to the RPS or NM community e.g., training, teaching, participation on working parties.

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