National Research Ethics Advisors' Panel

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

Date: **8 September 2010**
Time: **14:00 – 17:00**

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

MINUTES

Present:

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

In attendance:

Dr Janet Wisely
Mr Clive Collett (NREAP Manager)

1. Apologies: Sarah Dyer
2. Welcome of new member: Caroline Harrison
3. Declarations of Interest

   There were none
4. Minutes of meeting held on 11 August 2010

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

5. Matters Arising

5.1 Guidelines: Addenda to Information Sheets

The panel agreed that the minutes of the discussion in July were sufficient as a statement of the panel's view on the issue of the use of addenda to information sheets. They also endorsed the

proposed additional paragraph. The panel's full statement on the issue is now as follows:

> The panel sympathised with the concern expressed by researchers that RECs were being inconsistent in this matter with one REC even reported to be suggesting that addenda may not be used "as a matter of policy". It was noted by the panel that there was no such NRES 'policy' regarding the use of addenda.
>
> The panel considered that RECs had a responsibility to promote best practice with regard to the provision of relevant information in a timely manner to research participants. The prime ethical issue in such circumstances was the provision of important new information to research participants as quickly as possible and that it was not helpful to hinder this by entering into a prolonged debate regarding the specific format of the information or by prohibiting certain formats such as addenda to information sheets.
>
> It was agreed that it was perfectly acceptable for participants to be notified, by a separate record, letter or addendum to the information sheet, of amendments that did not affect their safety. It is NOT necessary for RECs to insist that the information sheet is redrafted and sent to all research subjects.

5.2 Proposed guidance for NREAP to issue to RECs regarding Medical Device Review and CI Conflict of Interest.

At the meeting held in August the panel discussed the proposed guidance and agreed that

> "…simply having a financial interest in the outcome of the research should not prevent an individual from being an investigator in that research nor result in that application receiving an unfavourable opinion purely for this reason. It was noted that investigators involved in any research project would have a vested interest in its outcome which may or may not give rise to a significant conflict of interest. Whilst RECs should always consider the potential for a conflict of interest each case should be considered on an individual basis."

The panel also agreed at that meeting to issue advice on this subject using the submitted NRES document as a starting point. However, following further communication between CC, AG and HD two issues were identified

1. The submitted NRES guidance paper would need to be completely rewritten as the "general" issue of conflict is extremely broad and not fully addressed by the proposed paper as it was written specifically to apply to device studies.
2. The production of robust guidance on the general issue of 'conflict of interest' would require further discussion by the panel.

The panel were asked to consider the following options for further action:

1. The panel do not issue their own guidance on this issue but endorse the previous minuted statement on this which supports the proposed guidance drafted by NRES.
2. Consider the wider issue of 'conflict of Interest' at a future meeting with a view to issuing NREAP guidance on the matter.

The panel agreed that the general issue of "conflict of interest" was an important issue that deserved further discussion and deliberation. Richard Tiner stated that the BMJ was about to publish a series of articles on 'conflict of interest' and thus felt it would be sensible for the panel to consider the issue at this time. However, it was agreed by the panel that the issue of any conflict of interest arising from a health care professional having a dual role both as a 'researcher' and a 'physician' would not be part of any discussion or guidance issued by the panel as there was already a large volume of literature on this particular issue.

It was acknowledged that potential conflicts of interests were inevitable in any research and that the

simple existence of a conflict of interest did not necessarily mean that an individual should not continue their involvement in the research. Any researcher will always have an interest in the successful completion of their research and conflicts do not always arise solely from financial interests but often, more importantly, from interests such as job security, career advancement etc. It was felt that the issue was not so much whether a conflict was present or not but whether that conflict was acceptable or unacceptable leading to the integrity of the research being compromised. The view that in all conflicts of interest 'transparency' and 'integrity' were key was broadly supported.

It was agreed that before discussing the general issue of "conflict of interest" at a future meeting it would be sensible to seek out existing guidance, evidence of particular conflicts of interest, examples of public opinion on this issue and any background information on which to base any further discussion. HD agreed to collate this information from NREAs to produce a future discussion document. Art Tucker (AT) and John Saunders (JS) agreed to assist HD in the collation of background information.

Agreed:

1. The panel endorsed the previous minuted statement on conflict of interest and supported the proposed guidance drafted by NRES regarding medical device review and CI conflict of interest.
2. HD would collate background information on which to base a discussion paper and the panel would consider the wider issue of 'conflict of Interest' at a future meeting with a view to issuing NREAP guidance on the matter.

Action: HD

5.3 MIST trial – update

At the last meeting of the panel gave their support to the proposed joint NRES/SHA letter to DH and GMC. Janet Wisely explained that the letters had now been sent and that she had received a reply from the GMC who had indicated that they would soon be issuing guidance regarding the consideration by the Interim Orders of whether a doctor under investigation should be allowed to continue their involvement in any ongoing or future research as an investigator.

5.4 Scientific or peer review of research and the role of Research Ethics Committees: guidance and a framework for review

HD informed the panel that following the panel's discussion of this issue at the last meeting that a workshop would take place on the 11th of January 2011 and will be chaired by Sir Iain Chalmers.

5.5 Research Ethics Review (RER)

JW explained that she had been in touch with the Research Ethics Review and that they were happy to consider the proposal that a member of NRES sits on the editorial board or, failing that, some other form of review process put in place to ensure that such articles correctly represented NRES procedures and policy.

6. NRES Update – Janet Wisely

JW explained that NRES was officially business as usual until announcements from AMS review were made and future hosting arrangements confirmed. However, notwithstanding this there was a need to continue with plans to transfer staff involved with operational functions to an NHS Host alongside the REC support staff. It had been agreed in principle that operational staff (including QA and training staff) would be transferred under TUPE arrangements to the Leeds Partnerships NHS Foundation Trust. Any

decisions regarding the future hosting of NRES corporate functions, currently hosted by the NPSA, would be taken following the outcome of the AMS review.

7. NREAP/AREC Response to the AMS second call for evidence - AG

- Received and discussed: NREAP/AREC Response to the AMS second call for evidence

The panel welcomed the draft NREAP/AREC response but felt that the document should be stronger in its assertion that R&D Offices are currently the major barrier to research in the UK. JS felt that the phrase ‘‘If a common regulatory body or system is set up that does not encompass the R&D function, then there will be little or no advantage to the researcher” could be expanded to state that not only would there be "little or no advantage" to researchers but also to patients and the wider community. He felt that the current R&D system with its attendant delay to research approval was in fact damaging to patients and public health. The panel supported this view. However, it was acknowledged that there were R&D offices that were helpful, facilitated research and could provide useful advice regarding the feasibility of a proposed piece of research.

The panel agreed with the proposal that NRES should form the basis of a single body that would receive the application, log it, maintain the necessary database and distribute relevant parts of the application to local RECs, Trusts and possibly other regulatory bodies, such as ARSAC).

During the discussion Sue Wilson raised the issue of "accredited researchers", an issue she felt should be widely promoted and suggested that the panel should discuss this at a future meeting. The panel asked Sue to produce a discussion paper for a future meeting.

AG would revise the application in collaboration with AREC for submission to the AMS by the 14th September deadline.

Action: AG

SWi: to produce discussion paper on "accredited researchers"

8. Ethical review of student research: guidance for students, supervisors and Research Ethics Committees

- Received and discussed with a view to issuing as NREAP/NRES joint guidance: Ethical review of student research: guidance for students, supervisors and Research Ethics Committees
- Received for information:
  - " IRAS: guidance on student applications"

The panel acknowledged that the educational value of student research is an important and worthwhile goal in itself aside from any scientific value or other benefits to be derived from such research. JS, whilst agreeing with this as a general statement, advanced the view that any project totally devoid of any scientific value should not be considered to be "research" at all as he felt that the ability to produce generalisable knowledge was a defining attribute of research. JW pointed out that RECs do occasionally provide opinions on projects which may not strictly be "research" where the Sponsor believes and wishes the project to be considered as research. Simon Woods (SWo) acknowledged that much student research, particularly at undergraduate or Masters degree level, did not contribute to scientific knowledge but still needed to be conducted to a high ethical standard. It was acknowledged that many student projects were by necessity underpowered due to the limited time and resources at hand but that even these projects needed to conform to the accepted view of what constituted "good science" in order to generate sufficient educational value. Such well-designed, but underpowered, studies whilst not

generating generalisable knowledge directly, could contribute to the greater sum of knowledge by their inclusion in meta-analyses conducted by other researchers.

Agreed:

The panel agreed that the draft paper should not be issued as NREAP guidance but were happy for NRES to revise and issue the guidance acknowledging the input and endorsement of the panel.

A number of suggestions were made regarding the draft guidance document:

- In paragraph 3 the sentence “Will not normally be of the same scientific quality or importance as other professional research, though may still contribute to knowledge or indicate areas for further study.” should be revised to state “*May not* be of the same scientific quality or importance as other professional research, though may still contribute to knowledge or indicate areas for further study.
- In paragraph 19 the panel felt that the sentence “In such cases, it is expected that the student will still complete the REC application form in IRAS on behalf of the CI.” could be amended as they did not feel it should be an “expectation" as from the RECs point of view it was not important *who* had completed the application form but rather that the application form had been correctly and accurately completed. It was suggested that the word "will" could be replaced with "can".
- The list of "responsibilities of the academic supervisors" in paragraph 29 should include the responsibility to ensure that the proposed project had real "educational value".
  In paragraph 32 the sentence "Where either an academic or clinical supervisor is named as CI for a study undertaken mainly for educational purposes, it is highly desirable that both the supervisor and the student should attend the REC meeting wherever possible” should be revised to make it clear that it was always desirable for supervisors to attend REC meetings even where they are not named as the CI.
    - Reference should be made to NRES guidance on information sheets with regards informing participants that the objective of the project is primarily educational

9. Proportionate Review Report - HD

- Received for Information: Proportionate Review Service: an assurance framework

Charles Warlow felt that it would be helpful if NREAs involved in the pilot of the PRS audit could also receive information on applications that were passed on to the full committee by the PRS . HD agreed. He also said we should review where studies should have been reviewed through PRS but were not, JW said this was an operational matter that would be addressed through operations and QA audits. Andrew George; Frank Wells; Charles Warlow; Richard Tiner; Sue Wilson and Jeremy Butler all volunteered to take part in the pilot of the proposed audit tool.

10. Proposed NREAP Procedure for items brought to the Panel for discussion/issue of NREAP Guidance

- Discussed: Proposed NREAP procedure for items brought to the panel for discussion/issue of NREAP Guidance

The panel welcomed and endorsed the proposed procedure subject to a number of minor revisions: the term "item" in paragraph 1 should be changed to "new item"; "consultation paper" should be capitalised; the term "REC community” in paragraph 5 should be changed to “REC community and/or others”.

The following revised procedure was therefore endorsed by the panel:

1. New item raised (e.g. by NREA, NRES, REC via NREA, or other stakeholder) and forwarded to NREAP Manager in writing together with the preferred action option (see below).

2. NREAP Chair and NREAP Manager decide whether the item should be taken forward for consideration by the Panel (either at a meeting or 'in correspondence').
3. If Panel Chair/Manager decide the item should be taken forward for consideration the submitted item is either emailed, where the item is considered suitable for consideration 'in correspondence', or placed on the appropriate meeting's agenda. The item may be taken forward as submitted or, if necessary, a meeting paper drawn up. The item will be put before the Panel with one of the following options for consideration/action to be taken:

    1) For information only;
    2) For endorsement;
    3) For discussion/advice without further consultation;
    4) For discussion/advice with a view to issuing NREAP guidance without further consultation.
    5) For discussion/advice and further consultation with a view to issuing NREAP guidance.
    6) Other action

4. Item discussed by the Panel and action agreed/decided upon.
5. Where the Panel agree/decide that the item requires further consultation with REC community and/or others before NREAP guidance issued a named NREA will, if necessary, be assigned to be the 'Lead NREA' for the consultation and a Consultation Paper drawn up. The consultation period should normally be decided at the panel meeting.
6. The Consultation Paper is published on the NRES hosted NREAP web page for consultation (responses to be addressed to the NREAP Manager).
7. At the end of the consultation period the consultation responses are reviewed and a paper/draft guidance produced for 'discussion with a view to issuing NREAP guidance' either with or without a recommendation for 'further consultation'.
8. Paper/draft guidance discussed (at NREAP meeting or in correspondence as appropriate) and further action agreed.
9. Final NREAP guidance issued.

11. **Single Issue Shared Ethical Debate - HD**

- Discussed with a view to issuing as NREAP guidance: "How long should potential participants have to consider the invitation to join a research project?"

The panel endorsed this paper and agreed that an NREAP paper based on this should be drafted for discussion with a view to issuing NREAP guidance without further consultation. It was agreed that the question title in IRAS question 31: the title "Time allowed to decide to take part" should be changed to "Time allowed to decide whether to take part or not"

12. **Incidental Findings in Imaging Research - HD**

- Discussed: Incidental Findings in Imaging Research: A framework for considering the ethical issues. Issue, guidance and a framework for consideration.

HD posed the question of whether it was acceptable to explain to research participants that, in the case of imaging undertaken as part of research, the scans were not "clinical scans" and any incidental findings not directly related to the research would not be reported back to participants.

CW emphasised that the problem of "incidental findings" was not insignificant and that in neurological research the chance of an incidental finding was around 1 in 37. HD stated that for abdominal MRI scans the chance of an incidental finding could be as high as 1 in 10.

Peter Heasman (PH) asked whether the question was related only to MRI images or were the panel meant to consider any radiograph? SWo added that the issue of incidental findings did not just apply to imaging modalities but also to any investigation that might be carried out as part of research e.g. blood tests. HD acknowledged that, whilst this paper had been generated in response to a conference specifically focusing on imaging research, the issue applied to any research investigation that had the

potential to uncover an incidental finding. SWo felt that it was up to the researcher to make the case for not reporting incidental findings back to the participant. In the case of genetic data it would clearly be inappropriate to feedback *all* of the data to the participant as the significance of much of that data would not be known and so would not necessarily be an “incidental finding". The onus was on the applicant to set out in any application to the REC, the strategy that would be followed in the event of an incidental finding of possible clinical significance.

The panel discussed the information that might be provided in the information sheet regarding the possibility of an incidental finding. Caroline Harrison (CH) felt that the "pathway" that would be followed in the event of an incidental finding should be set out for each project so that participants would know in advance both what the likelihood of an incidental finding being produced was e.g. 1 in 37, and also how such a finding would be dealt with. The panel agreed that this was sensible but also added that it would be useful to make clear that whilst there was the possibility that something with possible clinical significance *might* be found the researchers were *not actively looking* for such abnormalities.

FW raised the issue of whether an individual has the right to state that they do not wish to be told of any incidental finding with possible health significance. It was his view that there was such a right and CH expressed the view that this was correct. Both JS and CW were concerned that doctors often feel obliged to report incidental findings of no obvious significance which resulted in unnecessary distress for participants. CH stated that there was no duty of disclosure where that information was truly of unknown clinical significance. CW acknowledged this but felt that doctors were often "frightened" into revealing any incidental finding for fear of being sued.

PH agreed with the views expressed by the panel but wondered what the position was with regard to clinically significant findings that were *missed* by researchers. Would they be protected from legal action by appealing to the fact that the images had been looked at by non-clinicians with no expertise in formal diagnosis? CH felt that this was not a major problem as courts would apply the reasonable standard of competence applicable to the individuals involved. However, where a gross abnormality is missed, with deleterious results, by an individual who perhaps should have seen that there was a problem even though they did not have expertise in the area then they might be sued for negligence.

The panel agreed that NREAs would e-mail their comments on this issue to HD who would then produce a discussion paper that would be brought back to the panel for discussion at a future meeting

Action: HD

13. **Action Register**

- Received: NREAP Action Register

The panel reviewed the action register and discussed options for further action where required.

The action register would be updated accordingly and in future the register would be brought back to the panel every three months.

Action: CC

14. **Shared Ethical Debate 5 Workshop - 7th December 2010 - HD**

NREAs were asked to attend the shared ethical debate workshop in London on the 7th December 2010

Frank Wells, Simon Woods and Jeremy Butler all volunteered to attend the shared ethical debate workshop.

15. **Any Other Business**

16. **Date of Next Meeting:**

The next meeting of the National Research Ethics Advisory Panel will be held on 13 October 2010.
Time: 14:00 – 17:00.
Venue: Conference Room
Indian YMCA
41 Fitzroy Square
London W1T 6AQ