U.K. Radiopharmacy Group

NEWSLETTER
2011 Q3

UKRG INITIATIVES

Postgraduate Course in Radiopharmacy

The timing of the "Easter course" has been changed this year in order to better suit the timetable of the medics on the MSc in Nuclear Medicine Science for whom this forms the taught portion of their radiopharmacy module. The course will be held ***Tuesday 6 December to Friday 9 December*** in central London. The content has been re-organised slightly so that each day (more or less) has a single theme: background/review, radiopharmaceutical chemistry, regulatory issues, and clinical radiopharmacy. This year online registration is encouraged and for the first time electronic payments can be accepted.
https://www.kcl.ac.uk/prospectus/shortcourses/index/name/postgraduate-course-in-radiopharmacy/keyword/medicine

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

MOLYBDENUM

Molybdenum supplies

Availability of ^{99}Mo has been relatively stable for almost a year. There was one blip over the summer. However, Chalk River will be shutting down for planned maintenance next year and this will have knock-on effects.

Strategic report to Department of Health

The Department of Health has begun to assess the recommendations of the ARSAC report. UKRG is participating in the process.

Another OECD publication

The OECD has published yet another report in response to the ^{99}Mo shortage. This one is called "The Supply of Medical Radioisotopes: The Path to Reliability" and can be downloaded from the OECD NEA website:
http://www.oecd-nea.org/med-radio/reports/med-radio-reliability.pdf

REGULATORY ISSUES

^{82}Rb generators withdrawn

In a bizarre and totally unexpected development, the ^{82}Rb generator has been withdrawn from the market worldwide due to three detected cases of ^{82}Sr breakthrough. ^{82}Rb (t½ 75 sec) is a positron emitting agent for myocardial perfusion imaging which is infused directly from a generator loaded with ^{82}Sr (t½ 25 days). The generator is replaced once a month. The technology has been in use for 20 years and has an excellent safety record.

In June, three patients who had undergone ^{82}Rb PET several months earlier set off sensitive radiation detectors at border crossings in America. It was determined that they contained traces of ^{82}Sr (the parent) and ^{85}Sr (a contaminant, t½ 65 days). Initial estimates of the patients' radiation burden at 90 mSv have been revised downward to ~15 mSv; the effective dose from a ^{82}Rb study is 2.8 mSv, which is cited as one of its advantages over SPECT with ^{99m}Tc agents.

Two of the patients had been scanned a few days apart at a private cardiology practice in Florida, the third was from Nevada. Due to generator production problems, the 28 day expiry of in-use generators was extended to 42 days with FDA approval and the Florida patients received their studies at 40 and 44 days.

Standard QC for the generator includes a daily pre-elution which is allowed to decay for an hour to determine breakthrough.

In July the FDA issued a warning for physicians to stop using the generator and the manufacturer, Bracco, instigated a worldwide voluntary recall. Investigations ongoing include:

- Radiation measurements of other patients to determine how widespread the problem is;
- Review of daily QC data from users. Bracco claims that tests on all returned generators have been within specifications.

The investigation is expected to take until the end of the year. In the meantime, cardiac centres are struggling to handle the additional workload of myocardial perfusion SPECT studies.

Recent MHRA inspections

Issues which have come up in recent inspections have included:

- Failure to implement agreed actions from a previous inspection. *We would expect commitments made as part of the inspection response to be delivered in line with the submitted documentation. It is accepted that there will be occasions when, due to a change in circumstances, it may not be possible to adhere to the timelines agreed; under these conditions an interim RBI update form available on the website should be forwarded to the relevant inspector informing him or her of the change and explaining any additional actions to mitigate risk.*
- Inadequate change control
- Quality management system - a number of elements of the QMS were not effectively controlled including batch release, IMP controls and supplier approval/goods receipt
- Equipment validation and calibration.
- The designation POM should be removed from labels, as POM relates to marketing authorisation, and not individual products, so should not be on the label.
- If a product has a BP or EP monograph, then that is the name which should be used. This will be an education issue for customers, and the advice is to introduce new names slowly.

There is now a requirement for a site master file. Document retention time is now specified, as a GMP requirement rather than clinical governance. A signature log is required, for all personnel who sign worksheets. Verification of training effectiveness and change control are also required, as is an inventory of the documents used in the Quality Management System.

UKRG EVENTS

Radiopharmaceutical Quality Control Techniques: Theory and Practice

This 1.5 day course, which was first held 3 years ago, was offered in early September with 20 in attendance. The undergraduate labs at King's College London provide an excellent venue for a hands-on course. Radiochromatogram scanners were provided by LabLogic and Raytest UK, and a phosphor imager by PerkinElmer. Kits and chromatography media were donated by Agilent, Bartec, Covidien, Diagnostic Imaging Ltd, GE, and IBA. The feedback from the attendees was generally good but a number of suggestions will be incorporated in future courses, possibly as early as next summer.

European Nuclear Medicine Congress

For the first time in quite a few years the EANM meeting is being held in the UK, specifically in Birmingham. Although there are no formal UKRG events there will be many from the community in attendance. The EANM radiopharmacy committee is holding an open meeting on Sunday morning. While I haven't exhaustively trolled the abstracts, there are four presentations from two UK centres in the featured ^{68}Ga session on Tuesday afternoon.

RESEARCH NEWS

Battle of the sentinel node agents

We could have an epic battle on our hands. As you are aware, there is no agent specifically licensed for sentinel node imaging. A very promising agent, which I have discussed previously, is Lymphoseek. Unlike currently used radiocolloids, Lymphoseek is a soluble molecule, ^{99m}Tc-mannosyl-dextran. It targets mannose receptors on the surface of macrophages in lymph nodes. Being soluble, it migrates from the injection depot more rapidly and extensively, producing higher nodal counts.

Lymphoseek was designed by David Vera at UCSD and the rights were bought by the sentinel node probe company Neoprobe, who have since sold off their probe business to concentrate on targeted radiopharmaceuticals for intra-operative detection. Lymphoseek is in the final stages of regulatory approval in the USA and is expected to be launched next year. The developmental work has been done in the USA but the company recently announced they would be opening a European office, though no details are available.

So while Neoprobe sits cooling its collective heels, out of the blue Pharmalucence announces that it has FDA approval for ^{99m}Tc sulphur colloid for sentinel node detection in breast cancer, with the approval being based solely on a literature review of past clinical trials which demonstrated that the colloid was superior to blue dye. I find it extremely surprising that the FDA would accept retrospective analysis of heterogeneous studies of a heterogeneous agent. Because the colloid forms during boiling of a solution, the range of particle sizes varies between preparations. Moreover, some centres filter the product through 0.2 or 0.1 µm filters, selecting a range of smaller particles but losing a significant fraction of the activity in the process.

Neoprobe is understandably spitting nails, having performed prospective controlled trials and argued their validity while a competitor can gain approval based on a literature review.

Alpharadin gets fast tracked

Alpharadin, ^{223}Ra chloride, the alpha emitter being investigated for treatment of painful bone metastases, has been fast tracked for approval by the FDA. Earlier in the summer, Phase III trials were close early because of a significant survival advantage making it unethical to continue the placebo control arm. It featured on BBC News recently. The rights are owned by Bayer.

In other news, Bayer has announced that it is selling off its radiopharmaceutical division. This was the part of Schering which it didn't sell to IBA Molecular in 2006. They have been developing florbetaben, one of the ^{18}F-labelled amyloid agents for imaging Alzheimer's disease.

Somatostatin peptides – *Mea culpa*

In the previous Newsletter I made the mistake of speculating that the agent called SOMscan being developed by the new German company OctreoPharm was ^{68}Ga-DOTATATE. I understand that it is actually a novel second generation peptide.

Abstracts available

The abstracts from the ^{68}Ga-^{90}Y-^{17}Lu peptide meeting in Bad Berka are available at: www.wjnm.org

The abstracts from the International Symposium on Radiopharmaceutical Sciences in Amsterdam are available at: www.isrs2011.org/Abstracts/

Many presentations from the BNMS annual meeting in Brighton are available at: www.bnms.org.uk

While we are talking about free things, a new online journal with free access has been launched by the EANM, *EJNMMI Research.* www.ejnmmires.com

INDUSTRY NEWS

New contact details for iTLC-SG/SA

Varian brought iTLC-SG and -SA thin layer chromatography media back onto the market last year. Varian products are now sold via Agilent.
http://www.chem.agilent.com/en-US/products/columns-supplies/thinlayerchromatography/itlc-sg/Pages/default.aspx
The Agilent consumables team, Craig Douglas, David Smith & Jonny McLaughlin, are reachable at:

- telephone 0845 712 5292 option 3 option 2
- email to customercare_uk@agilent.com
- fax 0845 600 8356

Product shortages at GE

In what seems to be a standing item, GE has announced that SeHCat capsules will be off the market for a period due to production problems. Although it was hoped that the product would be available in early October this is not certain.

LabLogic Systems acquires Southern Scientific

Radiochromatography and nuclear medicine specialist LabLogic Systems has announced the acquisition of Southern Scientific, which manufactures and supplies radiation measurement, detection and analytical systems for the nuclear industry, hospitals and research.

"The key factor that links us with Southern Scientific is radioactivity," said LabLogic managing director Richard Brown. "We have had a friendly commercial relationship with them for many years; their strengths complement our own and they understand our technology, as well as having a similar ethos. We will be able to assist them with software development, and they will be able to contribute to our instrumentation programme - to our mutual advantage, and to the benefit of all our clients."

Southern Scientific's chairman and founder, Ken Frost, said "Becoming part of LabLogic will take the company to a new level. It is an exciting prospect for everyone concerned, and we all look forward to a bright future for the enlarged Group." Founded in 1983, Southern Scientific designs and supplies a comprehensive range of monitors and systems for medical, industrial, environmental and security applications, with full product support. The company has 10,000 sq ft of office and workshop premises in Sompting, near Lancing and 28 employees, including an eight-person direct sales force.

LabLogic Systems was founded in 1980 by John Clapham as a supplier of radio TLC and HPLC instruments and associated software and has gone on to develop many products of its own, notably the DEBRA LIMS for ADME studies and Laura software package for chromatography data capture and analysis. In 2007 LabLogic acquired IN/US, the USA-based manufacturer of the β-RAM radio HPLC detector for β-emitters. Today the company provides innovative solutions for the measurement and reporting needs of drug metabolism researchers, PET scientists and radio-chemists in 46 countries.

Further information about both companies is available at www.lablogic.com and www.southernscientific.co.uk.

Easy-to-use personal dosimeter is keenly priced

The TracercoT404 personal electronic radiation dosimeter, newly available to life science professionals from LabLogic Systems, is the easiest to read and operate on the market – and at half the price of others. Lightweight and drop-resistant, it has a large display showing radiation graph measurements for those who need precise figures, and a simple diagram of a human figure that fills with colour depending on the dose received – an unambiguous warning for the radiation non-professional. Completing the T404 package is the intuitive DoseVision™ software interface, a compact charging station/data upload dock which links to the user's PC through a USB interface – and even a quick-start guide edited by the Plain English campaign. What could be simpler?

UPCOMING MEETINGS

European Nuclear Medicine Congress
15-19 October, Birmingham. www.eanm.org

From Dosimetry to Biological Effect: Radiobiology as a Guide to Clinical Practice in Nuclear Medicine 5-8 Nov, Sorrento, Italy. www.nuclearmedicinediscovery.org

7th National Cancer Research Institute Cancer Conference 6-9 Nov, Liverpool. www.ncri.org.uk/ncriconference

International Conference on Clinical PET and Molecular Nuclear Medicine (IPET 2011): Trends in Clinical PET and Radiopharmaceutical Development 8–11 Nov, Vienna. www.iaea.org

4th International Conference on Radiopharmaceutical Therapy (ICRT-2011)
World Association of Radiopharmaceutical and Molecular Therapy (WARMTH), 28 Nov – 2 Dec, Ho Chi Minh City, Vietnam. www.icrt-2011.warmolth.org

Chemistry for Imaging SINAPSE Spirit
6 Dec, Glasgow. www.sinapse.ac.uk

UKRG Radiopharmacy Workshop 13 Jan, Bournville. www.ukrg.org.uk

16th European Symposium on Radiopharmacy and Radiopharmaceuticals 26-29 Apr, Nantes, France. Abstract deadline: 5 Dec.
http://esrr12.eanm.org

British Nuclear Medicine Society annual meeting 30 Apr - 2 May, Harrogate. Abstract deadline: 6 Jan. www.bnms.org.uk

Society of Nuclear Medicine annual meeting 9-13 June, Miami. Abstract deadline: early Jan.
www.snm.org

AS TIME GOES BY

The Committee held a grand send-off for **Barbara Wensworth** at a Thai restaurant in Birmingham during our July meeting. Hearts stopped momentarily when the server opened a bottle of Chateauneuf du Pape which she had brought in error rather than our usual plonk. When the error was detected (and an exception report filed), the correct item was brought (sigh) and the kitchen staff got the CNdP.

Another recent retirement is **Roger Pickett** from Amersham. I've managed to lose the email with the exact number, but he was with Amersham and its successors for something like 43 years. His earliest paper which I can verify was in 1970. He was on all the early HMPAO and Myoview papers. He was a font of knowledge on all things radiopharmaceutical. He has also been active in the Radioactive Drugs committee of the British Pharmacopoeia. But in spite of being a big shot at Amersham he always retained his interest in what was going on at the coal face and frequently contacted me about items which he had seen in the Newsletter, setting me straight on numerous occasions. Happy retirement, Roger.

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