

COMMITTEE ON THE SAFETY OF DEVICES

FRIDAY 6 March, 2009

10.30 – 1.00pm

ROOMS CR1/CR2

19 FLOOR, MARKET TOWERS, 1 NINE ELMS LANE, LONDON SW8 5NQ

Members Attending

Mr John Williams (Chair)
Mr Guy Alexander
Dr Steve Bennett Britton
Mr Christopher Earl
Dr Roger Evans
Mrs Shelia Fisher
Mrs Christine Glover
Professor Ian Learmonth
Professor Peter O'Donovan
Dr John Perrins
Dr Sheila Peskett
Dr Geoff Ridgway
Dr Charles Sears
Mr Arvind Singh
Professor David Sharpe
Professor Irving Taylor
Dr Gary Thorpe
Dr John Turney

MHRA

Dr Susanne Ludgate
Mr Clive Bray
Dr Christopher Brittain
Mr Philip Grohman
Mr Andrew Crosbie
Ms Valerie Field
Ms Hazel Randall
Dr Khalid Razak
Mr Stephen Lee
Dr Rosalind Polley
Mr Mike Peel
Mr Fred Huckle
Ms Laura Murray

Devolved Administration

Dr Sara Davies
Mrs Elizabeth Qua
Mr Peter Philips
Mr Richard Helmsley

Industry

Mr Mike Kreuzer
Dr Nigel Brassington

Apologies

Dr Anna-Marie Belli
Ms Cathy Cairns
Dr Karen Facey
Professor Julie Kent
Professor Ian Kimber
Dr Gordon Watkins
Ms Doris-Ann Williams
Dr Martin Donnelly
Mr Maurice Freeman
Mr Ray Hodgkinson
Mr Clive Powell
Mr Malcolm Carlisle
Mr Andrew Wong

1. Welcome

The Chairman welcomed everyone to the meeting, which would be his last as his term of office had come to an end. He took pleasure in announcing that Dr John Perrins had been appointed as Chairman from the next meeting. He was, however, unable to announce the new Committee Members as the appointments had not yet been finalised.

2. Apologies

Apologies were received from Dr Anna-Marie Belli, Miss Cathy Cairns, Dr Karen Facey, Professor Julie Kent, Professor Ian Kimber, Dr Gordon Watkins, Mr Malcolm Carlisle, Dr Martin Donnelly, Mr Maurice Freeman, Mr Ray Hodgkinson, Mr Clive Powell, Ms Doris Ann Williams and Mr Andrew Wong.

3. Minutes of the last meeting held on 28 November 2008 (09/01)

The minutes of the meeting were approved subject to a minor amendment to paragraph 5 under "Conflicts of Interest".

4. Matters arising/Action Points (09/02):

The Chairman informed the Committee that, since the last meeting, he had met with Professor Bruce Campbell, of the National Institute for Health and Clinical Excellence (NICE), concerning problems with the introduction of new innovative devices into the NHS, and felt that excellent progress was being made. However, he had also become aware of another body, the Technology Adoption Centre, which was also operating in this field. He had personally written to the Chief Medical Officer, Sir Liam Donaldson, to express his concerns.

(ii). Problems with blood glucose meters:

Dr Susanne Ludgate informed the Committee that work was continuing on the usability of the Patient Information Leaflets

(iii). Communication with Pharmacists:

Dr Ludgate once again thanked Mrs Christine Glover for her work on this. She also stated that she appreciated the excellent communication with the Royal Pharmaceutical Society.

The Committee were shown a mock up of the laminated information sheet, which would be sent to community pharmacists.

In reply to a question from the Committee, Dr Ludgate stated that legal responsibility, for the safety of a product, remained with the manufacturer and did not pass to the pharmacist.

(iv). **Audio Scanning for Babies**

Dr Ludgate stated that there had been a very successful resolution to this as:

- All problem devices had been removed from the market
- 100% of the affected patient group had been re-tested
- New devices were now on the market

5 Conflicts of Interest: A reminder

The Chairman reminded members of the need to declare personal specific, non-personal specific, personal non-specific and non-personal non-specific interests in the agenda items. No interests were declared.

6. Main Items.

(i). **The Efficacy and Mechanism Evaluation Programme (EME):
Assisting Translational Research**

Professor Ian Cree, Director of EME at the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), gave a presentation on the role of the programme.

He explained that, while the programme was funded by the Medical Research Council (MRC), with an annual budget of £15m, it was managed by the National Institute for Health Research (NIHR)

He stated that the purpose of the programme was to address the failure in translating research into practice, specifically between the prototype discovery and design and the clinical trial, and provided:

- Peer review
- Programme Board
- Post-award management
- Priority setting

It is aimed at significantly reducing the time spent on the application process, thereby speeding up the period between idea and implementation into practice, which was often around 15 years.

The EME would support specific types of clinical trials and evaluation studies that:

- Provided definitive evidence of efficacy
- Add significantly to the understanding of disease mechanisms
- Involve new scientific or clinical principles
- Include the development or testing of new methodologies
- Include validating surrogate markers as indicators of outcome

It would also support laboratory studies as part of a relevant main study.

The programme would not support:

- Incremental modifications
- Refinements of existing technologies
- Proof of concept
- Proof of mechanism in humans
- Confidence in effect
- Early phase clinical trials
- Global Health
- Research involving animals

The dedicated website offered help to those submitting applications with:

- Full information on the programme's remit
- Forms and documents for submissions
- FAQ's, guidance and useful resources

Since it first started operating, the timescale on funding decisions has been reduced from twelve to eight months.

Professor Cree gave two examples of studies the programme had supported:

- Intravitreal bevacizumab therapy for persistent diffuse diabetic macular oedema
- Continuous glucose monitoring and intensive treatment of type 1 diabetes

He concluded by encouraging the Committees' members to "get involved" with the programme.

In response to questions from the Committee, Professor Cree stated that the programme had a high degree of flexibility which enabled applications to be considered bearing in mind factors such as data recognition, well designed evaluation, cost effectiveness and research priorities. He further recognised the importance of quality assurance suggesting that it ought to be an integral part of cost effectiveness.

When asked about the programme's relationship with industry, he stated that part the remit was cooperation with other parties. He was of the opinion that there was more scope for this cooperation with devices rather than with drugs, because of the much smaller amount of money involved.

On other issues raised:

- The Translational Board includes members from MRC and NHIS
- An observer from MRC sits on the Board of EME
- The funding came from the central pool for Medical Research (currently around £1.1bn)
- The potential for tapping into funding from charities would be explored on a case by case basis. It was more than likely that studies would end up being funded by a combination of charity, the EME and industry

- The programme was available to applicants from throughout the UK

The Chairman thanked Professor Cree for his presentation and invited him to remain until lunch, when members would have a further chance to talk to him.

(ii). **Electronic Medical Device Alerts (eMDAs)**

Mr Clive Bray made a presentation to update the Committee on the progress of this new system. He reminded them that the MHRA (in consultation with the communications group, Liaison officers and the Devolved Administrations) had been developing a system with the following features:

- Be electronic and web based
- Have a clear layout
- Be suitable for England, Northern Ireland, Scotland and Wales

The eMDA summary would consist of a single page containing:

- Date and time of issue
- Product name (with picture if helpful)
- Brief description of the problem
- Action to be taken
- Who should take the action?
- Manufacturers contact details
- CAS* deadlines
- *Dept of Health Central Alerting System
- a link to the eMDA on the MHRA website

The eMDA provides full details of the product, problem and recommended action in a format easily navigable through the use of tabs. Specific pages can be used by the Devolved Administrations to provide local contact details and advice.

The format had been revised during trial runs and the system would be ready to roll out nationally on 1 April 2009. Mr Bray also stated that, for those who preferred something tangible, it would also be downloadable as a PDF. He finally wished to thank Monica Ponte, the Project Manager, for all her work on this.

In response to the Committee's questions, Mr Bray stated that, while it would almost certainly be possible to relocate the MHRA link from the bottom to the top of the page, making the eMDA more visible within (or having a separate window from) the MHRA website would have to be looked at as part of ongoing development. He also stated that existing MDAs would not be put retrospectively on to the system, but would still be available in PDF format.

The Chairman thanked Mr Bray for his presentation and congratulated him on the successful completion of the project.

(iii). **Medical Device Technology Forum**

Dr Christopher Brittain gave a presentation on the recent Forum which had been on Human Tissue Engineered Products. He reminded the Committee of the Forum's Remit, which is to "safeguard health, and limit unnecessary deterrents and obstacles to manufacturers in exploiting new technologies by ensuring:

- Early device research utilises the latest technology to deliver devices needed by patients and users
- Regulatory requirements and guidelines take account of scientific developments
- Industry has a clear understanding of the regulatory requirements in areas of scientific development

While a number of products had been discussed, Dr Brittain wished to focus on two specific areas that highlighted problems facing the industry.

Firstly, processed allograft bone products, which are regulated and available to patients in the US with a \$648M market. These are excluded from the current Medical Device Directive (MDD) as they contained no viable cells and therefore have no harmonised route to the EU market

Secondly, a presentation on Human Embryonic Stem Cell (HESC)-derived treatment for Age Related Macular Degeneration (ARMD) had raised the question of the relevance of animal testing.

Resulting from these discussions, a number of actions were suggested that the MHRA should consider:

Long-term:

- Appropriate harmonisation of EU and FDA requirements without adopting the current American legislation.
- Creation of an "Office of Regenerative Medicine" within MHRA, with UK and EU recognition.
- An EU database of international experts
- Increased investment in the industry
- A process of staged and conditional product approval

Short-term:

- Ensure that the issue of products not falling under the Advanced Therapy Medicinal Products (ATMP) Regulations or MDDs is discussed at European level.
- A clear road-map on the web for each stage of a products development.
- Improve the consistency of implementation of the MDD across all member states.
- Consider areas of cross-Agency involvement that could be streamlined.
- Consult with NIHCE on earlier engagement and assessment of products.
- Consider registries of regenerative medicine products.

- Assurance that the National Research Ethics Service (NRES) will be ready to ensure appropriate training for committees.
- Guidance on when animal models and testing are necessary.

In conclusion, Dr Brittain presented three immediate action proposals:

- Initiate proposals for an MHRA Office of Tissue Engineered and Somatic Cell Products.
- Discuss with NICE the addition of human tissue engineered products to their scope.
- Ensure that those products in the gaps between the regulations are covered at the European level.

In response to a question on the recast of MDD, Dr Brittain stated that this had been put on hold for the time being. He added that industry was in the process of developing new proposals and that industry and the regulator would continue to work together.

The Chairman thanked Dr Brittain for his presentation

7. Updates

(i). Mobile Phones

Ms Valerie Field informed the Committee that the Department of Health (DH) had issued an updated guidance – *“Using mobile phones in NHS hospitals – January 2009”*

After being consulted, early last year, the MHRA had concluded that, while rare cases of electromagnetic interference had been reported, even this level of risk was severely reduced by separations greater than one metre. It was felt, therefore, that it should be left to individual NHS Trusts to carry out risk assessments.

It was noted that the Royal College of Nursing had raised the issue of patient privacy and dignity. It was felt that this should be incorporated in local policies.

The MHRA advice remained unchanged:

“Areas of restriction are down to the individual hospital/trust but we recommend that mobile phones are not used in critical care areas such as intensive therapy units (ITU), special care baby units (SCBU) or where patients are attached to complex devices, as any effect on such equipment could be extremely detrimental to patient care”

The MHRA welcomed the clarification in guidance on the use of mobile phones in non-critical areas,

Mr Clive Bray stated that, on the closely related subject of Radio Frequency Identification Tags (RFIDs), there was a similar problem. He informed the Committee that advice on the use of RFID readers

had recently been placed on the HRA website. Current evidence suggests that the risk of interference with medical devices posed by the readers is similar to that created by mobile phones.

The Chairman thanked Ms Field for her report and Mr Bray for his comments.

(ii) **Labcor (Hazel Randall)**

Ms Hazel Randall updated the Committee on the case of the Labcor biological heart valve. Further to valve evaluation and testing, no inherent problems were found as all tests results were within the specifications. The latest status of the investigation is as follows:-

- The Norwegian notified body has reversed its suspension and the valve can now be legally sold again Europe
- The UK distributor has continued to suspend sales of the valve within the UK
- MHRA will be writing to the seven UK centres that implanted the valves to update them on the investigation findings
- The issue of pre-operative washing may have contributed to the failures and this has highlighted the need to flag up the importance of adhering to all washing requirements.
- MHRA is considering issuing a general MDA highlighting the strict procedures concerned with pre-operative washing.

The Committee suspected that this is a much wider problem than appreciated and stressed the importance of investigating such cases. The Committee also raised the issue of suturing techniques involved with heart valves and whether this should be included in the general MDA, which has been suggested. The Committee also asked whether devices other than heart valves are stored in gluteraldehyde which may also be affected by the washing process and if this needed to be addressed. Ms Randall replied that there were many types of such products.

The Chairman thanked Ms Randall for her presentation.

(iii) **Metal-on-metal soft tissue necrosis – (Khalid Razak)**

Dr Khalid Razak updated the Committee on the issue of metal on metal hip replacements. Further to the NJR, at the request of MHRA and BOA, sending out 569 questionnaires in September 2008 to revising clinicians performing revision surgery, to obtain more information about the occurrence of soft tissue reactions, 384 questionnaires have been returned out of the 569 that were sent out. Of the 384, 50 were identified as having possible soft tissue reactions. Questions raised from the data include:

- (a) Are metal-on-metal hip replacements performing better or worse than other hip replacements?

- (b) Is there an association between soft tissue reactions and any particular type of metal hip implant?
- (c) Is there an association with any other patient characteristic, eg, sex or age?

MHRA is continuing to collaborate with British Orthopaedic Association (BOA) and British Hip Society (BHS) to analyse data for possible correlations and contributory factors such as gender, angle of inclination and age. Advice on the statistical analysis of this data is also being sought from the Royal College of Surgeons (RCS)

The Committee regarded this as a crucial investigation and highlighted the need to look both backwards i.e. if there is an issue with metal-on-metal hip replacements (which represents approximately 40% of all hip replacements) what do we need to do about the high number of those who already have them and the need to look forwards i.e. the future of metal-on-metal hip replacements. There is also the need to investigate the high number of variables involved and any biological reactions, with a 25% revision rate in some patient groups. The issue of other joints other than hips being affected was also raised by the Committee.

The Chairman thanked Dr Razak for his presentation

(iv) Point of Care Testing Device Bulleting

Mr Stephen Lee updated the Committee on the device bulletin on Point of Care Testing which was issued in 2002. The document is now in the process of being updated and the MHRA is working closely with the Association for Clinical Biochemistry, the Institute of Biomedical Science and the Royal College of Pathologists. They have also received helpful input from the UK Accreditation Service. The Committee will be updated on progress at the next CSD meeting.

The Committee asked about the consequences in terms of training and education and if the professional bodies knew this update was in the pipeline. Dr Susanne Ludgate thought this update very timely what with the publication of the Carter report and the obvious need for training. Those involved were aware of the imminent update.

The Chairman thanked Mr Lee for his presentation.

8. Vignettes/Case Studies

(i) Northern Ireland Haemolysis issues

Mr Chris Earl presented the findings of the investigations into the problems associated with patients' haemolysing during and after their dialysis sessions. These involved 11 patients, on four different sites all in Northern Ireland, between September and December 2008.

The following factors were investigated:

- Manufacturing processes
- Water supply
- Storage of dialysates
- Dialyses practices
- Medical, technical, nursing and interventional harm

No common factors or causes were found. All major dialysis units in England and Wales were notified and asked to report back on any similar problems. No reports have been received. Other cases have been seen in other parts of the world but again without obvious causes. The investigation has been closed and a report will be published shortly by Dr Brown and made available to those involved in the investigation. These will include any points raised or learnt from the investigation. Chris Earl felt an important aspect to come out of the investigation was how well all the agencies* had worked together.

- *
- The DTS, Devices Clinical and Medicines Teams of the MHRA
 - The Register of Experts and the Committee
 - Northern Island Health Estates/NIAIC
 - Renal Association (Hub units)

The Committee commented on the difficulties that this case has highlighted i.e. how to investigate a serious problem which has no obvious pattern. It was noted that a similar clutch of events had occurred in the United States. The Food and Drug Administration (FDA) had been just as unsuccessful in identifying the cause.

The Committee would also like to see the issue of blood films addressed. Chris Earl believed the report by Dr Brown would address blood films. The issue of alerting haemolysis centres was raised and it was agreed that any incidents would be picked up through the regular blood monitoring process. The Chairman looked forward to the publication of the report.

The Chairman thanked Mr Earl for his presentation.

(ii) **HIV Group O problem**

Dr Rosalind Polley presented the findings concerning the HIV screening test. This third generation test which detects antibodies against HIV-1 Group M and O, and was found to have decreased sensitivity for Group O infections. This could potentially result in missed detection of HIV-1 Group O infection. Further to the completion of the investigation it was agreed that no further action was needed by the MHRA because of the following:-

- HIV-1 O infection detected at 10 – 15% normal levels, only those recently infected may be missed
- Detection of HIV – 1 group M and HIV-2 infections is unaffected
- NBS confirmed test not used to screen blood supply or follow up testing

- HIV-1 O infection is very rare in the UK (2 out of total 80,000 diagnosed infections)
- Minority of laboratories use this system, all confirmed receipt of FSN.

Because of these findings the expert advice concluded that the increased risk of the Siemens assay missing an HIV-1 Group O infection in the UK is negligible.

The Chairman thanked Dr Polley for her presentation.

9. Farewell to CSD: A Chairman's Look Back

Mr John Williams reflected on his years as Chairman of the CSD and how having completed his term as the Chairman of the National Confidential Enquiry into Perioperative Deaths, which embraced many of the same principles of Patient Safety' and being a member of the CMO's working group, he became the first Chairman of the CSD. He recalled that he had been "persuaded" by Lord Hunt, with the aid of both the in-coming and out-going Presidents of the RCS, to take this appointment. The new Committee on the Safety of Devices, which first met in March 2001, would be comprised of a Chairman, 25 – 30 experts representing the breadth of clinical practitioners along with two lay members to represent patients' interest.

The Chairman then highlighted some of the early issues the CSD encountered which has helped mould the work of the Committee:-

- Diathermy Burns: every speciality was involved in this issue which was also the principal cause of NHS negligence claims. This triggered discussions with industry, which are still ongoing today. As Chairman of the Committee, he could forge links with industry that the regulator could not. This also highlighted the need for co-operation and the responsibility of the Agency to promote education
- Education: the need for education of all involved with devices. MDA/MHRA staff, clinicians and users of medical devices has become apparent, resulting in educational links on the website such as those developed by Tom Clutton-Brock (Senior Lecturer in Anaesthesia & Intensive Care Medicine at the University of Birmingham) ie, the Anaesthetic Machine and Diathermy units. The Chairman remarked on how shocked he was to learn of a press release from Training Hub for Operative Technologies in Healthcare (THOTH) who have set up Medical Device Training centres without any reference to, or discussions with, MHRA. The Chairman informed the Committee that he had written to Sir Liam Donaldson informing him that educational and training modules were already in hand with the Agency, a role which had been adopted without any additional funding, whereas THOTH had very significant financial help.

- The Investigation of a hip prosthesis which was found to be causing serious problems (micro corrossions), several years after implantation was another issue the Committee faced. This led to an appeal by the manufacturer against the Agency which on appeal was not supported by the CSD. Ultimately this led to the creation of the National Joint Registry (NJR) following pressure on the Minister from CHD, which has become a point of reference and can assist in dealing with current issues such as Metal on Metal joint replacements and resurfacing. Without the NJR it would be much more difficult to obtain such data.
- Issues such as metal on metal implants and the new higher energy MRI machines have resulted in the Agency working closely with the individual organisations and manufacturers involved, together with the relevant Royal Colleges, which has developed communication between the different groups.
- Another responsibility the Committee assumed was the auditing of 5-10% of the Agency's work. These audits had proved to be of great benefit to Industry, clinicians and, not least, the Agency itself, in providing evidence of the quality of the work done.
- The effectiveness of the Agency's communication strategy was a concern of the Committee and, in particular, the distribution of the Medical Device Alerts and those who were ultimately responsible for taking appropriate action. Progress has been made with the format of the Alerts thanks to the establishment of a very effective communications group. The Chairman was very pleased that the electronic communication programme will be launched imminently. Another example is the improved links with Pharmacists covering areas such as availability of "over-the-counter" medical devices and the need for increased education of Pharmacists.
- Innovation and emerging technologies is a more recent challenge facing the Committee and Agency. The Medical Device Technology Forum and the presentation by Professor Riitta Suuronen highlighting the issues surrounding this area of medical development with a definite focus on post-market surveillance and outcome audit. Now, even more than previously, it was vital that new regulations, while ensuring patient safety, did not stifle innovation.

John Williams thanked the Committee members for their help and support during his time as Chairman.

Dr Susanne Ludgate then thanked the Chairman on behalf of the Agency for a fantastic job and providing so much support throughout his eight years. Dr Ludgate also thanked those members who were now at the end of their

second term and welcomed the new Chairman, Dr John Perrins. A gift was presented to those members who were now leaving the Committee.

10. **Any other business**

No other business

11. **Date of next meetings:** 9 July 2009
5 November 2009
25 March 2010