U.K. Radiopharmacy Group

Guidelines for the provision of radiopharmacy services in the UK

Report of a working group of the BNMS Radiopharmaceutical Sciences Group and the UK Radiopharmacy Group

Correspondence to ukrg@bnms.org.uk

1. Introduction

This document gives professional guidance for the provision of the safe, effective and responsive radiopharmacy service required for nuclear medicine. It identifies the role of the radiopharmacy staff, including key responsible persons as defined in relevant legislation.

The document builds on the advice issued in the previous version published in 2000. It is intended to assist managers and commissioners in NHS England for radiopharmacy and nuclear medicine services, taking into account the recommendations of the strategic report produced by ARSAC in December 2010 (www.arsac.org.uk/newsletter/documents/ARSACStrategicReport99Mo-99mTcfinalv2HQ.pdf). It recognises that the forward planning of radiopharmacy services in a streamlined NHS has to be justified and evidence-based, and must be consistent with the principles of medicines optimisation, Quality, Innovation, Productivity and Prevention (QIPP) (www.improvement.nhs.uk) – ensuring that each pound spent is used to maximise quality of care for patients.

2. Standards and Regulations for Radiopharmacy services

2.1 Radiopharmacy services are essential for the delivery of clinical nuclear medicine. Radiopharmaceuticals are Prescription Only Medicines that are manufactured, and in the case of Technetium-99m and PET radiopharmaceuticals, administered on the same day. Most radiopharmaceuticals are produced locally and are tailored to meet the needs of individual patients.

2.2 The preparation of radiopharmaceuticals in a hospital is an activity that must comply with the principles of Good Manufacturing Practice (GMP), as specified in European Directive 2003/94/EC and incorporated in the UK into the Human Medicines Regulations 2012 [1].

2.3 In radiopharmacies operating under Section 10 of the Medicines Act, radiopharmaceuticals are prepared under the supervision of a pharmacist and compliance with the principles of GMP is audited according to EL (97)52 [2] by an approved pharmacy Regional Quality Assurance Specialist. The standards expected of such units can be found in the Quality Assurance of Aseptic Preparation Services Standards document [3]

2.4 Radiopharmacies that operate under a Manufacturer's "Specials" Licence as issued under the terms of the Human Medicines Regulations 2012 are audited for compliance with the principles of GMP by the Medicines and Healthcare Products Regulatory Agency (MHRA). The minimum standards expected for such radiopharmacies can be found in the MHRA guidance for Specials manufacturers (Q&As) [4]

2.5 Under the clinical trials directive, radiopharmaceuticals may be classified as Investigational Medicinal Products (IMPs) and will therefore be prepared under a Manufacturer's Authorisation for Investigational Medicinal Products (MIA (IMP)).

2.6 Radiopharmaceuticals are among the most highly regulated of materials administered to patients because they are controlled both as medicinal products and as radioactive substances [5].

2.7 The Administration of Radioactive Substances Advisory Committee (ARSAC) advises health ministers on the granting of certificates authorising doctors and dentists to administer radioactive medicines to patients. A key part of the application is the identification of a scientist who will take responsibility for the quality of the administered medicinal products. This individual will be the person responsible for the radiopharmacy service.

2.8 The British Nuclear Medicine Society offers purchasers of nuclear medicine services a policy statement on standards for the safe practice of nuclear medicine [6].

3. Responsibilities of key personnel

Many different staff groups from a variety of backgrounds may be involved in radiopharmacy services. Elements of radiopharmacy practice, which may be performed by various staff groups, are identified in the UK Radiopharmacy Group Capacity Plan which is available at www.bnms.org.uk/ukrg/. General functions include:

- Manufacture and supply of radiopharmaceuticals
- Dispensing of individual patient doses
- Quality control of radiopharmaceuticals

- Quality assurance and pharmaceutical quality systems
- Education and training
- Clinical pharmaceutical service to nuclear medicine

3.1 The Radiopharmaceutical Scientist

Unlike the role of the Medical Physics Expert, the role of the Radiopharmaceutical Scientist (trained pharmacist/scientist) is not clearly defined. It is true that in some smaller units, there is not always a requirement for one, and other staff groups can, and do, manage the operation. In such cases it is important that there is a system in place which gives these units access to the expertise of a Radiopharmaceutical Scientist.

The Radiopharmaceutical Scientist's role comprises a wide variety of functions. They will usually be required to play a part in the manufacturing process. However, this is not their primary function. They will be an individual with a high level of experience and expertise in Radiopharmaceutical Scientist, and as such are able to also fulfil many additional functions. The list below is not exhaustive, and not all the roles are unique to the Radiopharmaceutical Scientist. It is intended to illustrate the value that such an individual adds to the radiopharmacy service.

1. Provision of specialist radiopharmaceutical advice, such as drug interactions and secretion of radiopharmaceuticals in breast milk
2. Optimise the use of radiopharmaceuticals for patient benefit
3. Investigation of altered bio-distributions and the effects of concomitant drug therapy
4. Development of new radiolabelling techniques
5. In-house manufacture of therapeutic products
6. Purchase of unlicensed medicines and associated legal requirements
7. Development of clinical trials
8. Development and maintenance of the radiopharmacy pharmaceutical quality system
9. Advising on the tendering process and the purchase of products of the appropriate quality
10. Audit to maintain and implement appropriate standards to protect patients
11. Adverse event monitoring, investigation and reporting
12. Conducting patient medicines utilisation reviews in nuclear medicine practice to ensure optimal diagnostic accuracy and therapeutic response
13. Design of radiopharmacy facilities within the legal framework

- Research and development

14. Planning and expansion of both clinical services and basic or applied research, for example provision of radiopharmaceuticals for positron emission tomography (PET)
15. Business development
16. Preparation of product dossiers

3.2 The Chief Pharmacist

The Chief Pharmacist is responsible for ensuring the safe and secure handling of medicines, and their optimal use on behalf of the Trust. With regard to radiopharmaceuticals, how this responsibility is discharged will vary depending on the type of facility supplying the radiopharmaceuticals to the Trust. Further details are contained in the UK Radiopharmacy Group document Responsibilities of Chief Pharmacists for the Purchase and Supply of Radiopharmaceuticals which is available at www.bnms.org.uk/ukrg/.

3.3 Personnel within a licensed radiopharmacy

Radiopharmacies operating under a Manufacturer's "Specials" Licence

There must be a named person responsible for production (Production Manager) and a different independent person responsible for Quality Control. The Production Manager cannot have managerial responsibility for the person named as Quality Controller. Staff members such as pharmacists, clinical scientists, technologists and radiographers, may be named on the Licence but will be determined for eligibility and suitability by the MHRA, depending on their knowledge, experience and expertise. These roles have clearly defined duties outlined in chapter 2 of the EU Guidelines to Good Manufacturing Practice [7].

In radiopharmacies with a Manufacturer's "Specials" Licence, the Quality Controller is responsible for release of products, although they may nominate a suitably trained individual to carry out the function. The responsibility cannot be delegated.

In hospital radiopharmacies that operate either under a Manufacturer's "Specials" Licence or under Section 10 of the Medicines Act [8], there is no requirement for products to be released by a Qualified Person (QP).

Radiopharmacies additionally holding an MIA (IMP) licence

Following the introduction of the Medicines for Human Use (Clinical Trials) Regulation 2004 [9], a radiopharmacy in which IMPs are prepared is required to name a QP on its MIA(IMP) manufacturing licence. No batch of medicinal product may be released unless an authorised

nominated QP has certified that it has been manufactured and checked in compliance with the laws in force. Release of products manufactured under an MIA(IMP) cannot be undertaken by anyone other than a QP named on the licence

Production and release functions must be independent processes and sufficiently staffed to meet these requirements. In the case of manufacture of an IMP, the QP cannot play any part in the manufacture of the product. The MHRA expect this principle to be followed with any licensed manufacturing process, and adequate staffing to ensure independent release must be in place.

The responsibilities and key regulatory documents relating to the QP are described in the Rules and Guidance for Pharmaceutical Manufacturers and Distributors [7].

3.4 Personnel within a radiopharmacy that operates under Section 10 of the Medicines Act [6]

The Chief Pharmacist has overall responsibility for the service and a Pharmacist must release any product for clinical use. This responsibility cannot be delegated.

The Accountable Pharmacist is responsible for all aspects of the radiopharmacy service. The duties include the approval of all systems of work and documentation. This person is also an Authorised Pharmacist.

An Authorised Pharmacist is a person designated by the Accountable Pharmacist to supervise the aseptic process and release products for use. An Authorised Pharmacist should be in the department and be in a position to intervene at any part of the radiopharmaceutical preparation process. He/she should be able to ensure that the process is carried out in the prescribed manner and must have knowledge of the pharmaceutical quality system, including any errors and incidents. There must be a system in place to ensure the Pharmacist releasing products is made aware of any errors or incidents which have occurred during the manufacturing process.

References

1. The Human Medicines Regulations 2012. SI 1916 London: TSO, 2012.
2. NHS Executive. Executive Letter (97) 52: *Aseptic Dispensing in NHS Hospitals.* London: Department of Health, 1997.
3. Quality Assurance of Aseptic Preparation Services: Standards 5th Edition. Editor Beaney A. The Pharmaceutical Society, 2016.
4. Medicines and Healthcare Products Regulatory Agency (MHRA) Guidance for Specials manufacturers (Q&As), 2015 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/400232/Guidance_for__specials__manufacturers.pdf
5. Hartman N.G. Regulation of radiopharmacy practice in the United Kingdom. In: Theobald T, ed. Sampson's textbook of radiopharmacy. London: Pharmaceutical Press, 2011: 495-500.
6. Nuclear Medicine Standards for Purchasers and Trusts. London: BNMS, 1997. http://www.bnms.org.uk/images/stories/downloads/documents/microsoft_word_-_standards_of_delivery_of_a_nuclear_medicine_service_.pdf
7. Current version of EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use. Eudralex website. http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm
8. The Medicines Act 1968. London: HMSO. 1968.
9. The Medicines for Human Use (Clinical Trials) Regulations 2004. London: HMSO, 2004.