U.K. Radiopharmacy Group

NEWSLETTER
2015 – Summer Edition

ACCREDITATION STANDARDS FOR RADIOPHARMACY SERVICES

The Academy for Healthcare Science has been commissioned by the Chief Scientific Officer for NHS England to develop an accreditation standard and improvement programme for all Clinical Engineering and Physical Science services encompassed within healthcare science (iCEPSS; Improving Clinical Engineering and Physical Science Services).

All Radiopharmacy services (including both MS Licensed and Section 10 Units) are included in this programme. In addition to core domain standards, separate CSES (Clinical Scientific or Engineering Service) domain standards have been developed for Radiopharmacy.

Nuclear Medicine departments who manufacture radiopharmaceuticals will also have to comply with the Radiopharmacy standards as well as the Nuclear Medicine CSES standards.

A number of Radiopharmacies have volunteered to pilot these standards. If you would like to volunteer as a pilot site, please contact Peter Jarritt (Peter.Jarritt@ahcs.ac.uk)

ADVERSE REACTION AND PRODUCT DEFECT REPORTING

The UKRG Radiopharmaceutical Adverse Reaction and Product Defect on-line Reporting Forms are available on the UKRG website. There are separate forms for reporting adverse reactions and product defects. If there are any problems in using these forms please contact: Neil.Hartman@bartshealth.nhs.uk

ERROR REPORTING

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.

A summary of results from a pilot study is given below:

- 81 error reports returned from 5 centres since 1st January 2015
- Breakdown of errors shown in following tables.

Product type	**Number**
Tc-99m kits	60
Other compounded kit	1
Finished product	6
Blood labelling product	2
Batch prepared products	6
Other non-active products	2
Not categorised	4

Error type	**Number**
Incorrect requests	2
Incorrect transcription	2
Patient dose calculation error	31
Worksheet calculation error	2
Incorrect assembly / preparation / radiolabelling	3
Incorrect dose measure	11
Labelling (paper) error	1
Dispatch error	20
Others	2
Not categorised	5

Staff category	**Number**
Person taking order	4
Person preparing paperwork in advance	40
Person preparing / labelling vials	12
Person preparing final product	10
Person checking	8
Person transporting products	1
Not categorised	1

Staff group	Number
Pharmacist / Radiopharmaceutical Scientist	3
Technologist / technician	71
ATO / SATO	2
Radiographer	1
Student / pre-reg. pharmacist	3
Not categorised	1

When was error detected?	Number
By self, when checking	2
First check, in assembly area	3
Operator check, in preparation area	11
During assembly, preparation, radiolabelling	6
During calibration	5
During labelling (paper)	1
Final check prior to release	13
At release	23
On receipt	3
In clinical area, prior to administration	7
Not categorised	7

Patient outcome	Number
None	73
Minor	5
Moderate	2
Major	1

GMP Outcome	Number
None	66
Other	13
Minor	0
Major	2

LYSINE-ARGININE SUPPLY

Currently this product is only available from Preston Pharmaceuticals. The product is expensive to manufacture and often there is expired stock. In order to plan for sufficient supply, Preston Pharmaceuticals would like collate information on user requirements.

If you are a user of this product please email Angela Nutman (Angela.Nutman@lthtr.nhs.uk) with your annual usage.

KEY PERFORMANCE INDICATORS

A UKRG working group is developing a Guidance Document on Key Performance Indicators (KPI's) for Radiopharmacy Services and would be interested to know what KPI's (if any) departments are currently using. If you are happy to share these please email davidgraham1@nhs.net

GALLIUM-68 UPDATE

An update on the current status of Ga-68 in the UK is attached in Appendix 1 of this Newsletter.

BOURNVILLE 2016 UKRG ANNUAL WORKSHOP

UKRG is pleased to announce that the 2016 Annual Workshop will take place at The Beeches Management Centre, Bournville, on **Friday 15th January 2016**.

Full details of the Workshop programme will be circulated in the next Newsletter

The UKRG would welcome suggestions for topics for the workshop. Please email any suggestions to Adrian.hall@rmh.nhs.uk

PLATELET RADIOLABELLING

There is a meeting on Monday 28th September 2015 at St Bartholomew's Hospital in London to discuss SOPs and practice and to formulate a national SOP guidance for the radiolabelling of platelets and their radiopharmaceutical release.

Further information including a programme and registration for the meeting can be obtained from Neil.Hartman@bartshealth.nhs.uk

KING'S POSTGRADUATE COURSE IN RADIOPHARMACY

The next running of the course will be from Tuesday 8th to Friday 11th December 2015 at St Thomas's Hospital, London. For further details see https://www.kcl.ac.uk/prospectus/shortcourses/index/name/radiopharmacy2015/keyword/medicine

BNMS ANNUAL SPRING MEETING 2016

The BNMS Annual Spring Meeting will be held from Sunday 17th April to Tuesday 19th April 2016 at the International Conference Centre, Birmingham

The UKRG would like to encourage people to submit abstracts to support the Radiopharmacy sessions. The deadline for submitting abstracts is likely to be early January 2016.

REGULATORY ISSUES

Update on EU GMP

It should be noted that the MHRA expect to see **Change Control** procedures followed, including impact assessments for updates and changes to EU GMP. 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 15 on **Qualification and Validation** has been revised and is available on the Eudralex website. The deadline for coming into operation is the 1st of October 2015.

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.

Several changes were made to Eudralex Volume 4, which were highlighted in the last newsletter. If you are not aware of these, the changes 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**.

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.

The Grove Centre's Diamond Jubilee

This year, GE Healthcare's Grove Center celebrates 75 years of innovation. What began in the 1940s as "The Radiochemical Center," then became, among other things, a luminous paint factory, continues now as a hub for some of the most innovative healthcare technologies of our time. In its Silver Jubilee year, 1965, the Grove Center launched the world's first commercial radioimmunoassay kit, for measuring insulin in the blood of diabetics. This became a universal clinical tool and the first in a long line of industry-leading healthcare products. The site remains a key center of research, as well as the global headquarters of GE Healthcare's Life Sciences division.

Full story with additional historical pictures can be found at http://newsroom.gehealthcare.com/the-grove-centres-diamond-jubilee-a-look-back-at-75-years-of-innovation/

Mallinckrodt improves labelling of Technescan HDP and MAG3 kits

As part of a plan to improve the labelling properties of radiopharmaceutical kits, Mallinckrodt has revised the summary of product characteristics (SPC) for Technescan HDP and MAG3.

The new HDP (Sodium Oxidronate 3.0mg) can now be labelled with a maximum activity of 11.1 GBq in a volume of 3-10 ml. Previously, the maximum activity was 7.4 GBq in a volume of 3-6 ml. Please refer to revised SPC (section 12) for further information.

The revised SPC for MAG3 now states that the maximum activity that can be added to the vial is 2960 MBq in a volume of 10 ml. The shelf–life of the radiolabelled product is 8 hours (when stored below 25^{o}C). Please refer to the revised SPC (sections 6.3 and 6.6.1) for further information.

GE Web Ordering

GE Healthcare's new Web Ordering system is now live and they are inviting customers to register to utilize the benefits it has to offer. This tool allows you to:

- Order products at your convenience 24 hours a day
- View your order history
- Search through your available product range
- Save items to your favourites
- View current order status
- Repeat your past orders with ease
- View your PO spending
- Check what orders have been placed by 'procurement' if you do not place orders directly

To register, please go to **ci.gehealthcare.com**
If you have any questions about Web Ordering, or need helping registering, please contact Customer Service on 0800 558822 our your local Key account Manager

GE: Updated SPC for Nanocoll

GE have revised the SPC for Nanocoll, which now includes an expansion of the licensed indications, such as identification of the sentinel lymph node draining a primary tumour in the following malignant diseases: melanoma, breast, prostate, penile, head and neck and female pelvic cancer.

NanoScan kits (PL 40129/0002)

NanoScan (Human Serum Albumin nano sized colloid 500 micrograms) kits are now available from Diagnostic Imaging Ltd. Licensed indications include conventional lymphoscintigraphy and sentinel node detection in melanoma and breast cancer. The shelf-life of the reconstituted product is 8 hours. Please refer to the SPC for further details.

NORMAN VEALL MEDAL 2015

Congratulations to Paul Maltby who was awarded the prestigious Norman Veall Medal at the BNMS 2015 Awards Dinner.

The award recognises a non-medical scientist who has made an outstanding contribution to the science and/or practice of nuclear medicine in the United Kingdom.

UPCOMING MEETINGS

Hospital Pharmacy Europe – LIVE

HPE LIVE is returning to **Birmingham** for its third consecutive year on **13th October 2015** with a programme designed to address innovation, clinical excellence and continuity of care.

Bringing together expert speakers at the forefront of modernisation and service improvement with an exhibition designed to showcase the latest technological, pharmaceutical and delivery products, this event will be a **unique opportunity to share experiences with colleagues from across the UK** whilst taking home practical ideas and solutions which will **impact the way pharmacy services in your department**.

Register early to secure your free place!

Launched in 2002, Hospital Pharmacy Europe is a market-leading brand serving a highly engaged audience of over 12,000 Hospital Pharmacists across Europe.

Hospital Pharmacy Europe magazine – affectionately known by its readers as the '**Purple Journal**' – delivers a potent combination of timely news and definitive, peer-reviewed clinical articles in every issue

This year, HPE LIVE are working closely with the UKRG, such that there will be a UKRG stand at the conference, manned by our Committee Chair, Jilly Croasdale. This joint collaboration may also see the UKRG featured in an upcoming issue of HPE.

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

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.

The next meetings of the UKRG Committee will take place in London, on 8th October and then in Bournville 13th and 14th of January for the Strategic and Committee meetings, followed by the annual workshop on the 15th of January. 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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APPENDIX 1:

UPDATE ON CURRENT STATUS OF ^{68}Ga IN THE UK

Are we any closer to having ^{68}Ga-DOTATATE routinely available?

RECENT PUBLICATIONS:

- *Ph Eur* monographs for ^{68}Ga chloride labelling solution and ^{68}Ga-edotreotide (DOTATOC) have been published; however, the limit for ^{68}Ge breakthrough has been challenged and might be relaxed
- UKRG has published guidance on introduction of a clinical ^{68}Ga labelling service

  http://www.bnms.org.uk/images/stories/UKRG/2014/GMP_and_Practical_Requirements_for_68Ga_Gallium_Radiolabelling__2014.pdf

CLINICAL USE:

- There are now four centres routinely producing ^{68}Ga-DOTATATE/etc
- Several other centres are close to introducing ^{68}Ga peptides
- Mallinckrodt at UCLH has expanded production
- Clinical interest remains as high as ever, despite delays in roll out
- Other indications, such as prostate specific membrane antigen, are promising

GENERATORS:

- IGG101 (Eckert & Ziegler/Imaging Equipment Ltd)
  - Received marketing authorisation in Denmark last year; through mutual recognition it is now licensed in Germany, Italy, and some other countries
  - No decision yet on applying for authorisation in UK due to cost
- ITG (ITG Garching/Diagnostic Imaging Ltd)
  - Redesigned column has largely addressed problems with ^{68}Ge breakthrough and high backpressure
  - Clinical grade generator (GMP certified) now available and proceeding toward eventual licensing
- iThemba (IDB/Link Medical)
  - Made to South African GMP standards
  - Can now be legally imported into UK by Link

REAGENTS:

- Peptides:
  - DOTATATE is now available from Mallinckrodt
  - DOTATOC and DOTANOC are freely available
  - HA-DOTATATE (Scintomics) is freely available
- Other reagents:
  - The three generators each use a different strength of HCl as eluent
  - Sterile GMP-certified ultrapure (low metal) 0.1 M HCl eluent available in 250 mL bags (Rotem, via Imaging Equipment)
  - Several NHS manufacturing units have made reagents to E&Z or ITG specifications, though this may not be on-going
  - Increasingly, manufacturers of synthesizers are now supplying GMP reagents with sterile cassettes

KITS:

- There are no licensed kits for preparation of ^{68}Ga radiopharmaceuticals
- However, there has been recent progress toward development of kit procedures using eluate of licensed generator (AAA and Octreopharm looking at this)

PROCESSING OF ELUATE AND/OR PRODUCT:

- Pre-labelling processing of eluate
    - All generators eluted with HCl, though each at different strength
    - Some labelling protocols require pre-concentration of eluate to reduce volume for more efficient labelling reaction, to raise the pH, and to reduce ^{68}Ge breakthrough
    - Anion or cation exchange methods have been used; recently reported cation method does not require use of acetone
    - ITG method avoids pre-concentration and uses 4-5 mL bulk eluate
    - Other alternative is to use hottest fraction, but this only works when generator is fresh
- Post-labelling purification of product
    - Most protocols use post-labelling purification (trapping product on C-8 or C-18 cartridge, elution with ethanol, dilution with saline) to ensure high radiochemical purity and low ^{68}Ge breakthrough

AUTOMATION:

- Eckert & Ziegler Pharmtracer (Imaging Equipment Ltd) probably most widely used in Europe
- ITG (Diagnostic Imaging) shielded manual synthesis unit has been modified
- Scintomics (LabLogic)
- Raytest (Diagnostic Imaging)
- The above are supplied with sterile cassettes and GMP reagents are available for most
- Amercare dose dispenser has been used

HOT CELLS:

- Several radiopharmacies are installing a dedicated hot cell to house ^{68}Ga generator and synthesis unit; quotes varied from £60k to £125k

QUALITY CONTROL REQUIRED:

- See UKRG guidance document

SUMMARY:

- Progress has been made, particularly with respect to:
    - Generator performance and regulatory status, though not UK licensing
    - Availability of GMP reagents
    - Availability of DOTATATE
- Two promising developments:
    - Progress toward kit procedures
    - New indications, particularly PSMA

Jim Ballinger/Pei San Chan/Maggie Cooper on behalf of the UKRG
May2015