National Research Ethics Advisors' Panel

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

Date: **02 April 2014**
Time: **14:00 – 17:00**

Venue: Room HRA 1
Skipton House
Health Research Authority
Skipton House,
80 London Road,
London SE1 6LH

MINUTES

Present:
Andrew George (AG) (Chair)
Malcolm Boyce (MB)
John Keen (JK)
Peter Heasman (PH)
Søren Holm (SH)
Ros Levenson (RL)
Mark Sheehan (MS)

In attendance:

Clive Collett (HRA Ethics Guidance & Strategy Manager)
Hugh Davies (HRA Ethics Advisor)
Sue Bourne (Head of Partnerships & Guidance)
Amanda Hunn (Patient and Public Engagement Project Manager)

1. Apologies: Simon Woods

2. Declarations of Interest: None

3. Minutes of meeting held on 15 January 2014

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

4. MATTER ARISING

1.1 Collated responses received from RECs after review of the SED12 Report

At the last meeting the panel noted that only a small number of RECs had provided feedback and asked CC to enquire whether any further comments had been received.

CC contacted QA and was informed that no further responses had been received.

5. NREA Activity Log

Panel members were invited to provide updates to the NREA activity log since the last meeting.

6. Action Register

Received and noted:

- NREAP Action Register

7. Consistency of REC Decisions?

Received for Discussion:

- Draft NREAP 'Consistency in REC Review' paper

MS informed the panel that his academic paper on consistency had been submitted to the American Journal of Bioethics and, subject to a few minor changes, would hopefully be published soon.

SH felt that paragraph 4 and paragraph 25 could be redrafted to read "there should not be an expectation of *absolute* consistency in terms of content". HD expressed the opinion that a formal statement that consistency should not be expected may be problematic for the HRA. RL agreed that such a statement would not be desirable and that we should amend the statement accordingly. MS clarified that whilst the starting point is that there should not be an expectation of content consistency there *are limits* to the amount of variation that would be acceptable.

AG suggested that it may be a simple matter of phrasing. He suggested that it could be revised to say "whilst we should strive for consistency of content there will always be cases where RECs may legitimately diverge" or similar. SB suggested that the first sentence of paragraph 4 might be deleted so that the paragraph begins "Different committees may legitimately come to a different decision about the same research proposal; however there are limits to the range of decisions that are acceptable.

RL commented that there was insufficient recognition of the values and preferences of patients as part of the contextualisation process. The panel agreed that this should be explicitly included. MS suggested that paragraph 7 be revised to add "patient groups and the public" to the phrase "broader engagement with researchers".

RL considered that paragraph 30 was a little "clunky" and did not think that the suggestion that committees should consider the ethical categories as if there was a "member of the committee who thought that the category was the overriding ethical category" present was helpful. She felt that this was just one example of how a committee might fully consider the issues. MS explained that this was an attempt to provide an account of what full consideration might mean in practice. RL felt that full consideration would be better achieved through the use of headings or checklists such as those included in the HRA ethical review forms.

AG suggested that the reference to 'advocacy' might be removed and the text revised to state "committees should consider each of the ethical categories as though it was the overriding ethical category for the given piece of research".

RL noted that the suggestion in paragraph 43 could lead to a conflict of interest if REC members were to be closely involved in the provision of early advice to researchers on their research proposal, although it was noted that if the advice were provided by members of a separate committee to the REC involved in the review then this might be acceptable. Both JK and PH noted that chairs do currently provide advice on specific applications and that where this occurs they would make it clear to researchers that their advice was being provided in a personal capacity and did not in any way represent the view of the committee. They would then declare their involvement and what advice was given at the meeting where the application was reviewed.

AG noted that one of the current ways in which contextualisation is facilitated is by the attendance of researchers at REC meetings and suggested that this be added to the "initiatives already in place/in progress" section.

The panel discussed whether paragraph 44 regarding "past decisions / decisions of other committees" should go into "operational" detail. It was felt that this section should not be too prescriptive, particularly with regard the suggestion that "applicants should be encouraged to ... present prior decisions" to RECs as it was felt that this should not be interpreted as a mandatory requirement.

MS suggested a number of revisions:

paragraph 13: could be deleted
paragraph 22: should state that the REC's reasons for their decision should make explicit reference to the ethical categories.
Paragraph 28: is a little wordy and includes two different meanings of the term "category".
Paragraph 39: should make more of the ShED exercises and their potential for promoting greater consistency.
Paragraph 43: add "patient groups and the public"

PH was of the opinion that this was an important document that he hoped would be read by all stakeholders and needed to be placed in the HRA "shop window". AG asked whether it would be reasonable to seek confirmation from NRES as to how this document would be used and circulated. The panel agreed that a description of the action plan for this document and its recommendations should be sought.

Agreed: CC would revise the document for circulation to the panel via email. Once the final document had been agreed by the panel it would be submitted to NRES and confirmation sought regarding the subsequent action plan.

Action: CC

8. **Proportionate Approaches to Consent**

Received for Discussion:

- Draft Guidance 'Proportionate Consent for Simple and Efficient Trials in the NHS (To be circulated later)

The Panel were asked to comment on draft guidance regarding proportionate approaches to consent which is intended to be put out for consultation in June 2014

Amanda Hunn (Patient and Public Engagement Project Manager) attended for this item.

Background:

The NIHR Health Technology Assessment Programme has issued a call for research proposals to allow either more rapid conduct, or lower costs, or both, when benchmarked against conventional pragmatic multicentre trials, while still providing data sufficiently robust to guide NHS or patient decisions. The Health Research Authority has issued a statement of support for the NIHR call for simple and efficient trials in which it undertakes to identify opportunities for proportionate consent in such simple trials, working with the MHRA to ensure they are compatible with Clinical Trial Registration and consulting with the REC community to provide an agreed ethical framework. In addition, NREAP will be available to provide guidance on the ethical issues presented by the applications to this call.

Background papers received for information:

- Pragmatic randomised trials using routine electronic health records: putting them to the test. Van Staa et al. BMJ 2012; 344 doi: http://dx.doi.org/10.1136/bmj.e55 (Published 7 February 2012) BMJ 2012;344:e55

  No Consent Argument:

- Ethics and informed consent for comparative effectiveness research with prospective electronic clinical data. Faden R, Kass N, Whicher D, Stewart W, Tunis S. Med Care. 2013 Aug;51(8 Suppl 3):S53-7. doi: 10.1097/MLR.0b013e31829b1e4b.

  The authors argue that in a learning health care system with ethically robust oversight policies, a streamlined consent process could replace formal written informed-consent procedures for many studies, and *patient consent would not be required at all for some trials*.

  Argument for Integrated (explicit) Consent:

- Informed Consent for Pragmatic Trials — The Integrated Consent Model
  Scott Y.H. Kim, M.D., Ph.D., and Franklin G. Miller, Ph.D.
  N Engl J Med 2014; 370:769-772February 20, 2014DOI: 10.1056/NEJMhle1312508
  http://www.nejm.org/doi/full/10.1056/NEJMhle1312508

  The authors argue that *informed consent is ethically necessary in pragmatic trials* that randomly assign individual patients to treatments, even when treatment options are within the standard of care. They propose integration of a streamlined consent process into routine practice.

SH expressed the concern that whilst there would be legitimate cases of research where proportionate consent would be appropriate there was always the possibility of "mission creep" such as the addition of an additional blood test or slight variation to the clinical dose etc. In addition, whilst existing treatments might be therapeutically equivalent they may differ in their "amenity factor". He illustrated this with an example: the antimalarial drugs Mefloquine and Malarone are both licensed and effective but Mefloquine is taken on a weekly basis whilst Malarone involves daily administration. Such differences would mean that the two treatments, whilst therapeutically equivalent, would not be broadly comparable.

RL was concerned that any moves to remove consent in any way would have unintended consequences such as undermining trust in health care professionals and clinical research/researchers more generally. RL cautioned that we would also need to be mindful of guidance such as the GMC "Duties of a doctor" which emphasise concepts such as "*communication, partnership and teamwork*" and "*maintaining trust*". In particular, she felt that the possibility of relying on posters to inform patients of their inclusion in research was not acceptable: there needs to be a conversation between the GP and the patient and recognition that, if such simple research trials are to be undertaken, adequate resources will need to be made available to fund the additional burden undertaken by GPs.

MS agreed noting that the use of posters alone would be effectively giving up on consent. He was of the opinion that the value of consent was too often closely keyed to the "risk" of the proposed research i.e. if there is no additional risk involved then consent would not be required. He felt that this misunderstood the reasons and justification for seeking consent i.e. that it respects persons and their autonomy. Where the risks involved are very low and that fact is obvious to everyone (including patients) then this opens up the possibility of a 'light touch' in seeking consent.

AG felt that proportionality was often treated as though it was a binary choice e.g. either a 20-page information sheet or 5 seconds of explanation from the GP. However, in reality we are dealing with a continuous range of possible consent processes involving increasing levels of information.

MB supported the idea of the simple, pragmatic trials and whilst he personally wouldn't mind if he was included in the trial of two licensed medicines without explicit consent he recognised that some patients would be upset by this. Thus, he felt explicit consent was still necessary in the conduct of these trials but that consent should be as simple as possible. He noted that whilst the pharmaceutical industry was responsible for making new medicines it was the responsibility of the physicians to conduct trials regarding their use.

HD noted that this initiative originated from the view that the burden of consent was too onerous and prevented trials from happening resulting in harm to patients through the use of untested treatments. He noted that, with regards CTIMPs and the information requirements, mixed messages may have been given regarding the level of information required in order to comply with the clinical trials regulations. Information sheets need only comply with the "principles" of ICH GCP[1] and not follow them to the letter in all cases.

CC asked if there were any general principles that could be included in the guidance. RL offered the view that informed consent is not something we would wish to see dispensed with and that the length of the information sheet does not equate to its' thoroughness. She reiterated that the risk of undermining trust in the NHS and the research process was too great to move to a system of recruitment to pragmatic trials *without* consent

AG suggested the principle that consent need only be sought in circumstances where the patient has a choice regarding the intervention they would receive. For example, where a ward was trialling a new mattress and the patient would receive the same mattress regardless of whether they consent to be part of the trial or not then consent for the use of the mattress was not required as it has no impact on the treatment received. However, consent for the use of their data would be required and should be sought for this aspect of the study. RL agreed stating that the point was to understand what we are asking patients to consent to: the *intervention* or *use of their data for research*?

[1] As set out in "ICH HARMONISED TRIPARTITE GUIDELINE FOR GOOD CLINICAL PRACTICE" E6(R1) version dated 10 June 1996

AG wondered if this might also apply in the case of a GP surgery that routinely prescribes one particular drug. SH noted that in many cases it would not be true to say that, in the context of a GP surgery, that the GP can only prescribe one drug. The GP would have the ability to prescribe from a number of possible treatments.

MS felt that there are already a number of "tools in the mix" for facilitating such research in a way that did not prejudge the level of risk and link this to the need for consent. He felt the "guidance" document should not be "guidance" per se but rather play out the scenarios to demonstrate ways in which proportionate consent might be acceptable with regards 'verbal/written consent', 'natural variation in standards of practice', 'intervention vs. access to data', 'role of CAG' etc.

SH felt it was important to keep the issue of "cluster randomisation" separate from the issue of pragmatic trials as they were quite distinct.

MS noted that it was important to decide what the level of information required to seek consent was proportionate to. He had previously noted that linking proportionality to risk was inadequate and failed to engage with the justification for seeking consent. Alternatively, linking the proportionality of consent procedures to the "ethical issues" at stake might be preferable but as the ethical issues would need to be judged on a case-by-case basis having formal "guidance" might preclude that.

AG expressed the concern that "ethics" was not seen as the "whipping boy" for any difficulties encountered in conducting such pragmatic trials. In the example of a trial involving different mattresses he found it difficult to believe that a requirement to seek consent, perhaps involving a few sentences of verbal explanation, would render the research impossible particularly when this requirement is weighed against the logistics of ensuring that the mattresses are delivered to the ward at the appropriate time so as to be available for the research and the patient.

The panel agreed that:

- Informed consent is desirable in all cases unless a strong justification is provided for dispensing with this requirement
- informed consent procedures should always be proportionate to the nature of what is proposed and the ethical issues at stake
- proportionate informed consent procedures should not solely be determined by the level of risk involved in the research
- consent should always be documented
- consent need only be sought for research activities that differ from the standard of care that the patient would otherwise receive (i.e. consent should be sought where the patient has the possibility to decline the intervention)

Action: CC to revise the draft document appropriately

9. **ShED14 Report**

Received for Information/Discussion:

- ShED 14 Report
- Anonymised individual REC feedback report

The question of whether there was an order effect involved in the opinion given by RECs was raised, both within the ShED exercise and also in their deliberation of real applications. It was felt that this might be a fruitful area to investigate.

The panel discussed whether the ShED reports should be made publicly available. MS felt that it was not immediately clear why such an internal "audit" process needed to be made public. The panel also felt that if the report were to be made public then this would need to be accompanied by greater explanation of the context of these exercises.

10. **Patient Information Leaflet (PIL) and Information Sheets**

Discussed:

Sheila Oliver (Head of NRES) asked the panel to provide guidance or a position statement on the following;

> The recent investigation of a recent complaint raised the issue of whether when a study involves the use of a licenced drug the information provided in the PIS should be a complete transcript of the Patient Information Leaflet (PIL) that would be provided with the medication had it been prescribed for normal care and treatment.
>
> The issue was raised for discussion at the recent round of NREAP hosted Chairs meetings and the general feeling was that there is no like for like matching undertaken by the REC between the PIL and the information in the PIS and that they would not expect that there would be a full transcript, though there was a suggestion that it could/should be added as an appendix.

HD asked the panel whether they would agree to the principle that where a research study involves licensed medicinal products then research participants should be given the same information they would have received if they were receiving the licensed medicinal product as part of their standard care.

The panel were content to agree with this but were keen to avoid duplication and an accompanying increase in the size of the information sheet and thus agreed that the information could be provided in a separate document along with the patient information sheet.

The panel endorsed the following statement:

"Potential participants in a clinical trial involving licensed medicines should be provided with information equivalent to that they would have received had they been prescribed those medicines as part of their standard care (i.e. the information contained in the Patient Information Leaflet (PIL)).

This information may be provided separately to the Participant Information Sheet (PIS)"

11. New Ethical Review Form (to assist in the production of a summary of opinion for publication)

Received for Information:

- Ethical Review Form
- Ethical Review Form (Mental Capacity Act)

It was noted that chairs at the recent London & South East Coast NREAP/chairs network meeting were sceptical about whether the introduction of these forms would improve ethical review. PH noted that, in his opinion, the documents had the potential to prevent repetition and improve the ethical debate, but only minimally.

AG wondered how NRES would assess the effectiveness of these forms and their impact upon the quality of ethical review and requested that CC put this question to NRES for an answer.

Action: CC

12. Meeting with Nuffield Council on Bioethics – Sham Surgery

Received for Information:

- Note of meeting between Nuffield Council on Bioethics (NCOB) and National Research Ethics Advisors' Panel (NREAP): Guidance on the Ethical Conduct of Research in using Sham Neurosurgery as Placebo Control. 27 February 2014

13. HRA Values

Received for Information:

- HRA Values

14. House of Lords Select Committee on the Mental Capacity Act 2005. Report of Session 2013–14: post-legislative scrutiny

Received for Information only:

The panel recently contributed to the HRA response to the House of Lords Select Committee appointed to consider and report on the Mental Capacity Act 2005. The committee has now published its report. **N.B.** NO specific recommendations relating to clinical research were made.

Key findings

The Committee's key finding is that the Act is not widely implemented. To address this the Committee recommends that responsibility for implementing the Act be given to an independent body.

The Committee's second key finding is that the Deprivation of Liberty Safeguards are not fit for purpose. The Committee recommends that they be replaced with new provisions. The **full text of the report** can be viewed here:

PDF version -
http://www.publications.parliament.uk/pa/ld201314/ldselect/ldmentalcap/139/139.pdf

HTML version -
http://www.publications.parliament.uk/pa/ld201314/ldselect/ldmentalcap/139/13902.htm

An **Easy Read summary of the report** can be viewed here:

http://www.parliament.uk/documents/lords-committees/mental-capacity-act/mental-capacity-act-2005-easyread.pdf

15. **Any Other Business**

There was none

16. **Date of Next Meetings**

2nd July 2014

8th October 2014