Notes for guidance on the clinical administration of radiopharmaceuticals and use of sealed radioactive sources

Administration of Radioactive Substances Advisory Committee

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Preface

These notes for guidance have been prepared by members of the Administration of Radioactive Substances Advisory Committee (ARSAC) past and present.

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Introduction

1 The guidance given in these notes is not mandatory and does not have the force of statutory regulations: nevertheless, it is based on national and international recommendations and represents the advice of the Administration of Radioactive Substances Advisory Committee (ARSAC). These notes can be considered to be a guide to good clinical practice in the UK for nuclear medicine and have been updated from the previous revision.

2 ARSAC will review these notes annually. Additional information will be provided through guidance published on the website. Notification of changes or updates will be made using the email subscription bulletin. To subscribe to receive updates use the following link: https://public.govdelivery.com/accounts/UKHPA/subscriber/new?topic_id=UKHPA_43

3 This document is uncontrolled when printed. The most up-to-date version of the notes is available on the website.

4 In this, September 2020 version of the notes, there are updates to the information in section 4 - Applying for research authorisation, reflecting the changes to this process following the launch of the online portal for submitting research applications to ARSAC.

Section 1

Licensing requirements of the Ionising Radiation (Medical Exposure) Regulations

Introduction

1.1 Article 28(a) of the EURATOM Basic Safety Standard Directive 2013[1] (BSSD) requires licensing for the deliberate administration of radioactive substances to persons for the purposes of medical diagnosis, treatment or research.

1.2 The medical exposure aspects of the BSSD were transposed into the Ionising Radiation (Medical Exposure) Regulations 2017 [2] in Great Britain (GB) (IR(ME)R). In Northern Ireland these were transposed into the Ionising Radiation (Medical Exposure) Regulations (Northern Ireland) 2018 [3]. These regulations include the licensing requirements of article 28(a) relating to medical exposures. IR(ME)R repeals the Medicines (Administration of Radioactive Substances) Regulations 1978[4] (MARS regulations) which transposed previous requirements.

Licensing Authority

1.3 IR(ME)R requires employers and practitioners to hold a licence for the administration of radioactive substances for a specified purpose.

(a) each employer is required to hold a licence at each medical radiological installation where radioactive substances are to be administered to humans

(b) every practitioner is required to hold a licence in order to justify the administration of radioactive substances to humans

1.4 Licences are required for any administration of a radioactive substance that results in an effective dose greater than 1μSv. This precludes the need to apply for a licence for the administration of the majority of substances that contain only naturally occurring levels of radioactivity.

1.5 The Licensing Authority for employer licences is:

(a) in England, the Secretary of State

(b) in Scotland, the Scottish Ministers

(c) in Wales, the Welsh Ministers

(d) in Northern Ireland, the Department of Health (NI)

1.6 The Licensing Authority for practitioner licences is

(a) in GB, the Secretary of State

(b) in NI, the Department of Health (NI)

1.7 ARSAC provides advice on the issue of licences to the relevant Licensing Authority. Applications are processed by Public Health England (PHE).

1.8 The purpose for which each radioactive substance specified in a licence may be administered is defined as research, diagnosis or treatment.

1.9 A licence may be revoked or varied by the Licensing Authority at any time.

1.10 A licence is valid for the period specified on the licence. The majority of licences are issued for 5 years; however licences with a shorter duration may be issued as appropriate.

Review

1.11 Any applicant who is aggrieved by a decision of the Licensing Authority or conditions attached to a licence may seek a review as specified in schedule 1 of IR(ME)R.

Processing of applications

1.12 Applications should be submitted as far in advance as possible of the date by which authorisation is required to allow sufficient time for processing and assessment.

1.13 Incomplete applications will be returned to the applicant, with a request for provision of the missing information before consideration by ARSAC. An acknowledgement will be sent to the applicant when the application has been accepted as complete and assessment has started.

1.14 PHE and ARSAC will aim to process all applications within six weeks of receipt of a **complete** application however; applications which require additional information or clarification can take longer.

1.15 If an application is referred back for additional information, it cannot be considered further until an appropriate reply is received from the applicant eg the practitioner or named individuals within the application (eg the Medical Physics Expert for employer licences).

1.16 No information about an application will be provided to any other persons except those named on the application form.

Urgent applications – particular patient licence (PPL)

1.17 In cases where the licence held by an employer and/or practitioner at a medical radiological installation is inappropriate for an administration that is urgently required, an application for a particular patient may be submitted. PPL applications cannot be accepted for research purposes. The committee would not normally approve PPL applications for novel procedures which have not been previously authorised by ARSAC. Advice about such applications, and other matters, can be sought from the ARSAC Support Unit.

1.18 Where more than one such administration is to be undertaken by an employer or practitioner, an amendment application must be submitted to add the procedure to the employer licence and the practitioner licence.

1.19 Employers who do not hold a licence at a medical radiological installation cannot submit a request for a particular patient licence.

1.20 Practitioners who do not hold a licence cannot request a particular patient licence. In cases of extreme urgency, the ARSAC Support Unit may be able to help such practitioners locate appropriate licence holders and advise on special circumstances when a standard referral to another medical radiological installation is inappropriate.

Transitional arrangements

1.21 Any valid ARSAC certificates after 6 February 2018 (when IR(ME)R came into force) are deemed:

(a) to be considered as legally equivalent to a licence until its expiry date

(b) to licence the employer at the medical radiological installation for the same scope and purpose (diagnosis, treatment or research)

(c) to licence the practitioner for the same scope and purpose

1.22 There is nothing in IR(ME)R to prohibit employers and practitioners from applying for licences at any time. This may result in a combination of licences and certificates being valid at an installation for any given exposure. A licence does not invalidate any existing certificates. Written procedures used locally should clearly state which authorisation method (a licence or certificate) is being used by the employer and practitioner to comply with the legal requirement for licencing.

1.23 Applications for licences should be submitted as far in advance as possible and at least 8 weeks before the expiry of a certificate to allow sufficient time for processing. Once a certificate expires, then employers and practitioners will no longer legally be allowed to administer the specified radioactive substances until appropriate licences have been issued.

Research involving the administration of radioactive substances

1.24 Employer and practitioner licences issued under IR(ME)R for research are not trial specific.

1.25 To take part in any ARSAC approved research trial, the employer and practitioner licences must include the specified procedure codes for the purpose of research.

1.26 Any valid research certificate is considered as legally equivalent to a licence for the practitioner and the employer at the radiological installation, to administer radioactive substances in accordance with the research trial detailed on the certificate until it expires.

1.27 Research certificates issued under the MARS regulations are trial specific and cannot be used for other research trials.

Section 2

Applying for an employer licence

Initial application

2.1 An employer licence is required for each employer at each medical radiological installation at which administrations of radioactive substances may occur. The Medical Director or Chief Executive Officer (or other equivalent individuals) may apply on behalf of the employer in conjunction with the supporting staff available at each medical radiological installation.

2.2 An application for an employer licence should be submitted as far in advance as possible but at least 8 weeks before the expiry of the last certificate or licence at a medical radiological installation for a required procedure to allow clinical services to continue.

2.3 Where there are multiple employers based at a medical radiological installation, all employers will need a licence covering the scope of service for which they are responsible. If more than one employer has a shared responsibility for the management of a service, then it must be clear which employer is taking legal responsibility for each exposure or aspect of each exposure. This may result in multiple employers holding a licence for the same procedure at the same medical radiological installation.

2.4 Details on how to apply and application forms are available on our website www.gov.uk/arsac. There are fees for employer applications, see section 2.25. To complete an employer licence application form, the following information is required:

(a) address of the medical radiological installation

(b) full legal name and address of the employer as it will appear on the licence

(c) name and address of the accountable representative of the employer under IR(ME)R. This is usually the Chief Executive Officer (or other equivalent individual)

(d) name and address of Medical Director

(e) name and contact details for the practitioners, Medical Physics Experts (MPEs) and relevant individuals responsible for radiopharmaceutical provision

(f) where appropriate, details of training of supporting staff

(g) procedures for which authorisation is sought and for which purpose

(h) for procedures not listed in these notes, local diagnostic reference levels (DRLs) where appropriate and effective dose to include references

(i) equipment and facilities available to the employer

(j) summary of governance arrangements for IR(ME)R, details of how the employer delegates the entitlement of duty holders and the system for ensuring compliance

(k) any other information as may be specified on the application form or may be reasonably required for the assessment of the application

2.5 Applications for an employer licence to include therapy procedures should detail the following:

(a) start-up discussions for procedures new to the medical radiological installation

(b) patient selection and onward management (eg multidisciplinary team meetings)

(c) facilities and supporting staff appropriate to the administered activity of the radioactive substance to include diagnostic facilities where appropriate

(d) details of designated in-patient accommodation as appropriate (for some treatments will require en-suite facilities and shielded rooms)

(e) number of procedures undertaken in the last 12 months and predicted numbers to be undertaken in the following 12 months

Toxicological and pharmaceutical safety

2.6 Employer and practitioner licences may be granted for radiopharmaceuticals or other products which do not have marketing authorisations. In this case, the employer retains responsibility for all aspects of the safety, quality and efficacy of such products. This also applies to the use of licensed products outside the terms of their marketing authorisation.

2.7 The fact that the radiological hazard to the patient from a particular product is considered acceptable subject to the clinical judgement of the practitioner, and that its use is within the competence of the supporting staff and the available facilities, in no way absolves the employer from their responsibilities to ensure pharmaceutical safety.

Supporting staff and services

2.8 At a medical radiological installation where administrations of radioactive substances are undertaken, it is expected that there will be a multi-disciplinary team involved with service provision. This will include practitioners, MPEs, radiopharmacists (if appropriate), and other healthcare professionals (eg radiographers, technologists, surgeons and nursing staff) with appropriate training and experience. The team will:

- **(a)** undertake clinical and non-clinical procedures (including calibration and assessment of technical performance of equipment)
- **(b)** evaluate the procedures for the performance of tests (including estimation of tissue dose)
- **(c)** assess radiation protection of patients
- **(d)** manufacture and draw up radiopharmaceuticals for administration
- **(e)** perform surgical or interventional procedures

2.9 IR(ME)R requires that employers must ensure that suitable MPEs are appointed and involved in exposures involving the administration of radioactive substances.

2.10 The availability and proximity of the MPE should bear a direct relation to the radiation risk involved with the procedures requested on the licence. There should be sufficient MPE support available based on the services provided. Guidance on what constitutes sufficient support has been published by the European Commission[5], the British Nuclear Medicine Society (BNMS)[6] and the Institute of Physics and Engineering in Medicine (IPEM)[7]. Multiple MPE's may be required dependant on the individual's training and the scope of service to be provided. For example, an MPE for a diverse therapy service should be readily available and normally employed at the medical radiological installation listed in the application. An MPE for an application including low dose procedures in a research laboratory could be based offsite and at some distance from the laboratory.

2.11 As nuclear medicine techniques and services develop, new functions and processes are expected to be undertaken by staff within the nuclear medicine department and may be undertaken by staff in locations that are outside the department. It is important that the employer's procedures specify how duty holders are entitled following demonstration of competence through appropriate training and experience.

2.12 The MPE should advise the employer on compliance with IR(ME)R.

2.13 The adequacy of other supporting services will depend upon the nature and complexity of the work involved[6]. Factors to be considered for medical exposures include the suitability of:

(a) equipment to undertake the procedure involved

(b) working areas and related laboratory equipment

(c) trained staff for the supervision, treatment and nursing of subjects to whom the radioactive substance is administered

(d) trained surgical teams for procedures involving administration of a radioactive substance and interventional or surgical procedures

2.14 Demonstration of initial competence for supporting staff can be provided through formal theoretical training, supervised practical experience and mentored practical experience. Theoretical understanding can be achieved through attending conferences or training courses. Practical training can be provided through formal visits to other centres with experience of a procedure, often acquired by involvement in early research applications.

Renewal of licences

2.15 An employer licence may be renewed on expiry. It should be noted that it is the responsibility of the employer to hold a valid licence for the scope of service provided. Renewals should be submitted at least 8 weeks prior to the expiry of a licence to allow sufficient time for processing.

2.16 The ARSAC Support Unit should be notified if the employer licence is no longer required.

Amendment to licences

2.17 An amendment to an employer licence should be submitted for the following circumstances:

(a) addition of a procedure

(b) change in purpose for a procedure (for example from research to diagnosis)

(c) request for authorisation for an administered activity above the DRL or for a significantly greater administered activity than previously authorised for any procedures not in these notes

2.18 Applications for an amendment can be made whenever required within the duration of a valid licence. There are fees for employer amendment applications, see section 2.25.

2.19 Where applications are made for a licence to include procedures that are significantly different from those already held, then further evidence of appropriate facilities and relevant training and experience of the supporting staff should be included in the application.

2.20 In recent years, some suppliers have developed training to support the introduction of new radiopharmaceuticals into the UK, where the use of the radiopharmaceutical demands expertise and skills not usually available within an existing nuclear medicine service. Reference to completion of this training within an amendment application will often enable applications to be processed more quickly.

2.21 Alternative local methods of developing appropriate skills can always be used, but recognised training schemes may be preferable as these provide evidence of competence that might be more easily transferable. Where local training is developed, this should be equivalent to existing formal schemes. Within any application to ARSAC, greater detail will be required about local training schemes so that the committee can satisfy itself as to the competence of all staff involved.

2.22 This competence must be maintained and demonstrated through appraisal and similar mechanisms. The requirement for maintaining competence applies to all staff, some of whom will be within the department management structure and some of whom will not.

Notification of material changes to licences

2.23 A notification should be submitted to the ARSAC Support Unit by email immediately of any material changes that may affect the validity of the licence. There is no fee for notifications. Such changes include, but are not limited to:

- **(a)** change in Chief Executive Officer or Medical Director
- **(b)** change to administrative details (eg legal name of hospital or trust)
- **(c)** replacement of existing equipment
- **(d)** change in level of support including addition or removal of named:
    - (i) MPEs
    - (ii) supporting staff for radiopharmaceutical provision
    - (iii) practitioners
- **(e)** change in provision of radiopharmaceuticals
- **(f)** suspension of service (eg during renovation works)
- **(g)** closure of department/services

Fees

2.24 Applications can only be processed on the payment of the correct fee.

2.25 Details of fees are as follows:

(a) new licence application: £250

(b) amendment to existing licence: £200

(c) renewal of an existing licence: £200

2.26 Full details of how to pay the fee will be provided once an application has been accepted. Standard payment method is using a debit or credit card through a secure online portal. Alternative payment methods using Bacs (Bankers Automated Clearing System) and invoices are available; please contact the ARSAC Support Unit for details once an application has been accepted.

Section 3

Applying for a practitioner licence

Initial applications

3.1 Practitioners must apply on behalf of themselves. A practitioner licence may only be granted to the practitioner who is clinically responsible for the justification of administrations of radioactive substances.

3.2 Currently, ARSAC will only support applications from practitioners who are medically trained. It is expected that practitioners are appointed in a substantive consultant post.

3.3 Every practitioner licence application must list all medical radiological installations where they are, or will be, entitled as a practitioner under IR(ME)R[2, 3]. It is expected that the practitioner will review and approve all protocols used at all medical radiological installations where they are entitled.

3.4 A licensed practitioner may work at any other medical radiological installation where they are also entitled to act as a practitioner and can provide sufficient support as specified in paragraphs 3.32 to 3.34.

3.5 Doctors who habitually authorise exposures under guidelines issued by a licensed practitioner may need to review their entitlement in line with their employer's procedures. If, for example, such individuals wish to work independently and justify exposures outside of these guidelines, it may be appropriate for them to apply for a licence and be entitled as a practitioner.

3.6 Details of how to apply and application forms are available on our website www.gov.uk/arsac. There are no fees for practitioner applications. To complete a practitioner licence application form, the following information is required:

- **(a)** name, address, qualifications and appointment of the applicant
- **(b)** the primary medical radiological installation in which they are entitled
- **(c)** procedures for which authorisation is sought and for which purpose
- **(d)** theoretical training relevant to the procedures applied for
- **(e)** practical experience relevant to the procedures applied for, to include confirmation of appropriate continuing medical education (CME) since training

(f) any other information as may be specified on the application form or may be reasonably required for the assessment of the application

3.7 Applications for a practitioner licence to include therapy procedures should detail the following:

(a) specific recent training and experience in the procedures applied for to include:

(i) indicative numbers of cases

(ii) the applicant's level of involvement

(iii) whether experience was gained during formal training or under the mentorship of another practitioner

(b) expected number of procedures to be performed over the next 12 months

(c) attendance at relevant training courses to include certificates and syllabus as appropriate

(d) details of involvement in relevant multidisciplinary team meetings for appropriate patient selection and onward management

Qualifications and experience of the practitioner

3.8 To hold a licence, it is essential to receive both theoretical and practical training in the procedures applied for. The degree of training required by a practitioner will vary with the nature of the procedures to be undertaken.

3.9 Practitioners who wish to apply for a licence to enable them to support a comprehensive diagnostic nuclear medicine imaging service should have satisfactorily completed the Royal College of Physicians (RCP) Nuclear Medicine Training Programme, the Royal College of Radiologists (RCR) Radionuclide Radiology Subspecialty Training Programme or demonstrate an equivalent level of training.

3.10 Holders of a CCT (certificate of completion of training) or CESR(CP) (certificate of eligibility for specialist registration (combined programme)) in nuclear medicine, would normally expect to receive a licence including most of procedures in table 5.1 and 5.3

3.11 Those who have successfully completed training in radionuclide radiology would normally expect to be licensed for most of those imaging procedures listed in table 5.1 for which training is included in the RCR Radionuclide Radiology Subspecialty Training Programme.

3.12 Practitioners who wish to apply for a licence to support a therapy service should have completed the RCP Nuclear Medicine Training Programme, the

RCR Clinical Oncology Specialist Training Programme or demonstrate an equivalent level of training.

3.13 Applicants who have not undertaken any of these structured training programmes are required to demonstrate equivalent training, experience and competence relevant to the procedures they wish to undertake.

3.14 Alternative local methods of developing appropriate skills can always be used, but recognised training schemes may be preferable as these provide evidence of competence that might be more easily transferable. Where local training is developed, this should be equivalent to existing formal schemes. Within any application to ARSAC, greater detail will be required about local training schemes so that the committee can satisfy itself as to the competence of all staff involved.

3.15 In recent years, some suppliers have developed training to support the introduction of new radiopharmaceuticals into the UK, where the use of the radiopharmaceutical demands expertise and skills not usually available within an existing nuclear medicine service. Reference to completion of this training within an application will often enable applications to be processed more quickly.

Additional requirements for positron emission tomography/computed tomography (PET/CT) or positron emission tomography/magnetic resonance imaging (PET/MRI)

3.16 Practitioners who wish to justify exposures as part of a PET/CT or PET/MRI service will require training and experience additional to that required for conventional nuclear medicine procedures. Such practitioners should already hold a licence for a comprehensive range of nuclear medicine procedures.

3.17 For those undertaking structured training through the Royal Colleges for a nuclear medicine CCT or CESR, a licence for routine diagnostic PET procedures will usually be granted on completion of the training grade.

3.18 For those who have not undergone structured training to include PET/CT and/or PET/MRI, additional information on post qualification training and experience will need to be provided to demonstrate adequate knowledge, experience, competence and skill. Specific details of practical experience required is detailed in section 3.27 to 3.31.

Theoretical training

3.19 Theoretical knowledge can be obtained through attendance at conferences and lectures as well as through keeping up to date with current literature.

3.20 A number of courses on PET/CT are available in the UK, Europe and North America and these will provide sufficient theoretical knowledge for the

applicant, when considered in conjunction with an existing broad knowledge of nuclear medicine.

3.21 The theoretical training in the core curriculum in table 3.1 is intended as a guide for applicants who have not completed formal training programs. It should be noted that this does not address the comprehensive medical knowledge required for the management of patients. The time taken to cover the relevant areas in table 3.1 will vary depending on the scope of the application. Sections that are not relevant to the application may be omitted.

3.22 The core curriculum is intended to provide sufficient detail so that the licence holder has an appreciation of all aspects of the procedures applied for but cannot provide the same depth of understanding that other professionals within the specialty will bring to the subject, eg radiopharmacists and physicists.

Table 3.1: Full nuclear medicine service core curriculum

1	***Fundamental physics of radionuclides***	
1.1	**Atomic structure**	Mass, atomic and neutron number Energy levels – nuclear and electronic
1.2	**Radioactivity**	Radionuclides Units of radioactivity Specific activity Physical half-life Decay constant Poisson (count) statistics
1.3	**Radioactive decay**	Mechanism of alpha, beta and gamma emission Electron capture and X-ray emission Isomeric transition, internal conversion Auger electrons Positron emission and annihilation
1.4	**Properties of radiation**	Excitation and ionisation Attenuation of X-rays and gamma rays Scattering and absorption Bremsstrahlung radiation
1.5	**Radionuclide production**	Production methods Isotope generators Cyclotron and nuclear reactors
1.6	**Radiation hazards and dosimetry**	Biological effects of radiation Risks and benefits of radiation Cellular radiobiology Biological and effective half-lives Absorbed dose, equivalent dose, effective dose and their units Application of MIRD concepts for calculating whole body, organ and tumour doses
1.7	**Radiobiology aspects for therapy**	Uptake ratios Cell cycles Cell killing Total lethal dose Radiosensitisation Tissue homogeneity
1.8	**Dosimetry for therapy**	Dose rate Fractionation Biological effective dose, dose volume histogram, tumour control probability Microdosimetry – residence and clearance Mass estimations
2	***Principles of radiation detection, instrumentation and equipment***	
2.1	**Detection of radiation**	Geiger-Müller detectors, proportional counters and ionisation chambers Scintillation and solid state detectors Spatial discrimination, collimators, basic design and function Energy discrimination, multichannel analysers and pulse height analysers Temporal discrimination, count-rate (dead-time) effects and corrections

Table 3.1: Full nuclear medicine service core curriculum

2.2	**Detection systems – general**	Radionuclide assay calibrators QA programmes and QC testing for radionuclide calibrators, and requirements for traceability Personal and Environmental contamination monitors Personal whole body and extremity dosimeters and dose rate meters Gamma sample counters; counting geometry and establishing protocols for counting External probe systems including intra-operative probes
2.3	**Detection systems – gamma camera**	Gamma camera detectors, camera systems and associated equipment Construction and function of main components Care of scintillation crystals Principles of collimation, and main designs Output signals – *X* and *Y* position signals, *Z* energy signal Digitisation of event data, formation of digital images and optimal selection of discrete matrices Spatial resolution, information density and noise Energy resolution Energy, linearity and uniformity (sensitivity) corrections Anatomical markers Static, dynamic, ECG-gated and scanned (whole body) imaging Planar quantification of radiopharmaceutical uptake, distribution and kinetics Image processing techniques, region of interest analysis and time–activity curve generation Techniques for background correction, motion correction, attenuation correction, scatter correction and partial volume correction QA programmes and QC testing for planar gamma camera imaging
2.4	**Associated electronic equipment**	Photomultiplier tubes and photodiodes Power supplies (high and low voltage) and amplifiers Analogue to digital conversion
2.5	**Single photon emission computed tomography (SPECT)**	Principles of single photon emission computed tomography Requirements for performing SPECT on a gamma camera system Centre of rotation correction Energy, linearity and uniformity (sensitivity) corrections SPECT/CT – appropriate CT protocols, registration and fusion of SPECT and CT data Reconstruction of projection datasets Filtered back projection and iterative reconstruction techniques Attenuation correction, scatter correction and partial volume correction Algorithms for reconstruction with resolution recovery SPECT quantification of radiopharmaceutical uptake, distribution and kinetics Acceptance testing, QA programmes and QC testing for SPECT and SPECT/CT systems

Table 3.1: Full nuclear medicine service core curriculum

2.6	**Image formation and quality**	Image quality – noise, contrast resolution and spatial resolution Image artefacts Optimisation of image quality and radiation dose Optimisation of image display, including windowing, thresholding, saturation and the use of grayscale and colour lookup tables Acceptance testing, QA programmes and QC testing of display devices Administered activity and DRLs Investigation time Counting statistics and 'information density' Choice of collimator (design and specifications – energy range, sensitivity and resolution) Acquisition protocols for dynamic study (spatial and temporal resolution) Acquisition protocols for SPECT (collimation, angular sampling, image matrix and projection time)
2.7	**Analysis of data**	Manipulation of data Image processing techniques, region of interest analysis and time–activity curve generation Correction techniques, background correction, decay correction and motion correction Quantification of uptake, retention, clearance and distribution Kinetic analysis, compartmental analysis and deconvolution Algorithms Physiological basis of models
2.8	**Computing**	Electronic image data storage, native and standard file formats (Interfile, DICOM) Structure of digital images and determination of image file sizes Anonymisation of image data Archiving of image data including RIS, PACS and VNA Major considerations regarding processing and review systems – hardware, performance and operating systems Image processing applications software Computing for tomography, requirements for data reconstruction and corrections Fusion, registration and visualisation of tomographic image datasets Acceptance testing and QA of processing and review systems
2.9	**Therapy equipment**	Design safety Control of administration including automated infusion devices Management of radioactive waste from administration and the patient
2.10	**Positron emission tomography (required for PET licences)**	Principles of tomography Principles of positron emission tomography Design of PET/CT systems – PET detectors, detector block architecture and performance Time of flight (TOF) Noise equivalent count rate (NECR) and optimised data acquisition protocols PET image formation, sinograms and data blocks, from 2D to 3D geometries PET image reconstruction, FBP and iterative reconstruction techniques PET/CT – appropriate CT protocols, registration and fusion of PET and CT data Use of CT for attenuation correction and anatomical fusion, CT artefacts and use of CT contrast Reconstruction with CTAC and scatter correction Quantification – requirements for calibration of PET systems PET quantification of radiopharmaceutical uptake, distribution and kinetics and SUV analysis Acceptance testing, QA programmes and QC testing for PET/CT QA and standardisation of protocols for clinical trials imaging

Table 3.1: Full nuclear medicine service core curriculum

2.11	**Computed tomography (required for licences including SPECT/CT or PET/CT)**	Construction, function and operation of a contemporary multislice CT scanner CT image reconstruction, FBP and iterative reconstruction techniques Factors controlling CT image quality Factors controlling CT radiation dose to patients Optimising CT radiation dose to patients Dose metrics for CT – DAP, DLP, CT dose indices (CTDI), effective dose, local and national DRLS and dose investigation levels (DIL) Radiation safety in CT Acceptance testing, QA programmes and QC testing for CT
3	***Calibration techniques***	
3.1	**Preparation of calibration sources and phantoms**	Preparing calibration sources and phantoms
3.2	**Quality assurance**	Pulse height and window selection Uniformity of field Spatial linearity Spatial resolution – intrinsic and at depth, point and line spread functions Count rate performance Sensitivity Collimator performance Image processing
3.3	**Routine quality control checks**	Standard tests, applicability, frequency of testing, action and remedial thresholds
3.4	**Calibration of therapy sources**	Calibrating therapy sources
4	***Radiopharmaceuticals***	
4.1	**Chemistry of relevant radiopharmaceuticals**	Principles of their localisation
4.2	**Tracer principles and techniques**	Kinetics of radioactive tracers used in nuclear medicine Use of principles of kinetics and modelling techniques applied to radionuclide investigations Physiological principles of tracer techniques Errors associated with quantitative measurement
4.3	**Preparation of radiopharmaceuticals**	Radiopharmacy and working practices in respect of radiation safety and microbiological safety Principles of labelling blood products Individual dose preparation Identification of prepared products Quality control – radiochemical sterility and pyrogens Documentation – packaging and transport of radiopharmaceuticals Monitoring of work areas and waste disposal Use of kits, dilution and transfer of activity Principles of pharmaceutical good manufacturing practice (GMP) Regulation of radiopharmaceutical production
4.4	**Generators**	Safe handling of generators Elution of generators

Table 3.1: Full nuclear medicine service core curriculum

5	***Management and radiation protection of the patient***	
5.1	**Patient selection**	Disease process and other investigations relevant to the disease Patient preparation and consent (as appropriate) Food and drug interactions Arrangements for radioactive patients in the hospital and home Administration of radioactivity – techniques and procedures, and apparatus Preparation and disposal of syringes and needles Documentation – for procedural requirements, clinical governance and regulatory compliance Hygiene in relation to radioactivity Reporting procedures (including accidents, adverse reactions, errors in preparation and administration) Non-medical imaging Special groups and contraindications: • pregnancy • breastfeeding • infants and children • the seriously ill
5.2	**Therapy aspects**	Planning of investigations including the selection of appropriate tests and imaging techniques for the diagnosis of malignant disease Formal consent for therapy administrations Interaction with other pharmaceuticals, foods and clinical investigations Criteria for discharge of the inpatient Radiation safety issues in public areas, the workplace and at home Possible toxicity of the therapy, both early and late Follow up, assessment of efficacy and retreatment
6	***Statutory and advisory publications and general radiation protection***	
6.1	**Statutory and advisory aspects**	Underpinning concepts of radiation protection: • justification, optimisation and limitation • application of the ALARP principle to practices • UK regulatory framework for radiation protection National and international regulatory requirements relevant to the practice of nuclear medicine National and international guidance on nuclear medicine
6.2	**General radiation protection**	Regulatory duty holders and their training and responsibilities: Radiation protection, with particular emphasis on: • shielding, preparation, dispensing and administration of doses • minimising radiation dose to staff, including pregnant and breastfeeding staff • prior risk assessment, restriction of exposure and dose monitoring • use of time, distance and shielding to reduce radiation dose • use of personal protective equipment to reduce exposure • environmental contamination monitoring of working areas • personal contamination monitoring of staff • decontamination procedures in dealing with spills • security, transportation and storage of radioactive substances • storage and disposal of radioactive waste • protection of the patient, their contacts and the wider public, and their comforters and carers

Practical experience

3.23 The amount of appropriately supervised practical experience needed for a licence will vary and can be restricted to those procedures which are to be undertaken.

3.24 The applicant should be able to demonstrate active involvement in protocol development, participation in patient selection, patient preparation, justification, participation in multidisciplinary team (MDT) meetings, clinical evaluation and, within the nuclear medicine facility, day-to-day running of the service. Such experience will prepare the applicant for patient management problems that may arise for both diagnostic and therapeutic procedures. The practical experience for diagnostic procedures should not be limited to reporting alone.

3.25 As a guide, applicants should have experience of supervising and reporting a number of procedures consistent with the curriculum of the European Board of Nuclear Medicine (EBNM) and the Joint Royal Colleges of Physicians Training Board (JRCPTB), for the procedures applied for.

3.26 Applicants for a comprehensive diagnostic licence are expected to have experience of approximately 3000 procedures. This level of experience will enable a practitioner to justify, perform, and develop the protocols for those procedures included within the issued licence.

3.27 For hybrid imaging, licences do not confirm the holder's knowledge, experience, competence and skill in relation to any use of CT as this is outside the scope of licence. The use of CT in nuclear medicine procedures is subject to clinical governance considerations[8].

3.28 Practical experience in PET/CT should be obtained through attendance at an established clinical PET/CT installation. Mobile PET/CT facilities may contribute to the experience of an individual but are not sufficient to be recognised as the sole source of training.

3.29 Applicants who wish to justify ^{18}F-FDG-based oncology procedures, should be able to demonstrate active involvement in approximately 600 cases typically over a period of about three months. This should be achieved in blocks rather than through sessional involvement and it is recommended that the blocks should be of no less than four weeks duration. Experience gained in this way should ensure a representative patient case-mix.

3.30 For non-^{18}F-FDG PET/CT procedures, ARSAC would normally expect applicants to demonstrate practical experience specific to each procedure applied for. For neurological PET/CT this should include the mentored review of approximately 50 cases (including library cases) for each indication. For cardiac PET/CT this should include the mentored review of approximately 100 cases (including library cases).

3.31 Practitioners who wish to justify cerebral amyloid PET/CT procedures need to include the following information within their applications:

- **(a)** confirmation of participation in, or feedback from, the relevant MDT and referring dementia experts
- **(b)** knowledge, experience and authorisation for ^{18}F-FDG imaging for differential diagnosis of dementia
- **(c)** specific understanding of brain amyloid imaging in dementia, following attendance at a reader training programme or equivalent
- **(d)** practical experience in the procedure requested to include mentored review of at least 50 cases

Remote working

3.32 ARSAC does not encourage remote practitioners. The committee considers that remote working makes it more difficult to ensure that the requirements for patient safety and appropriate standards of quality of care are maintained. ARSAC is of the view that wherever possible, the practitioner should regularly attend at each medical radiological installation for which they are providing support.

3.33 It is the professional responsibility of all licensed practitioners to ensure that they are providing adequate supervision for the appropriate justification of exposures and management of protocols.

3.34 Where a licensed practitioner is looking to extend support to additional medical radiological installations, the following should be considered:

- **(a)** practitioners should be entitled as a practitioner and as an operator for any other practical aspects that they undertake according to the employer's procedures
- **(b)** practitioners should hold a contract with the employer
- **(c)** the practitioner should review their licence to ensure that all procedures licensed at the medical radiological installation are included for the purpose specified
- **(d)** the practitioner should spend time on site providing supervision, the level of supervision should be commensurate with the complexity of the procedures performed
- **(e)** when the practitioner is not based on site, they should be contactable to provide support when the procedures are being undertaken

(f) the practitioner should approve and provide support for the ongoing review of all protocols

(g) the practitioner should review the employer's procedures under IR(ME)R to ensure they can comply with them

(h) if it is not possible for the practitioner to authorise every exposure, the practitioner should issue guidelines to allow the authorisation of exposures by appropriately entitled operators

(i) the practitioner should assess the arrangements to ensure that there are appropriate supporting staff available to them. This is particularly important where operators will be authorising under their guidelines

Renewal of licences

3.35 A practitioner licence may be renewed on expiry. It should be noted that it is the responsibility of the practitioner to ensure that they hold a valid licence. Renewals should be submitted at least 8 weeks prior to the expiry of a licence to allow sufficient time for processing.

3.36 Maintenance of competence is a clinical governance issue and an essential part of modern clinical practice. Practitioners are expected to undertake appropriate CME associated with the procedures on their licence as part of the appraisal and revalidation processes and to confirm this at the time of renewal.

3.37 The ARSAC Support Unit should be notified if the licence is no longer required.

Amendments to licences

3.38 An amendment to a licence should be submitted for the following changes:

(a) addition of a procedure

(b) change in purpose for an existing authorised procedure (eg research to diagnosis)

3.39 Applications for amendments can be added within the duration of a valid licence. These should be made as and when required. Evidence of appropriate training and experience specific to the procedures requested should be included in the amendment application.

Notification of material changes to licences

3.40 A notification should be submitted to the ARSAC Support Unit, by email prior to any material change in circumstances that may affect the validity of the licence. Such changes include, but are not limited to:

(a) change in appointment

(b) change of medical radiological installations where the licence holder is entitled as practitioner

(c) retirement or reduction in hours

(d) change of contact details

Section 4

Applying for research authorisation

Introduction

4.1 IR(ME)R[2, 3] addresses the exposure of individuals as part of biomedical and medical research. The principles of justification and optimisation also apply to research exposures. IR(ME)R requires the employer to establish either a dose constraint or target levels of dose for each research programme.

4.2 Regulation 11(1)(d) of IR(ME)R states that a person must not administer a radioactive substance in the course of a research programme unless it has been approved by an expert committee. ARSAC is this expert committee. It also requires such research programmes to be approved by a recognised research ethics committee (REC).

4.3 Under IR(ME)R, employers and practitioners wishing to take part in any ARSAC approved research trial, must ensure the specified procedure codes are included on their licences for the purpose of research.

4.4 Practitioners should be appropriately notified of the research protocol by the research sponsor during the setup of the research trial and prior to any administrations taking place at each radiological installation.

4.5 Further information on approvals for research trials by other bodies may be obtained through the Health Research Authority (HRA): www.hra.nhs.uk.

Applying for a research approval

4.6 ARSAC research approval must be obtained by the trial sponsor for all research trials as follows:

- **(a)** where the protocol requires the administration of radioactive substances regardless of whether this is considered standard care
- **(b)** where the protocol specifies the frequency, administration or processing for an exposure involving radioactive substances that would otherwise always be considered standard care

4.7 ARSAC research approval is not required for research trials where:

- **(a)** the protocol does not specify any administrations of radioactive substances

(b) the only administration of a radioactive substance mentioned in the protocol is an inclusion criterion that would be received by all participants as part of standard care (eg a trial where all participants must have received prior radioiodine therapy to be considered eligible)

4.8 The HRA have produced further guidance to aid sponsors in determining if the exposures within a trial are research exposures, this is available on their website https://www.myresearchproject.org.uk/help/hlpradiation.aspx.

4.9 Submissions to ARSAC should be made at the same time as ethical approval is sought. Submissions should be made via the ARSAC online portal (https://digitaltools.phe.org.uk/servicedesk/customer/portal/22). Applicants will need to set up an account to submit an application: https://digitaltools.phe.org.uk/servicedesk/customer/portal/22/user/signup. Further guidance on how to use the online portal is available here: https://www.gov.uk/guidance/how-and-when-to-submit-research-applications-to-arsac.

4.10 A preliminary research assessment (PRA) form is automatically generated for research trials which involve the administration of radioactive substances on the Integrated Research Application System (IRAS). The sponsor (or someone on their behalf) should submit the PRA form to the ARSAC Support Unit via the online portal with any relevant participant information sheets (PIS) and supplementary documentation. ARSAC does not routinely require the research protocol to be provided except for studies involving the administration of therapeutic radioactive substances. Where the trial involves novel radiopharmaceuticals, references or estimates of effective doses should be submitted (see section 4.20). If the study has gone through the HRA Radiation Assurance process, then F1 of the research exposure form should be submitted for ARSAC review.

4.11 There are fees for research approvals, see section 4.35.

4.12 A trial must receive confirmation of ARSAC approval prior to any administrations of radioactive substances taking place. The ARSAC research approval document will confirm the approved procedures within the trial. The trial sponsor must provide this to all relevant participating medical radiological installations.

Research amendments

4.13 Occasionally, a research trial may change after a trial has been approved. ARSAC should be notified of any changes concerning the administration of radioactive substances as this may affect the approval granted. Such changes include, but are not limited to:

(a) changes to the number of administrations of radioactive substances from section A1 of the original PRA

(b) addition or removal of a procedure involving the administration of a radioactive substance

(c) addition of a new population with a different clinical condition or healthy volunteers (including changing the age range for participants)

(d) changes to the radiation risk information in the PIS following a change to the protocol

4.14 Such changes normally meet the criteria for notifying substantial amendments to the REC (or Gene Therapy Advisory Committee). Research sponsors should apply to ARSAC for an amendment with the following information:

(a) short summary of the changes

(b) notice of the substantial amendment from IRAS when this is submitted to the REC

(c) updated PRA form if there are changes to the number of administrations or procedures involving radioactive substances (note that this requires revision of the integrated dataset part A and/or B3 and then creation of an up-to-date pdf of the PRA form via the submission tab)

(d) any other relevant enclosures (eg updated PIS to include any tracked changes)

4.15 All information should be submitted to the ARSAC Support Unit by email, further guidance is available on our website: https://www.gov.uk/guidance/how-and-when-to-submit-research-applications-to-arsac. ARSAC will contact the sponsor if any further information is required to process the amendment. There are fees for research amendments, see section 4.35.

Research notifications

4.16 ARSAC should be notified of minor changes to research trials to ensure the approval remains valid. Notifications should be made to the ARSAC Support Unit by email and are not subject to a fee.

4.17 Such notifications include, but are not limited to:

(a) change to the research trial title

(b) change to IRAS ID

(c) closure of a trial

Issues considered by ARSAC when assessing research trials

4.18 ARSAC has primary responsibility for assessing whether the proposed administration of radioactive substances in a research trial is appropriate. This includes consideration of:

(a) whether the administration of radioactive substances is appropriate to the trial objectives, taking into account international and UK guidelines

(b) the effective or target tissue dose per administration and per participant

(c) the risks to participants from these administrations in combination with other ionising radiation to be administered, taking into account the age, diagnosis and other characteristics of the research cohort

(d) measures to minimise the risks, in particular for individuals with child-bearing potential

(e) information in the PIS regarding the administration of radioactive substances and the risks

Activity administered and effective dose

4.19 The activity administered to individuals should be the minimum consistent with obtaining adequate information, especially for administrations to individuals who are not expected to benefit directly. Research involving high radiation doses may be approved if specific justification is provided. The justification must apply to the individual recipient as well as to the population as a whole. All unnecessary administrations should be avoided.

4.20 ARSAC expects that when an application for a research trial involving novel radiopharmaceuticals is submitted, estimates of effective dose will be based on the best information available at the time. Where such estimates are not possible from similar existing human studies, data from animal dosimetry studies, or where practicable from human studies involving extremely low radiation doses, should be submitted as part of the application. References to published works should be included on the PRA form with copies submitted with the application or, where this is not available; any unpublished data should be provided.

4.21 More accurate information on dosimetry may be available once the trial commences. To help ARSAC in its task of reviewing future applications, such information should be made available to the ARSAC Support Unit as soon as possible.

Age

4.22 Consideration must be given to the age of the subjects proposed for investigation. In particular, persons under 16 years of age should not be involved except where problems specific to their age group are under investigation. Special justification would be required for the inclusion of children and young persons in research trials.

4.23 Whenever possible, healthy volunteers should be aged over 50 years [9]. If the trial requires subjects below the age of 50 years, then explicit justification for the age range required should be included within the application. Upper age limits do not need to be stated in the application.

Multiple trials

4.24 Consideration should be given to the risks to an individual who is involved in several research trials. It is unacceptable that an individual should repeatedly take part in research trials leading to a substantial cumulated radiation dose. This is particularly relevant for healthy volunteers where an annual dose constraint of 10mSv from all research exposures (including those from non-nuclear medicine procedures) should be applied.

4.25 Investigators should always review the previous radiation exposure of the proposed participants. In the case of healthy volunteers, previous exposures as part of their clinical diagnosis or treatment should not be included as part of the proposed annual dose constraint of 10mSv.

Pregnancy

4.26 The possibility of early pregnancy should always be borne in mind in connection with the use of individuals of childbearing potential as research subjects.

4.27 Individuals who are pregnant or breastfeeding must not be involved in any trial, except where problems related to their condition are under investigation and alternative techniques that do not involve ionising radiation have been considered and rejected.

Communicating risk to research ethics committees, patients and research subjects

4.28 IR(ME)R includes a requirement for all research subjects to receive prior information on the risk of any exposures they may receive as part of a research trial. Knowledge and communication of risk to patients and research subjects form an essential element of modern medical practice and, without it; informed consent cannot truly be obtained.

4.29 When communicating risk, it is normal to discuss risk in terms of numbers. Care should be taken to ensure that the risks are not compared with practices that are unfamiliar or considered unacceptable. Comparing the risk associated with a paediatric procedure with that of smoking cigarettes or using internationally derived comparisons, such as drinking half a bottle of red wine a day, may give a false impression or trivialise the risk.

4.30 As the level of risk becomes greater, quoting risks in numerical terms may be helpful. At moderate levels of risk, it is likely that only in exceptional circumstances would a properly informed individual volunteer without a balancing individual benefit.

4.31 Where discussing the risk of a single administration the dose can be compared with the average dose to which people are exposed in a year in the UK (approximately 2.7mSv[10]). It would not be appropriate to compare the risk in a trial to an excessive number of years of background radiation.

4.32 ICRP Publication 62 [4] provides general guidance for assessing research proposals against radiation risk. When designing research trials, consideration should be given as to whether the extra information gained from the trial warrants the risk involved.

4.33 The HRA have also published guidance on representing risk to patients and research subjects and this is available on their website.

Fees

4.34 Research sponsor applications can only be processed on the payment of the correct fee.

4.35 Details of fees are as follows:

- **(a)** new multi-centre research trial: £350
- **(b)** new single-centre research trial: £300
- **(c)** new low dose research trial (<1mSv total participant dose): £200
- **(d)** research amendment: £250

4.36 Full details of how to pay the fee will be provided once an application has been accepted. Standard payment method is using a debit or credit card through a secure online portal. Alternative payment methods via Bacs (Bankers Automated Clearing System) and invoice are available.

Section 5

Routine procedures

Introduction

5.1 These notes contain information regarding a subset of procedures undertaken routinely in the UK using radioactive substances. This is intended to be neither exhaustive nor exclusive. Omission of a particular procedure does not imply that ARSAC will not approve an application for its use or that it is in any way unsatisfactory. ARSAC may review and update the procedure details within these notes periodically.

5.2 PET/CT evidence based guidelines published by the RCR and RCP [11] have been used by ARSAC to determine which PET procedures to include in the notes.

Considerations for diagnostic procedures

5.3 It is important that the administered activity for each individual exposure is optimised such that appropriate diagnostic information is obtained with the lowest practicable dose to the patient. This is the principle underlying optimisation.

5.4 IR(ME)R[2, 3] requires that employers regularly review and have available to operators diagnostic reference levels (DRLs). All procedures should be undertaken in accordance with departmental written protocols. Local DRLs should be specified in the written protocols.

5.5 The values for administered activity listed in these notes are to be considered as the national DRLs (NDRL) for investigations in adult patients of standard size eg 70kg. These levels are expected not to be exceeded for standard procedures when good and normal practice regarding diagnostic and technical performance is applied.

5.6 In many cases, it will be possible to administer activities less than the NDRL. This is encouraged in line with the optimisation principles above.

5.7 NDRL for CT exposures used as part of SPECT/CT and PET/CT procedures have been published and are available online: https://www.gov.uk/government/publications/diagnostic-radiology-national-diagnostic-reference-levels-ndrls/ndrl

5.8 The NDRL are to be regarded as guidelines and should be exceeded only in individual patients where clinical circumstances make it necessary, eg

patients who are very much overweight or unable to tolerate standard acquisition times. The guiding principle, however, remains that the activity administered should be the minimum consistent with acquiring adequate information from the investigation concerned.

5.9 Where administered activity is increased on the basis of an individual patient's weight, it is unnecessary to inform ARSAC. If such increased activities are used infrequently, they should be justified and recorded by the licenced practitioner. The requirement for this should be included in the employer's procedures. The actual activity administered must be recorded in the patient's medical or departmental records.

5.10 Where this becomes a regular process, but is still assessed for each individual patient, a basis for the increase in activity can be established and should be included in local protocols. This can then be applied by staff other than the licenced practitioner but the requirement to record the actual administered activity and the reason for the increase remains.

5.11 If, within the context of local circumstances (eg all patients for bone scans at the radiological installation have confirmed cancer and severe bone pain), all patients at a medical radiological installation will require a standard activity for a procedure higher than the NDRL, an amendment to the employer licence should be made to ARSAC, giving the justification for the increased activity. If agreed, this should be included within local written protocols

5.12 Many employers written protocols calculate the administered activity for radiopharmaceuticals dependant on the patient weight. ARSAC supports this, particularly for PET radiopharmaceuticals where patient specific administered activities are more common. ARSAC will accept applications with proposed administered activities indicated by weight eg MBq/kg. Values used should be based on published data and adapted for the capabilities of local equipment. This should be detailed in local protocols with the activity calculated for a 70kg person being less or equal to the NDRL stated in these notes.

5.13 Where applications are made for procedures by reference to functional groups or specific procedure codes within these notes, then the activities administered to patients should be those quoted in these notes or lower.

5.14 ARSAC expects routine clinical audits to be performed on the administered activity. Persistent administration of activities larger than those contained in these notes, without justification, would be cause for concern.

Considerations for therapeutic procedures

5.15 For treatments using unsealed sources, ARSAC considers the total activity administered to be a matter of clinical judgement by the responsible licensed practitioner. Where available, clinical guidelines should be taken into consideration.

5.16 IR(ME)R requires that practitioners ensure that exposures of target volumes are individually planned and their delivery appropriately verified taking into account that doses to non-target volumes and tissues must be as low as reasonably practicable and consistent with the intended radiotherapeutic purpose of the exposure. ARSAC recommends that:

(a) in cancer treatments with radioactive substances, the absorbed dose to the tumour, and to non-target volumes and tissues, following each administration should be measured and recorded, to permit subsequent optimisation of total doses

(b) for treatment of benign conditions or, where direct measurements are impossible, absorbed doses should be calculated or estimated and recorded

5.17 Applications for therapy administrations both in routine clinical practice and research, are therefore expected to specify what dosimetry will be performed, per course, on an individual patient basis. Employers should ensure that appropriate resources are available.

5.18 For treatments using sealed sources, where available, clinical guidelines should be taken into consideration for determining the prescription.

General techniques for dose reduction

5.19 A number of simple techniques can be used to reduce radiation dose. For example, many radiopharmaceuticals are excreted by the kidneys. Bladder doses can be minimised by drinking plenty of fluid and frequent bladder emptying.

5.20 Advice on the use of thyroid blocking agents is given in section 8.

5.21 Where two imaging investigations give equivalent information, and both are available to the patient within the time frame of their clinical management then, on radiation protection grounds, the investigation resulting in the lower dose should be selected.

5.22 In some cases, if the patient is healthy and cooperative, administered activity might be reduced and scan times increased. However, it is important that the diagnostic information produced is not compromised by any reduction in administered activity. An example might include lung scans for pregnant women.

5.23 Software programs (eg resolution recovery) that improve image quality may allow for a reduction in the administered activity while maintaining the required levels of diagnostic information. Where available, such programs should be used and optimised in local protocols.

Effective dose (ED)

5.24 The effective doses given in these notes have been calculated from the corresponding DRL using the methodology described in ICRP Publication 128 [12], using weighting factors from ICRP Publication 60 [13]. Revised weighting factors have been published in ICRP Publication 103 [14], but have yet to be applied to the ICRP models.

5.25 Although the concept of effective whole body dose was originally only intended for occupational risks, it provides a useful index when used in connection with radiopharmaceuticals.

5.26 The effective doses are based on clinically normal subjects and may vary considerably in pathological states. Caution should therefore be exercised in conditions where the abnormal retention of the radiopharmaceutical can result in a substantially higher absorbed radiation dose.

5.27 Information on radiation doses to patients from radiopharmaceuticals is provided in ICRP Publication 53 [15] and its addendums [16-18] and summarised in ICRP Publication 128 [12]. For those procedures not covered in ICRP publications, other published dosimetry estimates have been used[19-28].

5.28 Estimates of the dose to the uterus may be used as an indicative dose to the foetus in cases where pregnancy is known or suspected. Figures are derived from the literature, mostly from ICRP Publication 128. It should be noted that these figures do not include a component of dose from the cross-placental transfer of radiopharmaceuticals. IR(ME)R requires practitioners to consider whether the exposure could be delayed until it is confirmed whether the individual is pregnant, or the exposure can wait until the baby is born.

Functional groups

5.29 To simplify the application process, some of the procedures in table 5.1 have been organised into ‘functional groups’, relevant to patient pathology and physiology. Where all procedures within a functional group are required on a licence, the applicant can specify the functional group instead of listing individual procedures.

5.30 Procedures within the functional groups are listed in table 5.5 for imaging procedures and table 5.6 for non-imaging procedures.

Table 5.1: diagnostic procedures

Procedure code	Radio-nuclide	Chemical form	Investigation	Route of admin	DRL (MBq)	ED (mSv)	Dose to uterus (mGy)	Functional group	Old serials
111In-107-58	^{111}In	leucocytes	infection/inflammation imaging	IV	20	7.2	2.4	9	49a3
111In-131-132	^{111}In	pentetreotide	somatostatin receptor imaging	IV	110 220 SPECT	5.9 11.9	4.3 8.6	14	49a61i
111In-140-139	^{111}In	platelets	thrombus imaging	IV	20	7.8	1.9	10	49a5ii
111In-41-92	^{111}In	DTPA with non-absorbable compounds	oesophageal/gastric/intestinal motility studies	oral	12	3.8	2.0	6	49a1vii 49a6
123I-117-136	^{123}I	mIBG	sympathetic innervation imaging of the heart	IV	370	4.8[1]	3.7	1	53a5iv
123I-117-167	^{123}I	mIBG	tumour imaging	IV	400	5.2[1]	4.0	14	53a5iii
123I-93-142	^{123}I	iodide	thyroid imaging/uptake	oral or IV	2	0.6	0.02	23	53a1i
					20	6.1	0.17	11	53a1ii
123I-93-143	^{123}I	iodide	thyroid metastases imaging (after ablation)	oral (or IV)	400	10[5] (7.8)[5]	4.8 (4.8)	14	53a1iii
123I-96-15	^{123}I	ioflupane	brain imaging	IV	185	4.6[1]	2.6	4	53a71i
125I-84-101	^{125}I	human albumin	plasma volume	IV	0.2	0.04[1]	0.04	22	53b4iii
131I-93-142	^{131}I	iodide	thyroid imaging/uptake	oral	0.2	5.8	0.008	23	53c6i
131I-93-143	^{131}I	iodide	thyroid metastases imaging (after ablation)	oral (or IV)	400[6]	68[5] (52)[5]	18 18	14	53c6ii
14C-166-51	^{14}C	urea	H Pylori detection	oral	0.2	0.006	0.005	24	6a50

Procedure code	Radio-nuclide	Chemical form	Investigation	Route of admin	DRL (MBq)	ED (mSv)	Dose to uterus (mGy)	Functional group	Old serials
14C-79-19	^{14}C	glycocholic acid	breath tests	oral	0.4	0.14	0.06	24	6a 1
201Tl-157-83	^{201}Tl	thallous chloride	myocardial imaging	IV	80	11.2	4.0	1	81a1iv
201Tl-157-94	^{201}Tl	thallous chloride	parathyroid imaging	IV	80	11.2	4.0	11	81a1vi
51Cr-44-46	^{51}Cr	EDTA	GFR measurement	IV	3	0.006	0.008	25	24a4
51Cr-48-109	^{51}Cr	erythrocytes	red cell kinetics	IV	4	0.7	0.3	22	24a 1i 24a 1ii 24a 1iii
51Cr-48-48	^{51}Cr	erythrocytes	GI bleeding	IV	4	0.7	0.3	24	24a 1iv
75Se-1-7	^{75}Se	23-seleno-25-homotaurocholic acid (SeHCAT)	bile salt absorption	oral	0.4	0.3	0.3	20	34a 3
81mKr-74-75	^{81m}Kr	Gas	lung ventilation imaging	inhalation	6000	0.2	0.001	3	36a 1
99mTc-113-113	^{99m}Tc	MAG 3	renal imaging/renography	IV	100	0.7	1.2	8	43a13i
99mTc-125-92	^{99m}Tc	non-absorbable compounds	oesophageal/gastric/intestinal motility studies	oral	40	0.9	0.6	6	43a11i 43a11ii
99mTc-132-117	^{99m}Tc	pertechnetate	salivary gland imaging	IV	80	1.0	0.6	6	43a1iii
99mTc-132-142	^{99m}Tc	pertechnetate	thyroid imaging/uptake	IV	80 imaging	1.0	0.6	23	43a 1i
					40 uptake	0.5	0.3	11	43a 1ii
99mTc-132-39	^{99m}Tc	pertechnetate	ectopic gastric mucosa imaging (Meckel's)	IV	400	5.2	3	6	43a1iv
99mTc-132-42	^{99m}Tc	pertechnetate	first pass blood flow imaging	IV	800	10.4 (3[1])	6.5 (5.1[1])	1	43a1xvi

Procedure code	Radio-nuclide	Chemical form	Investigation	Route of admin	DRL (MBq)	ED (mSv)	Dose to uterus (mGy)	Functional group	Old serials
99mTc-137-11	^{99m}Tc	phosphonates and phosphates	bone imaging	IV	600 800 SPECT	2.9 3.9	3.7 5.0	5	43a4ii
99mTc-150-167	^{99m}Tc	sestamibi	tumour imaging	IV	900	8.1	7.0	14	43a15iv 43a15vi
99mTc-150-83	^{99m}Tc	sestamibi	myocardial imaging	IV	800[4] SPECT rest stress	7.2 6.3	6.2 5.8	1	43a15vii
99mTc-150-95	99mTc	sestamibi	parathyroid imaging and/or probe studies	IV	900	8.1	7.0	11	43a15i
99mTc-152-58	^{99m}Tc	sulesomab	infection/inflammation imaging	IV	750	6.0	4.4	9	43a18
99mTc-154-75	^{99m}Tc	technegas	lung ventilation imaging	inhalation	40	0.6	0.01	3	43a55
99mTc-156-83	^{99m}Tc	tetrofosmin	myocardial imaging	IV	800[4] SPECT rest stress	6.4 5.5	6.2 5.6	1	43w46v
99mTc-24-12	^{99m}Tc	colloid	bone marrow imaging	IV	400	3.6	0.4	5	43a7ii
99mTc-24-121	^{99m}Tc	colloid	sentinel node (breast) probe studies with or without imaging	interstitial/ peri-tumoural	20[2] 40	0.02 0.08[3]	0.001 0.003	15	43a7xi
99mTc-24-125	^{99m}Tc	colloid	sentinel node (melanoma) imaging and probe studies	interstitial/ peri-tumoural	40[2]	0.18	0.002	15	43a7xiii
99mTc-24-48	^{99m}Tc	colloid	GI bleeding	IV	400	3.6	0.4	6	43a7iv
99mTc-24-61	^{99m}Tc	colloid	lacrimal drainage	eye drops	4 (each eye)	0.04	–	13	43a7vi
99mTc-24-64	^{99m}Tc	colloid	liver and spleen imaging	IV	80 200 SPECT	0.7 1.8	0.1 0.2	7	43a7i

Procedure code	Radio-nuclide	Chemical form	Investigation	Route of admin	DRL (MBq)	ED (mSv)	Dose to uterus (mGy)	Functional group	Old serials
99mTc-24-76	^{99m}Tc	colloid	lymph node (lymphoedema) imaging	interstitial	20 (each limb)	0.09	0.001	2	43a7xvii
99mTc-24-92	^{99m}Tc	colloid	oesophageal/gastric/intestinal motility studies	Oral	40	0.9	0.6	6	43a7v
99mTc-30-133	^{99m}Tc	denatured erythrocytes	spleen imaging	IV	100	0.2	0.14	10	43a9
99mTc-33-112	^{99m}Tc	DMSA(III)	renal imaging	IV	80	0.7	0.4	8	43a6iii
99mTc-40-113	^{99m}Tc	DTPA	renal imaging/renography	IV	300	1.5	2.4	8	43a5i
99mTc-40-42	^{99m}Tc	DTPA	first pass blood flow studies	IV	800	3.9	6.3	4	43a5iii
99mTc-40-46	^{99m}Tc	DTPA	GFR measurement	IV	10	0.05	0.08	25	43a5xi
99mTc-40-75	^{99m}Tc	DTPA	lung ventilation imaging	aerosol inhalation	80	0.5	0.5	3	43a5xix
99mTc-43-15	^{99m}Tc	ECD	brain imaging	IV	750	5.8	6.9	4	43w49
99mTc-48-10	^{99m}Tc	erythrocytes	blood pool imaging (MUGA) /probe studies	IV	800	5.6	3.1	1	43a10iv
99mTc-48-48	^{99m}Tc	erythrocytes	GI bleeding	IV	400	2.8	1.6	6	43a10iii
99mTc-50-15	^{99m}Tc	exametazime	brain imaging	IV	750	7.0	5.0	4	43a17
99mTc-51-58	^{99m}Tc	exametazime labelled leucocytes	infection/inflammation imaging	IV	200	2.2	0.7	9	43a14
99mTc-5-70	^{99m}Tc	albumin macro-aggregates or microspheres	lung perfusion imaging	IV	100 200 SPECT	1.1 2.2	0.2 0.4	3	43a3i
99mTc-5-71	^{99m}Tc	albumin macro-aggregates or microspheres	lung perfusion imaging with venography	IV	160	1.8	0.4	3	43a3ii
99mTc-5-73	^{99m}Tc	albumin macro-aggregates or microspheres	lung shunt assessment	IV / IA	150	1.6	0.3	3	43a3xiv

Procedure code	Radio-nuclide	Chemical form	Investigation	Route of admin	DRL (MBq)	ED (mSv)	Dose to uterus (mGy)	Functional group	Old serials
99mTc-84-10	^{99m}Tc	human albumin	blood pool imaging (MUGA) /probe studies	IV	800	4.9	3.8	1	43a2vii
99mTc-88-132	^{99m}Tc	HYNIC-Ty3-octreotide	somatostatin receptor imaging	IV	740	3.7	3.0	14	43w70
99mTc-91-44	^{99m}Tc	iminodiacetate	functional biliary system imaging	IV	150	2.4	1.7	7	43a8

Notes

[1] with the thyroid blocked

[2] the activity should be increased in order to give a retained activity of approximately 10MBq at the time of surgery if probe studies, with or without imaging, are to be undertaken on the day following administration

[3] effective dose based on 18 hours from injection to surgery

[4] for combined rest–stress protocols carried out on a single day the total activity administered should not exceed 800MBq for planar imaging. For rest–stress protocols with SPECT, activity administered should not exceed 1600MBq. Two-day protocols are recommended on the basis of superior image quality, but it is recognised that these may not be practicable

[5] effective dose calculated without contribution from thyroid

[6] activities of ^{131}I greater than 30MBq should be considered as therapy administration for radiation protection purposes

Table 5.2: diagnostic procedures – positron emission tomography

Procedure code	Radio-nuclide	Chemical form	Investigation	Route of admin	DRL (MBq)	Activity by weight[1] (MBq/kg)	ED (mSv)	Dose to uterus (mGy)	Old serial
11C-20-52	^{11}C	choline chloride	hepatocellular cancer imaging	IV	370		1.6	0.7	6b74i
11C-20-105	^{11}C	choline chloride	prostate cancer imaging	IV	370		1.6	N/A	6b74
11C-111-17	^{11}C	L-methyl-methionine	brain tumour imaging	IV	400		3.3	2.7	6b2i
11C-111-96	^{11}C	L-methyl-methionine	parathyroid tumour imaging	IV	740		6.1	5.0	6b2ii
13N-6-83	^{13}N	ammonia	myocardial imaging	IV	550		2.0	1.4	7a22i
18F-19-52	^{18}F	choline	hepatocellular cancer imaging	IV	370	4.0	7.4	5.6	9a44ii
18F-19-105	^{18}F	choline	prostate cancer imaging	IV	370	4.0	7.4	N/A	9a44
18F-57-17	^{18}F	FDG	brain tumour imaging	IV	250		4.8	4.5	9a21iii
18F-57-37	^{18}F	FDG	differential diagnosis of dementia	IV	250		4.8	4.5	9a21v
18F-57-43	^{18}F	FDG	focal epilepsy	IV	250		4.8	4.5	9a21vi
18F-57-58	^{18}F	FDG	infection/inflammation imaging	IV	400	4.5[2]	7.6	7.2	9a21iv
18F-57-83	^{18}F	FDG	myocardial imaging	IV	400		7.6	7.2	9a21vii
18F-57-169	^{18}F	FDG	whole body tumour imaging	IV	400	4.5[2]	7.6	7.2	9a21i
18F-61-27	^{18}F	florbetaben	cerebral amyloid assessment	IV	300		5.8	4.9	9a59
18F-62-27	^{18}F	florbetapir	cerebral amyloid assessment	IV	370		6.9	5.8	9a40
18F-66-11	^{18}F	fluoride	bone imaging	IV	250		4.3	3.3	9a23i
18F-67-17	^{18}F	fluoroethyltyrosine	brain tumour imaging	IV	370		5.9	6.3	9a52
18F-68-87	^{18}F	fluoro-L-DOPA	neuroendocrine tumour imaging	IV	280	4.0	7.0	7.8	9a22iii

Procedure code	Radio-nuclide	Chemical form	Investigation	Route of admin	DRL (MBq)	Activity by weight[1] (MBq/kg)	ED (mSv)	Dose to uterus (mGy)	Old serial
18F-68-135	^{18}F	fluoro-L-DOPA	suspected congenital hyperinsulinism	IV	280	4.0	7.0	7.8	9a22i
18F-71-27	^{18}F	flutemetamol	cerebral amyloid assessment	IV	185		5.9	4.6	9a42
68Ga-37-132	^{68}Ga	DOTATATE / DOTATOC / DOTANOC	somatostatin receptor imaging	IV	250		6.4 TATE 4.2 NOC 5.8 TOC	3.7	31b29
68Ga-141-105	^{68}Ga	PSMA	prostate cancer imaging	IV	200		4.6	N/A	31b33
82Rb-18-83	^{82}Rb	chloride	myocardial imaging	IV	2220		2.4	2.2	37a20i

Notes

[1] these values should be used as a guide only, with the administered activity optimised locally. Further guidance on administering by weight is provided in 5.9 to 5.12

[2] for systems that apply a PET bed overlap of ≤30 %, the minimum recommended administered activity is calculated as follows:
FDG (MBq) = 14 (MBq·min·bed^{-1}·kg^{-1}) × patient weight (kg)/emission acquisition duration per bed position (min·bed^{-1})
for systems that apply a PET bed overlap of >30 %, the minimum FDG administered activity is calculated as follows:
FDG (MBq) = 7 (MBq·min·bed^{-1}·kg^{-1}) × patient weight (kg)/emission acquisition duration per bed position (min·bed^{-1}) [29]

Table 5.3: therapeutic procedures with unsealed sources

Procedure code	Radionuclide	Chemical form	For treatment of	Route of admin	Serial
131I-117-156	^{131}I	mIBG	treatment of malignancy	IV	0C10
131I-93-145	^{131}I	iodide	treatment of benign thyroid disease	IV or oral	0C 2 0C 3
131I-93-150	^{131}I	iodide	treatment of carcinoma of thyroid	IV or oral	0C 4
153Sm-46-146	^{153}Sm	EDTMP	treatment of bone metastases	IV	0C38
169Er-24-144	^{169}Er	colloid	treatment of arthritis	intra-articular	0C 8
177Lu-37-157	^{177}Lu	DOTATATE / DOTATOC / DOTANOC	treatment of neuroendocrine malignancy	IV	0C65
186Re-24-144	^{186}Re	colloid	treatment of arthritis	intra-articular	0C21
186Re-82-146	^{186}Re	HEDP	treatment of bone metastases	IV	0C39
223Ra-32-147	^{223}Ra	dichloride	treatment of bone metastases in castration resistant prostate cancer	IV	0C54
32P-136-163	^{32}P	phosphate	treatment of polycythemia vera and related disorders	IV or oral	0C 5
89Sr-18-146	^{89}Sr	chloride	treatment of bone metastases	IV	0C 9
90Y-27-144	^{90}Y	colloidal silicate/citrate	treatment of arthritis	intra-articular	0C 6
90Y-37-157	^{90}Y	DOTATATE / DOTATOC / DOTANOC	treatment of neuroendocrine malignancy	IV	0C66
90Y-89-155	^{90}Y	ibritumomab tiuxetan (Zevalin)	treatment of lymphoma	IV	0C53
90Y-118-153	^{90}Y	microspheres	treatment of hepatic malignancy	intra-arterial	0C35

Note

the activity per administration is a matter for clinical judgement; caution is advised in treatments for non-malignant disease especially in young patients

Table 5.4: Procedures with sealed sources

Procedure code	Radionuclide	Physical form	Indication	Old serial
106Ru-52-151	^{106}Ru	eye plaque	treatment of eye diseases	0T30
125I-148-164	^{125}I	seeds	treatment of prostate cancer	0T29
125I-148-67[1]	^{125}I	seeds	localisation of tumours	N/A
137Cs-7-164	^{137}Cs	appliances	treatment of prostate cancer	0T23
192Ir-169-148	^{192}Ir	wire/appliances	treatment of breast cancer	0T25
192Ir-169-154	^{192}Ir	wire/appliances	treatment of lung cancer	0T25
192Ir-169-159	^{192}Ir	wire/appliances	treatment of oesophageal cancer	0T25
192Ir-169-165	^{192}Ir	wire/appliances	treatment of rectal cancer	0T25
192Ir-169-166	^{192}Ir	wire/appliances	treatment of skin cancers and benign skin diseases	0T25
192Ir-7-152	^{192}Ir	appliances	treatment of gynaecological cancers	0T25
192Ir-7-164	^{192}Ir	appliances	treatment of prostate cancer	0T25
90Sr-7-151	^{90}Sr	appliances	treatment of eye diseases	0T24
90Y-144-162	^{90}Y	rods	treatment of pituitary tumours	0T21

Notes

the target volume dose and dose rate are a matter for clinical judgement for therapeutic procedures

[1] – This procedure involves the insertion and later removal of a seed for diagnostic purposes. The dose delivered will vary dependant on the activity of the seed, the number of seeds inserted, the time to removal and the volume of tissue excised. This procedure should be applied for under the diagnostic section of the application forms to include details of the local protocol and associated dose estimates.

Table 5.5: imaging groups

Group 1 I – cardiac

99mTc-48-10	^{99m}Tc	erythrocytes	blood pool imaging (MUGA)/probe studies
99mTc-84-10	^{99m}Tc	human albumin	blood pool imaging (MUGA)/probe studies
99mTc-132-42	^{99m}Tc	pertechnetate	first pass blood flow imaging
99mTc-150-83	^{99m}Tc	sestamibi	myocardial imaging
99mTc-156-83	^{99m}Tc	tetrofosmin	myocardial imaging
123I-117-136	^{123}I	mIBG	sympathetic innervation imaging of the heart
201Tl-157-83	^{201}Tl	thallous chloride	myocardial imaging

Group 2 I – vascular

99mTc-24-76	^{99m}Tc	colloid	lymph node (lymphoedema) imaging

Group 3 I – lung

81mKr-74-75	^{81m}Kr	gas	lung ventilation imaging
99mTc-5-70	^{99m}Tc	albumin macro-aggregates or microspheres	lung perfusion imaging
99mTc-5-71	^{99m}Tc	albumin macro-aggregates or microspheres	lung perfusion imaging with venography
99mTc-5-73	^{99m}Tc	albumin macro-aggregates or microspheres	lung shunt assessment
99mTc-40-75	^{99m}Tc	DTPA	lung ventilation imaging
99mTc-154-75	^{99m}Tc	technegas	lung ventilation imaging

Group 4 I – brain

99mTc-40-42	^{99m}Tc	DTPA	first pass blood flow studies
99mTc-43-15	^{99m}Tc	ECD	brain imaging
99mTc-50-15	^{99m}Tc	exametazime	brain imaging
123I-96-15	^{123}I	ioflupane	brain imaging

Group 5 I – bone/joint

99mTc-24-12	^{99m}Tc	colloid	bone marrow imaging
99mTc-137-11	^{99m}Tc	phosphonates and phosphates	bone imaging

Group 6 I – gastrointestinal

99mTc-24-48	^{99m}Tc	colloid	GI bleeding
99mTc-24-92	^{99m}Tc	colloid	oesophageal/gastric/intestinal motility studies
99mTc-48-48	^{99m}Tc	erythrocytes	GI bleeding
99mTc-125-92	^{99m}Tc	non-absorbable compounds	oesophageal/gastric/intestinal motility studies
99mTc-132-39	^{99m}Tc	pertechnetate	ectopic gastric mucosa imaging (Meckel's)
99mTc-132-117	^{99m}Tc	pertechnetate	salivary gland imaging
111In-41-92	^{111}In	DTPA with non-absorbable compounds	oesophageal/gastric/intestinal motility studies

Group 7 I – hepatobiliary

99mTc-24-64	^{99m}Tc	colloid	liver and spleen imaging
99mTc-91-44	^{99m}Tc	iminodiacetate	functional biliary system imaging

Group 8 I – genitourinary

99mTc-33-112	^{99m}Tc	DMSA(III)	renal imaging
99mTc-40-113	^{99m}Tc	DTPA	renal imaging/renography
99mTc-113-113	^{99m}Tc	MAG3	renal imaging/renography

Group 9 I – infection/inflammation

99mTc-51-58	^{99m}Tc	exametazime labelled leucocytes	infection/inflammation imaging
99mTc-152-58	^{99m}Tc	sulesomab	infection/inflammation imaging
111In-107-58	^{111}In	leucocytes	infection/inflammation imaging

Group 10 I – haematology

99mTc-30-133	^{99m}Tc	denatured erythrocytes	spleen imaging
111In-140-139	^{111}In	platelets	thrombus imaging

Group 11 I – endocrine

99mTc-132-142	^{99m}Tc	pertechnetate	thyroid imaging/uptake
99mTc-150-95	^{99m}Tc	sestamibi	parathyroid imaging and/or probe studies
123I-93-142	^{123}I	iodide	thyroid imaging/uptake
201Tl-157-94	^{201}Tl	thallous chloride	parathyroid imaging

Group 13 I – lacrimal

99mTc-24-61	^{99m}Tc	colloid	lacrimal drainage

Group 14 I – tumour

99mTc-88-132	^{99m}Tc	HYNIC-Ty3-octreotide	somatostatin receptor imaging
99mTc-150-167	^{99m}Tc	sestamibi	tumour imaging
111In-131-132	^{111}In	pentetreotide	somatostatin receptor imaging
123I-93-143	^{123}I	iodide	thyroid metastases imaging (after ablation)
123I-117-167	^{123}I	mIBG	tumour imaging
131I-93-143	^{131}I	iodide	thyroid metastases imaging (after ablation)

Group 15 I – sentinel node

99mTc-24-121	^{99m}Tc	colloid	sentinel node (breast) probe studies with or without imaging
99mTc-24-125	^{99m}Tc	colloid	sentinel node (melanoma) imaging and probe studies

Table 5.6: non-imaging groups

Group 20 NI – absorption

75Se-1-7	^{75}Se	23-seleno-25-homo-tauro-cholate (SeHCAT)	bile salt absorption

Group 22 NI – haematology

51Cr-48-109	^{51}Cr	erythrocytes	red cell kinetics
125I-84-101	^{125}I	human albumin	plasma volume

Group 23 NI – endocrine

99mTc-132-142	^{99m}Tc	pertechnetate	thyroid imaging/uptake
123I-93-142	^{123}I	iodide	thyroid imaging/uptake
131I-93-142	^{131}I	iodide	thyroid imaging/uptake

Group 24 NI – gastrointestinal

14C-79-19	^{14}C	glycocholic acid	breath tests
14C-166-51	^{14}C	urea	H pylori detection
51Cr-48-48	^{51}Cr	erythrocytes	GI bleeding

Group 25 NI – genitourinary

51Cr-44-46	^{51}Cr	EDTA	GFR measurement
99mTc-40-46	^{99m}Tc	DTPA	GFR measurement

Section 6

Investigations in children and young persons

Introduction

6.1 In diagnostic investigations in children, particular care must be exercised to ensure that the most appropriate investigation is chosen to answer the clinical problems. When considering the choice of investigation, factors which should be considered are risk/benefit ratios, economic cost, invasiveness and radiation dose.

6.2 The radiation dose from the administration of radioactive substances, when used in the appropriate clinical situation, is justifiable assuming the information gained cannot be obtained using diagnostic procedures with either a lower or no radiation exposure and/or a less invasive procedure. Where appropriate and practical, an investigation which does not involve ionising radiation should be chosen, assuming access to such procedures is available within a timeframe appropriate to the clinical management of the patient.

6.3 Nuclear medicine departments designed for adults often provide a poor environment for children. Successful nuclear medicine procedures for children require some simple modifications to the environment and normal procedures. Comprehensive practical information can be found on the EANM website under each specific examination: www.eanm.org. Consideration should be given as to whether it would be more appropriate to refer the child to a specialist centre.

6.4 Procedures involving children always take longer than the equivalent adult procedure. Children tend to be less predictable and more varied in their response than adults. It is advisable to schedule at least 50% extra time for paediatric procedures.

6.5 All staff involved in paediatric procedures should be familiar with local arrangements. Delay in carrying out parts of the procedure can often lead to the child being less cooperative. This can in turn lead to an increase in the time taken for the procedure or in some cases the procedure may not be successful.

6.6 The parent/guardian of the child should be fully informed about the procedure in advance of the imaging appointment. Leaflets providing full information on the particular examination should be given to the parent/guardian at the time of the appointment. On the day of the examination the entire procedure should be explained to the child and accompanying adult.

Activity administered

6.7 The activity administered should be the minimum consistent with obtaining a diagnostic result. As this is the same principle which is applied to adults, the normal activity administered to adults should be used as a baseline for the calculation of activity to be administered to children weighing less than 70kg. Advice has been provided by the Paediatric Task Group of the EANM[30]. This is presented in table 6.1. An update to this guidance was released in the form of a new paediatric dosage card in 2007[31] and further amended in 2014[32] to provide weight-independent scaling factors dependent on the class of investigation. This was supported by further guidance detailing scaling information for ^{18}F-FDG PET imaging[33].

6.8 It is recommended that for children or young persons, body weight should always be measured. With the exception of PET imaging, the adult administered activity should then be scaled down as shown in table 6.1. This will produce an image quality and an imaging time comparable with that expected for adults by maintaining the same image count density. The resulting effective dose by weight when compared to an adult will be higher.

6.9 Centres using PET for paediatric patients, while being cognisant of the most recent guidance from the EANM, should optimise the administered activity locally based on equipment settings and clinical reporting preferences. For ^{18}F-FDG whole body tumour imaging it is recommended to scale by body weight with the same scheme as used for adults. ARSAC is of the view that this area requires further research as technology and techniques are rapidly evolving.

Table 6.1 scaling of adult administered activity for children or young persons by body weight

Weight (kg)	Fraction of adult administered activity	Weight (kg)	Fraction of adult administered activity	Weight (kg)	Fraction of adult administered activity
3	0.10	22	0.50	42	0.78
4	0.14	24	0.53	44	0.80
6	0.19	26	0.56	46	0.82
8	0.23	28	0.58	48	0.85
10	0.27	30	0.62	50	0.88
12	0.32	32	0.65	52–54	0.90
14	0.36	34	0.68	56–58	0.92
16	0.40	36	0.71	60–62	0.96
18	0.44	38	0.73	64–66	0.98
20	0.46	40	0.76	68	0.99

6.10 As a general guide, activities less than 10% of the value of the equivalent adult activity should not be administered. For most purposes this simple approach will be adequate. For a number of procedures, however, if adequate image quality is to be achieved, the administered activity should be not less than that set out in table 6.2.

Table 6.2 recommended minimum administered activity for children

Radiopharmaceutical	Investigation	Minimum activity (MBq)
^{99m}Tc-DTPA	renal imaging/renography	20
^{99m}Tc-DMSA(III)	renal imaging	15
^{99m}Tc-MAG3	renal imaging/renography	15
^{99m}Tc-phosphonates and phosphates	bone imaging	40
^{99m}Tc-colloid	liver and spleen imaging	15
^{99m}Tc-colloid	bone marrow imaging	20
^{99m}Tc-colloid	oesophageal/gastric/intestinal motility studies	10
^{99m}Tc-denatured erythrocytes	spleen imaging	20
^{99m}Tc-normal erythrocytes	blood pool imaging/probe studies	80
^{99m}Tc-pertechnetate	first pass blood flow imaging	80
^{99m}Tc-pertechnetate	ectopic gastric mucosa imaging (Meckel's)	20
^{99m}Tc-pertechnetate	thyroid imaging/uptake	10
^{99m}Tc human albumin macroaggregates or microspheres	lung perfusion imaging	10
^{99m}Tc exametazime	brain imaging	100
^{99m}Tc exametazime labelled leucocytes	infection/inflammation imaging	40
^{99m}Tc-iminodiacetate	functional biliary system imaging	20
^{99m}Tc-tetrofosmin	myocardial imaging	50
^{99m}Tc-sestamibi	myocardial imaging	50
^{123}I-iodide	thyroid imaging/uptake	3
^{123}I mIBG	tumour imaging	70

Imaging technique

6.11 There should be specific protocols in place for imaging children in nuclear medicine departments. These should include the choice of collimator, imaging parameters and views for the various examinations. For example, in a bone scan, it is essential that the limbs should be imaged separately from the torso unless a whole body scan protocol is used. In this case, specific localised views of the knees and any abnormal focal areas are essential.

Sedation

6.12 A cooperative child will not normally require sedation or general anaesthetic[34] Sedation may be required for long examinations when movement should not occur. Before sedating the child, consideration should be given to the effect that sedation may have on function. This applies especially to SPECT studies, PET/CT[35] and pinhole views of the hips in the young child.

6.13 Sedation or general anaesthetic may, in some cases, be considered necessary, but this should be based on an individual assessment. Children in pain require analgesia and, if this is adequate, sedation may not be required.

Radiation protection

6.14 When a radiopharmaceutical is administered that is excreted by the kidneys, simple protective measures such as encouraging a high fluid intake, active bladder emptying or frequent nappy changing will enhance the process of elimination of the radiopharmaceutical and reduce gonadal and bladder doses. Additionally, the appropriate choice of radiopharmaceutical can result in a major reduction in radiation dose.

6.15 Where appropriate, thyroid blocking agents should be administered. Further information is provided in section 8.

Section 7

Pregnancy, conception, and breastfeeding

Pregnancy

7.1 When it is necessary to administer radioactive substances to an individual of childbearing potential, the radiation exposure should be the minimum consistent with acquiring the desired clinical information, whether the individual is known to be pregnant. Alternative techniques which do not involve ionising radiation should always be considered. Such consideration is particularly important when using radionuclides with long half-lives.

7.2 Only investigations which are imperative should be conducted during pregnancy. Investigations carried out on pregnant patients result in radiation doses to both the patient and the foetus.

7.3 Any individual of childbearing potential undergoing procedures involving radiopharmaceuticals should be asked whether they are or might be pregnant. The employer's procedures should describe when and how pregnancy enquires should be made and specify the age range of individuals who should be asked (eg 12 to 55 years old).

7.4 If the possibility of pregnancy cannot be excluded, the patient should be asked whether their menstrual period is overdue. Low dose procedures, in which the foetal dose is likely to be below 10mGy, can continue to be undertaken, provided that the period is not overdue. For procedures resulting in higher foetal doses, exceeding 10mGy, the procedure should only be undertaken during the first 10 days of the menstrual cycle[36]. If necessary, a pregnancy test can be performed to confirm the patient is not pregnant in accordance with the employer's procedure.

7.5 Where a patient is probably or definitely pregnant, the justification for the exposure should be considered by the practitioner following consultation with the multidisciplinary team responsible for the patient. It should be noted that a procedure of clinical benefit to the pregnant patient may be of indirect benefit to the foetus.

7.6 If the practitioner decides that the procedure should be undertaken in a pregnant patient, the exposure to both the patient and foetus must be optimised. Any reduction in administered activity must not impact on the likelihood of achieving a diagnostic outcome.

7.7 The response to pregnancy enquires should be documented as evidence that the employer's procedure has been followed.

7.8 Estimates of dose to the uterus are included in tables 5.1 and 5.2, for risk assessment purposes. No component of dose from cross-placental transfer of radiopharmaceuticals is included in these values. These dose estimates refer to early pregnancy, before organogenesis has proceeded far enough for there to be concentrations of radioactivity in particular foetal organs.

7.9 ARSAC recommends that where foetal doses exceed 1mGy, the practitioner should pay particular attention to the justification of these exposures. A dose up to 1mGy corresponds to a level of risk comparable to that due to variations in natural background radiation. The available evidence[37] suggests that the risk of an adverse effect (eg childhood cancer) from a dose of 1mGy is about 1 in 17,000.

7.10 Further information regarding biological effects after prenatal irradiation has been published by the ICRP[38].

Conception

7.11 There is no evidence that pre-conceptual irradiation of an individual can cause any abnormality in their offspring[37]. ARSAC does not consider that advice needs to be given concerning avoidance of conception for the majority of routine diagnostic administrations of radioactive substances.

7.12 The foetal thyroid gland is known to concentrate radioiodine avidly during the second and third trimesters of pregnancy; during this period the quantity of radioactivity within the pregnant patient should not exceed 0.1MBq of ^{125}I or 0.03MBq of ^{131}I. Consideration of the diagnostic procedure 125I-84-101 (0.2MBq ^{125}I human albumin) has shown that this will decrease to below 0.1MBq in 15 days: it is, therefore, unnecessary to issue any advice to delay pregnancy following this procedure.

7.13 Of the diagnostic imaging procedures listed in table 5.1, only 131I-93-143 (^{131}I-iodide, thyroid metastases imaging after ablation) requires advice to delay pregnancy. Any administered activity of ^{131}I greater than 30MBq should be considered as a 'therapy' administration for radiation protection purposes; advice on pregnancy in table 7.1 should be followed.

7.14 In some circumstances it will be necessary to advise patients to avoid conceiving for a period following the administration of long-lived radioactive substances.

7.15 The administration of therapeutic doses of ionic forms of longer-lived radionuclides is, however, a possible source of concern because of the appearance of larger quantities of such radionuclides in ejaculate and in sperm[39]. Following the therapeutic administration of ^{131}I-iodide, ^{32}P-phosphate or ^{89}Sr-chloride it is advisable to instruct individuals to avoid conception for four months as this is greater than the lifecycle of a sperm cell.

7.16 Individuals should be advised to avoid becoming pregnant for a period following therapy administration as given in table 7.1. The administration of activities smaller than those indicated in table 7.1 does not imply that the advisory period specified may be reduced.

Table 7.1 period following therapy administration for which individuals should be advised to avoid pregnancy

Radioactive substance	For treatment of	All activities up to (MBq)	Avoid pregnancy (months)
^{32}P-phosphate	polycythaemia and related disorders	200	3
^{89}Sr-chloride	bone metastases	150	24
^{90}Y-colloid	arthritis	400	0
^{131}I-iodide	benign thyroid disease	800	6 (at least)
^{131}I-iodide	thyroid cancer	6000	6 (at least)
^{131}I mIBG	malignancy	7500	3
^{153}Sm-colloid	bone metastases	2600	1
^{169}Er-colloid	arthritis	400	0

Diagnostic administrations to individuals who are breastfeeding or lactating

7.17 Before administering a radioactive substance to a patient who is lactating (eg breastfeeding, or expressing milk), consideration should be given as to whether:

(a) the test could reasonably be delayed

(b) the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of radioactivity in breast milk

(c) appropriate quality control measurements have been made (see 7.20)

7.18 Where the patient is breastfeeding, specific written instructions must be given, and these instructions should be recorded in their medical records.

7.19 Information on secretion of radioactivity into human breast milk is limited, and for most radiopharmaceuticals the advice given here is based on small numbers of measurements.

7.20 The presence of radionuclide impurities or free ions, such as pertechnetate or iodide, will incur additional radiation dose. ^{123}I should not be administered to breastfeeding patients unless it is pure (containing no ^{124}I or ^{125}I).

7.21 In addition to any potential radiation dose to the infant from ingestion of breastmilk, the external exposure from close contact with the patient for prolonged periods of time during feeding should also be considered.

7.22 Advice is given in the Medical and Dental Guidance Notes[40] that special precautions or restrictions are only required when patients have been administered more than 30MBq of ^{131}I, 120MBq of ^{111}In-pentetreotide, 150MBq of ^{201}Tl-thallous chloride, or 800MBq of ^{99m}Tc myocardial perfusion agents, such as sestamibi or tetrofosmin. Advice is also given for administrations of more than 10MBq of ^{111}In-labelled leucocytes; however, it is not recommended to administer greater than 10MBq to breastfeeding patients. Precautions may also be necessary after administration of positron emitting radionuclides.

7.23 Precautions should be taken to minimise the radiation dose to the breastfed infant from external and internal sources. A dose constraint of 1mSv is recommended.

7.24 Table 7.2 lists breastfeeding interruption times for a limited range of radiopharmaceuticals. The interruption times include an assessment of the dose to the infant from ingestion and external irradiation. The interruption time is calculated such that the dose to the infant should be less than 1mSv from a single administration. The annual dose to the infant should also be less than 1mSv and consideration of extending the interruption times should be given if multiple exposures are expected.

7.25 Breastfeeding may be restarted immediately after the interruption time has elapsed since administration of the radiopharmaceutical. In many cases this time is zero, and no interruption of feeding is strictly necessary. The principle of 'as low as reasonably practicable' (ALARP), however, indicates that even where no interruption time is recommended, it is usually appropriate to express the milk completely once and discard it.

7.26 For some radiopharmaceuticals the required interruption time would be so long that the patient should be advised to stop breastfeeding altogether.

7.27 Specific advice should be given as follows:

(a) wherever possible, at least one feed should be expressed and appropriately stored in advance of the administration

(b) the infant should be breastfed just before the administration

(c) three to four hours after the administration, the breastfeeding patient should express as much milk as possible - this milk should be discarded and alternatives used instead

(d) breastfeeding should not resume until after a total period of interruption as given in table 7.2, or as calculated from measured samples. During the period of interruption, milk should be regularly expressed as completely as possible and discarded

(e) breastfeeding can be undertaken following subsequent pregnancies

7.28 The interruption times in table 7.2 do not apply during the period of early lactation when colostrum is being secreted. During that period, feeding should be interrupted until measurements on milk samples demonstrate that it is safe to recommence.

7.29 The dose to the infant may be estimated by measuring the radioactive concentration in a sample (or in successive samples) of the breast milk.

7.30 ICRP Publication 72[41] details a method for the calculation of dose following the ingestion of radioactivity that can be used to provide an estimate of the dose to infants.

Table 7.2 breastfeeding interruption times by radioactive substance administered

Radioactive substance	Activity administered to mother (MBq)	Feeding interruption time (hours)
^{32}P phosphate	Any	STOP
^{18}F FDG	400	1
^{51}Cr EDTA	3	0
^{81m}Kr gas	6000	0
^{99m}Tc-pertechnetate	80 800	30 57
^{99m}Tc human albumin macroaggregates or microspheres	100 200	13 20
^{99m}Tc normal erythrocytes[1]	800	20
^{99m}Tc DTPA	300 800	0 5
^{99m}Tc DMSA(III)	80	0
^{99m}Tc-iminodiacetate	150	0
^{99m}Tc exametazime	500	0
^{99m}Tc-sulesomab	750	11
^{99m}Tc MAG3	100 200	0 2
^{99m}Tc sestamibi	400 900	0 3
^{99m}Tc colloid	80	0
^{99m}Tc phosphates and phosphonates	800	0
^{111}In leucocytes	10	0
^{111}In pentetreotide	220	60
^{123}I iodide	20	42
^{123}I mIBG	400	25
^{125}I human albumin	Any	STOP
^{131}I-iodide	Any	STOP
^{201}Tl-thallous chloride	80	10

Notes [1] for labelled normal erythrocytes the figures will be sensitive to changes in the labelling efficiency, which can vary substantially

7.31 External measurements of dose rate at 0.1m from the patient's torso may be used to estimate the external component of the exposure. The effective dose from the administration without any restriction on close contact may be calculated by multiplying the maximum external dose rate by the effective exposure time[42, 43].

7.32 Values of effective exposure time from commonly used radioactive substances are listed in table 7.3. The effective exposure time assumes a total contact time of 9 hours in a 24 hour period[44] consisting of 35 minutes in close contact at the start of each hour for the first 8 hours after radioactive substance administration, 35 minutes at the start of each fourth hour for the next 12 hours (modelling feeding times overnight), and 35 minutes at the start of each hour for the remaining 4 hours.

7.33 As the dose rate from the patient reduces over time through physical decay and biological excretion, the effective dose to the infant will also reduce. Estimates of interruption times based on physical decay will remove the need for repeated dose rate measurements from the patient.

7.34 Restrictions may be relevant for patients who are bottle feeding infants, where no dose is expected from ingestion.

Table 7.3 effective exposure time by radioactive substances administered

Radioactive substance	Effective exposure time (h)
^{18}F FDG	1.8
^{51}Cr EDTA	2.4
^{99m}Tc (all compounds)	3.9
^{111}In leucocytes	35.9
^{111}In-pentetreotide	10.9
^{123}I iodide (euthyroid)	4.2
^{123}I iodide (hyperthyroid)	5.5
^{123}I mIBG	4.4
^{131}I iodide (euthyroid)	27.4
^{131}I iodide (hyperthyroid)	32.2
^{201}Tl thallous chloride	30.2

7.35 The internal component of the effective dose(x) can be calculated using the following formula[42] which assumes a mono-exponential decrease of activity concentration with time:

$$x = \frac{D_{max}}{e^{\left\{\ln 2 \cdot \left(\frac{P - t_c}{t_{½max}}\right)\right\}}}$$

Where:

D_{max} = maximum value of effective dose to the infant (mSv) [42, 45, 46] (corrected for ARSAC DRL)

P = breastfeeding interruption time (hours)

t_c = time of first feed following administration of radioactive substance assuming no interruption (set at 3 hours, using a feeding interval of 4 hours and a feed 1 hour prior to administration)

$t_{½max}$ = maximum value of effective half-life (hours)

7.36 Table 7.4. summarises values of maximum effective half-life taken from published data[47-51] that may be used in this calculation.

Table 7.4 maximum effective half-life by radioactive substance administered

Radioactive substance	Maximum effective half-life (h)
^{18}F FDG	0.89
^{51}Cr EDTA	11
^{99m}Tc pertechnetate	8.26
^{99m}Tc human albumin macroaggregates or microspheres	7.01
^{99m}Tc phosphonates	6.83
^{99m}Tc DTPA	5
^{99m}Tc DMSA (III)	5.9
^{99m}Tc colloid	8.3
^{99m}Tc iminodiacetate	9.14
^{99m}Tc erythrocytes	9.5
^{99m}Tc MAG3	5
^{99m}Tc sestamibi	6.73
^{99m}Tc exametazime	3.77
^{99m}Tc sulesomab	3.14
^{111}In leucocytes	134
^{111}In pentetreotide	10.05
^{123}I iodide	10.4
^{123}I mIBG	8.56
^{131}I iodide	11.1
^{201}Tl chloride	43

Therapeutic administration to individuals who are breastfeeding or lactating

7.37 Whilst breastfeeding is completely contraindicated for therapeutic procedures using radionuclides which are excreted in breast milk (eg ^{I31}I for treatment of thyrotoxicosis or thyroid cancer), unusually there may be instances where, despite cessation of breastfeeding, continued lactation may result in significant dose to breast tissue. In the example of ^{131}I, ICRP Publication 95[52] gives the equivalent dose to the breast tissue (in the euthyroid case)

as 1.3 x10^{-9}Sv.Bq^{-1} for the lactating breast - an increase by a factor of approximately 20 compared to the non-lactating organ.

7.38 Advice from a lactation consultant is recommended and a balance should be struck between delaying treatment until lactation and the associated increased uptake reduces naturally (which may take over 6 weeks) versus side effects caused by medications which inhibit lactation.

Section 8

Thyroid blocking

Introduction

8.1 Thyroid blocking is used to reduce radiation dose[53]. Of the radionuclides commonly used in nuclear medicine, only technetium and iodine are concentrated by the thyroid.

Technetium-99m

8.2 ARSAC considers it unnecessary to use blocking agents to reduce the radiation dose to the thyroid following administration of most radioactive substances containing ^{99m}Tc.

Radioiodine

8.3 When ^{123}I, ^{125}I or ^{131}I is administered as iodine-labelled compounds, with or without iodide as a radiochemical impurity, a substantial part of the effective dose stems from irradiation of the thyroid. Thyroid blocking is recommended for all iodine-labelled compounds not intended for thyroid imaging or therapy.

8.4 Blocking will reduce the absorbed dose to the thyroid when radioiodine is administered as mIBG, albumin or as other labelled compounds. It should be performed if the absorbed dose to the unblocked thyroid will be greater than 50mGy. Assuming full metabolism of the labelled compound and uptake of 25% of the released radioiodine by the thyroid, guidance values which will give this dose are:

^{123}I	15MBq
^{125}I	0.2MBq
^{131}I	0.1MBq

8.5 Before administering a radioiodine compound which is metabolised to iodide or which contains radioiodine impurities, consideration should be given to blocking the thyroid if the administered activity will be greater than the values in section 8.4.

Blocking agent equivalents

8.6 Various formulations of iodide and iodate are available for oral and intravenous administration. The iodine contents of commonly used blocking agents are:

65mg potassium iodide contains 50mg iodine[54]

85mg potassium iodate contains 50mg iodine[55]

1ml of aqueous iodine oral solution BP (Lugol's Iodine) contains 130mg iodine[56]

8.7 If iodine is contraindicated, thyroid blockade can be carried out with potassium perchlorate (200mg adult dose). It should be noted that currently potassium perchlorate is not licensed in the UK. Sodium perchlorate (2ml vials containing 200mg for intravenous use) may also be available.

Blocking protocols

8.8 An oral dose equivalent to approximately 100mg iodine will reduce thyroid uptake to less than 1% of normal. This should be administered the day before the investigation and then daily for one (^{123}I) and five (^{131}I) days, respectively. In patients receiving ^{131}I-based treatments, even a prolonged protection protocol may not avoid a substantial likelihood of subsequent hypothyroidism[57]. The use of a blocking protocol using a combination of iodine and perchlorate could be considered in this situation[58]

8.9 If potassium perchlorate is used it should be given one hour prior to the procedure and repeated at eight hourly intervals until the estimated radioiodine levels have fallen to the levels shown in 8.4.

8.10 Where individuals have forgotten to take their thyroid blockade medication then the dose should be given to them at least one hour prior to the procedure. Use of potassium iodide two hours after exposure to ^{131}I still offers a 'protective effect' of 80% but blocking more than eight hours after exposure is unlikely to be effective[59].

8.11 When thyroid blocking agents are administered to children, consideration should be given to reducing the dosage. This should be broadly consistent with advice[60] given in relation to the use of thyroid blocking in the event of a nuclear accident:

children of 3 to 12 years old	50% of adult dose
children of 1 month to 3 years old	25% of adult dose
neonates (birth to under 1 month old)	12.5% of adult dose

8.12 In children, the dosage of potassium perchlorate required is 10mg.kg^{-1}. The maximum total dosage should be 500mg and the minimum total dosage is 50mg. Potassium perchlorate should be administered 30-60 minutes prior to administration of the radioactive substance. A second dose can be given as late as possible on the same day. If the thyroid gland is seen at the time of scanning the following day, then the child should be given another (third) dose of potassium perchlorate.

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