National Research Ethics Advisors' Panel

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

Date: **12 May 2010**
Time: **13:00 – 16:00**

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

MINUTES

Present:

Andrew George (Chair)
Jeremy Butler
Hugh Davies
Peter Heasman
John Saunders
Nalin Thakker
Richard Tiner
Art Tucker
Frank Wells
Sue Wilson
Simon Woods

In attendance:

Dr Janet Wisely
Sam Wigand
Mr Clive Collett (NREAP Manager)

Apologies: Sarah Dyer; Charles Warlow

1. **Declarations of Interest**

   There were none

2. **Minutes of meeting held on 14 April 2010**

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

3. **Matters Arising**

   4.1 **Disclosing Information about a Research Participant without Consent and Appropriate Action for a Researcher when Seeing Poor Practice.**

The panel noted that guidance on this issue was distributed by email to all RECs on 07/05/2010 as "NREA 01 dated 22-04-22 (v.3, 2010-04-22)".

4. **Responses to Independent Review of the Regulation and Governance of Medical Research:** Janet Wisely/Andrew George

- For Information: NRES management response to the Independent review

Janet Wisely (JW) explained that the draft response had been agreed by the DMG and the NPSA and would also be made available for information to REC members.

Andrew George (AG) explained that he had met with AREC last week and was currently working on the first draft of the NREAP response to the review. Once this had been completed he will e-mail the draft to all NREAs (AREC will also circulate the joint draft to its members) for initial comments and then make the resulting document available for information to REC members.

Nalin Thakker (NT) felt that the document should contain an initial section explaining who the major players were in the regulation and governance of medical research, particularly as the AMS call for evidence did not list NHS R&D Offices under the section "Bodies involved in regulation, governance and advice include:" Hugh Davies (HD) felt that the 'MRC Clinical Trials Toolkit' (http://www.ct-toolkit.ac.uk) provided an excellent overview of the regulation and governance processes and could be adapted and included in the NREAP response.

Frank Wells (FW) had just returned from an ethics working party in Brussels and explained that within the EU there was no doubt that the UK is leading the way with regards to training and quality assurance of RECs. This in turn meant that the ethical review process in the UK worked well and worked quickly. In addition he stated that IRAS had been a great success and was the envy of many EU countries. However, in his opinion, the biggest hurdle to performing medical research in the UK was the R&D system which was perceived by pharmaceutical companies to be time-consuming and expensive to negotiate.

The panel felt that of the two roles that R&D offices perform; governance and negotiating costs, it was the costing aspects that often caused delays in the system. It was agreed that heterogeneity and the lack of common organisation were the major problems with the R&D system. Richard Tiner (RT) stated that R&D Offices are the only group that do not have a statutory timeline with regards to clinical trials and that this may need to be looked at. RT pointed out that John Camm had published a paper detailing the two-year delay that the DARE study had encountered in seeking R&D approval from every trust in the country which might be useful to reference. HD also pointed out that Charles Warlow had published several papers regarding research governance impediments to clinical research.

Sue Wilson (SWi) felt that the National Information Governance Board for Health and Social Care (NIGB) also presented a major hurdle to performing research, particularly as they did not need to adhere to any published timelines. In addition, it was noted that occasionally the NIGB would contradict the opinion of RECs resulting in further delays. JW explained that NRES was currently in dialogue with the NIGB to produce a memorandum of understanding which would address these issues.

Agreed: The panel agreed that the NREAP response to the AMS call for evidence should robustly defend the position that the ethical review process was no longer a major hurdle to performing research in the UK and should point out the major improvements that had been introduced by COREC/NRES. The document should also highlight the fact that within the EU NRES was widely seen as having introduced excellent training and quality assurance procedures and had played a major role in the introduction of the IRAS system which had greatly streamlined the process for applying for permissions and approvals to conduct health and social care research.

It was agreed that the NREAs response should highlight their opinion that the major hurdle to performing medical research in the UK was now the R&D system which did not have to work to timelines and was extremely heterogeneous with individual offices appearing to interpret research governance requirements differently.

5. **Forum for Public Consultation:** Jeremy Butler/Sam Wigand

Received and considered:

- Suggested strategy for recruitment to the Forum
- Notes on the NRES Forum for Public Consultation Application Form
- Role Description: Forum Member
- Website addresses
- Letter of invitation

Jeremy Butler (JB) explained to the panel that it was intended that the forum should be composed of 12 individuals all of whom would be members of organisations but would not sit on the forum as representatives of their respective organisations. The forum would meet twice a year but it was expected that a large amount of committee work would be conducted in between these meetings.

The panel welcomed the introduction of the forum and made a number of comments on the form is provided to the panel. Simon Woods (SWo) suggested that the term "research participants" in the documents could be replaced by the term "people who may be invited to take part in research". The panel agreed that this reflected the target audience more closely and should be used.

It was felt that in the role description the requirement for a “Good understanding of the principles and purpose of public involvement in research” under the section “Knowledge” could be changed to “Willing to develop a good understanding of the principles and purpose of public involvement in research”

The panel discussed whether the application form should include the section regarding criminal convictions as having a criminal conviction did not necessarily preclude an individual from taking part in the forum. It was noted that current wording did not preclude individuals with a criminal conviction from joining the forum. It was agreed that the section should remain but that it would be up to the shortlist panel to decide on a case-by-case basis whether the nature of any past convictions precluded their involvement in the forum. This is in line with REC member appointment process.

It was also suggested that the application form might ask potential members whether they had any "track record" of community work or service to the community.

SWo expressed the opinion that it would be important to attempt to reach marginalised societal groups who traditionally were not represented on such bodies. He agreed to assist JB and Sam Wigand in formulating a strategy to reach such groups of people. In addition he offered to sit on any interview panel set up to interview potential forum members.

RT suggested that it would be useful to involve an individual with experience of volunteering for research studies as a healthy volunteer in the forum. He suggested that JB approach contract research organisations as they often maintained healthy volunteer panels.

6. **NHS Research Facilitators**

Received and considered:

- DH Draft Implementation Plan “Patient and Public Awareness: Approved NHS Research Facilitators”

The panel broadly welcomed the draft implementation plan but felt that there were questions over the utility of the proposed system. They suggested that the system should allow for the conduct of feasibility

studies where it would not be known how many patients were available for recruitment into specific trials. Such studies would not require anyone to contact patients but would simply need to indicate how many patients in each hospital would fit the inclusion criteria for a study. It was pointed out by Art Tucker (AT) that whilst it might be considered that there were potentially thousands of patients available to take part in, for example, a large cardiac study it would not be known how many other studies were currently competing for and recruiting the same patients.

SWi stated that in the past there had been a greater collaboration between academia and the NHS allowing academic staff to have honorary contracts which allowed them to have access to patients and patient data. It was suggested that it was suggested that the implementation plan should allow for academics to be "NHS Research Facilitators" as they had the appropriate skill set to understand the collection of patient data for research.

It was also suggested that it would be sensible to seek broad consent for the use of medical records for research at the point of entry to the NHS. Consent to such use could then be recorded on a national database.

Agreed: The panel agreed that the introduction of a 'feasibility' element into the implementation plan should be considered. Furthermore, the panel urged the DH to consider the possibility of seeking broad consent for the use of patient data in research at the point of entry into the NHS.

7. NREA Guidelines: Educational Projects and Research

The Panel are invited to consider whether they would like to issue any guidance to Universities, or support a letter from NRES management to Universities potentially regarding educational research projects.

For Information:

- Email correspondence between Janet Wisely and a REC Chair
- Email correspondence between Janet Wisely and attendee at the Southern Conference
- Current online NRES guidance regarding educational projects

Due to the pressure of time this item was held over for consideration at a future meeting.

8. PRS NMEIT Type III submission report for NREAP

- Report on Type III category research projects (Research using "extra tissue" (e.g. further blood taken at time of routine sampling or tissue taken at "clinically directed" operation)) reviewed during the pilot scheme for proportionate review of applications to Research Ethics Committees.

The committee had no concerns over the type III research projects reviewed during the pilot scheme so far. It was noted that a monitoring system would be developed as part of the proportionate review system and this would report regularly to the panel.

9. Nuffield Consultation on Ethics of Human Bodies in Medicine and Research

- Received and considered: the Nuffield Council on Bioethics consultation document "Human Bodies in Medicine and Research". Closing date for responses: 13 July 2010.

The panel welcomed the consultation but felt that the issues involved were somewhat confused by the bringing together of two aspects of research participation which were not felt to be closely connected i.e. the donation and use of tissue in medical research and participation in "first-in-human" clinical trials of new medicines.

It was noted that many of the questions in the consultation were of a generic nature whilst others required an individual response. It was agreed that the panel should only respond to the "generic" questions. Individual members could also respond in their own right if they so wished.

Agreed: The panel should respond to the consultation. NREAs should forward their initial thoughts on the generic issues to Simon Woods who would then present them to the panel at the June meeting for further discussion.

Action: SWo

10. **Examples of Good Minutes**

- For Information: two sets of minutes supplied by Joan Kirkbride: one from the NNT II REC written in the format of the pilot summary of opinion template and the set of model minutes developed to support the current minute taking guidance.*

The panel received the two examples of good minutes.

Peter Heasman (PH) raised the issue of terminology in minutes. He stated that some members of his committee wanted the minutes to reflect that there had not been unanimity in some of the decisions made. For example the phrase “the committee" implied unanimity whilst "members" implied less agreement. It was suggested that there should be an agreed lexicon for the production of minutes.

JW pointed out that the introduction of the summary of opinion method will change the way minutes are produced and the fact that members’ opinions will be published may also have an effect on what is said and how it is recorded.

JB commented that he had never seen the letters that are sent out following the committee meetings. It was agreed that Joan Kirkbride should be asked if she has good examples of outcome letters that could be presented to the panel for information.

Action: CC

11. **Any other business**

Withdrawal of Data Following Participation in a Study.

JW asked the panel for their views on how long after consent to take part in a study can a participant ask to have their data withdrawn.

Whilst the panel were not qualified to make any statements regarding the legal aspects of requests to withdraw data already collected in a research study they recognised that there was a tension between respecting an individual's wish to withdraw their data and the public interest in the validity of research and the integrity of research data. Whilst respect for autonomy demands that an individual has a right to withdraw their active participation in a study at any time, their right to withdraw data derived from their participation is clearly more complex and any specific advice will depend upon the details of the individual case.

However, in general the panel noted that it was accepted practice to include in information sheets and consent forms the statement that that whilst participants were free to withdraw their active participation at any time any data collected during the study would still be included in any analysis.

It is not clear whether "participation" could or should be deemed to extend to the later analysis of non-identifiable data collected from an individual, but the panel felt that, in general, the public interest in the integrity of data produced by research trials would normally outweigh the perceived harm that might result from the retention and analysis of an individual's non-identifiable data against their will.

In addition, the panel felt that consideration would need to be given to whether the removal of individual's data would result in insufficient data remaining to produce any meaningful results thereby threatening the integrity of the trial

The issue of "ownership" of the data was also discussed by the panel. A parallel was suggested by AG with discussions regarding property rights in tissue and cell lines derived from tissue. It has been argued that where the "remover" manipulates and “improves” the tissue he thereby acquires property rights over the tissue[1]. AG suggested that the processing and analysis of an individual's personal data may be deemed to transfer intellectual property rights over that data to the “processor” thereby removing the right of the individual to request the removal of the data (now owned by the researcher). However, SWo pointed out that these arguments with regards to property rights in tissue and cell lines were somewhat controversial and may have limited applicability to any case involving data.

Following the meeting the NREAP secretariat found the following guidance related to this issue that broadly support the NREAP position outlined above:

The FDA (U.S. Food and Drug Administration) has released guidance (Guidance for Sponsors, Clinical Investigators, and IRBs: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials - September 2008[2]) on the use of data following withdrawal:

> “III. DISCUSSION
>
> In summary, data collected on study subjects up to the time of withdrawal must remain in the trial database in order for the study to be scientifically valid. If a subject withdraws from a study, removal of already collected data would undermine the scientific, and therefore the ethical, integrity of the research. Such removal of data could also put enrolled subjects, future subjects, and eventual users of marketed products at an unreasonable risk. Finally, removal of data would fundamentally compromise FDA’s ability to perform its mission, to protect public health and safety by ensuring the safety and effectiveness of regulated products.”
>
> “IV. FDA POLICY
>
> If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject’s medical record or other confidential records requiring the subject’s consent. However, an investigator may review study data related to the subject collected prior to the subject’s withdrawal from the study, and may consult public records, such as those establishing survival status.”

In addition the Wellcome Trust has published guidance (Research involving people living in low and middle income countries: Position statement and guidance notes for applicants[3]) which highlights issues for applicants to consider when designing and submitting a research proposal to the Wellcome Trust for funding:

> “Withdrawal from participation in research
>
> The right to withdraw from ongoing participation in a research study is a fundamental right of any participant.
>
> Researchers need to give careful consideration to the implications of individuals withdrawing their participation from research. The feasibility and implications of withdrawing from research, and the extent to which that applies to the withdrawal of data and samples from a study, need to be clearly covered as part of the consent process.

[1] *Doodeward v Spence* (1908) 6 CLR 406

[2] http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf

[3] http://www.wellcome.ac.uk/About-us/Policy/Policy-and-position-statements/WTD015295.htm

The Wellcome Trust would consider it appropriate to retain data and samples within a study if they are anonymised, there is no link back to the participant, the risk to the individual of retaining the data is minimal and the withdrawal of the data threatens the integrity of the study.

12. **Date of next meeting:**

The next meeting of the National Research Ethics Advisory Panel will be held on 9 June 2010. Time: 14:00 – 17:00 Venue: Jubilee Room, Indian YMCA, London.