U.K. Radiopharmacy Group

NEWSLETTER
2014 – Q2
Edition

PROMOTION OF (RADIO)PHARMACEUTICALS

[Editor's note: *Mike Ward (IBA Molecular) has provided the following statement from the Nuclear Medicine Industry Association (NMIA) concerning the marketing of radiopharmaceuticals; only minor editorial changes – in square brackets [ ] - have been made for improved readability. Details of NMIA member companies can be found at this URL: http://www.bnms.org.uk/industry/nuclear-medicine-industry-association-members.html]*

The British NMIA would like to [remind UKRG Newsletter readers] that although the pharmaceuticals you use on a daily basis are diagnostic rather than therapeutic, and are also classified as Prescription Only Medicines (POMs), the ABPI code of practice / regulations still apply.

As such both healthcare professionals and industry colleagues are expected to respect this.

What is the ABPI? http://www.abpi.org.uk/

The Association of the British Pharmaceutical Industry (ABPI) represents innovative research-based biopharmaceutical companies, large, medium and small, leading an exciting new era of biosciences in the UK.

The ABPI Code sets standards for the promotion of medicines to health professionals and appropriate administrative staff in the UK. It includes requirements for the provision of information to patients and the public and relationships with patient groups. The Code also applies to a number of areas that are non-promotional.

The Prescription Medicines Code of Practice Authority (PMCPA) is responsible for administering the ABPI Code of Practice for the pharmaceutical industry at arm's length of the ABPI itself. http://www.pmcpa.org.uk/

The Code covers:

- Journal, direct mail and digital advertising
- The activities of representatives, including any materials used by them
- The supply of samples
- The provisions of inducements to prescribe, supply, administer, buy or sell medicines, by the gift, offer or promise of any benefit or bonus whether in money or in kind
- The provision of hospitality
- Promotional meetings
- The sponsorship of scientific and other meetings including payment of travel and accommodation expenses
- All other sales promotion including exhibitions and digital communications
- The provision of information to the public
- Relationships with patient organisations.

The detailed provisions in the Code aim to ensure that pharmaceutical companies operate in a responsible, ethical and professional manner.

The code can be downloaded here http://www.abpi.org.uk/_layouts/download.aspx?sourceurl=/our-work/library/guidelines/Documents/Code%20of%20Practice%202014.pdf

It is a lengthy document, but here are a few suggestions covering several aspects that will be of assistance in minimising any potential breaches that could occur when industry works with the community.

Meeting sponsorship
When planning meetings that will require industry sponsorship please avoid using lavish venues. In practical terms this means avoiding 5-star hotels, sporting venues and other places noted as being places of entertainment.

Promotion of products at meeting
POMs should not be promoted to the general public, so exhibition sites should not be in public view or in areas of public access such as entrance lobbies to venues. A practical example is that it is prohibited to have product brochures on a registration desk whereas flyers for forthcoming meetings and training events are fine.

Future/ Unlicensed products
These cannot be promoted commercially until licenses are obtained. Pre-marketing / research is allowed within strict guidelines and is most usually conducted by medical teams and 3rd party research groups.

Even if information / trials [data] relating to an unlicensed product is published, and in the public domain, a sales representative is not permitted to discuss these [unlicensed] products. Again, medical teams [will] support this aspect so do not be surprised if your conversation is cut short and your enquiry referred on.

Product Promotion / Supply Updates
There are strict guidelines for all aspects of product promotion regarding advertising, brochures and all aspects of communication between the industry and health care professionals.

Any product claim must be substantiated with clear reference to approved / appropriate sources and you will usually see at least abbreviated prescribing information alongside any piece.

All companies will have strict processes in place to prevent such breaches.

Please note that this does not necessarily apply to communications regarding product supply. An example here would be that informing customers of a manufacturing / supply issue.

A theoretical example would be the non-availability of a company's Sestamibi kit.

To help with work planning and to reduce patient impact, it is permissible and desired that such a shortage is communicated in a quick and straightforward manner with timelines where possible.

However if that communication then proceeds to expand as to why Sestamibi X is better than Sestamibi Y, then [that] communication piece [changes] from being non-promotional to promotional and thus would cause a breach of Code.

If a company / manufacturer believes that another organisation is in breach of any of the above, they are at liberty to make a complaint citing the instance which will include details of where the breach took place e.g. At a congress, in a third party publication, email, website etc

All companies strive to work within the Code and are keen maintain standards and ethical practices.

We thank you, as our customers, [and ask you] to encourage us to continue to work [within the Code] by considering the above points when engaging with us for our educational support.

UKRG ANNUAL REPORT

The UKRG / BNMS Radiopharmaceutical Sciences Group annual report for 2014 was presented at the BNMS Spring meeting held in Harrogate. A copy of the Report is included as an appendix to this edition of the Newsletter.

EU CLINICAL TRIALS REGULATIONS

The new clinical trials regulations were passed by the European Parliament on 16th April 2014 and published in late May: full details can be found at this URL:
http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:JOL_2014_158_R_0001&from=ES

Article 61, Paragraph 5(b) exempts clinical trials of diagnostic radiopharmaceuticals from the need for an IMP licence if performed in a hospital, health centre, or clinic. The exact legalities of how this would apply to university cyclotron units affiliated to a hospital remain to be worked out. This is an important precedent recognising the special characteristics of radiopharmaceuticals. The regulation will come into effect in May 2016.

AVOIDANCE OF GENERATOR SHARPS INJURIES

UKRG would remind readers that users have a responsibility to minimise the likelihood of a sharps injury from an unshielded generator needle, especially when returning expired generators. Whilst following good practice, the needle should be either removed and discarded or it should be securely capped, before the generator is packed for shipping.

DISPENSING OF Tc99m RADIOPHARMACEUTICALS: SAFE DRAWING UP GUIDANCE

The UKRG Guidance on the "Safe Drawing Up of Radiopharmaceuticals" outside of the controlled environment of a radiopharmacy has been updated to indicate that it refers only to Technetium-99m products. [By the time this Newsletter is published] the revised Guidance should be available on the UKRG Website at this URL:
http://www.bnms.org.uk/ukrg/guidance-notes/safe-drawing-up-of-radiopharmaceuticals-in-nuclear-medicine-departments.html

Newsletter readers are reminded that doses from multi-dose vials containing radiopharmaceuticals with a half life greater than 24hours should be drawn up in the Radiopharmacy controlled environment.

Ra-223-DICHLORIDE (XOFIGO®): SAFE DRAWING UP GUIDANCE

A joint UKRG/IPEM Working Party is preparing Guidance on the Safe Drawing Up of Ra-223-dichloride". The Guidance document will be available on the UKRG website; look out for details of its publication in a future edition of the Newsletter.

EMA REVIEW OF NEW MEDICINAL PRODUCTS

The EMA publishes a monthly list of **a**pplications for centralised marketing authorisations for human medicines [including radiopharmaceuticals] that are under evaluation by the European Medicines Agency's Committee for Medicinal Products for Human Use **(**CHMP**).** The list can be found at this URL:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/document_listing/document_listing_000349.jsp&mid=WC0b01ac05805083eb

Mo99/Tc99m SUPPLY STABILITY

Back in November 2013 Guy Turquet de Beauregard, President of AIPES (*), published an article in the French Newspaper *Le Monde* about the Mo99 supply position over the next few years, and calling for an extension to operation of the Osiris reactor at Saclay (France) which is due to close in late 2015, specifically calling for an extension to late 2018. In the article he explains something of the anticipated reactor operations over the coming few years.

Availabilities of reactors between 2015 and 2018 show a strained situation. Indeed two of the four main reactors will come to a halt during these three years: the Canadian NRU reactor will definitely stop in October 2016 at the latest, the Belgian BR2 reactor will undergo maintenance for a long 18 months between 2015 and 2016. Thus if the Osiris reactor were to come to a halt late 2015, the level of available Tc99m would reach, during this period, a potentially unstable zone in case one of the other two most productive reactors suffered a non-programmed halt, namely HFR in the Netherlands and Safari in South Africa. We could then be faced with several weeks' of significant medical examination shortage. On average, these research reactors operate 60-70% of the year, the rest of the time being dedicated to nuclear safety and maintenance.

After 2018, projects in progress will reach completion to take over: the Munich FRM2 reactor, the increased capacities in Australia (Opal) and the Korean reactor project solely dedicated to Nuclear Medicine. Lastly, the new French Jules Horowitz reactor, under construction, should be operational after 2018.

The full text of the *Le Monde* article is available at this URL:
http://www.aipes-eeig.org/files/guyturquet_lemonde.pdf

(*) AIPES is the Association of Imaging Producers and Equipment Suppliers.

[Editor's Note: *Jim Ballinger (Guys) has provided the following update on the position in the UK*]
NHS England has commissioned BNMS to prepare a report to be entitled "Developing Sustainable Supplies of Medical Radioisotopes for the UK". The report will look at the background to the current situation, alternative imaging modalities which can be used, a survey of the potential routes to produce Mo-99 and/or Tc-99m, specific issues with the production of Tc-99m by cyclotron (including logistics and dosimetry), workforce issues, and other radionuclides. The Science and Technology

Facilities Council has funded a UK delegation (to include UKRG members) to visit Edmonton and Vancouver, Canada, where cyclotron production of Tc-99m is being implemented. One potential solution would be a chain of 2-4 cyclotrons around the UK which would produce Tc-99m on overnight runs and then either supply bulk pertechnetate to regional radiopharmacies or centrally prepare radiopharmaceuticals. However, this picture would be greatly different from the current situation and the report will likely recommend that UKRG maintain oversight of potential developments.

REGULATORY ISSUES

Update on EU GMP

Readers are reminded that the current status of EU GMP can be checked on the Eudralex website at this URL:
http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm

Details of recent changes are summarised below:

The revised Chapter 2 on **Personnel** became effective from 16th February 2014.

Chapter 3 on **Premises and Equipment** is being revised; the deadline for comments on the draft has now passed.

Chapter 5 on **Production** is being revised; the deadline for comments on the draft has also passed.

The revised Chapter 6 on **Quality Control** was published on 28th March 2014, with a deadline for implementation of 1st October 2014.

Chapter 8 on **Complaints and Product Recall** is being revised; the deadline for comments on the draft has now also passed.

Annex 3 on the **Manufacture of Radio-pharmaceuticals** is unchanged; the version from September 2008 is still current.

Annex 15 on **Qualification and Validation** is being revised; the draft is still available on the Eudralex website although the closing date for comments is stated as 31st May 2014. It is expected that the revision will be effective from some time in October 2014.

Annex 16 on **Certification by a Qualified Person and Batch Release** is being revised; the deadline for comments on the draft has now also passed.

MHRA Symposium GMP/GDP 2014

The MHRA is pleased to announce the dates for the next GMP/GDP Symposium: **9-12 December 2014**, London. Due to the ever increasing demand for the symposium, this year the symposium will run over four days, comprising of two GDP days (9th and 11th December 2014) and two GMP days (10th and 12th December 2014).

The purpose of the 2014 GMP Symposium is to introduce the latest changes to EU GMP and to continue to give inspector led training as has been popular at previous MHRA symposia. Currently, the topics considered to be most relevant are Annex 16, Annex 15, Chapter 3 and 5 on prevention of cross contamination and the latest developments in the implementation of the Falsified Medicines Directive (FMD). The Agency is also looking to build on the information presented at last year's symposium on data integrity issues. We would like to ask you to complete this short questionnaire to ensure that we are providing the right information, discuss what is important and ensure the event is beneficial to those who attend.

Similarly the purpose of the 2014 GDP Symposium is to review and consider the impact of the EU GDP Guidelines 2014, the Falsified Medicines Directive (FMD).

MHRA therefore requests your assistance in identifying topics of interest for the 2014 events by completing and on-line survey. Completing this short survey will only take a few minutes and you will be given a **survey respondent's special discount code** for use against early-bird bookings registration fees for the event. Please complete this survey by **30 June 2014.** The special discount code will be sent to everyone who completes the survey when the symposium is announced.

These surveys are aimed at individuals from organisations involved in manufacturing and distribution activities of both drug substances and drug products. These may be either commercial or non-commercial (NHS) activities. Such individuals will include QPs & RPs and those working in QA, QC, manufacturing, distribution and regulatory compliance.

The GMP Survey is at this URL:
https://www.surveymonkey.com/s/GMP2014

The GDP Survey is at this URL:
https://www.surveymonkey.com/s/GDP14

INDUSTRY NEWS

UKRG Disclaimer: Much of the information in this section is proffered by UKRG Industry colleagues. Inclusion in the Newsletter does not imply endorsement of any particular product by the UKRG. In addition UKRG is not responsible for any claims made individual companies.

GE Healthcare agreement with SHINE Medical Technologies, Inc. (SHINE Medical) to ensure the long-term supply of Molybdenum-99 (Mo-99)

GE Healthcare is pleased to announce that it has signed a supply agreement with SHINE Medical, a Wisconsin USA-based company dedicated to the production of medical isotopes, as a future source for Mo-99. This agreement ensures the long-term supply of Mo-99 and associated "cold kits" from GE Healthcare for vital diagnostic procedures for your patients.

GE Healthcare believes SHINE Medical is a promising and viable new source of non-reactor produced Mo-99. SHINE Medical will use low enriched uranium (LEU) instead of highly enriched uranium (HEU), which is being phased out because of proliferation concerns. This is in support of the US National Nuclear Security Administration charge to eliminate all HEU produced Mo-99 by the year 2020. SHINE Medical will provide Mo-99 to GE Healthcare on a regular basis when its planned manufacturing facility is operational.

The Mo-99 produced by SHINE Medical will work seamlessly with existing Tc-99m generators, including the proprietary GE Healthcare generator, Drytec®.

With this strategic agreement and cooperation with our current suppliers, GE Healthcare is working to ensure an uninterrupted supply of global Mo-99 to its own customers after the NRU reactor in Canada discontinues Mo-99 production in 2016.

If you have any questions, please contact your local GE Healthcare representative.

We thank you for your continued support of GE Healthcare.

[Editor's note: *further information about SHINE Medical can be found on the company's website at this URL:* http://shinemed.com/]

GE changes vial supplier for I-123 products from 1st July 2014.

In July 2014 there will be a change in the supplier of glass vials used for the following GE Healthcare's products

- •Sodium Iodide (123I) Injection,
- •AdreView,
- •[123I]-IBZM Injection,
- •DaTSCAN.

[Editor's note: *Steve Forman, GE, has advised UKRG that the supplier of the new vials will be Gerresheimer AG ; details at this URL:* http://www.gerresheimer.com/]

These products will continue to be supplied dispensed in 10 ml medicinal vials of Type I pharmaceutical glass and this change will not affect the quality or the stability of the dispensed products.

This change is part of our on-going plans to standardize and simplify our Supply Chain processes where ever possible.

GE Healthcare would however like to draw your attention to this change as it relates to the measurement of the dispensed iodine-123 radioactivity amount. The decay of Iodine-123 is associated with the emission of 159 keV gamma photons used for imaging, and furthermore also with the emission of low-energy X-rays (27 and 31 keV). This low-energy X-ray radiation is absorbed (to a greater or lesser extent) by the glass vial and the levels of this absorption may differ slightly with the change of vial.

With this in mind GE Healthcare recommends that customers reassess the calibration of their ion chamber in conjunction with the use of the new vial.

Any vial delivered on or after the **1st of July 2014** will be from the new vial supplier.

If customers have any questions, they should not hesitate to contact their local Customer Service representative in the first instance.

Adelphi Healthcare Packaging launches new protective vial sleeves

Once heat shrunk to the vial, the protective vial sleeves are designed to trap toxic substances within the unit if the glass vial is compromised through a breakage or surface damage, thereby reducing possible contamination of production equipment and minimising the possibility of product contact for operators and clinical physicians alike.

The protective vial sleeves are available in transparent PVC or PET and with or without a rigid base cap, which offers extra protection against impact damage.

The sleeves can be supplied pre-applied to vials and are suitable for use with standard 10ml Sterile Nitrogen Filled Vials.

Further information can be found on the Adelphi website at www.adelphi-hp.com; any enquiries should be addressed to sales@adelphi-hp.com or call Gavin Crauford Taylor on +44 (0)1444 472300

TRAINING EVENT: PHARMACEUTICAL QUALITY SYSTEMS FOR MANAGERS

UKRG is pleased to publicise the following training event being organised by Quality Control North West (QCNW).

Title: **Pharmaceutical Quality Systems for Managers**
Date: **Monday 8th September 2014**
Venue: **Macdonald Townhouse Hotel, Manchester**

The course is designed for Aseptic Unit Managers, Operational Managers and Senior or Chief Technicians with a responsibility for service delivery. It will highlight the importance of a Pharmaceutical Quality System (PQS) [Editor's note: *a (radio)pharmaceutical quality system even!*] and to identify the key steps to implementing the system. By the end of the course the delegate should be able to:

- Understand the principles of a PQS
- Understand what constitutes a robust PQS
- Identify the key documents in a PQS and how to structure the content, for example:
  - Capacity Plan
  - Site Master File
  - Quality Manual
  - Product Quality Review
  - Technical Agreements
  - Procedures/Specifications/Worksheet

For further information about the course, or to request a booking form, please contact Suzanne Cooke at QCNW at this e-mail address (Suzanne.cooke@stockport.nhs.uk

UPCOMING MEETINGS

2014

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

BNMS / IPEM joint Autumn Meeting 2014
2 September 2014, Glasgow, UK
Website: www.bnms.org.uk

5th International Workshop on PET in Lymphoma
19-20 September 2014, Menton, France
Website: http://eitti.free.fr/

EANM Annual Meeting 2014
18-22 October 2014, Gothenburg, Sweden
Website: http://eanm14.eanm.org

2nd Cardiac PET Meeting
14 November 2014, Manchester, UK
Info from: Peter.Nield@cmft.nhs.uk

GMP/GDP Symposium 2014
9-12 December 2014, London, UK
Website:
http://www.mhra.gov.uk/ConferencesLearningCentre/Conferences/index.htm

2015

BNMS Annual Spring Meeting
26-19 April 2015, Brighton, UK
Website: http://bnms.org.uk

From the Editor

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

The next meetings of the UKRG Committee will take place in Birmingham, 3rd July 2014; the one after that at in London, on 9th and 10th October 2014.

If readers have any issues they wish to be discussed please raise them with your regional rep on the Committee (full details at this URL: http://www.bnms.org.uk/ukrg/general/ukrg-committee-list-2011.html).

Alternatively, comments on the Newsletter content or on any radiopharmacy issue can be sent direct to the Editor at the address below.

www.ukrg.org.uk

Newsletter 2014-Q2
Publication date: 18/6/2014

Editor: Bob Ardley

Regional Medical Physics Department
University Hospital of Hartlepool
Holdforth Road, Hartlepool, UK, TS24 9AH
Phone: 01429-522681; Fax: 01429-860052
E-mail: bob.ardley@nth.nhs.uk

Appendix - BNMS Radiopharmaceutical Sciences Group Annual Report 2014

Radiopharmacy Error reporting
UKRG has now launched a new on-line Radiopharmacy Error Reporting (ER) scheme which all members of the radiopharmacy community are encouraged to use. The on-line version of the form is available on the BNMS website. The form is designed to be easy to use; it opens as a "form-fillable" PDF in Adobe Acrobat Reader. Many of the entries are selected from pull-down lists. A major feature of the new ER system is that information submitted on-line will be collated by UKRG to produce an anonymous snapshot of radiopharmacy quality and frequently encountered errors or near misses across the UK.

MHRA Guidance on EU GMP
In October 2013 the MHRA issued a "Q&A Document" giving up-to-date guidance on how it interprets EU GMP as it relates to holders of a Manufacturer's "Specials" Licence.
http://www.mhra.gov.uk/home/groups/commsic/documents/websiteresources/con326474.pdf
The guidance has been developed to ensure consistency during routine Good Manufacturing Practice (GMP) inspections and to ensure MS license holders are aware of MHRA expectations in this complicated area. It is planned as a 'living' document which will be updated as required. A period of 6 months (up to 1 April 2014) will be given for MS Licence holders to become familiar with this document and implement any changes to their operations and quality systems which may be required.

Purchasing of radiopharmaceuticals outside of Radiopharmacy control, and UKRG Guidance on the Safe Drawing up of radiopharmaceuticals:
The UKRG Guidance on the safe drawing up of Radiopharmaceuticals and the purchase of radiopharmaceuticals refer to the need for a documented agreement between Radiology, Nuclear Medicine and Medical Physics departments and the Trust's Chief Pharmacist. This agreement should describe the responsibilities for delegating the purchase of radiopharmaceuticals, as well as a requirement to discuss with the Chief Pharmacist any purchase of unlicensed materials. An "agreement template" is being prepared by UKRG and will be made available on the UKRG website. In addition to the template agreement, UKRG is developing an audit proforma for users to test their compliance with the Guidelines which will also be available on the UKRG website along with the Guidelines which can be found at this URL: http://www.bnms.org.uk/ukrg/guidance-notes/

Education and Training:
The UKRG held its annual workshop at Beeches Management Centre in Bournville, Birmingham. The meeting focussed on new radiopharmaceutical products, developments in professional issues. The afternoon workshop sessions were arranged to allow a more in depth discussion about KPIs, critical impact assessment and stratifying responses to molybdenum shortages.

Clinical Pharmaceutical Scientist training:
The joint task force set up by Modernising Scientific Careers and Modernising Pharmacy Careers board have now established a Clinical Pharmaceutical Scientist training scheme. This involves rotation between Radiopharmacy, Pharmaceutical Production, Aseptic preparation and Quality Control. From over 130 applicants nationally for the scheme 10 trainees were appointed and commenced in post in September 2013. There have been expressions of interest in hosting a trainee from September 2014.

Needle re-sheathing:
The Health and Safety (Sharps Instruments in Healthcare) Regulations 2013 came into effect on 11th May 2013. The EU Directive on which the UK Regulations are based is 2010/31/EU; it contains statement that: "re-sheathing of needles is not permitted". Following a consultation process on the implementation of this EU directive, to which the UKRG contributed, the HSE have acknowledged that there are specialist areas where it is appropriate to recap needles as long as certain conditions are met. The specialist areas include radiopharmacy and nuclear medicine. The conditions that must be met include use of appropriate risk assessments as well employment of suitable devices that adequately control the risk of injury during the recapping process. HSE has produced Health Services Information Sheet 7 - Health and Safety (Sharps Instruments in Healthcare) Regulations 2013 to provide guidance on how to comply with the Regulations. UKRG guidance on the re-capping of needles in radiopharmacy and nuclear medicine has now been published and can be downloaded from the UKRG website at this URL:
http://www.bnms.org.uk/images/Recapping_needles_UKRG_guidance_v5_UKRG_format.pdf