U.K. Radiopharmacy Group

NEWSLETTER
2016 Q1

REVIEW OF THE 2016 UKRG ANNUAL WORKSHOP IN BOURNVILLE

The editor would like to thank Peter Bartholomew for providing this report on the Bournville conference – his first. (*The opinions and views made by the author of these reports are not necessarily reflective of the UKRG.*)

The Annual UKRG Workshop was held at Bournville, Birmingham on Friday January 15th. The morning session involved invited talks and proffered papers. Clint Waight opened the batting (the sporting metaphor is deliberate – Clint entertainingly presented his team in the style of Sky Sports) with a talk on the radiopharmacy aspects of Selective Internal Radiation Therapy (SIRT). He demonstrated the physical differences between glass and resin spheres and the practicalities of their use, and usefully pointed us to the SIRT UK network for further information. He showed that in his own hospital he felt it was important for radiopharmacy to be involved in the preparation of the doses and the administration sets.

Maggie Cooper's talk "Nanocolloid Kits – are they all the same?" was a comprehensive review of relevant material. Maggie showed that particle size affects clearance and that there were differences between the manufacturers in particle size profile, however there was conflicting evidence relating particle size to efficacy. There was a valuable summary of the TLC methods used for quality control and discussion on what volume to inject, including and retention of activity in syringes. I was grateful to Maggie for pointing out the differences in licensed indications between the brands, so pay particular attention if you do sentinel node work in areas other than breast cancer. Kimberley Wright from University Hospitals Birmingham next gave us a talk on her perspective of the Scientists Training Program (STP) in Clinical Pharmaceutical Science. She first described the STP and guided us through the work based training and OLAT (online assessment tool). She told us that this 3 year MSC program, working in an NHS trust full-time, would lead to an MSc and briefly described her research project (using ^{90}Y spheres) as well as the competencies needed for OLAT. I was impressed by Kimberley's confidence and enthusiasm for the course, and suspect that a lot of hard work had gone on in the background both by Kimberley and the staff teaching her. Next up was Alison Beaney from Newcastle Hospitals with a talk entitled "New Standards from 'Quality Assurance of Aseptic Preparation Services, Edition 5.'" We were guided through the relevant chapters with particular emphasis on key changes for radiopharmacy. The new format has a pragmatic philosophy with "*What to Do*" chapters and "*How to Do*" appendices and aims to provide easily auditable statements. It also now includes a specific section on prescribing in radiopharmacy. There are significant changes that you will need to be aware of but the good news is that the document is likely to be published by the Royal Pharmaceutical Society in print and digital form.

Scott Edmonds, another STP Trainee, described his work on cell-labelling with ^{89}Zr and guided us through the theory of cell tracking and the potential for this PET isotope to provide better performance than our current main SPECT equivalent, ^{111}InOxine. He showed that ^{89}Zr had been chelated with Oxine and that successful murine imaging of various cell types had been accomplished, although there was considerable work to be done before this breaks through into routine clinical work. Peter Jarritt gave a talk on accreditation in radiopharmacy and its place in Health and Social Care Quality Assurance. He described iCEPSS (Improving Clinical Engineering and Physical Science Services) a quality improvement and Accreditation project to cover all MSC services. Radiopharmacy is included in the Nuclear Medicine IPEM Standards Advisory Group (SAG – a good memory for acronyms is necessary in this area) and is well represented by experienced members of UKRG. Peter described a Quality Improvement Programme (QIP) being piloted at Barts using a self-assessment tool (SAIT). iCEPSS funded by HEE and AHCS and involving UKAS via the IPEM SAG and using its QIP (with the SAIT) working towards BS7000 (as an interpretation of ISO 17025 and 15189). *Beat that sentence for acronym density!* Acronyms aside, this is very important work – in a heavily regulated environment, but amongst many potential benefits, it is very likely that compliance with this accreditation will greatly facilitate compliance with regulations.

The last talk was by Professor Hans-Jürgen Wester describing the latest state of play with ^{68}Ga

and theranostic pairs (a diagnostic agent used to predict the therapeutic benefit of another). He suggested that the recent work using ^{68}Ga labelled somastatin analogues was significant but limited to a small patient population which alone may not make ^{68}Ga commercially viable. However this radionuclide has much wider potential – he described the advances that have been made in designing chelator moieties for ^{68}Ga and how several exciting new bio conjugates have been attached to them. He showed some wonderful images of PET/CT and PET/MRI using ^{68}Ga PSMA in the early detection of prostate cancer but I was most impressed by the images of positive uptake in areas of infarction using ^{68}Ga RGD. Watch this space!

The afternoon session involved syndicate work. "You get out as much as you put in" would be a suitable motto for these sessions – fortunately the groups were well led and most attendees felt comfortable enough to contribute. In "*How to perform risk / impact assessments*" we were given some useful tips on defining and using risk and using the information (make sure you put risks on the Trust Risk register if you want action) and ensure you integrate risk assessments into your CAPA processes. In "*Methods for detecting radioactive contamination*" we went from basics like 'higher than background' measurements on a monitor, through to a discussion of simulation kits (vapour doesn't simulate technetium contamination very well, apparently). It was also useful to discover that Public Health England do RPS Courses at various locations that are free to the referring Trust. In "*Trending in Radiopharmacy*" the groups were invited to contribute the areas where they trended data. The take home messages were to ensure that deviations were trended and a reminder that the MHRA Q&As indicate that capacity should be assessed monthly (or more frequently). There was strong encouragement for us all to contribute to the UKRG Error Reporting System.

Reflection on the meeting:
This was my first such meeting and I can't stress how useful I found it. As a grumpy pedantic old man, I believe the word "workshop" should not be used outside the context of light engineering and I don't think the word does this event justice in any regard. As well as the interactive, reflective aspects suggested by the word, it was also a proper mini-conference with regulatory updates, a chance to meet industry as well as see research and development presentations. There were a good number of exhibitors (enough to fill two big rooms) and their availability saved me a lot of work back at base. The talks were a well-balanced lot with the necessary dry material interspersed with some interesting (and in some cases jaw-dropping) clinical work. See you next January!

CLARIFICATION SOUGHT ON SPORICIDAL USE IN RADIOPHARMACY

The UKRG is currently seeking further clarification on the exemption for radiopharmacies in the use of sporicidal agents for the transfer of materials to a Grade A working environment. Clarification is being sought as to whether radiopharmacies are exempt from using sporicidal agents at all in the transfer process, or whether the exemption relates only to the transfer of components known to be susceptible to the effects of these agents.

In the meantime, all radiopharmacies are encouraged to independently conduct a robust risk assessment for their material transfer process, whether it includes sporicidal agents or not. The previous issue of the UKRG newsletter contained information, including references of the data supporting the risks of using sproicides in the Radiopharmacy, and other studies have also been published identifying the risks associated with various disinfectant agents. All licensed units should have adopted the recommendations in the MHRA's Guidance for Specials Manufacturers on material transfer to the Grade A working zone (Section 3.5.20), which includes a two stage transfer process, with spraying and wiping at both stages (see link below):

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

An update on any further information and the expectations of the MHRA will be provided in upcoming UKRG newsletters.

UKRG SUPPLIER AUDITS

The UKRG have previously conducted audits of suppliers of radiopharmaceuticals or components used in Radiopharmacy production. This programme is to be reintroduced and the results made available to all Radiopharmacy units who require the information. Further detail of these audits will be provided in the next newsletter, including how to access the reports. This will save individual units having to collect the same information for their Approved Suppliers Lists that are a requirement of GMP. The MHRA recently published a blog on supplier responsibilities, which can be found at:
https://mhrainspectorate.blog.gov.uk/2016/03/17/qualification-of-suppliers-a-helpful-reminder-of-the-3-steps-needed-to-assure-supply-chain-integrity/

ERROR REPORTING

Those who attended the Annual Conference at Bournville in January would have received an annual report of all errors submitted to the National Error Reporting System. The on-line Error Reporting Form is available on the UKRG website. The UKRG would like to encourage centres to use this scheme as the results can be analysed to provide valuable information on future training requirements.

Please continue to use the national error reporting system, or if you have not done so before, try it out for the first time. What's the worst that could happen?

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

KEY PERFORMANCE INDICATORS

A UKRG working group is developing a Guidance Document on Key Performance Indicators (KPI's) for Radiopharmacy Services, and comments were requested in the last newsletter. From the feedback, the UKRG are looking to develop a suite of KPIs for radiopharmacies to use, some of which will be recommended as being suitable for all units, while others KPIs will be listed as suggestions from which you can choose what best suits your unit.

At present, a set of core KPIs from the UKRG may include indicators suchs as:

- Adherence to capacity plans
- Time taken to close out incident investigations (CAPAs)
- Time taken to resolve complaints

The work is still in progress, so please keep an eye out on the UKRG website, or future editions of this newsletter, for updates.

MHRA BLOGs

In recent years, the MHRA have made significant steps toward making sure they communicate effectively to manufacturers in the UK. One of the most useful initiatives has been the introduction of the MHRA blogs, which are routinely posted on their website, see link below:
https://mhrainspectorate.blog.gov.uk/

These blogs explain what can sometimes be complicated and rather uninspiring legislation, in an easy to understand format to help us to interpret their recommendations. All radiopharmacies, particularly units with an MHRA licence, should subscribe to these blogs if they wish to keep abreast of GMP updates, or if they wish to find out more information on a particular topic. An example of this might be Data Integrity.

DATA INTEGRITY: A NEW LOOK AT AN OLD TOPIC

Does anyone really know what they want when it comes to Data Integrity? Many radiopharmacies have been inspected and found to be deficient in this area, largely due to them not understanding the expectations of the licencing authority. In a series of three blogs, the MHRA have given a clearer indication of what they want to see when it comes to data integrity in our units. The first blog looks at organisational behaviour in relation to data integrity, the second blog looked at ways to design systems to be compliant and the third blog explored the impact of procedures and behaviour on reliable data in medicines manufacture.

At the very least, we should all have a written data integrity policy, and have conducted some form of gap analysis on our own systems to gauge where we are in relation to regulatory expectations. If we can't comply fully, we should at least have a plan as to how we can comply in the future, and these blogs will assist in that process.

REGULATORY ISSUES

Feedback from recent GMP inspections

It's always good to know what the hot topics are on the MHRA inspectors' agenda to help us all to identify and rectify any gaps in our own units before the inspector arrives. From the inspections carried out in 2015, these are some of the areas for improvement that the MHRA have noted in the radiopharmacies they have inspected:

1. Poor completion of investigations for deviations.
2. Documentation, such as SOPs not being kept up to date.
3. Clear SOPs and policies on issues such as remote release of products.
4. Lack of investigation for environmental monitoring deviations – particularly on excessively high results.
5. Failure to fully investigate failures in sterility tests, including an impact assessment.

We'll keep you up to date on this issue in the newsletter, on at least an annual basis.

Update on EU GMP

In addition to keeping up to date with MHRA guidance, it is a good idea to routinely check for updates on the EudraLex website at this URL: http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm

Annex 16 on **Certification by a Qualified Person and Batch Release** has been revised. The deadline for coming into practice is **the 16th of April 2016.**

Annex 17 on Parametric Release is being revised. A consultation was launched on the 15th of September 2015 on a draft revised version of Annex 17. The consultation closed on the 11th of December 2015.

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 by individual companies.

End of an era: Discontinuation of the Capintec CRC-15R
As many of you may already know, the staple of many radiopharmacy and nuclear medicine departments, the Capintec CRC-15R has been discontinued. While this was announced some time ago, Southern Scientific are continuing to provide service and support for a short time, but parts are no longer available.

A new radiopharmaceutical (^{99m}Tc-Tektrotyd)

^{99m}Tc Tektrotyd is manufactured by Rotop and distributed by Imaging Equipment Ltd in the UK, and is now available as a licensed product. This is an Octreotide-labelled ^{99m}Tc tracer that can be used as an alternative to ^{111}In-Octreoscan. It is licensed for use in adults for the investigation of gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs), for localizing primary tumours and their metastases.

Improved labels for Stamicis (sestamibi)
As a result of reports from the UK market of product vial labels not being able to withstand the wet boiling procedure required for the reconstitution of Stamicis (sestamibi, CIS Bio International, IBA Group) IBA Molecular have subsequently invested a lot of time and resource investigating a different type of label and have announced that following a long process of validation by a UK Radiopharmacy, all batches of Stamicis now are manufactured with a new reinforced label. The new label came into effect on the 23rd of February 2016, following batch number F004HA which is currently being despatched from Alliance Medical Limited

The integrity of the new label during wet boiling, including the adhesive performance and print, has been validated at temperatures up to 150°C. Any further questions relating to this product can be directed to :
Leisl Anderson – Northern UK 07786 963 765
Mike Ward – Southern UK 07885 464 638

Draximage Product Recall on Medronate

Draximage recently issued a product recall on their medronate kits, following the discovery of glass particles (DMRC file reference MDR 090-02/16 - Jubilant DraxImage MDP recall). All units of the offending batch have been used or successfully recalled by the company without further reports of this issue being identified.

Raytest Acquisition: Radiopharmacy LIMS Systems

Raytest GmbH have announced that the company has been acquired by Elysia SA, a Belgian company offering quality control (QC) systems to radiochemistry laboratories around the world, integrating their LIMS software with instruments from Raytest and other providers into a compact, integrated, QC package. This new partnership will extend the range of products on offer as well as providing financial stability.

In the UK, Diagnostic Imaging Ltd (DIL) will continue to represent this expanded group. Enquiries regarding how Raytest can assist radiopharmacies in complying with current regulations on data integrity in QC, can be directed to Andy Holley at andyholley@diagimaging.com.

UPCOMING MEETINGS

2016

The Clinical Pharmacy Congress*
The future of Clinical Pharmacy
22-23 April, 2016
ExCel London, Royal Victoria Doc 1 Western Gateway, London

*In 2016, the Clinical Pharmacy Congress will be working closely with UKRG and will include lectures on radiopharmaceuticals in clinical practice. More details on these lectures will follow.

BNMS Annual Spring Meeting 2016 (Celebrating 50 years)
17-19 April, 2016, ICC, Birmingham

SNMMI 2016 Annual Meeting
11-15 June, 2016 San Diego, USA
Website: SNMMI Annual Meeting 2016

From the Editor

My thanks to all who contributed items for inclusion in this issue of the Newsletter, in particular to Peter Bartholomew for submitting the Bournville report.

The next meetings of the UKRG Committee will be on the 27th April, July 6th and October 5th. The Strategic Group will meet on July 5th and in January 2017. 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

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