U.K. Radiopharmacy Group

NEWSLETTER
2012 Q3

UKRG INITIATIVES

UKRG Annual Report 2011-12

An annual report on UKRG activities [*Editor's note: or should that be UKRG radioactivities?*]during 2012-12 was presented to the BNMS AGM, and to the BNMS Radiopharmaceutical Sciences AGM during the BNMS Annual Meeting in Brighton. A copy of the Report is attached as an Appendix to this Newsletter.

UKRG advice on the safe drawing up of radiopharmaceuticals

UKRG makes no apologies for reminding readers about the Guidance on the "Safe drawing up of radiopharmaceuticals in nuclear medicine departments". It is intended to provide guidance to Nuclear Medicine Departments on the provision and design of clinical facilities, procedures, documentation, training and audit in order to minimise the risks that arise from drawing up patient doses of radiopharmaceuticals in areas other than controlled pharmaceutical environments. It has been prepared by the UKRG on behalf of the BNMS, and is available on the UKRG website at this URL:
http://www.bnms.org.uk/images/stories/UKRG/UKRG_Drawing_up_Feb-12.pdf

CR-UK / ECMC / UKRG WORKSHOP: RADIOPHARMACEUTICAL IMPs IN EARLY PHASE CLINICAL TRIALS

This first joint Cancer Research UK, Experimental Cancer Medicines Centres, and UKRG Workshop will take place on 23rd October 2012 at the Royal Institute of British Architects (RIBA), 66 Portland Place, London W1B 1AD. The Workshop will provide an opportunity to discuss the challenges and demands of manufacturing radio-pharmaceutical IMPs for early phase clinical trials, sharing successful approaches and identifying best practice as well as next steps.

Registrants will hear:

- Case studies exemplifying the key issues encountered when setting up and conducting early phase trials with radiopharmaceutical IMPs
- An update on the interface between ARSAC and clinical trials
- The logistics and approvals necessary for setting up early phase trials from a radiopharmacist and an industry perspective
- How the clinical trial regulations apply to early phase trials with radiopharmaceutical IMPs and about the common issues that the MHRA tends to see with CTA applications involving these agents

The faculty for the Workshop comprises:

- Elaine Godfrey (MHRA)
- Tim Meyer (UCL)
- Kim Orchard (UCL)
- Maggie Cooper (KCL)
- Mark Gaze (UCLH)
- Glenn Flux (CTRad)
- C Gillies O'Bryan-Tear (Algeta ASA)
- Jonathan Bull (CR-UK)
- Nigel Westwood (CR-UK)
- Speaker TBC(ARSAC)

Registration is free. For details please contact Hannah Brown (hannah.brown@cancer.org.uk)

NHS "SPECIALS"

National Database of NHS "Specials"

As mentioned in the last Newsletter, readers are reminded that Version 2 of the National Database of NHS "Specials" is operating at this URL: www.pro-file.nhs.uk Registration is required to use the site but once logged-in much useful information is available to you.

National Advisory Board

UKRG understands that the National Advisory Board NHS Medicines Manufacturing and Preparative Services has been "wound up".

Withdrawal of Products / Supply Issues

C^{14} breath test products

Perkin Elmer have taken over the production of several C^{14} breath test products from GE. It has been reported that they have produced several batches of C^{14}-Glycocholic Acid which have given unwanted peaks. Perkin Elmer have been made aware of RCP issues by an NHS radiopharmacy, so there are intermittent supply problems at the moment.

GE

GE has advised that there are no (other) product supply issues at this time.

Draximage Medronate (MDP)

The UK distribution arrangement for Draximage MDP are still to be confirmed. Hopefully we can publicise the details in the next Newsletter.

SPC Updates

Responsibility for advising users of changes in SPCs lies with the supplier of the product. However, UKRG is pleased to offer suppliers space in the Newsletter for the wider dissemination of information relating to SPC changes.

GE DaTSCAN® and thyroid blockade

GE have asked the UKRG to remind the community that in the most recent issue of the DaTSCAN SPC, dated 8th June 2011, the guidance on thyroid blockade has changed to a simpler regime. The guidance is now that: "Patients must undergo appropriate thyroid blocking treatment prior to injection to minimise thyroid uptake of radioactive iodine, for example by oral administration of approximately 120 mg potassium iodide **1 to 4 hours prior to injection of DaTSCAN**".

IBA/CISBio PentaCIS®

IBA have announced an SPC update for PentaCIS for all product released after 6th August 2012. The following sections have been changed:

4.1 Therapeutic indications,
4.2 Posology and method of administration
4.3 Contraindications
4.4 Special warnings and precautions for use
4.6 Fertility, pregnancy and lactation
4.7 Effects on ability to drive and use machines
4.8 Undesirable effects
5.1 Pharmacodynamic properties
5.2 Pharmacokinetic properties
11 DOSIMETRY

INDUSTRY NEWS

Latex-free?

A statement on the absence of Latex in CISBio products is available from your IBA Molecular Rep.

New Type A Transport Container for shipping pre-filled syringes

ONET Technologies UK Ltd has been selling the GP3708 & GP3400C Type Transport Packagings to radiopharmacies for 12 years and has recently reviewed and upgraded the two designs. This is in response to market changes and a drive to simplify labelling. Both designs now come with label holders which will accommodate a 200 x 100mm laminated label that may be reversed.

The GP3400C now has a custom made syringe carrier and the exposed lead shield is painted to aid cleaning.

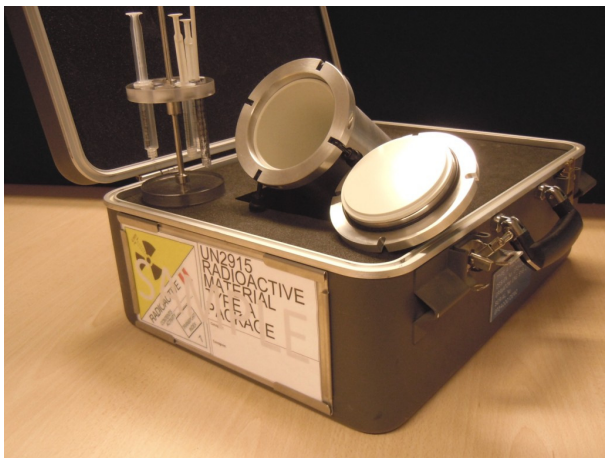
Some of the packagings have been in the field now for 10 years and as such are outside their nominated life. Consequently Onet has inspected some of the older designs which have been used on a daily basis for 10 years and generally (apart from replacing rivets and lid hinges) the packagings are good for several years more. This is a testament to how the radiopharmacies have looked after the packaging and also the robustness of the original design.

We are now able to state that radiopharmacies should, with careful use, get at least 10 years' service from the design.

We are also able to retrofit the new label plates to existing designs.

The revised certificates and operating instructions for the new design will be added to our website at the end of October. For details please go to this URL: www.onet-technologies-uk.com

Contact Gerry Holden or David Windley, Onet Technologies UK Ltd; gholden@onet-uk.com or dwindley@onet-uk.com for further details.



REGULATORY ISSUES

Human Medicines Regulations 2012

These new Regulations (SI 2012:1916) came into effect on 14th August 2012. They are the result of the initiative by the Medicines and Healthcare products Regulatory Agency (MHRA) to consolidate and review UK medicines legislation. **They replace much of the Medicines Act 1968 and around 200 statutory instruments**, in the process repealing much obsolete law and contributing to the government's drive for burden reduction.

Key Regulations relevant to Nuclear Medicine and Radiopharmacy are:

The exemption in Reg 173 from the requirement for Authorisation (as in Reg 46) for radio-pharmaceuticals prepared for "immediate use", subject to certain conditions.

The exemption in Reg 240 for the requirement for a prescription (as in Reg 214(2)) for a Prescription-Only-Medicine (POM) radiopharmaceutical or an adjunctive medicinal product used for a nuclear medicine procedure, subject to certain conditions.

Reg 263 covers the requirement for package leaflets for radiopharmaceuticals.

Chapter and verse is quoted in an Appendix to this Newsletter.

Revision of Clinical Trials Directive

The European Clinical Trials Directive (CTD) which came into force in 2005 was intended to protect patient safety and ensure the quality of clinical trial data. However, it has had the unintended effect of significantly reducing the number of clinical trials undertaken. The requirements of the CTD were aimed at the pharmaceutical industry and were ill suited to academic trials. The CTD was certainly seen as an impediment to trials of radiopharmaceuticals and led to the establishment of the MHRA-MRC PET expert panel.

There was a review of the CTD after it had been in place for 5 years. Many organisations in the UK and Europe submitted evidence of its negative impact, in particular EORTC and EANM.

The draft of the revised legislation, as a regulation rather than directive and hence enforceable in all member states without needing to be passed into law individually, was released for comment in July. Significant changes have been proposed which will lighten the regulatory burden. Most importantly, clinical trials of diagnostic radiopharmaceuticals are to be exempt. This is exactly what we had hoped for but did not dream of obtaining. However, these changes would not take effect for about 4 years as the legislation works its way through the European Parliament, and no doubt there will be lobbying to remove the exemption for radiopharmaceuticals. There is still reason for hope, but also a need for vigilance and political action.

http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf

Recent MHRA inspections

During 2012-Q2 only two radiopharmacies had received a GMP Inspection; there were no major points of non-compliance found. Other (minor) points of non-compliance with GMP were:

- Aseptic practices were not as consistent as they should be in that holding times for wipe/spray transfers were not being monitored.
- Sterile facemasks were not always worn when working in open cabinets.
- Critical Supplier Audits:- An agreement needs to be in place re approving them and the reports need to be specifically detailed enough for follow up actions to be taken.

MEETING REPORTS

BNMS Autumn Meeting 2012

I am grateful to Jim Ballinger for providing this report.

The autumn BNMS meeting was held 12-13 September in Oxford. While it was heavily slanted toward physics as it dovetailed with the IPEM meeting, there were some sessions of interest to radiopharmacy. Most importantly, there was a robust defence of myocardial perfusion imaging (MPI) by Dr Nik Sabharwal, a cardiologist from Oxford. He pointed out the limitations of recent publications which claimed cardiac MR was superior to SPECT MPI. The prime advantages of SPECT MPI are its prognostic value (though presumably over time this will be established for MR) and its provision of quantitative information.

The afternoon session focussed on audit. The physicists have been conducting audits for a number of years and this has led to improvements in service. For example, an audit of GFR determinations revealed discrepancies even when the same raw data were provided to each institution. This led to revised BNMS guidelines on GFR determination. More recently the BNMS has begun a national clinical audit of DaTSCAN reporting. About half the centres which use DaTSCAN participated and the concordance rate was reassuringly high. Finally, clinical audit has been a component of the private sector PET provision since the beginning and again the overall quality of reporting is very high.

This was the last autumn BNMS meeting. In the future there will be one day single topic symposia, the first being in Birmingham next September.

Postgraduate Course in Radiopharmacy

Here is a reminder, carried over from the last Newsletter, about a useful CPD opportunity.

The Postgraduate Course in Radiopharmacy will be held ***Tuesday 11 December to Friday 14 December*** at St Thomas' Hospital, London. The content has been organised so that each day (more or less) has a single theme: background/review, radiopharmaceutical chemistry, regulatory issues, and clinical radiopharmacy. Online registration is encouraged and electronic payments can be accepted. Details can be found at this URL:

https://www.kcl.ac.uk/prospectus/shortcourses/index/name/postgraduate-course-in-radiopharmacy-2012/alpha//month//day//header_search/radiopharmacy

If the link doesn't work, please go to www.kcl.ac.uk, select Study, then Short Courses, then search on Radiopharmacy.

Thanks to the UKRG members who participate in this course and who have sponsored attendance by their members of staff.

UPCOMING MEETINGS

2012

European Association of Nuclear Medicine (EANM) Annual Congress
27–31 October, Milan, Italy
www.eanm.org

EANM Short Course: Trends in PET Methodologies
17-18 November 2012, Vienna, Austria
www.eanm.org/education_esnm/edu_facility/pet_methodologies/pet_methodologies_intro.php?navId=314

ICRT 2012 – 7th International Conference on Radiopharmaceutical Therapy
25-29 November , Levi, Finland
www.eanm.org

2013

UKRG Annual Workshop
11 January, The Beeches Conference Centre Bournville, Birmingham, UK
www.ukrg.org.uk

Radiopharmacy Course
4-15 February, IEO - European Institute of Oncology, Milan, Italy
www.eanm.org

2nd World Congress on ^{68}Ga Molecular Imaging (PET/CT), Targeted Radionuclide Therapy and Dosimetry (SWC-2013)
28 February – 2 March 2013, Postgraduate Institute for Medical Education and Research, Chandigarh, India
www.2ndworldcongress-ga-68.de

British Nuclear Medicine Society (BNMS) 41st Annual Meeting
22-24 April, Brighton, UK
www.bnms.org.uk

20th International Symposium on Radiopharmaceutical Sciences
12–17 May 2013, International Convention Centre, Jeju, Korea
Website: www.isrs2013.org

Society of Nuclear Medicine (SNM) 60th Annual Meeting
8–12 June 2013 , Vancouver, British Columbia, Canada
Website: www.snm.org

EANM'13 Annual Congress of the European Association of Nuclear Medicine
19-23 October, Lyon, France
www.eanm.org

2014

ESRR'14 European Symposium on Radiopharmacy and Radiopharmaceuticals
24-27 April, Pamplona, Spain

11th Congress World Federation of Nuclear Medicine and Biology (WFNMB)
27-31 Aug, Mexico
www.wfnmb.org

From the Editor

My thanks to all who contributed items for inclusion in this issue of the Newsletter.

The next meeting of the UKRG Committee will take place in London on 24th October 2012. If readers have any issues they wish to be discussed please raise them with your regional rep on the Committee. Alternatively, comments on the Newsletter content or on any radiopharmacy issue can be sent direct to the Editor at the address below.

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Issue 2012-Q3 Published 24th September 2012	This and previous issues of the Newsletter are available from the UKRG web site and are posted in the library section at www.VirRad.org

Appendix to the UKRG Newsletter 2012-Q3

BNMS Radiopharmaceutical Sciences Group Annual Report 2011-12
Report compiled by Jilly Croasdale, Chair

2011-12 has been a busy year, with much going on and reasonable progress in several areas:

1. Patient information leaflet for Potassium Iodate tablets: This has been produced by Medicines Information Royal Liverpool University Hospital following comments that the current PIL for the licensed indication covers Nuclear Incidents and is not fit to give out to patients having Nuclear Medicine studies. The leaflet will soon be available on the BNMS website once it has had final approval by Council.

2. Radiopharmacy Support to Nuclear Medicine services: This document, previously published in 2000, was reviewed. Much of the content of the previous version is now covered in the UKRG Capacity Planning toolkit, and has been removed. It provides additional information about the Qualified Person as well as information on the role and function of the Radiopharmaceutical Scientist.

3. Safe Drawing Up of Radiopharmaceuticals: This document is now being put on the BNMS website, and gives guidance to Nuclear Medicine departments on safe practices to adopt when drawing up radiopharmaceuticals.

4. QA of Radiopharmaceuticals document: The UK Radiopharmacy Group and the National Pharmaceutical Quality Assurance Committee have reviewed this document and it is now in the public arena. The reviewed document sets out minimum standards, whereas the previous version gave best practice guidelines. This review was subject to extensive consultation with both the QA Committee and the MHRA, and will be used to inform Farwell and MHRA auditors.

5. Needle re-sheathing: The Council Directive which will be incorporated into law in this Country in May 2013, states that where there is a risk of injury, needle re-sheathing is banned. The BNMS Radiopharmaceutical Sciences Group and the UK Radiopharmacy Group have been liaising with the HSE to highlight the problems this will cause Radiopharmacy. It is hoped that subsequently, the use of resheathing devices (supported by a risk assessment) will be permitted.

6. Radiation Dose to the lens of the eye: Whilst many practices in Nuclear Medicine will never expose the operator to the proposed new lower limit of 6mSv, it may be wise to document an assessment of the operator's eye dose for PET procedures and therapy administration, based on some practical measurements. Discussions with the HSE are on-going.

7. Adverse Drug Reactions to radiopharmaceuticals reporting: The process for ADR reporting using the long established BNMS scheme is currently undergoing a review.

8. Radiopharmacy Audit tool: As part of the BNMS organisational audit document, this standalone document is currently being reviewed. It is anticipated that the new document will be available by the end of the year.

9. UKRG website: This is now located on the BNMS server, but remains an independent website. www.bnms.org.uk/general/ukrg-homepage.html

10. MDP supply: Due to a change in the distribution arrangements for MDP in the UK there has been an interruption to the supply of the licensed kit from Draximage. The same product (although with a French pack insert) is being made available from the original distributor but as an unlicensed product. This issue has highlighted (again) the fragility of continuity of radiopharmaceutical supply in the UK

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Reg 263 covers the requirement for package leaflets for radiopharmaceuticals.

Requirement for authorisation

46.—(1) A person may not sell or supply, or offer to sell or supply, an unauthorised medicinal product.

(2) A person may not sell or supply, or offer to sell or supply, a medicinal product otherwise than in accordance with the terms of—
(a)a marketing authorisation;
(b)a certificate of registration;
(c)a traditional herbal registration; or
(d)an Article 126a authorisation.

(3) A person may not possess an unauthorised medicinal product if the person knows or has reasonable cause to believe that the product is intended to be sold or supplied to another person within the European Economic Area.

(4) A person may not in the circumstances mentioned in paragraph (5)—
(a)manufacture or assemble a medicinal product; or
(b)procure the sale, supply, manufacture or assembly of a medicinal product.

(5) Those circumstances are that the person knows or has reasonable cause to believe that the medicinal product has been or is intended to be sold or supplied contrary to paragraph (1).

(6) For the purposes of this regulation a medicinal product is unauthorised if none of the following is in force for the product—
(a)a marketing authorisation;
(b)a certificate of registration;
(c)a traditional herbal registration; or
(d)an Article 126a authorisation.

(7) This regulation is subject to—
(a)Part 10 (exceptions to requirement for marketing authorisation etc); and
(b)Article 83 of Regulation (EC) No 726/2004 (authorisation of placing on the market of medicinal product for compassionate reasons).

(8) A medicinal product is not unauthorised for the purposes of this regulation if—
(a)it is sold or supplied, or offered for sale or supply, for export to an EEA State; and
(b)the product may lawfully be sold or supplied in that state by virtue of legislation adopted by that state in compliance with the 2001 Directive.

(9) Paragraphs (1) and (2) do not apply to the sale, supply, or offer for sale or supply, of a medicinal product to a person outside the European Economic Area.

(10) Paragraphs (1) and (2) do not apply to the sale, supply, or offer for sale or supply, of an investigational medicinal product to a person specified in regulation 13(1) of the Clinical Trials Regulations for the purposes of administering that product in a clinical trial, provided that the conditions specified in regulation 13(2) of those Regulations are satisfied.

(11) Paragraph (3) does not apply to possession of an investigational medicinal product by a person who knows or has reasonable cause to believe—
(a)that the investigational medicinal product is intended to be sold or supplied within the European Economic Area; and
(b)that paragraph (10) will apply to the sale or supply.

Exemption for certain radiopharmaceuticals

173. Regulation 46 (requirement for authorisation) does not apply where a radiopharmaceutical is prepared—
(a)at the time when it is intended to be administered;
(b)in accordance with the manufacturer's instructions (*) and by the person by whom it is to be administered (**);
(c)from radionuclide generators, radionuclide kits and radionuclide precursors in respect of which a marketing authorisation is in force; and
(d)for administration in accordance with regulation 2 of the Medicines (Administration of Radioactive Substances) Regulations 1978(**1**).

Bob Ardley comments:
(*) It seems it is essential that we follow the manufacturer's instructions for preparation of the radiopharmaceutical in order to make use of the exemption on Reg 173
(**) I take "the person by whom it is to be administered" to be the ARSAC Certificate Holder, or a person working under his or her written directions.

Sale or supply of prescription only medicines

214.—(1) A person may not sell or supply a prescription only medicine except in accordance with a prescription given by an appropriate practitioner.

(2) A person may not (Bob Ardley comment: but see the exemption in Reg 240) parenterally administer (otherwise than to himself or herself) a prescription only medicine unless the person is—
(a)an appropriate practitioner other than an EEA health professional; or
(b)acting in accordance with the directions of such an appropriate practitioner.

(3) The following are appropriate practitioners in relation to any prescription only medicine—
(a)a doctor;
(b)a dentist;
(c)a supplementary prescriber;
(d)a nurse independent prescriber; and
(e)a pharmacist independent prescriber.

240.—(1) Regulation 214(2) does not apply to—
(a)a radioactive medicinal product, administration of which results in a medical exposure; or
(b)any other prescription only medicine if it is being administered in connection with a medical exposure, if the following conditions are met.

(2) Condition A is that the prescription only medicine is administered by an operator acting in accordance with the procedures and protocols referred to in regulation 4(1) and (2) of the Ionising Radiation (Medical Exposure) Regulations 2000(**1**) which apply to the exposure.

(3) Condition B is that the medical exposure has been authorised by—
(a)an IRME practitioner; or
(b)where it is not practical for an IRME practitioner to authorise the exposure, by an operator acting in accordance with written guidelines issued by an IRME practitioner.

(4) Condition C is that the IRME practitioner mentioned in paragraph (a) or (b) of paragraph (3) is the holder of a certificate granted pursuant to the Medicines (Administration of Radioactive Substances) Regulations 1978(**2**).

(5) Condition D is that the prescription only medicine is not a controlled drug.

(6) Condition E is that, in the case of a prescription only medicine that is not a radioactive medicinal product, it is specified in the protocols referred to in paragraph (2).

(7) In this regulation—
"IRME practitioner" means, in relation to a medical exposure, a practitioner for the purposes of the Ionising Radiation (Medical Exposure) Regulations 2000;
"medical exposure" has the same meaning as in the Ionising Radiation (Medical Exposure) Regulations 2000; and
"radioactive medicinal product" means a medicinal product which consists of, contains or generates a radioactive substance so that, when the product is administered, the radiation it emits may be used.

Leaflets relating to radionuclides

263.—(1) The licensing authority must ensure that a detailed instruction leaflet is enclosed with—
(a)radiopharmaceuticals;
(b)radionuclide generators;
(c)radionuclide kits; or
(d)radionuclide precursors.

(2) The leaflet must include the information specified in Schedule 27.

(3) The leaflet must also include—
(a)any precautions to be taken by the user and the patient during the preparation and administration of the medicinal product; and
(b)special precautions for the disposal of the packaging and its unused contents.

Summary prepared by Bob Ardley
17th September 2012.