Health Research Authority
National Research Ethics Service

National Research Ethics Advisors' Panel

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

Date: 13 June 2012
Time: 14:00 – 17:00

Venue: Room 133B
Health Research Authority
National Research Ethics Service (NRES)
Skipton House,
80 London Road,
London SE1 6LH

MINUTES

Present:
Andrew George (Chair)
Hugh Davies
Caroline Harrison
John Saunders
Nalin Thakker
Richard Tiner
Art Tucker
Frank Wells
Simon Woods

In attendance:
Mr Clive Collett
Janet Wisely

1. Apologies: Sarah Dyer; Jeremy Butler; Peter Heasman
2. Declarations of Interest:

   7.0 RCP Guidelines on The Practice of Ethics Committees In Medical Research With Human Participants. HD stated that as an ex officio member of the panel employed by the HRA that he might be conflicted by discussion of this item. The panel decided that HD should remain in the meeting but he would not take part in the discussion or any recommendations made by the panel.

   10.0 TOPS. HD informed the panel that he was a trustee of TOPS.

3. Minutes of meeting held on 09 May 2012

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

4. Matters Arising

4.1 **Confidentiality, Privacy and Secrecy**

Since the last meeting the membership of the "information governance review panel" Chaired by Fiona Caldicott (see http://www.caldicott2.dh.gov.uk/) has been announced:

http://mediacentre.dh.gov.uk/2012/05/28/membership-of-information-governance-review-panel-announced/

Their wide remit will no doubt impact on any guidance we issue regarding the use of personal data in research and thus, following discussion with Hugh, it has been decided to put the draft "Confidentiality, Privacy and Secrecy" guidance document on hold until the review panel has produced its report towards the end of this year. This was felt to be preferable to issuing guidance now that may have to be revised once the "Caldicott 2" report is published.

4.2 **11 July NREAP Meeting**

It was noted that the meeting scheduled for 11th July 2012 would still take place as it was taking place some time before the Olympics opening ceremony and did not involve overnight accommodation for the attendees.

4.3 **Joint Government/GMC letter regarding requests from doctors for absence to undertake national work of benefit to healthcare systems across the UK.**

Received for information:

- Joint Government/GMC letter regarding requests from doctors for absence to undertake national work of benefit to healthcare systems across the UK

RT reiterated that Sally Davies had personally confirmed that the letter also applied to taking part in research ethics committee work. The panel agreed that it would be useful to ensure that this letter was circulated through the NREA hosted chairs network meetings and via the NREAP-badged HRA e-mail communication channel.

RT also noted that the Health and Social Care Act now placed a duty upon The Secretary of State to "promote (a)research on matters relevant to the health service, and (b)the use in the health service of evidence obtained from research." He commented that there was an opportunity here for the HRA to state that their work and the work of RECs was 'promotion of research on matters relevant to the health service'.

5. **NRES/HRA Update – Janet Wisely**

JW confirmed that Professor Jonathan Montgomery has been appointed as the Chair of the Health Research Authority (HRA). Professor Montgomery is currently Professor of Health Care Law at the University of Southampton, Chair of the Nuffield Council on Bioethics and Chair of Hampshire Primary Care Trust. He plans to withdraw from his role as Chair of Hampshire Primary Care Trust as soon as handover arrangements have been agreed.

She informed the panel that the event to launch IRAS as the system platform for the unified approval process took place on the 12th June with a demonstration of the new e-submission functionality. It was explained that the "go live" date for e-submission will be in a few weeks after testing is completed and HRA is confident the system changes were understood and expected. A number of important initiatives were also presented at the launch:

Changes to SOPs including a follow-up reminder to applicants one month following a provisional opinion (rather than three months as currently) and a withdrawal notice issued two months following a provisional opinion (rather than four months as currently).

Favourable opinion with conditions letters would now include a paragraph explaining that any revised documents changed in order to comply with conditions should be submitted to the REC coordinator who would issue an acknowledgement letter. These SOP changes come into effect on 29th June.

Plans to enable ARSAC certificates issued for "diagnosis" to also cover “research" procedures. Initial assessment would still be done in parallel with the research ethics committee review but ARSAC would only have an input where the practitioner does not have a certificate for diagnostic purposes. This would not entail a change to the existing regulations, as it would comply with the current EU directive. A memorandum of understanding would be put in place between NRES and ARSAC to facilitate this change. It was hoped that this might eliminate around 80% of the research applications currently received by ARSAC. Work will begin immediate with a go-live date expected in early 2013

It has been agreed with R&D departments that Question 23 “Authorisations” on the Site-specific information form could be replaced with a single declaration by the applicant that they had discussed this study with R&D prior to submission. The target date for this change is September 2012.

JW informed the panel that the concept of "notifiable" and "non-notifiable" changes had been agreed in principle with R&D. It had further been agreed that the HRA could set out standards regarding what should and should not be notified to R&D departments.

Ethics officers had now been appointed and the role would be piloted in two phases. The first phase will include a "diary" phase where ethics officers would keep notes on their work and this would then be followed by the “real” pilot, which would run for six months beginning September 2012. It was noted that SiWo had been appointed as an ethics officer along with four others. SiWo would also be involved in the oversight of the pilot.

6. What do Potential Research Participants Want To Know?

Received for information/discussion: A presentation by Ms Helen Kirkby (HK), Dr Melanie Calvert (MC), Professor Heather Draper (HDr)

- Summary: “What do potential Research participants want to know?”
- What potential research participants want to know about research: a systematic review - BMJ Open 2012;2:e000509. doi:10.1136/bmjopen-2011-000509

The panel were invited to discuss the applications of the results of this study with the researchers

Professor Draper explained that they would like to seek the panel's views on two issues:

1. The format and use of the ‘reduced’ information sheet
2. How to take this work forward

SiWo explained that as a REC vice-chair his REC frequently advised researchers to produce information sheet similar to the "reduced" information sheet presented to the panel. However, he wondered how such a patient information sheet (PIS) would fit in to the overall informed consent process. Where did the PIS sit within this process? He noted that the GMC state that in taking consent researchers “must ensure that any individuals whom you invite to take part in research are given the information which they want or ought to know, and that is presented in terms and a form that they can understand.”[1] The question of what the participant ought to know is an area that RECs will have an opinion on.

[1] GMC, Research: The Role and Responsibilities of Doctors (2002) para 19. http://www.gmc-uk.org/Research_the_role_and_responsibilities_of_doctors_2002.pdf_31588009.pdf

(NB guidance withdrawn April 2010 and replaced by ’Good practice in research and Consent to research – supplementary guidance’ (04 May 2010) which now states: “You must give people the information they want or need in order to decide whether to take part in research. How much information you share with them will depend on their individual circumstances. You must not make assumptions about the information a person might want or need, or their knowledge and understanding of the proposed research project.” http://www.gmc-uk.org/static/documents/content/Research_guidance_FINAL.pdf

HDr asked, if we accept that the role of the consent interview is more important and takes precedence over the information provided in the PIS, what things must be patients know before deciding whether to take part in a piece of research. She also asked whether the "24-hour rule" might be reduced in appropriate circumstances. The panel informed HDr that allowing potential participants at least 24 hours to consider their participation had never been a "rule" nor stipulated in any guidance.

SiWo stated that patients rely on many sources of knowledge some of which they have prior to being approached to take part in research e.g. knowledge gained from being a patient etc. AG agreed stating that RECs may not always take into account the prior knowledge of the intended audience.

JS commented that the study population in the team's research was probably younger than the average clinical research participant. HK acknowledged that one of their concerns was that the use of technology might not be appropriate for many older people.

JS stated that the PIS was not as important as what is said verbally to potential participants and their relationship with the researcher/HCP. RT commented that whilst this was probably correct it highlighted the need for impartial written information to be provided.

JS felt that the issue of gaining consent had parallels with the 'paradox of enquiry' presented in Plato's Meno: "*…man cannot enquire either about that which he knows, or about that which he does not know; for if he knows, he has no need to enquire; and if not, he cannot; for he does not know the, very subject about which he is to enquire.*[2]" i.e. potential research participants do not know what it is they need to know. HDr agreed saying that there were circles of information: patient judgement was overlaid with what is required to be given to the patient. However, we do have a consent process whereby patients are verbally given information that it is considered necessary for them to know.

AG commented that if a REC thinks there are a core number of items that potential participants should know then that REC has to decide what they are. It might be possible that the researcher or other person taking consent might then test the participant on those core items to ensure that they have taken in the essential information. HDr agreed but felt that there would then need to be guidance on what the core items should be. If a participant did not wish to know one of those pieces of information then they might be barred from the research.

SiWo explained that he had been working recently on the concept of therapeutic misconception and noted that if patients do fail to perceive that research aims are different to the aims of treatment that at least the current governance framework means that we are dealing with well-defined and relatively "safe" research studies. Participants who took part in such studies even though they had an incomplete understanding of the true aims would at least be taking part in a relatively safe activity.

RT noted that all medicines come with an information leaflet included in the box. If something untoward happens to the patient then they immediately go to the leaflet. He felt this was similar to research information sheets in that there needed to be a document that participants could refer to when needed. SiWo noted that there are occasions where clinical trials will have very serious side effects and asked whether we can really afford for patients not to be made aware about such things. RT agreed and felt that this is where the interview process comes in.

RT felt one of the main issues was one of "trust". He felt that patients in this country particularly are still very trusting of their healthcare professionals, not as much as they once were still more than in other countries. This culture of trust was still very important factor in a patient's decision to take part or not in research, as they will tend to trust an invitation coming from their doctor or other healthcare professional.

NT was concerned that the research presented to the panel involved a lower risk study and that there was a real danger in extrapolating from this to other higher risk studies. In addition, he felt that not

[2] http://classics.mit.edu/Plato/meno.html

everybody would be able to access the extra layers of information provided through the Internet. He stated that he felt the purpose of a PIS was for future referral and also as a "legal" document to prove that the researchers have provided the necessary information to the participant.

HDr asked whether the panel thought that RECs would be happy if the use of streamlined information was applied to higher risk studies. She added that the more complex the study the more likely patients are to return to the study information and that by using an Interactive Information Sheet (IIS) it would be possible to track exactly what information they are accessing and how often.

NT stated that he understood where Prof Draper's team were coming from but felt it was important to note that RECs do constantly ask for information sheets to be simplified. FW agreed but felt that information sheets still required a number of essential items. NT agreed but felt that these could be much shorter for low-risk information sheets.

AT stated that in his opinion information sheets are primarily intended to provide protection for the pharmaceutical industry. The reason that 20 page information sheets are produced by pharma companies was so that they can avoid being sued for not providing sufficient information.

AG noted that RECs would often use the information sheet as a test of whether the researcher was able to communicate effectively. An incomprehensible information sheet would invite the REC to question whether the researcher would be able to communicate the necessary information to the patient verbally.

HD congratulated the team on the work and stated that he would be very happy to work with them to take this work forward. He suggested that at this stage it might be sensible to collect more data in high risk studies regarding what information patients are actually using before going on to conduct a randomised trial of different PIS formats. He also thought that they might usefully talk to Pfizer as they were currently in the process of setting up studies using Internet-based information. HD also noted that Jane Kaye was looking at similar areas and referred Prof Draper's team to her recent article in 'Nature Reviews Genetics 13, 371-376 (May 2012), doi:10.1038/nrg3218 "From patients to partners: participant-centric initiatives in biomedical research"[3] he also felt it might be useful to discuss this with the EFGCP in order to investigate proceeding with this work as there were a large number of people in Europe who would be interested. He suggested they contact Jan Geissler at EFGCP (http://www.efgcp.be/Bio.asp?membid=753).

RT also suggested that they might like to talk to INVOLVE about this work and how to take it forward.

HDr asked whether the panel thought they would be able to get REC approval for such studies.AG felt that the use of IISs might be extended to higher risk studies provided that appropriate safeguards were put in place such to ensure that all participants have real access to the full information if they required it. An easy way to initially simplify and stratify information provided would be to separate the information along the lines of the current part one and part two sections of the NRES standard information sheet format. Information regarding insurance, confidentiality etc might be separated out into a separate layer of information that could be accessed if required. AG felt that whilst there was clearly a risk in trialling the use of reduced information he also noted that it was in line with NRES' wish to produce more evidence-based guidance.

HD suggested that it might be useful if they attend the EFGCP Annual Conference in Brussels on 29 & 30 January 2013 entitled "Virtual Future: what are the ethical dimensions of using emerging technologies in clinical trials and research?".

7. RCP Guidelines on The Practice of Ethics Committees In Medical Research With Human Participants – John Saunders

Received for information/discussion:

[3] http://www.nature.com/nrg/journal/v13/n5/abs/nrg3218.html

- RCP Guidelines on the practice of ethics committees in medical research with human participants - Fourth Edition
- Email from John Saunders

JS stated that he would like the panel to support an update of these guidelines and recommend to NRES that hard copies of the updated guidance be provided to all RECs.

AG noted that whilst there was clearly material in the current edition that would require updating e.g. because of changes in the regulatory environment, he felt that around 80% of the text concentrated on "solid ethical issues" and was unlikely to require major revision. JS agreed that this was a fair assessment of the revision required. He noted that he was uncomfortable with the section on patient record research and felt this was in need of revision. However, he felt that the overall structure of the guidelines, could be kept as it is i.e. divided into 10 main chapters.

FW noted that a single copy per REC may not be sufficient for all members to access.

SiWo acknowledged that the guidelines were a very good resource containing a good deal of sound advice. He noted that such guidelines would be very useful for anyone undertaking the ethics assurance officer role. He asked whether finance was a factor that would influence whether the revision is undertaken not. JS stated that he was unsure but that if undertaken then it was likely that it would result in a printed version. He also noted that, as previously, the guidelines are likely to be made available online free of charge one year after publication. He noted that he would most likely be the chair of any revising group and that he would like to have and NREA involved as part of that group. The current hardcopy of the guidelines were sold for £15.

AG questioned whether hard copies were required. He noted that in his own experience the raising of a purchase order for a single copy was often more trouble than it was worth. The panel noted that in all likelihood any revised guidance would end up being available online for free.

RT suggested that the Academy of Medical Royal Colleges might be invited to endorse the guidelines or be encouraged to buy into it being a joint document.

Agreed: The panel endorsed and supported the revision of these important guidelines

8. **Disruption of Research – Caroline Harrison**

Received for information/discussion:

- A verbal presentation by Caroline Harrison regarding legal remedies to counter organised disruption to research

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CH started her presentation by indicating that there was no easy answer to the question of whether there were legal remedies available to counter any organised disruption to research. The fundamental difference was between criminal offences (which may be prosecuted once committed; but where pre-emptive remedies are more difficult and of less ‘value’ in terms of protecting researchers) and conduct regulated by the civil law, where pre-emptive remedies to govern future conduct may be obtained. In criminal law, the offence is committed when all the necessary ‘elements’ have occurred. Those elements are the ‘actus reus’ and the ‘mens rea’ – i.e. the actions + accompanying mental intent. Crimes may also be ‘attempted’, but only if acts have been done which are ‘more than merely preparatory’ to the substantive offence. Conspiracy to commit crime is also an offence, but proving the requisite degree of agreement to amount to a conspiracy is difficult. Hence criminal law has its limitations, in this context. However, she noted that if the desired objective was to protect researchers and ancillary staff from

actual violence, or the imminent threat of violence, then this would primarily fall within the domain of criminal law and could be prosecuted once sufficient evidence was available. Prosecutions may be undertaken privately, or by the police. However, assaults also amount to a trespass against the person, and so the civil law *could* be used to restrain people from committing such acts, if there are good grounds for suspecting that this will occur or recur.

Concerted campaigns by groups to disrupt research (where the conduct of the group's members falls short of threatening violence) was a much vaguer and more controversial area. Legal remedies to combat e.g. non-violent or abusive campaigns to dissuade researchers from undertaking certain types research was in practical terms a "nonstarter", because the courts would have to balance the rights of researchers to go about their daily business, with the rights of protesters to free speech and freedom of expression. Where that balance will be struck in any one case, will be a matter of fact in any situation, and will be difficult to predict in advance. There were also practical problems, such as identifying defendant(s) – see below.

There is no specific statutory provision that CH could find, that was designed specifically to protect staff involved in clinical research. CH stated that she could not conceive of legislators or ministers being persuaded that there *should be* some specific regulation that should be passed, that would apply to researchers, but that did not also apply to the general public. She noted that within the existing law, there were three statutes that may have the greatest relevance to this area:

1) Protection from Harassment Act 1997;
2) Public Order Act 1986; and the
3) Malicious Communications Act 1988

CH noted that under civil law injunctive relief can be used to limit certain behaviours (e.g. preventing people from going to specified locations, or from contacting the claimant(s) etc., but it cannot require them to do positive acts). However in order to be able to bring a claim under the civil law, a claimant has to be able to identify an actual defendant that is recognised in law (i.e. something that has legal personality, such as a limited company, or an unincorporated association, or an individual person). Without this, there is no-one to sue, and no-one upon whom to serve papers, or to punish for breach of any Order made by the Court. This is likely to cause a real difficulty in the case of research disruption, because the people engaged in such conduct are likely to be part of a loose grouping of like-minded individuals; they may be difficult to identify as individuals, and many will have have no assets or insurance. Like the Hydra, once you cut off one head, more will spring up in its place

The real problem in both criminal and civil cases is the balance between an individual's right to freedom of expression and the rights of others to carry out their business without harassment.

CH explained that there were two main cases in this area that provided useful parallels:

1) Connolly v. DPP [2007] EWHC 237 (Admin); [2008] 1 W.L.R. 276[4] and
2) Novartis Pharmaceuticals UK Ltd & Ors v Stop Huntingdon Animal Cruelty ('SHAC') & Ors [2009] EWHC 2716 (QB) (30 October 2009)[5]

Connolly v. DPP concerned a woman who sent graphic images of aborted foetuses to pharmacies. She was a Roman Catholic who objected to the morning after pill. She was prosecuted under the Malicious Communications Act 1988. The court held that all the necessary elements of the offence were made out and so her appeal was rejected, but it also rejected the defendant's argument that the prosecution violated her right to freedom of expression under Article 10 of the European Convention on Human Rights. The court held that the restriction on her Article 10 right to "freedom of expression" was justified because the images were grossly indecent and offensive, and the restriction was justified as being a proportionate limitation on her rights, when balanced against the the rights of others to work without being subjected to grossly offensive material that was plainly intended to shock.

[4] http://www.bailii.org/ew/cases/EWHC/Admin/2007/237.html
[5] http://www.bailii.org/ew/cases/EWHC/QB/2009/2716.html

In **Novartis Pharmaceuticals UK Ltd & Ors v Stop Huntingdon Animal Cruelty ('SHAC') & Ors** the claimants applied for amendment of the injunction to address concerns about a protest planned for Halloween. Among other things, the claimants sought orders that the protestors must not:

- wear clothing or costumes splattered with blood;
- wear balaclavas, masks or face coverings;
- use banners to accuse Novartis and/or its employees of murdering, torturing or abusing animals.

Mr Justice Sweeney refused to amend the injunction to prevent the protestors from wearing blood splattered clothing or costumes. He held that such a restriction was not a proportionate restriction on their freedom of expression, and was unlikely to be practically enforceable. He also refused to prevent the protestors from wearing masks, but acknowledged that that issue was less 'clear cut'. In reaching his decision, he balanced the potential for ghoulish masks to cause distress and conceal the identity of people who intend to harass others against:

- the practical problems that a ban on masks would cause for the Police;
- the risk that such a prohibition would heighten tensions; and
- the rights of people to wear innocuous masks.

CH concluded by stating that she saw no realistic mechanism by which medical research could be singled out as a special category of work, and specifically protected beyond the scope of the general law which already regulates people's conduct. She noted however, that civil law injunctions might be a valid option where the conduct was egregious (indeed, they may be the only realistic option in some cases), and that they did have real "teeth", because breach of such injunctions is a contempt of court, and the ultimate sanction for persistent and deliberate contempt, even in a civil case, is imprisonment. Thus limited means/the lack of insurance may not be relevant if what you are really seeking to do, is to prevent identifiable individuals from threatening research workers.

9. The need to inform participants GPs of their patients taking part in research

The panel were invited to discuss and endorse the following statement:

"Informing GPs of their patient's participation in research is not a universal requirement. It should only be mandatory in the following circumstances:

i. Where the GP may have information about the patient that might influence the consideration as to whether it is safe for the patient to join the study;
ii. Where participation in the study would impinge on the provision of routine health care to that patient by the GP."

The current NRES "Information Sheets & Consent Forms Guidance for Researchers & Reviewers" (March 2011) states:

> **"6.2.5 Involvement of the General Practitioner/Family doctor (GP)**
>
> You should explain if the participant's GP (or other health care practitioner) needs to be notified of their participation, and seek consent for this. You should explain what information will be exchanged. There may be circumstances in which informing the GP may not be necessary, acceptable or possible."

FW stated that he always thought it important that the participants GP was aware that their patient was taking part in a trial. AT suggested that this was not necessary for low risk trial such as a trial simply taking a person's blood pressure. RT agreed but stated that in an interventional trial the notification of the GP was important. FW agreed that it was particularly important that the GP was alerted to any of their patient's participation in an interventional clinical trial.

AG noted it might be important where the participant is likely to be discharged back to the care of their GP. He noted that in some cases the REC might feel it was essential that the GP being informed and in such cases agreement to this would become a condition of taking part in the study.

The panel felt that the current statement should remove the word "routine" from the phrase “impinge on the provision of routine health care". In addition, it was felt that other healthcare professionals may also want or need to be informed about their patient's participation in a research study and thus the statement should be expanded to include all "healthcare professionals".

Agreed: the panel endorsed the following revised statement:

Informing GPs and other healthcare professionals (HCPs) of their patient’s participation in research is not a universal requirement. It should only be mandatory in the following circumstances:

i. **Where the GP or HCP may have information about the patient that might influence the consideration as to whether it is safe for the patient to join the study;**
ii. **Where participation in the study would impinge on the provision of health care to that patient by the GP or other HCP.”**

10. **TOPS paper**

Received for information:

- TOPS: an internet-based system to prevent healthy subjects from over-volunteering for clinical trials – Boyce et al., Eur J Clin Pharmacol DOI 10.1007/s00228-012-1231-8

The panel noted and welcomed the results of this paper confirming that TOPs was an effective measure for the prevention of over volunteering in clinical trials.

11. **NREA-Hosted Chairs network Meetings - Minutes**

Received for information:

- Minutes of the North West NREA-Hosted Chairs Network Meeting - 21 May 2012
- Minutes of the South West NREA-Hosted Chairs’ Network Meeting 18 May 2012

RT noted that in section 6.4 of the North West NREA-Hosted Chairs Network Meeting minutes the suggestion was made that the number of substantial amendments permitted for one study should be limited. RT had sympathy with this but pointed out it was not practical. AT agreed and asked what limit would be placed on the number of amendments.

RT noted that in section 8.1 comment was made that retired clinicians still qualified as "expert" members. He noted that this is an issue that may need to be reconsidered following the implementation of revalidation of doctors in 2013 (see http://www.gmc-uk.org/doctors/revalidation.asp).

Both SiWo and FW who hosted these two meetings stated that all attendees found the NREA hosted meetings extremely useful.

12. **Any Other Business**

13. **Date of Next Meeting:**

The next meeting of the National Research Ethics Advisory Panel will be held on 11 July 2012.

Time: 14:00 – 17:00
Venue: Skipton House
Health Research Authority
National Research Ethics Service (NRES)
Skipton House,
80 London Road,
London SE1 6LH