

BOURNVILLE 2018 UKRG ANNUAL WORKSHOP

Editor's note: *The review of the Annual Bournville workshop each year is written by a member of the UKRG Committee who kindly volunteers to pay sufficient attention to each presentation and summarise them for you in this article. This year, our thanks go to Catherine Humphreys, Principal Nuclear Medicine Scientist at Singleton Hospital in Swansea. Thank you Catherine!*

The annual UKRG Bournville Workshop was held on Friday 12th January at the Beeches Hotel, Bournville. This year saw a record number of delegates and many thanks must go to Dr. Neil Hartman and the organising team for putting together such an interesting programme and making the day a success.



The first presentation of the day was from Louise Fraser, ARSAC Scientific Adviser, and was entitled '**Changes to Medical Exposure Regulations in 2018**'. The focus of Louise's presentation was the new IR(ME)R regulations which are in force as of the 6th of February 2018. From that date, the ARSAC licensing application process changed to a 'dual licensing' system for Practitioners and Employers. The Employer is required to apply for licences to administer radiopharmaceuticals at each hospital site. Each application captures the scope of the service at each site, and incorporates diagnostic, therapeutic and research applications into a single document. Each Practitioner will apply for a licence which is based on their experience and practice. The Practitioner licences are 'portable' so they can be used in multiple hospital locations. However, it is essential that the Practitioner works within the scope of the Employer's licence at each hospital site. Current ARSAC certificates are still

valid until they expire and cover both the Practitioner and Employer during this time.

The theme of new regulations continued with the second speaker, Darren Morgan, a Clinical Scientist from Oxford. He spoke about the "**Practical Implications of IR(ME)R 2018 for Radiopharmacies**." Darren recommended having an 'Entitled Duty Holders Register' for those members of staff who are duty holders under IR(ME)R. He highlighted the role of the Medical Physics Expert (MPE) and recommended that Radiopharmacies take advantage of working with their MPE to help reduce potential IR(ME)R incidents.

The next speaker was Sarah Collen, Senior Policy Manager at the NHS European Office in Brussels, who delivered a much anticipated presentation on '**Brexit and the NHS**'. Since the 24th of June 2016, the NHS European team have been working on mitigation of the impact of Brexit on the NHS. This includes working towards agreement on rights for EU nationals who make up approximately 10% of the UK clinical workforce. They are planning how to manage the supply of medicines into and out of the UK on leaving the EU Single Market. Sarah explained that although leaving Euratom has legal implications for the trade and supply of radioactive materials, the UK government stance is that radiopharmaceuticals should fall outside of this scope as they are non-fissile. The team are also working towards mitigating any adverse effects on clinical research work within the UK, as currently the UK receives significant funding from Horizon 2020, an EU research funding program.

The meeting moved on from UK border control to clean room border control, as Dr. Maggie Cooper presented on '**The Use of Sporicides in Radiopharmacy**'. Maggie referred to the Yellow Cover Document on *Guidance for Aseptic Transfer Processes in the NHS: Addressing Sporidical Issues* written by the NHS Pharmaceutical Micro Protocols Group. A link to this document is provided below:

['Guidance for Aseptic Transfer Processes in the NHS: Addressing Sporidical Issues'](#)

This report recommends a first stage disinfection using a sporicidal wipe followed by an alcohol spray and a second stage disinfection using an alcohol spray followed by an alcohol wipe. The MHRA Q&A document states that there is an exemption for

the use of sporicidal agents where evidence exists that products are affected by sporicidal residues. Maggie summarised several research findings where radiopharmaceuticals have been shown to be adversely affected by very small amounts of oxidizing sporicidal agents. Her advice is that sporicides can be used in the first stage disinfection of most materials, excluding radiopharmaceutical kit vials. When commencing work with sporicidal agents, Maggie suggests increasing the rate of routine radiochemical purity testing and trending the results.

Dr. Paul Scully, a Cardiology Research Fellow at Barts Hospital, gave a clinical presentation on '**DPD Imaging in Clinical Nuclear Cardiology**'. He described the grading system for reporting of Tc99m DPD images when diagnosing different types of cardiac amyloidosis. He also displayed some clinical examples, allowing the delegates to suggest which grades they represented, with very good results!

An additional presentation was added to the agenda on the '**National Aseptic Services Review**' and was delivered by Steve Brown, and Kholia Khan. A national review of aseptic services has been funded by NHS Improvement, but this review only captures information from Pharmacy departments, so Radiopharmacies that are managed by Medical Physics or Nuclear Medicine departments, are currently excluded from the process. However, this may change in the future. The review questionnaire is already with the relevant departments for completion.

For those of us involved in transportation of radiopharmaceuticals between hospital sites, the next talk from Anna Mayor, Principal ONR Inspector on '**Transportation of Radiopharmaceuticals**' was insightful. Anna highlighted some common inspection failures, with the most common being poor emergency planning, including lack of rehearsal of emergency plans. She also made us aware that the ONR has written guidance documents relating to radioactive transport which can be accessed via the ONR website, or by following the link below:

<http://www.onr.org.uk/transport/guidance.htm>

Changes to come this year include revised Radiation (Emergency Preparedness and Public Information) Regulations (REPIR) and amendments to the Carriage of Dangerous Goods (CDG09) Regulations 2009 as part of the Basic Safety Standards Directive implementation. Anna informed all users that the remit of ONR inspections includes CDG and IRR compliance, so make sure you've got your prior risk assessments and contingency plans up-to-date for transportation of radioactive materials! Finally, she reminded us that organisations need to follow the graded application

process to HSE (under IRR17) for transport of radioactive materials.

The day was rounded off with parallel syndicate workshops on Qualification and Validation, CAPAs and GMP Training. Many thanks to Prof. Chris Marshall and Rebekka Hueting for the first workshop and special thanks to Jilly Croasdale, Clint Waight, Tom Murray and David Graham who delivered the remaining workshops with very little notice. All in all, a very successful day, packed full of content. Don't miss it next year!

MHRA GUIDANCE ON DATA INTEGRITY PUBLISHED

The MHRA published their GxP Data Integrity Guidance on the 9th of March 2018. In case you're wondering, "GxP" encompasses all of the good practice that the MHRA regulates against, including GMP for manufacturing, GCP for clinical trials and GDP for distribution. The published guidance may differ from the draft guidance you perhaps read last year, following the 1300 comments the MHRA received from professional groups and the pharmaceutical industry! The final version of the guidance document is available using the link below:

[MHRA GxP Data Integrity Guidance](#)

Now that you have read it, remember, the minimum requirement is to have a data integrity policy and a gap analysis comparing these standards to your current practice. Have fun with that!

7 DAYS NOTICE FOR MHRA INSPECTIONS OF SPECIALS MANUFACTURERS

The MHRA has recently communicated to units operating under a Manufacturer's "Specials" Licence that there has been a change to the period of notice they will give specials manufacturers for an upcoming GMP inspection. Instead of the previous 28 day notice period, the MHRA will be giving a maximum of seven days notice for a GMP inspection, as of the 1st of April 2018.

The reasons behind this change were that several MHRA inspections of 'Specials' activities during 2016 and 2017 resulted in compliance management escalation, or regulatory action. Serious non-compliances identified by MHRA inspections have often been linked to a lack of financial and technical resources to consistently maintain the pharmaceutical quality system. Indicators suggest that organisations reduce focus on regulatory compliance until an inspection

notification is received, at which time the unit it is given additional resource to reach a reasonable level of regulatory compliance.

Therefore, to ensure senior management focus on the regulatory requirement to consistently maintain compliant and adequately resourced operations, the MHRA has changed its approach to inspection notification for Specials manufacturers. The MHRA states that this approach ensures that senior management are engaged in maintaining compliance, rather than performing cyclical increases in activity following inspection notification.

There will be no change to the standards used to assess compliance.

UKRG SUPPLIER AUDITS

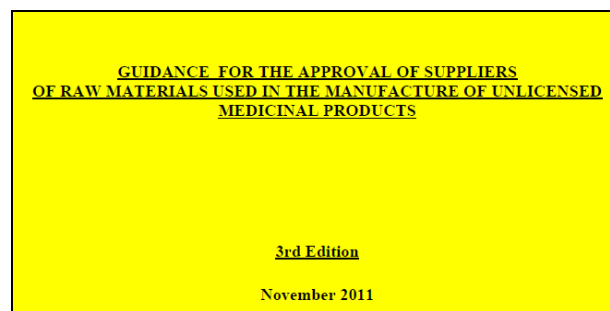
Auditing suppliers is a GMP requirement, but not every radiopharmacy can audit every supplier themselves. The UKRG are going to be running a series of supplier audits on behalf of all UK radiopharmacies, with the audit reports being made available to those that require them on request. Rob Lowe, has provided a summary of supplier audits and GMP requirements for specials manufacturers.

Traditionally, the sourcing of raw materials, by NHS Specials' manufacturers, has been focused on procuring the relevant material or service from a supplier who is able to supply an appropriate pack size, at an acceptably low cost. The availability of information from the supplier of TSE certification or certificates of analysis is also important both in terms of regulatory compliance and also because the ability to fully QC test incoming raw materials may be limited. However, the MHRA now expects manufacturers to have a greater understanding of the supply chain 'pedigree' for raw materials that are procured and the associated risks inherent in this operation. The supplier approval process must be supported by evidence of effective GMP compliance of the active pharmaceutical ingredient (API) manufacturing sites. The regulatory expectation is often that this will be confirmed via audit of the API manufacturing site by or on behalf of the manufacturing unit. Audits should be conducted at intervals not exceeding three years, by persons with appropriate training and experience, to confirm the current GMP status of the site.

The difficulty faced by NHS Specials' manufacturers is the need to source materials of suitable quality, within a reasonable delivery time and in quantities suitable for small-scale manufacturing. Further difficulties are caused by the fact that the majority of APIs are manufactured

outside the UK and often outside of the EU and therefore there are financial constraints to audit manufacturers for each of the APIs used. A further complication arises if the manufacturer of an API is unwilling to host an audit with a small scale manufacturer or asks for a substantial fee to be paid to allow access for auditing at the manufacturing site. Finally, it must also be considered that because the quantities of raw materials needed may be small, Specials manufacturers often source materials from distributors or brokers, rather than from the API manufacturer directly. Because of these difficulties a risk-based strategy for the evaluation and selection of raw material suppliers is usually employed. This provides a risk assessment score which ranks suppliers based on factors such as past experience, certification by national or EU regulators, the number of brokers in the supply chain between the manufacturer and the supplier you obtain the API from, information provided with the API etc. and dictates what level of audit scrutiny is required.

A Yellow Cover Document providing guidance on the approval of suppliers of raw materials for manufacturers is available from the NHS Pharmaceutical Quality Assurance Committee, using the link below:



<https://www.sps.nhs.uk/wp-content/uploads/2010/05/Supplier20Approval20Guidance20version203.pdf>

Note: registration on the SPS website is required.

This strategy requires identification of potential supply chain risks through the use and evaluation of supplier questionnaires and the sharing of audit reports between NHS manufacturers and Quality Assurance Specialist leads from across the NHS.

For suppliers of services a full technical agreement (TA) detailing the key aspects of the service, responsibilities and KPIs needs to be in place. This needs to be more than a standard template document and must consider specific local circumstances and needs. Realistic expectations of service provision must be agreed between both parties and responsibilities for quality must be defined in a technical (quality) agreement. Such a TA must be a meaningful, live document that

describes how the outsourcing arrangements and associated responsibilities of each party will be managed. It must not simply be seen as a regulatory or financial requirement. The TA should be drawn up, agreed and signed by both the purchaser and the provider of the service. It should define in practical terms the responsibilities of both parties with regards to the safety and quality aspects of the products or services provided. A service level agreement (SLA) will also be needed, defining the arrangements for the provision of a timely, cost effective and efficient service. A standard template for a TA is included in the 5th Edition of the Quality Assurance of Aseptic Preparation Services book (QAAPS5).

A TA should not just outline the service to be provided, but should specify if the service provider can sub-contract to another party, and if so how this is notified to the customer. Aspects of change control should be outlined so that the customer is kept aware of changes in the facility, process or materials used. How unplanned deviations are communicated and how complaints are investigated should also be covered. Finally, audit of the service provider needs to be specified. The customer is responsible for assessing the competence of the contractor to successfully undertake the work required. This may be through their own audit of the supplier or through the review of a relevant audit performed on behalf of the NHS by a third party (e.g. a QA Specialist). The TA should be clear that the service provider is expected to undertake regular internal audits and perform audits of any outsourced activities. The customer is entitled to audit the contractor's facilities relevant to the service being provided. In QAAPS5 the suggested frequency is bi-annually by mutual agreement with at least 4 weeks' notice, but if there is a specific problem or incident then a "for cause audit" must be undertaken promptly with a suggested time frame of 1 working days' notice.

A final word of caution is that while a supplier audit will give a valuable independent insight into actual activities at a supplier's site; it is only a "snapshot" on the day of the audit. Reliance will often be placed on an audit conducted by a third party. Obtaining a copy of an audit report is only the start of the process. There needs to be a formal consideration of the audit report with regards to specific local circumstances of the purchaser. This should consider:

- Knowledge and experience of the auditor
- When was the audit performed and is it still relevant?
- What was the scope of the audit and if this is relevant to the service required
- What was the outcome of the audit and what recommendations were made?
- What was the supplier's response to the recommendations and was this appropriate and timely?

RADIOPHARMACY UK EMAIL DISCUSSION LIST

After launching the Radiopharmacy UK Email Discussion List a good number of professionals and colleagues have joined the conversations.

If you belong to the UK Radiopharmacy community in the NHS or the academic sector you can still join the discussion list by following the link www.jiscmail.ac.uk/radiopharmacyuk.

Come and join in today! We all can contribute to find answers to frequent problems in our daily routine, share best practice or anything else you may think is useful for our Radiopharmacy community.

RADIOPHARMACY EUROPE EMAIL DISCUSSION LIST

With the closure of VirRAD activities, we have lost a valuable tool to communicate about clinical, academic, legislative and practical Radiopharmacy issues across Europe. As mentioned in the last newsletter, a European-wide discussion group has also been established where anyone in Radiopharmacy (academic or hospital) in Europe can ask to join by sending an email to the discussion group administrator at the following address: neil.hartman@bartshealth.nhs.uk



The email should include your first name, surname, email address, institution address and a brief sentence of which aspect of hospital or academic Radiopharmacy you are involved in. All communications will be strictly limited to the group and won't be able to be searched from any other source. The group email address is: europa-radiopharmacy@jiscmail.ac.uk but this is only accessible once you have been added to the subscription list.

“Is it just me?”

Is it just me, or is there not really enough room in this newsletter for this section in this issue?

No, it's not just you. This newsletter is already packed full of content, and significantly past its deadline, so apologies folks, but we'll maybe hold our “*Is it just me?*” questions until the next issue.

If you would like to ask another “*Is it just me?*” question, email the UKRG Newsletter editor at clint.waight@nhs.net, with the title “*Is it just me?*” and I'll anonymously ask the question here for you.

NEW IRMER REGULATIONS and ARSAC LICENCES

The new IRMER regulations came into force on the 6th of February 2018. The recommendations made by the UKRG in relation to the new ARSAC licensing process were generally accepted and most of you have had the pleasure of completing the new Employer and/or Practitioner application forms. Links to the application forms and the associated guidance document are provided below for those that have not yet begun the process.

[New Employer Licence Application Form](#)

[New Employer Application Guidance Document](#)

[New Practitioner Application Form](#)

[New Practitioner Application Guidance Document](#)

Remember, all of your current ARSAC certificates are still valid and you only need to change to the new Employer and Practitioner Licence model when you wish to introduce something that would have previously required a new ARSAC certificate. This includes new research studies, so centres performing research may be required to complete these applications sooner than others.

REGULATORY ISSUES

There's loads!

The MHRA and other GMP regulatory authorities have not spent the festive period resting on their laurels. Here's what they've been up to:

Publication of Data Integrity Guidance

As per the article on page 2, here's the link again to the [GxP Data Integrity Guidance](#).

New GMP Guidance for Investigational Medicinal Products

On the 16th of September, the European Commission published its new GMP guideline on Investigational Medicinal Products for human use.

In 2015, the European Commission conducted a consultation to determine whether there should be separate EU regulations for medicinal products for human use and Investigational Medicinal Products. As a result, the Commission has published separate documents, which can be viewed by following the link below:

[New EU GMP Guideline for IMPs - ECA Academy](#)

Draft Guidance on the update to Annex 1 of EU GMP

The European Commission has conducted a consultation on the new EU GMP Annex 1: the Manufacture of Sterile Medicinal Products. While the consultation has now closed, the draft document is still available to view by following the link below. This might help you to stay ahead of the game when the final document is published.

[Draft consultation document for EU GMP Annex 1](#)

MHRA Guidance on Out Of Specification (OOS) results

The MHRA have identified a deficiency in the way that out of specification results are handled in QC laboratories. Many of us in Radiopharmacy conduct a decent amount of our own QC testing in the form of radiochemical purity testing, and the handling of out of specification results can vary between sites. We conducted a small workshop on this issue at Bournville this year, but the MHRA have produced an excellent flow chart document to guide you through how to investigate OOS results in your department. The link to the document is given below. It's well worth a look and will be very useful in writing your own procedures for handling such events in the future.

[MHRA OOS Guidance](#)

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.

Withdrawal of UK Marketing Authorisation for Leukoscan

Immunomedics GmbH have taken the decision to withdraw their marketing authorisation for Tc99m-sulesomab (Leukoscan[®]), for commercial reasons. The marketing authorisation was officially withdrawn on the 21st of February 2018. There are no identical generic products available, however there is at least one alternative EU licensed product available for similar indications to Leukoscan[®].

Lutathera[®] approved by the EMA

Lutetium-177 oxodotreotide (Lutathera[®], Advanced Accelerator Applications) has received approval for use by the European Medicines Agency for the treatment of gastroenteropancreatic neuro-endocrine tumours (GEP-NETs). The approval was based on the results from the NETTER-1 trial where progression free survival was estimated at the 20 month data cut-off point, as being 65% in the Lutathera[®] group and 11% in the control group.

Lutathera[®] is given as four separate intravenous infusions of 7.4 GBq, at eight week intervals. Lutathera[®] is given concurrently with long-acting octreotide 30mg injections, 4-24 hours after the infusion and short acting octreotide for symptomatic relief.

UPCOMING MEETINGS

31st Annual Congress of the European Association of Nuclear Medicine

13th – 17th October 2018, Dusseldorf

Website: www.eanm.org/congresses-events/future-congress

12th Congress of the World Federation of Nuclear Medicine and Biology

20-24 April 2018, Melbourne, Australia

Website: <http://wfnmb2018.com/>

SNMMI Annual Meeting

Society of Nuclear Medicine and Molecular Imaging
Annual Meeting
23-26 June, 2018
Philadelphia, US

Note: BNMS are running a session on Lung V/Q SPECT imaging on Monday 25th June at this meeting, including the manufacture and use of Krypton and other ventilation agents.

UKRG Annual Workshop 2019

Friday 11th January 2018, Bournville, UK
Website: www.ukrg.org.uk

CAREER OPPORTUNITIES IN RADIOPHARMACY

Radiopharmacy posts are advertised in your local area by several means, including the Radiopharmacy UK email discussion list and other forums. If you are looking to advertise a post in your Radiopharmacy, or you are looking for career opportunities, the following websites and mail-bases may be of use to you.

See what's out there at:

NHS England: www.jobs.nhs.uk
Health in Wales: Health in Wales
NHS Scotland: www.jobs.scot.nhs.uk
Northern Ireland: Health & Social Care NI
UK Radiopharmacy email discussion list:
www.jiscmail.ac.uk/radiopharmacyuk

From the Editor

The newsletters are all published on the UKRG website, so if you're interested, please go to www.bnms.org.uk/ukrg/general/newsletters.html where you can read the entire back-catalogue if you wish!

The next meeting of the UKRG Committee will be on 24th of April 2018. If readers have any issues they wish to be discussed please raise them with your regional rep on the Committee <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 2017-Q2

Publication date:

Editor-in-Chief: Clint Waight

Department of Pharmacy,
The Royal Infirmary of Edinburgh,
51 Little France Crescent,
Old Dalkeith Road, Edinburgh, EH16 4SA
Phone: 0131 242 2929; Fax: 0131 242 2931
Email: clint.waight@nhs.net