Health Research Authority
National Research Ethics Service

National Research Ethics Advisors' Panel

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

Date: **14 March 2012**
Time: **14:00 – 17:00**

Venue: Room 126A
Health Research Authority
National Research Ethics Service (NRES)
Skipton House,
80 London Road,
London SE1 6LH

MINUTES

Present:

Andrew George (Chair)
Sarah Dyer
Peter Heasman
Nalin Thakker
Richard Tiner
Charles Warlow
Frank Wells
Simon Woods
Jeremy Butler
Art Tucker

In attendance:
Mr Clive Collett

1. Apologies: Janet Wisely; John Saunders; Hugh Davies, Caroline Harrison; Sue Wilson
2. Declarations of Interest

   There were none
3. Minutes of meeting held on 08 February 2012

   The minutes were approved subject to a minor amendment under item 4.2 Presentation of Precedents to RECs (Payments to Participants. JS asked by email that the word "unreasonable" be changed to "unethical".

4. Matters Arising

4.1 GAfREC Erratum/RGF clarification

Noted:

Update to confirm completion two actions from the last UKECA/UKHDs research governance officials meeting on 11th January:

The GAfREC erratum has now been published at:

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_126474

and the RGF clarification at:

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4108962

An amendment to the Health Research Authority Directions 2011 has also been proposed so that HRA can comment on potential breaches.

NT explained that he had recently advised David Neal on the updated algorithm "Does my project require review by a REC?", which guides researchers through the legislation and policy requirements for ethical review, and deals with excepted categories. This was revised in order to capture the erratum to GAfREC published last month. In revising this document the opportunity was also taken to address issues regarding tissue research. The following text was added to the algorithm:

"Researchers are encouraged to consider making a voluntary application for REC review where the exclusion applies but the study raises significant ethical issues, in particular where a generic consent given previously may not be adequate in the circumstances of the current study. For example, where a study could generate sensitive and clinically relevant information for the donors and/or their relatives, and the samples are linked anonymised potentially enabling donors to be re-contacted, it would be appropriate to apply to a REC to seek ethical advice on whether further specific consent should be sought and/or how feedback of results would be handled. The Research Ethics Service will accept voluntary applications raising ethical issues of this nature. It is helpful if researchers indicate clearly in their application why they are seeking voluntary review.

Research teams undertaking a programme of research with stored samples are also encouraged to make use of the NRES voluntary scheme of generic ethical review for Research Tissue Banks / Biobanks. Further guidance is at http://www.nres.nhs.uk/applications/approval-requirements/ethical-review-requirements/research-tissue-banks-biobanks/.

In cases where review by a REC is not necessary, academic researchers are recommended

to seek ethical review by a university REC as an alternative. The Code of Practice on Research from the Human Tissue Authority (HTA) recommends that any research with human tissue is conducted with ethical approval and that a HTA storage licence should not be seen as an alternative.

Researchers should always seek advice from the local R&D office (and from the Designated Individual in the case of HTA licensed institutions) on the appropriate arrangements for review of their research."

The updated guidance is now ready for issue as part of a package including Version 5.1 of SOPs (incorporating a set of minor changes to SOPs).

4.2 A consensus statement on research misconduct in the UK - FW

FW informed the committee that he had informally met with James Parry, Acting Head of UKRIO, in order to establish a positive working relationship with UKRIO. James Parry had agreed to take part in a forthcoming HRA meeting "Misconduct and fraud in health research: what is the REC's role?" taking place on Thursday, 19 April 2012 at Skipton House, London. This workshop will consider the roles of the Health Research Authority in supporting good research conduct and the Research Ethics Committees role within SOPs in reviewing an opinion in light of reported misconduct and fraud.

James Parry had drawn FW's attention to the work of "Public concern at work" (http://www.pcaw.org.uk) a whistleblowing charity established in 1993. The charity aims to play a key role in anticipating and avoiding the serious risks that arise in and from the workplace.

5. Proposal for National Research Ethics Advisors' Panel (NREAP) – Janet Wisely/Andrew George

Received for discussion:

- Proposal for National Research Ethics Advisors' Panel (NREAP) v1.4

JS had e-mailed comments regarding the revised draft of the proposal suggesting that the membership would need to include representation from both Scotland and Wales. The panel discussed this issue and felt that with a relatively small membership this would be unduly onerous. It was felt that the panel members need only have an "understanding" of the health service within the devolved nations and that whilst members from the devolved nations would be encouraged to apply it was felt that there was no need to specifically build in such representation into the membership requirements. It was agreed that paragraph 3.8 of the proposal document v1.4 should be removed. Instead the panel asked that para 1.3 be revised in order to make it clearer that, whilst the Health Research Authority Directions 2011 apply only in England the panel is a resource available to all RECs, funded by the UK Health Departments, within England and the devolved nations.

There was general concern amongst the panel that the current proposed membership was too small for the panel to function effectively. AG explained that the smaller number of panel

members had been proposed in recognition of the fact that the panel would engage more fully with RECs in future and seek their views. FW felt that it may not be possible to fulfil this aim with the proposed panel members, even with a full-time NREAP manager. AG suggested that para 3.2 might be revised to say "The proposed revised membership *should* include:". This would infer that the categories of members described was only a minimum requirement and thus leave it open to recruit more panel members and additional categories of member if considered necessary (in addition to co-option for specific time-limited appointments). The panel agreed that this was an acceptable solution.

CW suggested that the membership category "Experienced academic researcher" be changed to "Experienced academic *clinical* researcher". The panel agreed to this.

AGREED: the panel agreed that the changes identified above should be made to the proposal which would then be submitted to UKECA at their meeting on 15 March 2012.

ACTION: CC

6. **Re. HRA development project – creating an effective national role for the HRA**

Background:

The HRA has established a senior project team to complete a system review of research in the UK, from idea, through funding, approval, conduct, compliance and inspection, publication and translation to inform and identify an effective national role for the HRA in providing a unified approval process and promoting proportionate standards for compliance and inspection.

The project team wish to invite views from the NREAP.

Received for discussion:

- HRA Development Project letter from Janet Wisely
- HRA Development Project Powerpoint Presentation

Janet Messer (JM) and Sandra Holley (SH) from the HRA Project Team attended the meeting at 3pm.

FW expressed the opinion that now that the ethics review system was working smoothly the project team would need to grasp "the nettle" of R&D governance. Whilst he accepted that NHS Trust's were independent institutions he felt that the HRA should produce guidance for R&D offices as the HRA should have a role in ensuring that governance is dealt with efficiently and effectively. JM said that such guidance already existed. FW agreed but felt that evidently it wasn't working. Guidance was required to streamline the R&D process.

AT felt that the project team should pick someone from the research networks and find out where the blocks in the system are. Whilst the Trusts were independent there were some fundamental similarities in their systems and the HRA must use their authority to rein in those trusts that were holding up research. RT countered that the HRA doesn't actually have that authority, they had the potential for authority and indeed this authority was envisaged in the AMS review. However, this authority had been watered down

in the Government's "Plan for Growth"[1] published in March 2011. He noted that whilst the Health and Social Care Bill gives Trusts autonomy it also places a duty upon the Secretary of State and the commissioning groups to 'promote research'. He felt that potentially this duty could be used to place pressure on R&D offices to ensure that research was not held up unduly.

RT noted that at a recent conference he attended entitled " Advances in Medical Science: Collaboration for Growth" he heard evidence regarding one Trust in Lancashire that was doing phenomenal work in ensuring that research involving innovative medical technologies was given swift approval, sometimes in as little as a week. However he noted that this was primarily down to the R&D lead in place within that particular Trust. He asked how we can get such good examples picked up by other R&D departments around the country when, as others had remarked, Trusts were independent whilst research was a UK wide activity. JM agreed stating that the NHS was becoming more local whilst research was not.

RT explained that the proportion of clinical trials being conducted in the UK over the last 1 to 2 years was dropping significantly whilst increasing in the rest of the world.

AG wondered whether R&D timelines should be published? JM explained that these are already published and that the Guardian newspaper currently publish trust research activity league tables online (http://www.guardian.co.uk/healthcare-network-nihr-clinical-research-zone/trust-research-activity-league-tables).

JM acknowledged that R&D approval was an issue but explain that we needed to get beyond that simple assertion and drill down into the detail of that problem.

AG felt there was a problem with the culture. Often the dominant culture within R&D was one of not taking risks. How could this be turned around? JM commented that interestingly around 90% of the time taken to reach approvals within R&D departments focused on the finance aspects of research study. AT agreed stating that Trust finance offices can often play with the figures in order to increase the amount of money they receive from research clients. Research was often seen by Trusts as a "money pot". He suggested that research projects might be assigned a "chaperone" who knows the governance system. The chaperone would oversee the research project on its journey through the various governance processes, and where the project gets bogged down, they would intervene in order to move it on. He suggested that the HRA could approach the top 10 Pharma companies and offer such a scheme to them. Such individuals, working within the HRA, could also help Pharma companies communicate with researchers both within and outside the research networks, steer their research through the process and have power over Trusts to resolve difficulties. This would show that the UK can deliver research on time and make it a more attractive place to conduct research.

AG wondered whether a single R&D permission would be useful. JM stated that there had already been some conversations regarding the acceptance of assurances from other bodies. Of course there would always be some detail that needed to be looked at locally but many of the things looked at by R&D departments e.g. costings, contracts etc was standardised and could be looked at by a single individual or single office. She noted that many of the local checks carried out were demanded by NHS managers and not always by R&D departments.

JB felt that there was a training issue involved. If the majority of Trusts were all working in different ways then surely that meant there was a training issue that needed to be addressed. The HRA has the opportunity to lead on this issue and produced a training programme to bring disparate Trust's

[1] http://cdn.hm-treasury.gov.uk/2011budget_growth.pdf

together. JM agreed the training is key and that historically there had been no training programmes in place prior to last year. There was now such training in place in England including the use of e-learning.

RT felt that every Trust should have a board member with responsibility for R&D. This would make R&D directly accountable to the Chief Executive of the Trust. If research is a core function then the responsibility and accountability lies with the Chief Executive. NT felt that standards needed to be set and audited. It may also be appropriate to instigate a system of penalties for those Trusts not meeting these standards. RT noted that there were beneficial financial effects that accrued to Trusts who conducted research. Additional money was available from the Department of Health for promoting research. Whilst any such money would be marginal it was likely to be one of the larger "marginal" streams of income for a Trust.

AG wondered how a change in behaviour can be affected. What was in it for R&D departments to be more efficient? More money for Trusts if they were effective and efficient with regards R&D governance? Conversely should money be removed where targets were not met? JM explained that under the 'Plan for Growth' there was a 70-day benchmark for Trusts to recruit the first patient to a trial, with NIHR funding contingent on achieving this. However she noted that it was always possible to play games with these figures.

RT explained that industry was also partly to blame for the problem. Pharma companies would often continue to place research in Trusts that do a poor job of R&D governance. Such companies will often rather bid for 50 patients in a global trial in hope that they might get 45 patients recruited rather than bid for 100 patients and only gets 70 patients recruited. The metrics used by pharmaceutical companies means that 90% recruitment is preferable to 70% even if this represents fewer patients in the study.

NT suggested that Trusts should be "kite marked". This combined with a chaperone/concierge service that ensures the project is shepherded through in the shortest possible time would be of immense help.

SH stated that whilst many institutions conducted their own quality assessments regarding the research process these tended to use different standards. Shared standards were required. CW felt that those shared standards were already in place for most types of research even if only informally signed up to. SH agreed but the standards she was referring to were not 'science' standards but standards of 'management'. Such standards were not so clearly shared. AG noted that different bodies were assessing research using different scales. For example an ethics committee is only concerned that a piece of research is "good enough" whilst a research funder may wish to only fund research studies in the top 10%. Thus there is a difference in standards. He wondered whether standards regarding whether a particular investigator was a "finisher/completer" might be useful i.e. did they always publish their research once approval had been given.

SiWo noted that, in his experience, an ethics committee might take an extremely long time discussing an acupuncture project whilst spending only 5 minutes reviewing a complex clinical trial. If there was a system by which an application would arrive in front of the committee with certain assurances of quality attached this would help immensely.

PH said that if you wish to look at the 'quality' of research then you need to separate out the quality of 'science' from the quality of 'process' (including publication). Currently, there is very little focus on a piece of research after it has received favourable opinion. The review of progress reports by RECs was essentially a 'token' process and he felt that if the review by the HRA of research was more akin to that conducted within academic institutions it would be preferable i.e. to ensure that the research being undertaken within a particular institution was quality assured. The HRA need to identify what it is they

should be looking at aside from the quality of science. JM agreed that there was little oversight what actually happens to research. There appeared to be no 'memory' and each time a researcher submits a new piece of work it is considered without any reference to their record of conducting research. PH felt that this could be done, the data was there it's just that no one was looking at it.

SD felt that the risk for R&D in approving a piece of research is that something goes wrong. This needed to be reversed i.e. the risk for an R&D Department should be 'inactivity'. This perspective would make sense of the two parallel conversations that were currently taking place regarding the assessment of the quality of the piece of research and getting research through the governance hurdles more quickly. Researchers might be accredited whereby they had been shown to have gone through the system successfully and had a good publication record and thus were a lower risk for R&D departments. Researchers with a proven track record could be deemed to be low risk and thus fast tracked through the governance systems.

RT noted that whilst there was a lot of conversation around the things we thought were a problem we did not always actively promote those things that we are good at in terms of UK research. He stated that in the UK 1 in 6 patients with cancer were enrolled into a clinical trial. This compared with around 1 in 20 in the United States. In addition he noted that Scotland was also becoming one of the best places in the world to do database research. We are not getting out there and attracting the research into this country that we are really good at.

AG suggested that R&D Department should be subjected to comprehensive reviews in the same way that academic departments were. Academic departments were subject to review every six years and he felt that this could be translated to R&D departments. Such reviews could assess where timelines and processes are different from the national average and this data published.

JM thanked the panel for all of their comments and noted that they felt that the main priority for the HRA was the improvement of R&D governance processes. She noted that it had taken 10 years for RECs to get to where they are now and that R&D will need to make the same improvements in a much shorter timeframe. However, she was confident that the signs of hope were already there. There were many good R&D departments and the challenge was to ensure that all R&D offices came up to the same standard as these.

7. **Amendment to S51 of the Adults With Incapacity (Scotland) Act 2000**

The panel were invited to comment on a consultation paper where Scottish Ministers propose amending S51 of the Adults With Incapacity (Scotland) Act 2000 to allow the research provisions for incapacitated adults in clinical trials of investigational medicinal products (CTIMPs) to be extended so that research can go ahead with the consent of the patient's doctor and in urgent situations for non-CTIMPs.

Received for discussion:

- Urgent research - consultation on allowing research for incapacitated adults in non-CTIMPs

The panel welcomed the proposal contained in the consultation paper.

Si Wo stated that he was in favour of the proposal in principle but that the changes to the Scottish legislation should take note of the differences that exist in England and Wales between CTIMP and non-CTIMP research as set out in the Mental Capacity Act 2005 (MCA) in particular the additional safeguards in place to protect adults who lack capacity (ALC).

He drew attention to the following points:

1) It should be noted that in England Wales there are differences in the provisions for Adults who lack capacity (ALC) in research between CTIMP and non-CTIMP research. In the latter there is no provision for consent which represents the presumed will of the person but rather a duty for the researcher to consult appropriate others before making a decision to enter an ALC into a study.

2) There is a lower threshold for an ALC to be entered into a non-CTIMP study as set out in 31 (3a and b) of the MCA 2005:

3 (a) Research must have the potential to benefit P without imposing a disproportionate burden, *or*

(b) Provide knowledge of the causes or treatment of others with same condition, *and* involve

negligible risk to P, not interfere significantly with freedom of action or privacy, or be unduly invasive or restrictive.

It is suggested that changes to the Scottish legislation might consider a similar differentiation between CTIMP and non-CTIMP research.

3) The MCA also sets out additional safeguards at S33:

- Nothing must be done to which P appears to object unless it is to protect him from harm, or reduce or prevent pain or discomfort.
- If P indicates he/she wishes to be withdrawn, this must be done without delay unless there would be a significant risk to health.
- Any advance statement by P must be respected.
- Interests of P must be assumed to outweigh those of science and society.

4) Another difference between CTIMP and non-CTIMP research is the provision made for loss of capacity. In a non-CTIMP a participant who loses capacity does not automatically remain in the study unless Section 30 approval is in place (appropriate body approval) and the researcher consults with a consultee. It may be useful to think through the issue of loss of capacity for any proposed emergency provisions with a view to considering whether further safeguards are necessary.
5) It is strongly recommended that any change in legislation is also seen as an opportunity to produce suitable guidance as can be found in the MCA Code of Practice and the 'Guidance on nominating a consultee for research involving adults who lack capacity' (Department of Health 2008). In addition specific and more robust guidance should be provided for researchers and members of research ethics committees on the issues involved in emergency research.

6) Any change in legislation might also be seen as an opportunity to provide further training to researchers and REC members.

CW felt it should be more explicit that this proposal did not only cover randomised trials but other forms of research such as observational research. He felt the panel should make it clear in any response that they support this proposal not only for a randomised clinical trials but for other forms research.

AGREED: The panel welcomed and supported the proposal but felt that the amendment to the Adults With Incapacity (Scotland) Act 2000 should be accompanied by guidelines that set out what additional legal safeguards are in place to protect the interests of adults with incapacity.

8. Nuffield Council on Bioethics Consultation: Novel neurotechnologies: Intervening in the brain

Received for information:

- Nuffield Council on Bioethics Consultation: Novel neurotechnologies: Intervening in the brain

It was not proposed that the panel formally respond to this consultation document. However it is brought to the panel's attention so that any member with an interest may respond as an individual.

The panel felt that this was an extremely well drafted and useful document but agreed that the panel need not formally respond as there was no direct research related component that fell within the panel's remit to comment upon. However, individual panel members indicated that they would be responding through other channels.

It was agreed that REC members might wish to contribute to the workshops being held by Nuffield Council on Bioethics and that these should be circulated to all RECs.

The panel would look at the guidance once published and abstract relevant parts for dissemination to the REC community.

9. NRES Appeals/Complaints and Breach of GCP/RGF/Potential Fraud & Misconduct Registers

Received for information only:

- NRES Complaints Register
- Breach of GCP/RGF/Potential F&M

The panel commented that the new format, showing aggregated data in graphical form, did not provide sufficient detail for them to form any useful view regarding the information.

They asked that the detailed line listings for any outstanding complaints and breaches be sent for the review at the next available panel meeting.

10. Any Other Business

10.1 Social media and patient recruitment

The panel had recently received two communications: 1) an e-mail from a REC member regarding ethics and social media and the need to focus on how evolving social media communication platforms such as YouTube and Twitter are being used by researchers and pharma companies to reach out to potential patients; and 2) an e-mail from a member of the Independent Cancer Patients Voice charity concerning a suggestion that patients who have already been recruited to a particular trial could help in recruitment of new participants in the same trial by talking to them and answering lay questions about taking part in the trial.

The Panel welcomed both communications and were particularly pleased to receive a communication from a patient group. SiWo commented that from his experience of conducting training in research involving adults lacking capacity (ALC) and CTIMPs researchers often tell him that they are often under a lot of pressure to reach recruitment targets, particularly in ALC studies. He noted that in such cases the safeguards present in the Mental Capacity Act i.e. to take time and consult were often in tension with the need to recruit quickly. In addition, patient organisations will often keen to encourage patients to get involved in clinical trials. In one case an organisation who was the custodian of a patient database use the database to write to parents of children with a specific rare gene in order to ask them to take part in an ongoing study. There was always a pressure between promotion of research and the responsibility to protect potentially vulnerable participants.

FW agreed but felt that the researcher is always the gatekeeper and that the use of patients to recruit other patients could be a good thing.

SiWo noted that many patient groups were self-organising in respect of recruitment trials and it was not necessarily an issue for the panel. It was also noted that it was not only patients who might be used to recruit other patients healthy volunteers were also often paid to recruit other healthy volunteers. AT felt that this was acceptable as long as it was always conducted in a transparent manner.

The panel felt it might be useful if more detail of what was proposed could be provided for further discussion (i.e. how the patient-recruiters would be selected, what training they might receive if any, how they would be introduced and at what stage etc.) along with the Independent Cancer Patients Voice's (ICPV) views of the issue. Given that the ICPV is an organisation of patients for patients and has a wealth of expertise in this it was felt that they would be well placed to provide the panel with the views of patients on this issue. CC would convey the Panel's comments to the ICPV member.

It was noted that HD had invited the REC member who raised the issue of social media to attend one of the workshops at the members training day where this issue was due to be discussed.

ACTION: CC

10.2 HRA

AG informed the panel that he had attended the official opening of the HRA. He noted that the adverts for the chair and non-executive appointments to the HRA board were soon to be published.

10.3 Charles Warlow

Charles Warlow informed the panel that this would be his final meeting and that he was about to sail around the British Isles for the next five months. The panel thanked him for all of his work on the panel over the last 2 1/2 years and wished him well for the future and a bon voyage!

11. Date of Next Meeting:

The next meeting of the National Research Ethics Advisory Panel will be held on 09 May 2012.

Time: 14:00 – 17:00
Venue: Room 128A Skipton House

Health Research Authority
National Research Ethics Service (NRES)
Skipton House,
80 London Road,
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