A meeting of the National Research Ethics Advisors' Panel held on:

Date: **12 October 2011**
Time: **14:00 – 17:00**

Venue: **Room 223**
Primary Care Clinical Sciences Building,
School of Health and Population Sciences,
University of Birmingham
Edgbaston
Birmingham B15 2TT

MINUTES

Present:

Andrew George (Chair)
Jeremy Butler
Hugh Davies
Peter Heasman
John Saunders
Charles Warlow
Richard Tiner
Frank Wells
Simon Woods

In attendance:
Mr Clive Collett
Janet Wisely

1. Apologies: Nalin Thakker, Art Tucker, Caroline Harrison; Sarah Dyer; Sue Wilson
2. Declarations of Interest

   Item 8: incidental findings - John Saunders declared that he was the member responsible for RCP's position on this issue.
3. Minutes of meeting held on 14 September 2011

   The minutes of the previous meeting were agreed as a true record.

4. Matters Arising

4.1 Participant Recruitment and Commitment to Complete Research Studies

Richard Tiner asked whether there had been any increase in the numbers of CTIMPs that are terminated early. JW stated that she was not aware of an increase in the early termination of such studies and explained that the original agenda item was raised by a REC chair following receipt of two progress reports indicating early termination where the research was no longer in line with the pharmaceutical company's commercial interests.

5. NRES Update – Janet Wisely

JW introduced Sue Bourne, the recently appointed IRAS manager to the panel. The panel warmly welcomed her and wished her well in her new role.

JW informed the committee that Marc Taylor (Deputy Director of R&D; Head of R&D Systems and Governance at Department of Health) had now retired and that she had attended a lunch to mark his retirement. She was pleased to report that Marc expressed his thanks to both NRES and Prof Dame Sally Davies for working so effectively together across both NRES and DH.

Janet Wisely informed the panel that she had been appointed as the Interim Chief Executive of the HRA and Debbie Corrigan will be appointed as Interim Deputy Chief Executive of the HRA both with effect from 01 December 2011. JW would be directly accountable to Simone Bayes who in turn is accountable to Russell Hamilton Simone Bayes will also be directly accountable to Candy Morris for the transition of the HRA from an SHA to a fully fledged body.

The NRES Business Unit will be moving on 17th October 2011from Maple Street to Skipton House and will be located on the ground floor of Skipton House, 80 London Road, London SE1 6LH.

Initially the HRA board would consist of JW and Debbie Corrigan and the first board meeting will be held on 01 December at Skipton House to ratify all the relevant policies to enable the HRA to operate. It was explained that in addition Hugh Davies (NRES ethics advisor) would advise the board, particularly in his capacity as a clinician and the board would have access to NREAP who will be an advisory body to NRES at the HRA.

JW explained that at the meeting of the NRES NMG earlier that day the proposals put forward in the document "NRES at the HRA - Considerations for NRES" and updated in line with feedback from recent NRES centre events had been signed off. It was hoped that the proposals would result in a reduction in the number of items seen at REC meetings and that this would allow members to spend more time considering relevant guidance and reflecting upon the ethical issues in conjunction with the proposed ethics assurance officer. The draft strategic plan will be circulated within NRES and JW would now hold meetings with key stakeholders in order to discuss the proposals contained in the document. The revised document would then be brought back to NRES/NREAP before being taken to DH for approval

The proposed role of “ethics and assurance officer "would be piloted initially in two REC centres in order to evaluate the role and see how the officer interacts with researchers/staff and REC members. It was hoped that the role of the ethics and assurance officer would also facilitate better communication between NREAP and NRES RECS.

6. Incidental findings - Hugh Davies

The panel were asked to revisit ‘Incidental Findings in Imaging Research: a framework for considering the ethical issues’ revised in the light of the recently published ‘Management of Incidental Findings Detected During Research Imaging (Wellcome - SINAPSE – RCR) - 2011’

Received for discussion:

- Incidental Findings in Imaging Research: a framework for considering the ethical issues

Received for information:

- Management of Incidental Findings Detected During Research Imaging (Wellcome - SINAPSE – RCR) 2011 http://www.rcr.ac.uk/docs/radiology/pdf/BFCR(11)8_Ethics.pdf

It was noted that the Wellcome/SINAPSE/RCR document stated that the "majority opinion" was that

"participants who are not prepared to have information from research imaging fed back to them if an incidental finding were to be noted should probably not participate in research imaging studies". FW disagreed with this and felt that it was important that individuals who did not want to know about the results of any incidental findings should have the right “not to know" and that this should not prevent them from taking part in research. He emphasised that this approach would be in line with current guidance on genetic research and felt that there should be a consistent approach to this issue. SiWo explained that the "right not to know" was not enshrined in either law or ethics and was problematic where the incidental information also had implications for individuals other than the participant. RT agreed that genetic information was very different to imaging data given that genetic data would always have implications for other individuals. He felt that the Wellcome/SINAPSE/RCR guidance was an impressive document addressing a very complex area in which there were no hard and fast rules.

JS explained that he was not happy with rights-based approaches to these issues and felt that claims based on imputation of ‘rights’ were simply “empty rhetoric”. He felt it would be more useful to return to a "best interests" test of whether the incidental findings should or should not be fed back to the participant. Such an approach he felt would be conceptually more useful in this context.

The Panel felt that in cases of research where there was likely to be the possibility of incidental findings the researchers would need to have explicitly address this possibility and clearly stated in the application to the ethics committee how they propose to manage such findings.

Action: HD

HD would revise the document ‘Incidental Findings in Imaging Research: a framework for considering the ethical issues’ to reflect the panel's discussion and bring back to a future NREAP meeting.

7. Strategic Planning

The panel were invited to propose topics that they think that the NREAs should discuss over the coming year.

In doing so the panel were asked to consider the following Nature article which identifies novel clinical trial methodologies. In particular the panel are asked to consider and discuss the issue of ‘adaptive trials’ and the information and guidance RECs may need to adequately review them.

Received for discussion:

- “4 Ways to Fix the Clinical Trial” (Published online 28 September 2011 | Nature 477, 526-528 (2011) | doi:10.1038/477526a) http://www.nature.com/news/2011/110928/full/477526a.html

Received for information:

- “What You Need to Know About Adaptive Trials” - Pharmaceutical Executive (01 July 2006) http://pharmexec.findpharma.com/pharmexec/article/articleDetail.jsp?id=352793

RT explained that phase "0” trials did not need a Clinical Trials Authorisation (CTA) as they were not considered to be a CTIMP. As the MHRA would not be involved in the review of such trials this placed a certain amount of pressure on RECs to assure themselves that the IMP, even at a micro- dose level, was safe.

CW mentioned a recent article referring to the withdrawal of permission to use their data by participants in a study looking at whether there is a link between CFS and xenotropic murine leukaemia virus related virus (XMRV). All six participants withdrew their data with only two deciding to reinstate their consent for the use after the researchers had discussed this with them. The panel thought that the issue of when participants can legitimately withdraw their data from existing research would be useful to follow up at a future meeting.

RT also suggested the topic of upper age limits as a pure exclusion criterion for a trial. He explained that at a recent symposium held by the Faculty of Pharmaceutical Medicine it was decided that age alone should not be a basis for exclusion. RT also noted that 3 EU member states currently insist upon formal age ranges in drug trials.

Peter Heasman informed the panel that the Chairs of the last Northern NREA-hosted meeting considered that 'exclusion of non-English speakers from research' is an issue that all of their RECs have to deal with and causes some debate and discussion at most meetings. He also suggested that there should be a standing item on the agenda whereby NREAs can feedback issues from these meetings to the Panel who/which can then decide whether it needs to be taken further.

Action: AG, HD, CC

AG, HD and CC would consider the following suggestions raised by the panel and decide which should be brought back for further discussion at a later date:

1) Adaptive trials/emerging trial methodologies
2) Withdrawal of data from research
3) Discrimination and equality

8. Use of FOI Requests for the Purposes of Research – Hugh Davies

The panel were invited to consider and discuss the use of FoI requests in order to conduct research or to gain access to existing research data held by investigators. The panel were invited to consider whether they would wish to respond to the BMJ article.

Received for discussion:

- "Use of Freedom of Information Act to produce research on the cheap?" Aodhán S Breathnach, Peter A Riley, and Timothy D Planche - BMJ 2011;343:d6129 doi: 10.1136/bmj.d6129
- "University fights Philip Morris tobacco research bid" – BBC News, 1 September 2011 http://www.bbc.co.uk/news/uk-scotland-tayside-central-14744240

HD expressed his opinion that the use of Freedom of Information (FOI) Act requests to compel public authorities to expend time and money searching for and supplying data in order to comply with the request was not an appropriate way to conduct research. He urged the panel to consider drafting a response to the BMJ article.

JS noted HD's concern but felt that this was an issue of what is and what is not allowed under the FOI and that the only way to curb such requests was to change the law. HD acknowledged that this was true but felt that it would still be helpful to state that in the panel's opinion this was an "unfair" use of the law. CW pointed out that the Data Protection Act trumps FOI requests where such requests involve personal identifiable data.

PH stated that whilst he was somewhat equivocal on the matter he would support an overarching statement that it was inappropriate and disappointing to see the FOI used in this manner to conduct research and that it was not within the ethos of openness and collaboration in research.

RT also stated that he would support the encouragement of the publication of all research data so that it was in the public domain.

Agreed: The panel supported the drafting of a rapid response to the BMJ article "Use of Freedom of Information Act to produce research on the cheap?". HD would draft the response and circulated to all NREAs for their comments and revisions before submission for publication.

Action: HD

9. Conflict of Interest: NIH Update of Guidelines – Hugh Davies

Received for discussion:

- "NIH updates its conflict of interest guidelines - How much does the public need to know about reports of conflicts?" BMJ 2011;343:d5493 doi: 10.1136/bmj.d5493*

JW explained that the initial impetus for the consideration by the panel of this issue came from feedback from operations that some RECS were giving unfavourable opinions on medical device studies mainly because the Chief Investigator had a financial interest in the device under investigation. However, given the nature of device studies if a clinician has an idea for a novel device and patents it and manages to get a company to take it forward for manufacture then that clinician is almost certainly going to be the CI for the ensuing clinical investigations. Joan Kirkbride drafted guidance on this particular issue which the panel endorsed but it was not issued as NREAP guidance. The issue was then given further importance in the wake of the libel action taken by NMT Medical against Dr Peter Wilmshurst[1]. HD also produced guidance on this issue which was included in the NRES induction material for new members. JW felt, however, that there was still a need for detailed guidance on this issue to be issued by the panel or firmer and specific endorsement of the guidance and a minuted statement that RECs should look to appropriate measures to manage such conflicts, not dismiss applications on the basis of conflicts. Such guidance could draw upon Joan Kirkbride's guidance on medical device studies as well as the induction material produced by HD.

HD explained that he felt that there should be practical advice given to RECs on how to manage declared conflicts of interest. All research where any conflict of interest is identified should be subject to a plan such that the data are not subverted by the declared conflict of interest.

CW felt that in the case of research being undertaken by single investigator such conflicts of interest could be managed by the data being overseen by an independent body/individual. In the case of pharmaceutical research it is preferable for the data to be jointly co-owned by the chief investigator and the company.

RT pointed out that under the ABPI's revised code of practice the pharmaceutical industry would

> "Be required to collect and declare information about the total payment to healthcare professionals and others for services such as speaker fees and participation in advisory boards, as well as declaring the number of consultants employed. Similarly companies will have to declare sponsorship for attendance at meetings organised by third parties. The first annual declaration of payments to be made in 2013 for payments in 2012"[2]

PH agreed that the main thrust of any advice should be that RECs should assure themselves that once any conflict of interest is identified that it would be managed in such a way that it will not impact negatively upon the participant, CI, sponsor or the successful completion of the research. The REC should enter into a dialogue with the CI and the Sponsor so that this can be achieved without the need to resort to an unfavourable opinion if no other substantial ethical difficulties justifying such an opinion were present.

The panel felt that the relevant question(s) in the IRAS form should be reviewed to ensure that researchers are fully aware of the need to fully describe how conflicts are managed and to be aware that this is an issue the REC will consider very carefully.

Agreed: It was agreed that the panel would issue guidance on conflict of interests, based on Joan Kirkbride's 'medical devices' document and HDs induction guidance material, which gave practical advice regarding the management of such interests where identified. CC would draft the initial guidance

[1] http://www.healthwatch-uk.org/awardwinners/peterwilmshurst.html
[2] http://www.abpi.org.uk/media-centre/newsreleases/2011/Pages/240211.aspx

and bring back to the panel at the November meeting.

Action: CC

10. Seeking Consent – Hugh Davies

HD explained that NRES will be revising their existing guidance on information sheets next year. He invited the NREAs to provide initial advice, ideas, references etc in order to inform this work. 4 regional meeting (London, Bristol, Manchester and Edinburgh) will take place to seek the views of stakeholders and NREAs were asked to take part in these.

Agreed: It was agreed that an item would be placed on the November NREAP meeting agenda for feedback from NREAs on this issue to inform the revision of the existing NRES information sheet guidance.

11. Notification of EFGCP Annual Conference 2012

Received for information:

- EFGCP Annual Conference 2012 Informed Consent – How Less Could Be More: Effecting a paradigm shift so we do inform participants. 24 & 25 January 2012. Venue: Résidence Palace, Brussels, Belgium

12. Any Other Business

JS explained that he and CC attended the UKDEC one-day workshop in London on "Donation after Cardiorespiratory Death for Paediatric and Adult Cardiac Transplantation" held to clarify and address the complex ethical issues associated with the donation after cardiorespiratory death for cardiac transplantation.

JS explained that, whilst there is no legal definition of death, for many years the definition of death used by doctors in the UK has been based upon the irreversible loss of all function of the brainstem. This definition was most notably expounded by Chris Pallis in the BMJ's ABC of Brainstem Death[3] (1983, second edition 1995). Advances in medical technology have now made donation following cardiorespiratory death possible, however at the time of cardiorespiratory death the brainstem is not necessarily dead and so there are now two competing definitions of when somebody has died. In the context of donation of organs following cardiorespiratory death, UK DEC recommend that

"death can be confirmed after five minutes of continuous absence of cardio-respiratory function. The diagnosis of death in these circumstances depends upon there being no intention to attempt cardiopulmonary resuscitation or institute any measure that might result in restoration of blood flow to the brain"[4].

JS remarked that the use of cardiorespiratory criteria for diagnosing death might result in the removal of organs from people who, if one considers the brainstem death criteria to be definitive, are not truly dead.

13. Date of Next Meeting:

The next meeting of the National Research Ethics Advisory Panel will be held on 09 November 2011.

Time: 14:00 – 17:00

[3] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1500621/pdf/bmjcred00633-0047.pdf

[4] An Ethical Framework For Controlled Donation After Circulatory Death – Consultation. UK DEC, Academy of Medical Royal Colleges. January 2011. http://www.aomrc.org.uk/publications/reports-guidance/doc_download/9322-an-ethical-framework-for-controlled-donation-after-circulatory-death.html

Venue: Jubilee Room
Indian YMCA
41 Fitzroy Square
London W1T 6AQ