U.K. Radiopharmacy Group

NEWSLETTER
2014 – Q3
Edition

BOURNVILLE 2015: UKRG ANNUAL WORKSHOP

UKRG is pleased to announce that the 2015 Annual Workshop will take place at The Beeches Management Centre, Bournville, on **Friday 16th January 2015**.

Full details of the Workshop programme will be circulated shortly (via your local UKRG Rep, and in the 2014Q4 Newsletter) but we can confirm one speaker: Ian Oxley of IBA [Editor's Note: *now of AML?*] will be giving a talk on, and leading a workshop on, "quality risk management and financially-prioritised risk assessments".

Ra-223-DICHLORIDE (XOFIGO®): SAFE DRAWING UP GUIDANCE

The joint UKRG/IPEM/BNMS Guidance on the "Safe Drawing Up of Ra-223-dichloride (Xofigo®)" is now available on the UKRG website at this URL: http://www.bnms.org.uk/images/stories/UKRG/2014/Addendum_to_Safe_Drawing_up_document_for_223Ra_Radium_Chlor1.pdf

SNOMED CT UPDATE

The SNOMED Clinical Terms (CT) group at the Health and Social Care Information Centre (HSCIC) has been working to incorporate radio-pharmaceuticals into the SNOMED CT Project. UKRG has been concerned to ensure that this is robust and has been pleased to contribute to the exercise over the past year or so. An overview of SNOMED CT can be found at this URL: http://systems.hscic.gov.uk/data/uktc/snomed

Details of the Project's current status can be found at this URL: http://systems.hscic.gov.uk/data/uktc/news/radiopharmaceuticals

RADIOPHARMACEUTICALS IN CLINCIAL TRIALS: AN UPDATE ON "CERT"

CERT is the "CR-UK(*) ECMC(**) UK Radiopharmacy Taskforce". It has the key aim of acting as the primary interface between the radiopharmacy community and regulatory authorities. The emphasis will be on creating a common understanding of the regulatory requirements for the development and delivery of clinical trials that involve radiopharmaceuticals, primarily at ECMCs but also all other relevant UK clinical trial units.

CERT will also actively influence clinical trial regulations and guidelines to take into account the specialised nature of radiopharmacy clinical trials, ensuring that coherent implementation into practice happens across the UK radiopharmacy community.

CERT's remit is to:

- Steer the activities of CERT by identifying priorities for the development of the Taskforce and taking them forward
- Understand and influence the clinical trial regulations, and how they can be uniformly applied to clinical trials needing radiopharmacy involvement
- Provide advice on interfacing with industry and the regulators with respect to radiopharmacy activities in clinical trials
- Ensure that coherent networking within the radiopharmacy community takes place
- Facilitating expertise and knowledge sharing between ECMCs and throughout the UK research radiopharmacy community
- Identify options and practical solutions for sharing best practice and knowledge

- Discuss scientific, strategic and resourcing issues relating to radiopharmacy in early phase cancer trials
- Identify priority areas where insufficient or out of date guidance exists and develop new or updated guidelines
- Raise the profile of early phase cancer trials involving molecularly targeted radio-pharmaceuticals
- Implement innovative approaches to ensure radiopharmacy support for trials can be delivered more consistently and effectively across the UK
- Assist research groups in the development and completion of clinical trials involving radiopharmaceuticals

The CERT website can be found at this URL:
http://www.ecmcnetwork.org.uk/network-groups/cert-group/

The purpose of this resource is to provide guidance and advice related to the set-up of clinical trials using radiopharmaceutical Investigational Medicinal Products (rIMPs). It includes:

- A detailed step by step overview of the process from building the initial study concept to submitting your CTA application to the MHRA
- A roadmap highlighting each step in the above process
- An IMPD advice document which has been written specifically for radiopharmaceuticals
- Links to useful websites/groups and contact details to experts who are willing to provide help with many of the aspects involved in setting up these studies

Currently the resources the group is developing are accessed through the members-only logon; for access to this please contact James Ritchie by e-mail (james.ritchie@cancer.org.uk)

[Editor's note*: "CRUK" is Cancer Research-UK, and the ECMC is the "Experimental Cancer Medicine Centre", an initiative jointly funded by CRUK, the National Institute for Health Research (NHIR) in England, and the Departments of Health for Scotland, Wales and Northern Ireland*]

EANM GUIDANCE ON PREPARING AN IMPD

In August 2014 the EANM published guidance to help in the preparation of an IMPD.

The preparation of an Investigational Medicinal Product Dossier (IMPD) for a radiopharmaceutical to be used in a clinical trial is a challenging proposition for radiopharmaceutical scientists working in small-scale radiopharmacies. In addition to the vast quantity of information to be assembled, the structure of a standard IMPD is not well suited to the special characteristics of radio-pharmaceuticals. This [new EANM] guideline aims to take radiopharmaceutical scientists through the practicalities of preparing an IMPD, in particular giving advice where the standard format is not suitable. Examples of generic IMPDs for three classes of radiopharmaceuticals are given: a small molecule, a kit-based diagnostic test and a therapeutic radiopharmaceutical.

The EANM Guidance can be found at this URL:
http://www.eanm.org/publications/guidelines/2014_published_RP_IMPD.pdf

SEVEN DAY WORKING IN HOSPITAL PHARMACY SERVICES

UKRG is aware of the publication by the Royal Pharmaceutical Society (RPS) of a document entitled "Seven Day Services in Hospital Pharmacy: Giving patients the care they deserve".

This has been published by the RPS in response to the recommendations of NHS England's "NHS Services, Seven Days a Week Forum" that high quality treatment and care should be available in NHS hospitals every day of the week. The document was published to report on an RPS meeting held on 20th May 2014 to discuss the challenges posed in providing seven-day services; four themes arose from the meeting:

- Joining up hospital and community pharmacy services;
- The pharmacy workforces and ways of working;
- Targeting where to deliver seven-day services; and
- Affordability and building a case (for seven-day working) at an organisational level.

Newsletter readers will be interested to note that there is no mention of radiopharmacy or nuclear medicine anywhere in this document.

Mo99/Tc99m SUPPLY STABILITY

The OECD and NEA have published a review document on "***The Supply of Medical Radioisotopes***", subtitled "*Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the 99Mo/99mTc Market, 2015-2020*"

This document is commended to Newsletter readers for a better understanding of the Mo99/Tc99 supply situation. It can be found at this URL: http://www.oecd-nea.org/med-radio/reports/sen-hlgmr2014-2.pdf

REGULATORY ISSUES

MHRA Feedback on GMP Inspections

UKRG is pleased to welcome a Medicines Inspector at its meetings, in order to keep up-to-date with the MHRA approach to GMP issues. The attending Inspector is also able to give feedback on recent GMP inspections. Richard Funnell, GMP Inspector, attended the July UKRG meeting and provided the following feedback.

It appears that, in general, radiopharmacies have been found to be complying well with GMP at inspection. Most of the issues raised at inspections related to the sites' Quality Management Systems (QMSs):

- Quality Exception Reports are not always investigated in a timely manner and not fully analysed for root cause and identification of resultant CAPAs.
- The supplier approval process is not always up to scratch with more justification needed of why a unit is purchasing from a given company. This mainly relates to the purchasing of un-licensed 'cold' kits.
- There are sometimes issues where the labelling process being used is a bit 'confused'.
- There are some situations where commitments made to address deficiencies raised at a previous inspection have either not been fulfilled or not done in the agreed time frame. In this situation units should inform the MHRA via an interim compliance report (*) that agreed actions are not on course.
- There have been some issues with the sterilising of products manufactured from non-sterile starting materials.

Richard stated that it is often appropriate to have more than one person named on the Specials Licence for a given role (i.e. QC or production manager). This would enable a deputy to be identified.

(*) Richard was asked about other situations where the MHRA would expect an interim compliance report to be submitted. He gave some examples such as staff changes or where there was long term sickness (> 3 months) of someone named on the licence. It would be unusual to have to submit more than two such reports between inspections.

MHRA Investigation into the marketing of "stabilised" Medi-Exametazime by Link Medical Ltd.

Newsletter readers may be aware that the Enforcement Group at the MHRA conducted an investigation into the marketing of so-called "stabilised" "Medi-Exametazime" by Link Medical Ltd. UKRG has received the following statement from the MHRA on the conclusion of its investigation.

[The MHRA] investigation into Link Medical Ltd has now been concluded.

Link Medical Ltd, in the form of Mr Peter DOBSON and Mr Bob KENNY, has been issued with a formal warning with regard to supplying and offering to supply an unlicensed medicinal product in the form of a 'stabilised' version of MEDI-EXAMETAZIME with Cobalt Chloride. (The un-stabilised version of MEDI-EXAMETAZIME was and still is a properly licensed product). This formal warning has also included the fact that they made changes to a Summary of Product Characteristic (SmPC).

You may also be aware that Link Medical Ltd had its Wholesale Dealers Licence (WDL) suspended. However, on 17th March 2014 their WDL was reinstated by the MHRA. The range of regulatory actions which we are able to take against licences and the persons named on them is limited. In order for Link Medical Ltd to have their licence reinstated a number of variations were made which included the removal of Mr DOBSON as the Responsible Person. They now have a new Responsible Person. - Dawn Chivers.

We will of course continue to monitor the company's compliance with medicines legislation. In this respect if you or your colleagues become aware of any issues please do let me know.

Lastly, I would like to thank [you] and your department for the help they gave the MHRA during this investigation.

Contact details of the MHRA Officer dealing with this investigation can be obtained from the Editor on request.

As a result of this MHRA investigation UKRG is aware that some radiopharmacies, eg in the North West of England, are removing Link Medical Ltd from their list of approved radiopharmaceutical suppliers.

MHRA Guidance Note 5 (Manufacturer's Licence) and Guidance Note 6 (Wholesaler Dealer's Licence) have been updated

These guidance notes have been updated following the consolidation of medicines legislation into the Human Medicines Regulations 2012 and the implementation of the Falsified Medicines Directive.

These guidance notes have been published to help applicants and those who hold a manufacturer's licence, wholesale dealer's licence (WDA(H)) or broker registration. They outline the key obligations for maintaining the licence/registration.

Details can be found at this URL:
http://www.mhra.gov.uk/Howweregulate/Medicines/Medicinesregulatorynews/CON432946

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

13th August 2014 was a "red-letter-day" for GMP Updates. Details of recent changes are summarised below:

The revised Chapter 2 on **Personnel** became effective from 16th February 2014.

The revised Chapter 3 on **Premises and Equipment** was published on 13th August 2014; the deadline for implementation is **1st March 2015**.

The revised Chapter 5 on **Production** was also published on 13th August 2014; the deadline for implementation is also **1st March 2015**.

The revised Chapter 6 on **Quality Control** was published on 28th March 2014, with a deadline for implementation of 1st October 2014.

The revised Chapter 8 on **Complaints and Product Recall** was also published on 13th August 2014; the deadline for implementation is also **1st March 2015**.

A **revised Part II: Basic Requirements for Active Substances used as Starting Materials** was also published on 13th August 2014, with implementation 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 closing date for comments is stated as 31st May 2014. It is expected that the revision will be effective from some time in October 2014.

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.

MHRA Symposium GMP/GDP 2014

A reminder to readers that the next MHRA Symposium on GMP/GDP will be held on **9-12 December 2014** in London. Due to the ever increasing demand for the symposium, this year the symposium will run over four days, comprising of two GDP days (9th and 11th December 2014) and two GMP days (10th and 12th December 2014).

The purpose of the 2014 GMP Symposium is to introduce the latest changes to EU GMP and to continue to give inspector led training as has been popular at previous MHRA symposia. Currently, the topics considered to be most relevant are Annex 16, Annex 15, Chapter 3 and 5 on prevention of cross contamination and the latest developments in the implementation of the Falsified Medicines Directive (FMD). The Agency is also looking to build on the information presented at last year's symposium on data integrity issues.

Similarly the purpose of the 2014 GDP Symposium is to review and consider the impact of the EU GDP Guidelines 2014, the Falsified Medicines Directive (FMD).

For details of the Symposia, and to book, visit the website at this URL:
http://www.mhragmdp.co.uk/

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

Products currently under evaluation by the CHMP include the following:

- Lutetium (Lu-177) (Chloride)
- [Technetium (Tc-99m)] Tilmanocept (trade name: Lymphoseek®)

[Editor's Note: ***STOP PRESS: on 25/9/14 the EMA recommended that Tilmanocept be granted a Marketing Authorisation.***]

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 IBA Molecular UK Ltd.

In the 2013Q3 edition of the Newsletter we reported that Alliance Medical Ltd (AML) had taken full ownership of Erigal, and had also acquired IBA Molecular's UK F^{18}-FDG production facility. In the 2014Q1 edition of the Newsletter we reported that AML had been referred by the OFT to the Competition and Markets Authority (CMA). On 15th August the CMA cleared AML's acquisition of IBA Molecular's facility. Full details can be found at this URL:
https://www.gov.uk/cma-cases/alliance-medical-iba-molecular

Following the CMA clearance of this acquisition AML has also now become the exclusive UK distributor for IBA's SPECT radiopharmaceutical business. Mike Ward, AML Market Development Manager, has provided the following Press Announcement:

Alliance Medical, Europe's leading provider of medical imaging services, has secured a deal to become the exclusive UK distributor of IBA's SPECT radiopharmaceuticals (including Mo-99 generators) as part of their goal to provide a secure supply of radionuclides / radiopharmaceuticals to UK patients and the UK diagnostic imaging market.

This business integration will allow hospitals to have a single point of contact for both their SPECT and PET radiopharmaceutical needs, helping to creating a more streamlined service around their individual needs, with less duplication and greater economies of scale. The transfer of the business will not impact or affect arrangements with existing customers. IBA Molecular continues its long term commitment to SPECT radiopharmaceuticals which will allow for a better service and, over time, allow a guarantee of the secure supply of radionuclides to the UK.

The announcement comes as Alliance Medical continues to expand its molecular imaging business, following their acquisition of FDG producer Erigal and the FDG business of IBA Molecular UK, and now creating the UK's only integrated PET/SPECT radiopharmaceutical supply and imaging service.

Over recent months Alliance Medical has furthermore presented to both the BNMS Isotope Development group and UK Radiopharmacy group its longer term plans to further support nuclear medicine in the UK by considering the installation of cyclotrons powerful enough to also manufacture Tc-99m (as pertechnetate) so that variations in the world Mo-99 supply would not necessarily adversely affect the availability of Tc-99m in the UK.

Howard Marsh, Managing Director, Alliance Medical Molecular Imaging said: "*We are delighted to have been chosen by IBA Molecular as the exclusive distributor of their SPECT radiopharmaceuticals in the UK. This agreement is another step forward for us in our ambition to become the most relevant organisation for the provision of molecular imaging services in the UK."*

Mike Ward, Market Development Manager, said: *"We're really pleased to have the support of the Alliance organisation in providing even better support to all our UK customers, both current and future and to enhance the options for patient management."*

Further details can be obtained from Mike Ward,
Tel: 01483 203204, e-mail: mward@alliance.co.uk

Mallinckrodt News

UKRG has received the following update from Mallinckrodt.

The original Cardiolite (manufactured now by Lantheus in the US) will be distributed through Mallinckrodt via the usual free phone number from the UK. Other Lantheus products may follow by this route.

Also, DOTATATE kits (manufactured by Polatom) used as part of Neuroendocrine diagnostic therapy work up with Indium-111; therapy with 90Y and follow up of therapy with Indium-111 will be available soon from Mallinckrodt. Likewise DOTATATE as a GMP grade starting material for Ga68 synthesis for PET treatment planning and monitoring.

GE Healthcare product and SPC updates

GE has revised its production schedule for Sodium (Cr-31) Chromate (CJS.1P); instead of the previous "made-to-order" two-weekly production process this will now be made on a scheduled four-weekly production cycle, available in all current pack sizes with no order deadline.

GE has also updated the SPCs for their Sodium (I-131) Iodide therapy (Theracap®) and diagnostic capsules following the removal of the printed name from the capsule.

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

Eckert & Ziegler Ga-68 Generator News.

At the end of June 2014 Eckert & Ziegler received marketing approval from the European Medicines Agency (EMA) for the E&Z Ge-68/Ga-68 generator. Approval for sale of the generator in the respective countries of the EU should by now be in place. The EW&Z Press Release can be found at this URL:
http://www.ezag.com/home/press/press-releases/detail/article/eckert-ziegler-european-approval-process-for-gallium-68-generator-successfully-completed-worl.html

Diagnostic Imaging Ltd acquire *raytest* distributorship for the UK and Ireland.

Diagnostic Imaging Ltd are pleased to announce that they have been appointed UK and Ireland distributors for *raytest*. As you would expect from a German company the *raytest* products are precision engineered with a high level of reliability. The range of products includes: Radio TLC, Radio-HPLC, Radio Synthesis (including a fully automatic Ga-68 Cassette Labelling System), Spectroscopy, QC Lab Equipment, Radio-GC plus much more. The products are supported from UK by highly experienced engineers.

For more information please visit the DIL website www.diagimaging.com or call Mike Barker on 0845 226 0520.

Imaging Equipment Ltd (IEL) Update on the Netter-1 Study

The Netter-1 Study into peptide receptor radiotherapy (Lu-177 Dotatate) for patients with mid-gut somatostatin positive neuroendocrine tumours is reaching completion and recruitment will close in mid-November 2014. The international multi-centre study has successfully randomised 172 patients into the Lutetium 177 Dotatate arm and into a Somatostatin 60mg control arm, and several UK sites have received special mention from the trial sponsor for their contribution to the study. The Royal Free Hospital London, under the leadership of Professor Martyn Caplin, has recruited the second largest number of patients into the study

from within Europe, and the team at King's College London led by Dr Raj Srirajaskanthan has been singled out for praise following recruitment of patients into the Dosimetry Sub-Study which is looking at how different patient doses affects treatment outcomes. The Netter-1 Study is the first fully randomised controlled trial in peptide receptor radiotherapy and both the scientific and clinical community is looking forward to seeing the results of follow-up at both the interim stage in 2016 and the final report stage which will be in 2018.

UPCOMING MEETINGS

2014

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

2nd Cardiac PET Meeting
14 November 2014, Manchester, UK
Info from: Peter.Nield@cmft.nhs.uk

GMP/GDP Symposium 2014
9-12 December 2014, London, UK
Website:
http://www.mhra.gov.uk/ConferencesLearningCentre/Conferences/index.htm

Postgraduate Course in Radiopharmacy 2014
9-12 December 2014, London, UK
Website:
https://www.kcl.ac.uk/prospectus/shortcourses/index/name/postgraduate-course-in-radiopharmacy-2014/keyword/medicine

2015

UKRG Annual Workshop 2015
16 January, Bourneville, UK
Website: www.ukrg.org.uk

10th European Molecular Imaging Meeting
18-20 March, Tübingen, Germany
Website: http://www.e-smi.eu/index.php?id=2575

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

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 9th and 10th October 2014; and the meetings after that in Bourneville, on 14th and 5th January 2015. 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.

Please support the new Newsletter Editors!

My retirement from RMPD-Hartlepool, and from the NHS, at the end of November 2014 coincides with the end of my term as UKRG Newsletter Editor (there will be a 2014Q4 issue!).

I should like to take this opportunity to thank all the readers of the various issues for which I have been responsible, and to ask you all to give your support to the new joint-Editors as they take over the reigns from January 2015.

I am pleased to report that the new Editorial Team comprises:

- **Clint Waight (Editor-in-Chief), Edinburgh**
- **Bev Ellis (Assistant Editor), Manchester**
- **Maria Palmer (Assistant Editor), Bristol**

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