U.K. Radiopharmacy Group

NEWSLETTER
2014 – Q1
Edition

UKRG ANNUAL WORKSHOP BOURNVILLE 2014

[Editor's note: *I am grateful to Paul Hillel (Sheffield) for providing the following report.*]

The annual UKRG workshop which took place in Bournville on 17th January was well attended as always. For those staying over the night before there was the usual evening meal out which was the ideal opportunity for informal networking. However, there was a radical break from tradition with an excellent restaurant in Birmingham's China town being chosen as the venue in place of the usual Moseley curry house. A good night was had by all.

The morning session of the workshop kicked off with talks from four pharmaceutical companies highlighting some of their new radiopharmaceutical products. First there was Nick Stevens from **Imaging Equipment Ltd**. who explained some of the advantages of working with a smaller scale pharma company such as ROTOP, their German partner company. He gave details of the formulation for their licensed non-boil MAG3 product and their Nanocoll generic (NANOTOP) which will soon be available in the UK as a licensed product [*Editor's note: see below in the Industry News section*]. Next to speak was Omer Ahmed from Bayer who described their Radium-223 dichloride product **Xofigo** and its use for treating bone metastases in castration-resistant prostate cancer. He showed very promising results from phase III trials which demonstrated, amongst other benefits, a significant increase in patient survival for those treated with this product. Matt Green from Lilly was up next to give details on **Amyvid**, the exciting new Fluorine-18 PET tracer for imaging beta-amyloid plaque formation in the brain. Matt explained how this product has been licensed for use in cognitively-impaired patients being investigated for Alzheimer's Disease or other forms of dementia. He explained how plaque formation begins relatively early in the disease process in relation to other biomarkers. Some example PET images were shown (both positive and negative) and delegates were informed about an on-line image reader training program.

The final company presentation was given by Ann Maloney from Navidea who was visiting the UK from the US to talk about **Lymphoseek**. This radiopharmaceutical, which is for use in the detection of sentinel lymph nodes, works differently to the current colloid agents in that it binds to protein receptors near the surface of lymph nodes. Ann explained how this extends retention time in nodes, enabling their detection up to 30h post injection and reducing tracer uptake down stream of the sentinel node(s).

The final three talks in the morning session related to CPD, training and quality systems. Rachel Dixon from Guys and St Thomas first gave a very informative demonstration of the **Technical Professional Development (TPD) portal** and explained how this is already being used by other pharmaceutical technical services. Funded by NHS Pharmaceutical Technical Specialists Education and Training (TSET), this portal is designed to enable all grades and types of pharmacy staff to manage their training, CPD, and career development. A large number of relevant competencies are already defined on the system and radiopharmacy-specific ones could be added. Delegates were encouraged to explore the system by registering for a free account – here is the link: (www.tpdportal.org.uk). The next talk was by Bev Ellis from Manchester who gave an update on the **Modernising Scientific Careers STP for clinical pharmaceutical sciences**. She clearly explained the background to this new training program which was developed in order to address the future work-force needs in the fields of manufacturing, QA services, aseptics and radiopharmacy. There was an explanation on how the academic blocks given at Manchester University fit in with the work-based rotations and how the program differs to other STPs such as that for Medical Physics training. Next up was Adrian Hall from the Royal Marsden Hospital to publicise the new **UKRG error reporting form** which is now available on-line through the UKRG website. Adrian gave a demonstration of the form and delegates were strongly encouraged to report all errors and near misses via this system so that national issues can be collated and results fed back to the radiopharmacy community. [See the previous UKRG newsletter for further details of this error report form].

Before lunch was taken, Maria Palmer (UKRG chair) gave a short impromptu speech to inform delegates that this would be the last workshop that Paul Maltby would be organising due to his well deserved retirement later in the year. She acknowledged Paul's sterling work over the years and the audience showed their sincere appreciation with an extended round of applause [*Editor's note: I'll echo that!!*].

After an excellent lunch there was time for delegates to peruse the exhibition. The number of companies exhibiting their wares was up on recent years so people were able to find out about a wide range of available equipment and products. Delegates were split into three groups for the afternoon workshop sessions. The first group, which was lead by Jilly Croasdale, discussed how a **critical impact assessment** could be used to assess a unit's compliance with the UKRG guidelines on the QA of radiopharmaceuticals. In the feedback session Jilly reported how the group had worked through the different sections of the guidance document to consider the potential consequences of not performing the various tasks/QC checks or of failed results. The second group was lead by Maria Palmer and they considered **responses to Molybdenum shortages**. The group felt that most radiopharmacies and nuclear medicine departments had already increased the efficiency with which they use ^{99}Mo/^{99m}Tc in response to previous supply issues. The potential for further efficiency savings (driven both locally and nationally) were considered, most of these requiring better communication between regional radiopharmacies and also between radio-pharmacies and the nuclear medicine departments they supply. Government and industry responses offer mainly medium to long term solutions and were thought likely to result in price increases. David Graham led the final workshop group in a discussion about potential **key performance indicators (KPIs) for radiopharmacy**. The group felt it was important to clearly separate those KPIs required to confirm compliance with GMP with those required by Trusts and higher management. It was thought best to start with only 3 or 4 KPIs that are easy to measure/trend and to use simple traffic-light colour coding to express the level of compliance. GMP related KPIs considered included a compliance rating following MHRA inspection, timely completion of CAPAs and the rate of operator or environmental out or specifications.

An excellent day was closed with Paul Maltby reassuring everyone that this annual radiopharmacy workshop would be running as usual next year despite his retirement. Why not plan to attend in 2015?

[*Editor's note: UKRG is grateful to Adrian Hall for volunteering to take over from Paul the organisation of the 2015 Annual Workshop. Watch out for details in a future edition of the Newsletter*]

UKRG OFFICERS

From 1st April 2014 the UKRG Officers will be:
Chair: **Jilly Croasdale** (Birmingham)
Hon. Secretary: **Phil Hillel** (Sheffield), with support from Sue Ackrill (Birmingham)
Hon. Treasurer: **Adrian Hall** (Sutton)
BNMS Council Rep: **Bev Ellis** (Manchester)

KEY PERFORMANCE INDICATORS (KPIs) FOR RADIOPHARMACY

In many parts of the NHS Key Performance Indicators (KPIs) are used by a service to demonstrate how well it is performing. The KPIs can be developed by the service themselves, or, more often, are "imposed from on high" by management. UKRG has decided that the radiopharmacy profession would benefit from having a set of nationally agreed KPIs, and it would be better if these were developed from within the profession rather than outside it. To that end UKRG has established a KPI Working Group under David Graham's (Aberdeen) co-ordination. This Group is to produce a National Guidance Document for Radiopharmacy KPIs which looks at both Management KPIs and GMP KPIs. It seems that mostly, where KPIs are already in use, those KPIs focus only on numbers and timeliness of service but this does not give a true indication of the quality of service. It has been agreed that the Guidance Document would only need to focus on 4 or 5 KPIs that do not just focus on getting the product out of the door. Once the Guidance has been prepared it will be publicised in a future issue of the Newsletter.

Cr^{51}-EDTA

Single-use or multi-use of GE Cr^{51}-EDTA vials

GE have taken the reference to Cr^{51}-EDTA being a multi-dose vial out of the SPC; however, neither do they state that it is for single use only. The UKRG view is that users of this product can carry on using it as a multi-dose vial, but should recognise that if

they choose to do this, the Cr^{51}-EDTA will be being used "off licence" and will have to be classed as an unlicensed product. They should write a justification for using it based on the fact that the product has not changed and the risk assessment should state that doses must be drawn up in a Radiopharmacy and that the product only has a 28 day shelf life after first opening. We re-iterate the advice given in the 2006-Q2 issue of the Newsletter:

Discussion continues on the thorny issue of multi-dose use of Cr^{51}-EDTA injection. Two issues were raised at this (April 2006) meeting:
1. EU guidelines state that multi-dose vials should not normally be used more than 28 days after first puncture. The reference document is: CPMP/QWP/159/96 corr, which is available [*Editor's note: still available*] at this URL:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003476.pdf
2. Whatever means a radiopharmacy chooses to use, they must be able to present the MHRA with evidence validating the sterility of the product throughout its assigned shelf-life.

CANCER DRUG FUND (CDF) LIST

NHS England has published an updated Cancer Drug Fund (CDF) list which includes pomalidomide and **radium-223 dichloride** both of which were approved pending license on the previous CDF list. The list also includes dabrafenib for melanoma and trastuzumab emtansine for HER-2 positive breast cancer. Eight drugs/indications were not approved. Details can be found at this URL:
http://www.england.nhs.uk/wp-content/uploads/2014/02/ncdf-list-feb14.pdf

UKRG discussed Xofigo® (Ra^{223}-dichloride) Concerns were raised that this product may be purchased directly by Oncologists and drawn up in uncontrolled areas by inappropriately qualified staff. Newsletter readers are reminded that any Pharmacist/Physicist who signs the ARSAC application Part C for use of this product needs to be certain where and how it is going to be used. UKRG also raised some concerns about the radiation protection issues surrounding use of an alpha-emitting radionuclide; advice from an RPA will be essential.

REGULATORY ISSUES

Investigation of Out Of Specification (OOS) results

The MHRA has recently published some FAQs on how to manage OOS results; also a guidance document. The FAQs are available at this URL:
http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodManufacturingPractice/FAQ/OOSFAQs/

The guidance document is available at this URL:
http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con100182.pdf

Recent MHRA inspections

At the January meeting of UKRG Norman Gray (MHRA) reported on four recent GMP Inspections of "Specials" licensed radiopharmacies which included NHS "technetium" facilities and NHS and commercial PET facilities. GMP themes arising from these inspections are summarised below.

- If you have a near-miss/event recording process and also a deviation recording system MHRA would expect the near miss/events to be documented in a manner which includes a root cause analysis and determines corrective and preventative actions.
- MHRA would expect sites to have some Microbiological expertise available and one PET site did not have access to this resource.
- The investigation of adverse Environmental monitoring results was poor, investigation was poor, staff were not interviewed to determine any possible reasons and excursions were not raised until 3 months after the event.
- Poor validation documentation for a Hidex generator where the protocols had been written by the Swedish supplier themselves.
- Media fills did not cover all manufacturing activities only those done in the preparation isolator and not those in the dispensing isolator.

BNMS SPRING MEETING 2014

The 2014 BNMS Spring Meeting will be held in Harrogate, 11th-14th May 2014. There is an exciting radiopharmacy session on Tuesday 13th May at 8.30-10.30am with a programme comprising both invited review papers and proffered papers, as follows:

- Update of new PET tracers in the UK
- Radiopharmaceuticals: What is on the table and in the oven?
- Hybrid fluorescent-radioactive tracer (indo-cyanine-green ^{99m}Tc-nanoclloid) for sentinel node identification
- How quickly do ^{99m}Tc complexes form?
- The battle of the MAG3s

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.

Alliance Medical Ltd and the supply of F^{18}-FDG

In the 2013Q3 edition of the Newsletter we reported that Alliance Medical Ltd (AML) taken full ownership of ERigal, and had also acquired IBA Molecular's UK F^{18}-FDG production facility. UKRG now understands that AML has been referred by the OFT to the Competition Commission. Details can be found at this URL:
http://www.oft.gov.uk/news-and-updates/press/2014/20-14#.UzSan7mPO1t

Exametazime available from Diagnostic Imaging Ltd

Diagnostic Imaging Ltd (DIL) has been appointed as UK distributor for Medi-Radiopharma. This means that the licensed un-stabilised Medi-Exametazime is available for immediate delivery from DIL's GMP facility at Welford, Northants. Further details are available from Mike Barker and Mike Scholes at DIL (tel 0845 226 0520).

DIL have also advised that Medi-Radiopharma made a typo error in the SPC in their submission to the MHRA. The stability for both infection and brain imaging should have been stated as 60 minutes not 30 minutes. An amended SPC for this product (revision date 14/2/2014) is now available on the MHRA website; it can be found at this URL:
http://www.mhra.gov.uk/Safetyinformation/Medicinesinformation/SPCandPILs/ : search for "medi-exametazime" You will have to tick the disclaimer to view and download the SPC.

Steve Schroeter retires from UK Radiopharmaceutical sales.

[*Editor's note: Steve Schroeter has written an open letter to the NM and RP community, which I am pleased to reproduce in this edition of the Newsletter.]*

Dear All,

After 27 years in the business I decided in November, with the full support of IBA Molecular, to retire gracefully. Some of you will be aware of the issues I face (how it broke my heart to go for that DATScan!). IBA were aware of my diagnosis before they took me on board so full marks to them for their support, both on a corporate basis and from my immediate colleagues, who latterly carried an increasing amount of the workload which should have been mine.
I started out with pre-MAG3 Mallinckrodt in 1986, moving on through Medgenix, (Technegas), du Pont (SestaMIBI), Immunomedics, (Leukoscan), Cyclomedica (Technegas again), QADOS, and finally to IBA, with a few "etceteras" and a teaching qualification in the middle.
What of the future? Well, I got married in August, and we're having a new house built. The asparagus in the garden will soon be ready, and the trout fishing season starts on 1 April. So life's good really.
Many thanks for the kindness and tolerance you and your departments showed me over the years, it was always a delight to visit you. Thank you also for the many cups of tea.
Take care, and remember Voltaire: "Life's a shipwreck (but keep on singing in the lifeboats)"
Best wishes and goodbye.

Steve Schroeter, Bishop Auckland, Co. Durham.
(steveschroeter@hotmail.com)

Nanotop 0.5mg kit now available from Imaging Equipment Limited (IEL).

ROTOP GmbH (Dresden, Germany) has received full marketing authorisation for the distribution of Nanotop 0.5mg radiocolloid cold kit for Sentinel Node Imaging in the UK (PL 41222/0002). Nanotop 0.5mg, a generic albumin nanocolloid, has been manufactured by ROTOP since 2011, is sold in 10 different countries, has been injected in over 100,000 patients and has an excellent safety profile.

Nanotop 0.5mg is available to UK hospitals through IEL, with immediate effect.

The composition, and pharmacokinetic properties of the human albumin colloidal particles are identical to Nanocoll® 500 micrograms (GE, Amersham), which was the reference product for the generic

marketing application with 95% of particles having a diameter of ≤ 80 nm; less than 5% free Tc^{99m} after radiolabelling, and a pH of 7-8. Importantly, the mean particle size is highly consistent and varied by only ± 1.3 nm over a sample of 22 batches due to the same manufacturing process for both products, utilising colloid formation through a process of thermal denaturation. This consistency between the products enables surgeons, nuclear medicine specialists and radiopharmacists to switch between products with minimal disruption.

Although it is a generic, Nanotop 0.5mg does have several non-clinical variances to Nanocoll® 500 micrograms (see Table 1), and is the only product licensed for sentinel lymph node imaging and able to be stored at room temperature.

Table 1

Nanotop 0.5mg	
Storage:	Room temperature
Shelf life:	18 months
Nanocoll® 500 micrograms	
Storage:	Refrigerated 2-8 °C
Shelf life:	12 months

IEL are pleased to announce the distribution of this newly licensed radiocolloid as an addition to their existing cold kits - IELMAG3 and Cardiovis – and will continue to license other radiopharmaceutical tracers where there is a potential threat to continuity of supply.

Additional information (including the SPC) is available from Imaging Equipment Limited by phone (01761-417402), or online via the website at www.imagingequipment.co.uk. *[Editor's note: the SPC is also available from the MHRA website at this URL:* http://www.mhra.gov.uk/Safetyinformation/Medicinesinformation/SPCandPILs/]

Mediam products now available in the UK direct from the manufacturer.

Choledíam, Hepatate and Stannous Agent are now distributed directly to the UK by Mediam Pharma.
To place order, please email contact@mediam-pharma.com .
The postal address is: Mediam Pharma, 85 rue N. Mandela, 59120 Loos, France
Tel : +33 (0)3 20 49 72 58
Fax : +33 (0)3 20 88 16 71

UPCOMING MEETINGS

2014

ESRR'14 European Symposium on Radiopharmacy and Radiopharmaceuticals
24-27 April, Pamplona, Spain
http://esrr14.eanm.org

ANZSNM Annual Meeting 2014
25 April, Adelaide, Australia
Website:
http://www.anzsnm2014.com.au/index.html

BNMS Spring Meeting
11–14 May 2014, Harrogate, UK
Website: www.bnms.org.uk

Molecular Imaging – Solution to tomorrow's Healthcare?
12-14 May 2014, Odense, Sweden
Website: www.odensespringmeeeting.com

3rd PET/MR and SPECT/MR Conference: Paradigms for Combined Modalities in Molecular Imaging
19-21 May 2014, Kos Island, Greece
Website: http://www.pet-mri.eu/psmr14.html

SNMMI Annual Meeting 2014
7-11 June, St Louis, Missouri
Website:
http://interactive.snm.org/index.cfm?PageID=13055&navItemNumber=581

Nuclear Medicine Molecular and Hybrid Imaging Symposium (BIR/BNMS)
9-11 June, Manchester, UK
Website: www.bnms.org.uk

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

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

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 London, 2nd April 2014; the one after that at Aston, Birmingham on 3rd July 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-Q1
Publication date: 28/3/2014

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