U.K. Radiopharmacy Group

NEWSLETTER
2008 Q1

SENSIBLE ADVICE

One of the roles of the UK Radiopharmacy Group is to provide "sensible advice" to the nuclear medicine community on issues which arise involving radiopharmaceuticals. Here are two such issues.

Erythrocyte sedimentation agents for leukocyte labelling procedures

We are reaching a crisis due to the withdrawal of various forms of hetastarch (Hespan) used for erythrocyte sedimentation. The original Hespan disappeared several years ago. One of the NHS pharmaceutical specials manufacturing units (PMU) has been preparing an equivalent product but their source has dried up and the last batch produced will be expiring soon. None of the available licensed alternatives performs satisfactorily.

Alternative agents

One of the attractions of hetastarch was its low incidence of allergic reactions. Two alternatives, dextran and methylcellulose, are effective but are associated with higher rates of adverse reactions. The formula for preparation of 2% methylcellulose can be found in the product information for GE Healthcare ^{111}In oxine. It is also available from an NHS PMU; details are available from the Editor.

A sensible precaution

Whatever sedimenting agent is used, it is advisable to minimise the potential for adverse reactions by setting aside 10 mL whole blood at the beginning of the procedure, free of sedimenting agent. This can be spun down to yield about 5 mL "virgin" plasma for final resuspension.

Slow speed centrifugation

As an alternative to a sedimenting agent, slow speed centrifugation can be used to remove erythrocytes. Spinning at 14***g*** for 15 minutes should yield cell rich plasma, though not as rich in cells or great in volume as the standard technique. However, not all centrifuges can be set to such a low g-force.

Dilution

Diluting whole blood with saline (approx 1 vol saline to 2 vol blood) will reduce the viscosity and accelerate sedimentation by gravity, though again will yield fewer cells and they will be more dilute.

The search for an alternative

The UKRG is working with suppliers to arrange import of a suitable agent. Information will be distributed via the usual channels.

Preparation of tetrofosmin

In 1999 the tetrofosmin (Myoview) preparation instructions were amended to include venting the vial with air immediately after reconstitution. This is to avoid the formation of degradation products under nitrogen atmosphere, accelerated by high radioactivity concentration.

However, the instructions do not mention what to do in the case of subdispensing. If this is performed, it is essential to vent both the kit vial and the subdispensed vial(s) in order to prevent degradation.

UKRG EVENTS

BNMS annual meeting 2008

This year's BNMS congress will be held in Edinburgh 12-14 May. The final programme will be available on the BNMS website imminently. There is talk of a radiopharmacy pub crawl on the Royal Mile. The deadline for early registration is 11 April. (Pre-registration is not required for the pub crawl, though paracetamol might be).

Summer school in radiopharmaceutical quality control testing

Plans will be finalised shortly for a 2-day summer school offering lectures and practical experience in radiopharmaceutical quality control testing. It will be held at the Waterloo campus of King's College London. The tentative dates are 17-18 July and full details will be distributed shortly. Please contact jim.ballinger@kcl.ac.uk.

Postgraduate course in radiopharmacy

The UKRG Easter course at King's College London was held 10-13 March with 32 participants.

UKRG INITIATIVES

Error reporting

As announced previously, a form (available from paul.maltby@rlbuht.nhs.uk) for reporting errors or near misses in radiopharmacy has been devised based on a system developed by the national CIVAS group (www.civas.co.uk). Completed forms will be treated confidentially and reported to the national scheme anonymously. The system is now fully up and running. Those not yet participating are encouraged join in.

REGULATORY ISSUES

Sinks in radiopharmacies

It has long been recognised that the HSE and MHRA have differing views on sinks in radiopharmacies. A meeting was held between representatives of the two agencies and the following is an unofficial report of the compromise proposed.

Background

In order to comply with the Ionising Radiation Regulations 1999, Regulation 18, part 7 "suitable and sufficient washing and changing facilities" and associated monitoring facilities are required at (normally immediately inside) the exit from any "controlled or supervised area".

The GMP guide prohibits sinks and drains in grade A/B areas, and it has been Inspectorate policy to discourage sinks in areas where aseptic processing takes place, including isolator rooms and the changing rooms/airlocks leading to such rooms.

A number of HSE inspectors have expressed concern that GMP inspectors have criticised the positioning of sinks at such points and in some cases have required that they be removed.

Controlled area

As defined in the Ionising Radiation Regulations, this is the area subject to special rules for the purposes of protection against ionising radiation and to which access is controlled. In, for example, a nuclear medicine department it is the area where radiopharmaceuticals are handled and where there is deemed to be risk of contamination. The area is designated by the site owner or employer (which means that its extent is largely at his discretion.)

The Controlled Area is not necessarily identical to or coterminous with the clean or aseptic areas in a radiopharmacy. It may include areas peripheral to the clean rooms, including, for example, laboratories and support areas.

Solutions

To comply with both the Ionising Radiation regulations and the GMP guide, washing facilities would be sited in a non-sterile area within the controlled area, for example the support room to the clean areas. This would require the Controlled Area to be more extensive than the clean area, and for the exit from the clean rooms to be via the non-sterile support area containing the washing facility.

Proposed policy

Inspectors should accept the need for washing facilities within radiopharmacies, provided these are sited in a support area outside the clean areas but within the Controlled Area.

Where in existing or proposed radiopharmacies sinks are sited in changing rooms, inspectors should seek their relocation within the controlled area but not insist on their complete removal.

In certain existing radiopharmacy facilities the exit from the clean room/suite may be directly into an uncontrolled corridor. In these circumstances it may not be possible to site suitable washing facilities outside the clean area. It may be necessary to accept washing facilities on the "dirty" side of the change room, pending remodelling or redesign of the unit.

Administered activities for myocardial perfusion imaging

The last issue of the Newsletter reported that ARSAC had authorised an increase in administered activities for myocardial perfusion imaging. The paper on which this is based has now been published: *Eur J Nucl Med Mol Imaging* 2008; 35(2): 329-335.

In the Newsletter we noted that this change presents (at least) three challenges to radiopharmacy:

- To cost of the additional kits which will be required (fewer patients per kit)
- The additional pertechnetate which will be required; cost and licensing issues for larger generators
- The higher extremity doses to those preparing the tracers.

An astute reader (is there any other kind?) has pointed out an additional challenge:

- Licensing issues for higher levels of radioactive waste.

INDUSTRY NEWS

New Qados partnership

Qados are pleased to announce the new partnership with COMECER in the UK. Qados will act as sales agents for COMECER.

COMECER, based in Italy, produce and sell worldwide radiation protection systems for medical research and industrial applications. The main areas are PET, cyclotron labs and nuclear medicine labs. COMECER was established over 30 years ago. All the mechanical, electrical and software packages are produced in house in the factory with no sub contractors used. Closely linked with the commitment to safety COMECER believe in product development. Many systems produced are the result of innovative projects.

COMECER hot cells are GMP compliant and are supplied with all the necessary documentation to obtain appropriate validation certificates. COMECER implements a rigorous quality assurance program. The German management system TUV has certified that the quality system of Comecer is compliant with UNI EN ISO 9001:2000 and UNI ISO 13485. COMECER has a large installed base worldwide.

Please contact Qados for further information 01252-878-999, sales@qados.co.uk

BMS becomes Lantheus

Avista Capital Partners assumed ownership of Bristol-Myers Squibb Medical Imaging effective 8 January 2008 and will operate under the name Lantheus Medical Imaging. In the United States, Medical Imaging is now operating as an independent company within the Avista family of healthcare companies. In the European Union, Medical Imaging is working with Bristol-Myers Squibb to transition the business to its new ownership, a process that is expected to take up to six months. In the UK, during this period, the business remains committed to both a high level of customer focus and communication and it is definitely business as usual.

In a statement, the company said that "it greatly values its relationships with its customers and looks forward to continuing to provide them with the same quality products and superior service they have come to expect to expect from us." The business' products include CARDIOLITE® (Kit for the Preparation of Technetium Tc99m Sestamibi for Injection) and LUMINITY® (Vial for Perflutren Lipid Microsphere Injectable Suspension).

If you require any further information please do not hesitate to contact your local account manager or our Customer Service Department: Customer Services, Medical Imaging, Bristol-Myers Squibb Pharmaceuticals Limited, Lakewood, Heronsway, Chester Business Park, Wrexham Road, Chester CH4 9QW. Tel: 01244 581236 or fax 01244 586279, E-mail: ukmicustomer.service@bms.com

Hepatate unavailable

Tin colloid (Hepatate, GE Healthcare) is currently unavailable due to the need to validate a new supplier of the active ingredient, stannous fluoride. The product could be off the market for as long as a year. ARSAC has been informed and will expedite applications for the use of pertechnetate in place of colloid in lacrimal drainage studies. The UKRG is working with suppliers to find alternative agents.

MEETING REPORTS

Radiopharmacy Workshop 2008

The UKRG Radiopharmacy Workshop was held on Friday 18 January at the Beeches Management Centre, Bournville, Birmingham. Attendance was good, maintaining the high levels of the last few years. For those who thirst for such details, the traditional Thursday curry night supplemented by off licence beverages was a great success once again.

The first morning session, "Current radiopharmaceutical research", kicked off with Pei-San Chan from the Royal Free who talked about antibody labelling practicalities and pitfalls. Dan Lloyd from U Kent at Canterbury presented data on selective toxicity of ^{64}Cu ATSM to hypoxic cells. Jim Ballinger then presented results obtained by King's MSc student Kofi Mensah on development and validation of a simplified preparation of pentavalent ^{99m}Tc DMSA. The final talk in the session was Prof Alan Perkins from Nottingham talking about aptamers, a new vector for diagnosis and therapy.

The next session was "Radiopharmacy practice research". Chandra Solanki from Addenbrooke's presented validation of alternative methods for radiochemical purity measurements. This was followed by Sanjay Patel from Guy's and St Thomas' who described the optimal formulation for batch production of ^{51}Cr-EDTA. Both of these speakers recently completed the MSc portion of their PTQA programme.

The final morning session was "New horizons in clinical practice" in which David Turner described

the use of SIRSpheres (^{90}Y microspheres) in the treatment of advanced liver cancer.

The afternoon session consisted of two parallel workshops. In one of these, Stuart Hesslewood (who needs no introduction, and thus will get none) moderated a session on GMP training for radiopharmacy staff. The following is a stream of consciousness summary: Why do we do GMP training? It is a regulatory requirement, but the real reason is patient safety. We are, in general, rubbish at documenting our GMP training. There are two peculiarities in the application of GMP in radiopharmacy: radiation protection and the conflicts between MHRA and HSE requirements. A fundamental component of GMP is a quality management system. We would be wise to keep this as simple as possible and to adhere to it rigidly. Assessment of competence can be performed in three ways: observation, oral questions, and written questions. Finally, all of us are involved in this to a greater or lesser extent, and there are real opportunities for sharing training material to avoid reinventing the proverbial round transportational device.

The other afternoon session did not have a very promising title: "Disinfectants in the radiopharmacy". However, it turned out to be a remarkably refreshing discussion moderated by Phil Hunt, head of microbiology in QC North West and a member of the NHS Pharmaceutical Quality Assurance Committee. His main points were as follows: Review monitoring results and trends, and use them to help you decide what cleaning is required. Remember to remove all sources of moisture and nutrients. Use a sporicide only when needed. Ask for advice if you need it. Don't be afraid of questioning inspectors (easier said than done). He also exploded some myths. Resistance is not a problem in the cleanroom so there is little justification for rotating disinfectants. Using a sledgehammer will damage the isolator more than the bugs. Mild detergents are adequate in most circumstances. He also distributed draft recommendations from the QA committee which reflect the approach described above. More detail can be obtained from his paper entitled "Surface decontamination in hospital pharmacy cleanrooms" in *Hospital Pharmacy Europe*, May/June 2007. This is available following free registration at: www.hospitalpharmacyeurope.com
I wasn't looking forward to this session but it turned out to be the most reasonable discussion of the topic I have ever witnessed.

UPCOMING MEETINGS

14th European Symposium on Radiopharmacy and Radiopharmaceuticals 24-27 April, Skopje, Macedonia. http://esrr08.eanm.org

British Nuclear Medicine Society 36th annual meeting 12-14 May, Edinburgh. www.bnms.org.uk

Society of Nuclear Medicine annual meeting 14-18 June, New Orleans. www.snm.org

Probe Development in Molecular Imaging and Therapy American Chemical Society, 17-21 Aug, Philadelphia. www.acs.org

World Molecular Imaging Congress 10-13 Sept, Nice, France. Abstract deadline: 15 May. www.wmicmeeting.org

British Nuclear Medicine Society autumn meeting 25-26 September, Liverpool. Abstract deadline: 27 June. www.bnms.org.uk

National Cancer Research Institute 5-8 October, Birmingham. www.ncri.org.uk

European Nuclear Medicine Congress 11-15 October, Munich. Abstract deadline: 13 April. www.eanm.org

7Th International Meeting on the Effects of Low Doses of Radiation in Biological Systems: New Perspectives on Human Exposure 27-29 Nov, Lisbon http://www.lowrad2008.itn.pt/

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