U.K. Radiopharmacy Group

NEWSLETTER
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Edition

BOURNVILLE 2015: UKRG ANNUAL WORKSHOP

[Editor's note: I would like to thank Susan Ackrill for the following report]

The annual UKRG workshop, which was held in Bournville on 16th January, was well attended as always. This was the first workshop to be arranged by Dr Adrian Hall following the retirement in November of Paul Maltby who had been the workshop organizer for many years. The day was a great success, and Adrian is to be congratulated on organizing a most interesting and relevant workshop.

The morning session of the workshop covered a wide range of topics. Professor Alan Perkins and Dr Beverley Ellis jointly gave the first presentation, which was aptly entitled "Good Golly, Miss Molly". They looked at current and future provision of ^{99m}Technetium for medical imaging, focusing in particular on the likely impact of the molybdenum shortage predicted from 2016. Currently 5 reactors produce over 90% of the World's supply. The NRU reactor in Chalk River, Canada currently produces 40% of the World supply, and will cease molybdenum production on 31st October 2016, with the Osiris reactor in France (3%) shutting down at the end of 2015. Professor Perkins outlined the plans for future provision, including the 100MW Jules Horowitz reactor planned in France, the HFR replacement in Holland, and a new reactor planned in Munich. In Canada investment is being directed towards alternative technology, specifically cyclotron production of ^{99m}Tc. He discussed the findings of the UK working party, which visited Canada to look at the two cyclotrons at the University of Alberta, Edmonton and the TRIUMF cyclotron in Vancouver. The findings of the BNMS report have now been published on the BNMS website (see link below in *Future Supply of Medical Radioisotopes for the UK* section).

In summary, by 2025 production of ^{99}Mo/^{99m}Tc will be via a combination of:

- Existing reactors
- New or upgraded reactors
- New technology (cyclotrons)

Dr Ellis continued the presentation, looking at the work being undertaken to validate kit preparation and the regulatory requirements for the introduction of cyclotron-produced ^{99m}Tc. The radionuclidic impurities present in cyclotron produced ^{99m}Tc lead to a 10% increase in radiation dose to the patient. However, cyclotron production of ^{99m}Tc looks to be very promising, to supplement reactor produced molybdenum.

Mrs. Anne Black, Assistant Director of Pharmacy QA, Newcastle upon Tyne, then gave a very interesting presentation entitled "Introduction to advanced therapy medicinal products". An ATMP is a biological medicine, and regulation (EC) No 1394/2007 classified ATMPs as:

- Gene therapy medical products
- Somatic cell therapy medicinal products
- Tissue engineered products
- Or any combination of the three

She spoke about cellular therapies for example dendritic cells, as medicinal products these are the responsibility of Pharmacy. Chief Pharmacists have responsibility and need a governance mechanism in place. This is a rapidly developing field with an evolving regulatory landscape.

Dr Alison Beaney followed with a presentation on "Changes to Chapter 1 of the Rules and Guidance for Pharmaceutical Manufacturer's; the new Q and A document and how these are being interpreted by the MHRA". The changes to EU GMP Chapter 1 are a significant set of changes, with key issues for aseptic units. Chapter 1 deals with Pharmaceutical Quality Systems (PQS), and key changes include design of a PQS incorporating risk management principles e.g. root cause analysis. MHRA expectations as a result of the revised Chapter 1 will include a robust deviation process, and clearly defined roles and responsibilities of senior management. The main learning points were to be aware of the new requirements and to perform "gap analysis" so that change control for implementation of Chapter 1 is managed appropriately. Senior management support is essential for adequate resourcing of staff to implement these changes.

Sallyann Randerson, Lead Radiopharmacy Technician at Hull Royal Infirmary then went on to present her PTQA MSc dissertation entitled "Assessment of an alternative meal for solid gastric

emptying scintigraphy". She looked at alternative meals, and concluded that cheese was a promising meal alternative to egg, although this still requires validation.

Dr John Rhodes, Laboratory Manager, Stockton Quality Control Laboratory then provided a review of microbiology methods. He looked at sources of microbes in the clean room, in particular human sources of particles. He then went on to discuss appropriate media for microbiological monitoring, broth kits, operator validation tests, and product testing. He also looked at the effect of spray and wipe using IMS - sporicide. He discussed the identification of organisms at Genus or species level, comparing the traditional biochemical test with the new MALDI TOF equipment now in use.

Mr. Wayne Goddard, Quality Control Professional Manager, Stockton Quality Control Laboratory was next to present his PTQA MSc dissertation entitled "Detection and significance of fungi in hospital clean air environments". To date there is little work published on the types of fungi present in clean air environments. The project involved sampling of radionuclide generators and containers in Radiopharmacy units, and identification of fungi from routine test samples using the MADI-TOF rapid ID system. Moulds were recorded on 0.54% of plates, and accounted for 6.2% of colonies. Radiopharmacies had 17.9% from critical zones compared with 10.2% from pharmacy critical zones. Four main species of fungi were identified from the generator transport container, including Penicillium and Aspergillus species. Penicillium biofilms can survive high free chlorine concentrations. Wayne's conclusions were that control measures for dealing with fungi are required. These may originate from a variety of sources and without genus and species information it is difficult to trace these.

During the break for lunch there was an opportunity to see a presentation by Elvir Zahirovic on the SPECTra LIMS system for radiopharmacy, and also to visit the exhibition. Delegates were able to find out about a wide range of available equipment and products.

As an introduction to the afternoon syndicate work Ian Oxley, GMP and validation expert from IBA Radiopharma Solutions gave a very informative introduction to Quality Risk Management. His take home message was that QRM is here to stay, but here to help. He looked at the current regulatory framework, and the importance of an integrated GMP approach.

Delegates were then split into three groups for the afternoon syndicate sessions.
Group 1 led by Ian Oxley discussed Quality Risk Management. In the feedback session he reported the importance of using the correct terminology and knowing your products and processes, in terms of:

- CQA – Critical Quality Attributes
- CCP – Critical Control Points
- CPP – Critical Process Parameters

Considering all the above in terms of processes and facilities produces valuable key points to be incorporated into risk assessments.

Group 2 led by John Rhodes discussed microbial monitoring. In the feedback session he focused on incubation of plates, use of contact plates and swabs, and operator and process validation.

Group 3 led by Jilly Croasdale looked at capacity planning and seven day working. She reported back on the pros and cons of operating a seven day service. It was agreed by all that the challenges of seven day working (increased staff requirement for radiopharmacy, Nuclear Medicine for imaging and medical staff to report) far outweighed the advantages. Although greater use would be made of the generator (seven days instead of five), the cost of additional staffing would exceed any benefit gained.

This feedback concluded a very informative and enjoyable day, and it was agreed by all that Adrian had done an excellent job of stepping into Paul's shoes (hopefully not literally).

FUTURE SUPPLY OF MEDICAL RADIOSOTOPES FOR THE UK

A joint publication from BNMS and Science & Technology Facilities Council is available on the BNMS website detailing the issues leading to the expected worldwide shortage of ^{99}Mo over the next few years. The full document is available from: http://www.bnms.org.uk/images/stories/moly_updates/BN6249-RadioisotopesReportLIVE_v5_2.pdf

With the expected closure of two of the world's nuclear reactors involved in the production of ^{99}Mo, the report assesses the potential impact of this on healthcare services in the UK. Of particular interest, the report discusses options for non-reactor production of ^{99m}Tc, including cyclotron-produced ^{99m}Tc, which is already at an advanced stage in Canada, with two sites in Edmonton, Alberta and at TRIUMF, Vancouver BC producing ^{99m}Tc in this manner.

With the expected shortage possibly beginning as early as 2016, the report describes the current status of Nuclear Medicine services in the UK, and explores ways of using available resources more efficiently. Radiopharmacy and Nuclear Medicine departments are encouraged to try and get the most out of their ^{99}Mo generators, by reviewing services and investigating alternative generator

sizes and delivery times. Investigations into such issues are not only useful to conserve the ^{99}Mo resource, but may also offer you some financial savings, of which we are all being pressed to strive for.

REBOOT OF VIRRAD

VirRAD is a community platform that provides a web-based interface for Radiopharmacy staff and others in the Nuclear Medicine community to communicate with colleagues all over the world. This helps those involved in Radiopharmaceutical Sciences to share their ideas, solve everyday difficulties, disseminate best practice and develop innovative solutions to universal problems.

This important resource is soon to be re-launched, supported by the EANM Radiopharmacy Committee. Initially, only the Forum section will be activated, but this is a great way to communicate with colleagues and keep informed of issues in Radiopharmacy. Keep an eye on the site, but following this link:

http://www.virrad.com/

A date for re-launching the site has yet to be set, so until then, you may have to get by with the UKRG Newsletter!

ERROR REPORTING

National reporting of errors is a requirement of good practice for both Section 10 aseptic units and MHRA licensed facilities. The UKRG website has an established error reporting form that is available to all radiopharmacies to submit errors to satisfy the national reporting requirement. Use of the UKRG error reporting form has not yet been widespread among radiopharmacies, so readers of the newsletter are all encouraged to test the form, and report any errors that they feel may be a worthwhile contribution to the national register.

Error reporting and recording of deviations is not only a requirement of good practice, in both licensed and non-licensed facilities, but it is also a useful resource for education and identifying issues with products. We've all been told in the past "you're the only place that's having this problem," but sometimes you're not.

Why not just fire in a quick one on the website now? Here's the link, so you don't even have to get up:

http://www.bnms.org.uk/error-reporting-form/error-reporting-form.html

REGULATORY ISSUES

NEW MHRA GUIDANCE DOCUMENTS: Q&A FOR "SPECIALS" LICENCE HOLDERS

The MHRA have published a revised 2015 version of their very useful MHRA Guidance for Specials Manufacturers (Q&A document), which can be found using the link:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/400232/Guidance_for__specials__manufacturers.pdf

The Guidance is presented in an easy to read, Q&A style format, giving concise recommendations for radiopharmacies working under an MHRA "Specials" Licence. There have been a number of changes since the original 2013 document was released, including:

- More specific detail regarding capacity planning
- Guidance on cleaning validation
- The design of aseptic processes
- The use of ampoules in aseptic preparation
- Pooling of raw materials in aseptic compounding
- More detail on process validation tests and media fills
- Identification of microorganisms to species level in Grade A environments
- Minimum sanitisation expectations for transfer of materials to a Grade A working zone*

There has been much discussion regarding the last point on sanitisation of materials being transferred to Grade A working zones, in particular regarding the use of sporicidal agents. It should be noted that radiopharmacies have a full exemption from using sporicidal agents in material transfer procedures, due to the risk of oxidisation of the components of radiopharmaceutical kits (thank you Paul Maltby!).

DATA INTEGRITY: WHAT DOES THAT MEAN?

Many of us that enjoy the pleasure of a visit from an MHRA inspector from time to time are being questioned about their "data integrity" procedures and safeguards. After much scratching of heads from those trying to answer such an enquiry, the MHRA have kindly provided a document explaining what is meant by data integrity, and more importantly, what is expected of us. The document,

entitled “MHRA GMP Data Integrity Definitions and Guidance for Industry January 2015” is available on the MHRA website, using the link:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/397853/Data_integrity_definitions_and_expectations_v3_4__ack.pdf

Have a read through it, it is extremely helpful and has been written in a user-friendly format.

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

Several changes have been made to Eudralex Volume 4 since the last newsletter. These are summarised below:

The revised Chapter 3 **Premises and Equipment** was published on 13th August 2014 and became effective from 1st March 2015.

The revised Chapter 5 on **Production** was also published on 13th August and became effective from 1st March 2015.

The revised Chapter 8 on **Complaints and Product Recall** was also published on 13th August 2014 and also became effective from **1st March 2015**.

Just a reminder that a **revised Part II: Basic Requirements for Active Substances used as Starting Materials** was also published on 13th August 2014, and implemented from **1st September 2014**.

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 public consultation has now closed. It was expected that the revision would be effective from October 2014, but we are still awaiting a date for this.

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.

EMA REVIEW OF NEW MEDICINAL PRODUCTS

The EMA publishes a monthly list of applications 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

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.

We are a bit light on industry news this month – possibly due to the changes to the Editorial Team, but hopefully, once better connections are established, we can bring our readers more information from more companies.

Mallinckrodt moves Customer Services Department to the UK

With immediate effect, Mallinckrodt has brought their Customer Services Department for Nuclear Medicine into the United Kingdom. All calls will be diverted from the same free-phone Customer Services number (0800 234 6682) via an options menu. To reach the UK-based Customer Services Team, dial 1.

Mallickrodt Customers Services will also be moving from their Covidien-owned premises into their own premises on the 3rd of April 2015. The new address will be:

Mallinckrodt Pharmaceuticals
Suite G30, Regus, Ground Floor,
Building 1000, Western Road,
Portsmouth, Hampshire PO6 3EZ

As they are in the process of setting up the new office, they cannot accept orders by fax, so please **email all orders to the new Customer Service Team email address:**

cs.rpuk@mallinckrodt.com

GE Healthcare product and SPC updates

GE have updated the SPC on their ^{99m}Tc Drytec Generator. The revision is a substantial change to the previous version (June 2008) and was updated in May 2014. The changes have been made to ensure the SPC complies with current European Guidelines, expanding a few sections to include more detail.

CNS provides Safe and Secure transportation of radioactive materials within the UK

Vanessa Cummins, CNS Accounts Handler, invites Newsletter readers to consider **Courier Network Systems** as a possible logistical alternative for their current radioactive transportation requirements within the UK.

CNS offer a complete managed service for the safe and secure movement of radioactive materials particularly in the scientific and medical sectors. We are a London based courier company ideally situated to provide urgent same-day requests and next-day timed deliveries.

All our drivers are ADR trained, wear a C.N.S. uniform and carry photographic ID. We issue each driver with an XDA which provides us with an immediate proof of delivery and allows C.N.S. to track the vehicle at all times. Our business development has been fuelled by impeccable service and shaped by interpreting specific customer needs. We have built a great reputation in this field and can provide references from our many pleased clients.We have recently been audited by the ONR and VOSA and were found to be compliant.

For further information contact Vanessa at:
CNS, Block H03A, Tower Bridge Business Complex, 100 Clements Road, London SE16 4DG.
Tel 0207 231 9030

UPCOMING MEETINGS

BNMS Annual Spring Meeting
26-29 April 2015, Brighton, UK
Website: http://bnms.org.uk

10th International Conference on Radiopharmaceutical Therapy (ICRT-2015)
[World Association of Radiopharmaceutical and Molecular Therapy – WARMTH]
4-8 May, Innsbruck, Austria
Website: http://warmth.org/

SNMMI 2015 Annual Meeting
6-10 June, Baltimore, USA
Website: http://www.snmmi.org/am2015

EANM 28th Annual Congress
10-14 October, Hamburg, Germany
Website:
http://www.eanm.org/congresses_events/congress_calendar/calendar_detail.php?navId=24&eventId=859&year=2015&month=0

2016

UKRG Annual Workshop 2016
15 January, Bournville, UK
Website: www.ukrg.org.uk

11th European Molecular Imaging Meeting
8-10 March, Utrecht, Netherlands
Website: http://www.e-smi.eu/index.php?id=2652

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, on 15th April and then Birmingham on the 8th and 9th of July for the Strategic and Committee meetings. 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 (be nice, I'm new!).

New Newsletter Editors!

As you all may have already heard, Bob Ardley retired from the NHS, and as a result, also as UKRG Newsletter Editor. I would like to take this opportunity to acknowledge the splendid work that Bob put into this publication, especially now that I have seen how much work goes into it! On behalf of all of the readers of the Newsletter, I'd like to wish Bob all the best for his retirement, and to offer him the opportunity to return as a locum Editor in Chief if he ever feels the notion to come back!

We now have a new joint-Editor set up in the UKRG Newsletter Editorial Room (which does not actually exist as a physical structure), so you may see some variation in editions as we find our way. In addition to myself, the other Co-Editors are:

- **Bev Ellis, Manchester**
- **Maria Palmer, Bristol**
- **Jose Calero, The Christie, Manchester**

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