National Research Ethics Service

NHS Health Research Authority

## National Research Ethics Advisors' Panel

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

Date: 11 July 2012
Time: 14:00 – 17:00

**Venue:** Room 5C1 - 5th Floor
Health Research Authority
National Research Ethics Service (NRES)
Skipton House,
80 London Road,
London SE1 6LH

# MINUTES

1. Apologies: Hugh Davies; Sarah Dyer; Caroline Harrison; Art Tucker; Janet Wisely
2. Declarations of Interest

   There were none
3. Minutes of meeting held on 13 June 2012

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

### 4. Matters Arising

#### 4.1 Phase 1 Advisory Group

For Information:

Dr Siobhan McGrath will be leaving ORECNI and as a result will no longer manage the Phase 1 Advisory Group. CC will take over the management of the business for the group, which will become an advisory group that reports through NREAP. The group will initially be chaired by Richard Tiner until a member of the newly appointed NREAs has been identified to take on the chairing of this group.

#### 4.2 HRA Emergency Research workshop - 21 June 2012 – London – Andrew George

Received:

- Verbal update on the HRA Emergency Research workshop held on 21 June 2012

On the 21st June the Health Research Authority organised a meeting to bring together researchers and members of research ethics committees (RECs). Presentations and consequent discussion indicated that this research is complex, difficult and sometimes frustrating and the different national regulatory frameworks only add complexity when this work crosses national boundaries. Despite this, researchers described how research in this area can be done, and done well.

As for all areas of health care, it is only through research that we will improve care. It was claimed, with little counterargument, that patients are dying as a result of this dearth of evidence. While it was agreed that the acutely ill, who need urgent treatment, and cannot give consent are a vulnerable group, it was contended that without research they are "doubly vulnerable". Not only are they unable to represent their own interests but without this research, they will be given treatments which may not work or even be harmful.

Some have argued and presented evidence that the current ethos is often meaningless and may seriously harm patients and participants.[1] Yet this need not be so. Law and moral considerations give us a framework to help us decide when "consent at the time" should or shouldn't be waived. If this is understood and followed by both researchers and Research Ethics Committees, ethical research in which public and patients will have trust can be facilitated, regulated and conducted.

Those at the meeting were agreed on several points:-

1. Ethical research has to replicate, and therefore cannot change, practice. Separate treatment standards and schedules are ethically and scientifically unjustifiable.

2. Support for the following principles (while recognising the difficulties these present in emergency care research)

- People must be assumed to have capacity unless it is established that they lack capacity.
- Before treating people as unable to make a decision, all practicable steps to help them do so must be tried.
- People should not be treated as unable to make a decision merely because they make an unwise decision.
- Acts or decisions on behalf of people who lack capacity must be in their best interests. Before any act or decision, the person responsible must consider whether the purpose could be achieved in a less restrictive way

3. There was also support for the conditions for fair emergency trials without "consent at the time"

- Treatment is needed urgently and the nature of the trial also requires urgent action
- It's impractical to seek consent or consult others
- There is equipoise or uncertainty about the better treatment
- An NHS REC has given favourable opinion

SiWo noted that there was no evidence that RECs present a barrier to the conduct of emergency research. He noted that there were provisions within current law to permit emergency research and there needed to be a greater awareness of these by both researchers and ethics committee members. The law demands that researchers should always consider other routes of recruitment as stipulated within both the Medicines for Human Use (Clinical Trials) Amendment (No. 2) Regulations 2006. Statutory Instrument 2006 No 2984[2] and the Mental Capacity Act 2005[3].

AG noted that there appeared to be some confusion around the concept of "retrospective consent". Those present at the meeting were in agreement that the term did not make sense, as consent could not logically be given for events that had already taken place, and should not be used. The enrolment of participants unable to give consent was provided for in law and either a researcher has obtained informed consent from the adult's legal representative (under the Clinical Trials Regulations), sought

[1] Roberts et al, Effect of consent rituals on mortality in emergency care research. Lancet March 24, 2011.
[2] www.opsi.gov.uk/si/si2006/20062984.htm
[3] http://www.legislation.gov.uk/ukpga/2005/9/contents

"advice" from a consultee (MCA) or enrolled the participant under the provisions of The Medicines for Human Use (Clinical Trials) (Amendment No.2) Regulations 2006. Where the treatment to be given to an incapacitated adult as part of the trial needs to be given urgently, time may not allow for the written consent of a legal representative to be obtained first. The amendment allows incapacitated adults to be entered into a trial prior to consent being obtained from a legal representative provided that:

- Having regard to the nature of the trial and the particular circumstances of the case, it is necessary to take action for the purpose of the trial as a matter of urgency but
- It is not reasonably practicable to obtain informed consent prior to entering the subject, and
- The action to be taken is carried out in accordance with a procedure approved by the ethics committee.

Where an incapacitated adult is recruited in an emergency situation without prior informed consent, steps must be taken to seek informed consent either from the subject (if capacity has been recovered) or from a legal representative as soon as practicable after the initial emergency has passed. Where consent is withheld, the subject must be withdrawn from the trial.

It was also discussed at the workshop whether participants who had been enrolled into emergency research should be able to withdraw their data once they regained capacity. SiWo felt that the retention of non-identifiable data was allowed and legally robust however, the retention of data in an identifiable form might be open to legal challenge. It was agreed that clarity on this issue would be helpful.

It was also noted at the workshop that just because participants in emergency situations might lack the full capacity to give informed consent to participation in research did not mean that information should not be given to them in proportion to the limited capacity they had.

It was noted that HD was currently preparing report and guidance on this issue for circulation to participants at the workshop and RECS.

### 4.3 **Information Governance Review**

The HRA chair, Jonathan Montgomery, attended an evidence giving session on Tuesday 10 July 2012 for the 'Regulation and Governance' perspective of the Information Governance Review chaired by Dame Fiona Caldicott[4]. A briefing report was put together for Jonathan by CC which included the panel's concern regarding the need for clarity over requests for the withdrawal of data from research by participants once they have left a research study[5].

### 4.4 **Non-Executive Directors of Health Research Authority confirmed**

Sally Cheshire, Julie Stone and Dr Allison Jeynes-Ellis have been confirmed as Non-Executive Directors of the Health Research Authority (HRA). Sally will also be the Audit Committee Chair.

The new Non-Executive Directors will support the Chair by contributing to the effective governance of the Health Research Authority.

- Sally Cheshire has spent 13 years as a Consulting Director with one of the leading global professional services firms and is a Chartered Management Accountant by profession. She is currently Vice Chair of NHS North England and Audit Chair of the Human Fertilisation and Embryology Authority.
- Julie Stone is a medico-legal, ethical and regulatory academic and policy advisor. She is currently a Non-Executive Director of NHS Cornwall and Isles of Scilly, lay member of the

[4] http://caldicott2.dh.gov.uk/
[5] See NREAP Minutes of 12 May 2010 and 09/06/2012

General Osteopathic Council and member of the Ministerial Advisory Group on Mental Health Strategy.

- Dr Allison Jeynes-Ellis is a senior pharmaceutical physician with experience of working in the life sciences industry and a research and development specialist in oncology. Her current roles include Independent Pharmaceutical Consultant working across the life sciences and member of the General Medical Council.

## 5. HRA Statement "Training requirements for researchers"

Received for information/discussion:

- HRA Statement "Training requirements for researchers"

The panel were asked to support the statement contained in the attached document.

The panel welcomed and supported the statement. FW suggested that the HRA might seek the support of other institutions and suggested that they should approach the BMA's Medical Academic Staff Committee (MASC). SW noted that as a member of the committee he would be happy to be the point of contact for this approach. JS also noted that the support of the Royal College of physicians might be sought through him.

**Agreed:** The panel supported the statement.

## 6. ABPI/DH/BIA/CCRA/NRES Compensation in the event of injury in phase I Clinical Trials

Received for Information:

- Industry guidance – 'Insurance and compensation in the event of injury in Phase 1 clinical trials'
- Statement of Insurance Cover
- Insurance and compensation in Phase 1 trials - guidance for RECs

The Association of the British Pharmaceutical Industry (ABPI), the BioIndustry Association (BIA) and the Clinical Contract Research Association (CCRA) have jointly published guidance on insurance and compensation for Phase I clinical trials. The guidance, which has been developed in consultation with the Department of Health and the National Research Ethics Service (NRES) within the Health Research Authority (HRA), is for trials including first-in-man studies involving healthy volunteers. The guidance also applies to studies conducted in patient volunteers without the target disease to provide additional pharmacokinetic data about the medicine under research.

The guidance is intended for use by Phase I clinical trial sponsors, clinical research organisations and ethics committees. It has been developed to provide authoritative recommendations on the level of insurance and other aspects of insurance cover. The guidance is based on industry best practice and complements wider industry guidance on conducting Phase I clinical studies.

Published alongside the guidance is a template Statement of Insurance Cover, which has been developed by NRES, to give clinical trial sponsors a consistent document to provide to the ethics committee. The statement will be incorporated into the standard application for Phase I clinical trials within the Integrated Research Application System for health and social care research in the UK. The statement must be submitted with all commercially sponsored Phase 1 applications with effect from 1 August 2012. In due course, the statement will be incorporated into IRAS.

The panel welcomed and supported this guidance.

RT questioned why paragraph 1.3 indicates that the "guidance set out below applies only to Phase I studies sponsored by industry" as other organisations also sponsor phase I research e.g. Wellcome trust, CRUK, universities and others. He noted that ABPI documents tend to be adopted by other organisations but, as this had only just been released, he thought the question worth asking of the authors. It was noted that the accompanying REC guidance does not make this distinction and the panel wished to know whether the guidance to RECs was intended to apply to all phase I studies regardless of their sponsor.

RT also noted that para 3.2 states that "The undertaking to compensate the volunteer will be construed in accordance with English law" and wondered what the status of this guidance was in relation to phase I research conducted in Scotland and Northern Ireland.

RT further noted that whilst para 6.4 states that:

> "The Investigator and other physicians involved in Phase I studies must have appropriate insurance or indemnity against claims based upon negligence. This could be provided under the insurance of the Sponsor or of the CRO or through personal membership of a medical defence organisation or a policy of insurance purchased personally by the Investigator and other relevant physicians"

He felt that membership of a Medical Defence Union is unlikely to cover that individual for phase I research activity.

AG wondered whether the definition of "first into man" studies as "the administration of a new molecule to man (healthy subjects and or patients) for the first time by dose (single and repeated) and /or by route of administration. A new molecule is a unique molecular structure irrespective of whether the molecular class or the therapeutic target is known" might present difficulties for those researchers who modified existing molecules, e.g. peptides, whose safety profile was well-known but wished to manipulate molecule in such a way as to alter its stability thus changing its half life.

FW raised a query over paragraph 5.8.i.e. is there an inconsistency either in including the second bullet point on the regulatory requirement that the study be authorised by the competent authorities but not including a fifth bullet point on the ethical requirement that the study be given a favourable opinion by an NRES research ethics committee; or, in the absence of a bullet point relating to the requirement for ethical approval, including one on the regulatory requirement for competent authority authorisation? This query arises because of the requirement for both regulatory and ethical approval for a Phase I clinical trial; either both requirements should be included, or neither.

**Agreed:** the panel agreed that NRES should be asked the following questions regarding this guidance:

- Was it intended that the guidance to RECs should apply to all phase 1 studies regardless of their sponsor?
- Para 5.8: Is there an inconsistency either in including the second bullet point on the regulatory requirement that the study be authorised by the competent authorities but not including a fifth bullet point on the ethical requirement that the study be given a favourable opinion by an NRES research ethics committee; or, in the absence of a bullet point relating to the requirement for ethical approval, including one on the regulatory requirement for competent authority authorisation?
- Para 3.2: what was the status of this guidance was in relation to phase 1 research conducted in Scotland as para 3.2 indicates that "The undertaking to compensate the volunteer will be construed in accordance with English law"

## 7. ABI leaflet: Clinical research trials and insurance - Information for people who are planning to take part in a clinical research trial (January 2011)

The panel were invited to comment on the ABI leaflet "Clinical research trials and insurance Information for people who are planning to take part in a clinical research trial"

- Clinical research trials and insurance - Information for people who are planning to take part in a clinical research trial (January 2011)
- ABI Leaflet: DH - Issue and Background
- HD Comments on "Clinical research trials and insurance - Information for people who are planning to take part in a clinical research trial"

The ABI Leaflet is also available online at: http://www.abi.org.uk/Information/Consumers/Health_and_Protection/Health__Protection_Insurance_.aspx

Whilst the panel felt that there was a real need to have clear communication and guidance on this issue for research participants it was felt that this document was not well written and would benefit from being redrafted.

The panel were of the opinion that the leaflet was unclear, unnecessarily harsh with regards to seeming to group phase 3 with phase 1 & 2 trials and it was felt that any patient reading this leaflet would not fully understand the relevance of the questions being raised. The document should much more clearly describe what effect taking part in clinical research would have on their private health insurance.

RT noted that the leaflet did not fully address the issue of what insurance cover might be in place should a patient, who had taken part in a trial, became ill whilst abroad. Who would be responsible for repatriation, medical treatment etc.

FW drew the panel's attention to his and Hugh Davies' involvement with MARSH, the principal broker for the insurance industry on clinical trials. The panel agreed that it might be useful to involve MARSH in any discussion with the ABI over appropriate revisions to this leaflet.

**Agreed:** The panel agreed with the concerns raised by the Department of Health over this leaflet and ask that Hugh Davies, in collaboration with Frank Wells, take this issue forward with the ABI.

## 8. HM Government/ABI Concordat and Moratorium on Genetics and Insurance

Received for Information Only:

- HM Government/ABI Concordat and Moratorium on Genetics and Insurance

  Available online at: http://www.dh.gov.uk/health/files/2012/06/Concordat-and-Moratorium-on-Genetics-and-Insurance-20111.pdf

  The agreement with the Association of British Insurers (ABI), the Concordat and Moratorium on Genetics and Insurance, continues to guarantee that anyone who has had a predictive test to assess their susceptibility to genetic conditions, such as breast and ovarian cancer, can take out significant insurance cover without disclosing the results.

  The agreement has been extended to 2017 and sets out that all future reviews of the agreement will take place three years before the provisional end date. This will give consumers enough time to prepare if there are any changes. The agreement has also been simplified to make it easier to understand. The next planned review will be held in 2014.

The document states that:

*"Insurers agree to the following:*

*a. customers will not be asked, nor will they be put under pressure, to take a predictive genetic test to obtain insurance cover;*

*b. customers who have taken a predictive test before the date of this Concordat will be treated in the same way as customers taking tests under the terms of the Concordat;*

*c. customers will not be required to disclose any of the following:*

*i. a predictive genetic test result from a test taken after the insurance cover has started, for as long as that cover is in force;*
*ii. the predictive test result of another person, such as a blood relative; or*
*iii. a predictive or diagnostic test result acquired as part of clinical research. To avoid doubt, customers may be asked to disclose details of any symptoms, diagnosis or treatment received outside of the clinical research programme, even if those relate to a condition they found out about through the research programme.*

*d. customers making relevant insurance applications will be required to disclose a predictive genetic test result only if all of the following apply;*

*i. the customer is seeking insurance cover above the financial limits set out in the Moratorium;*
*ii. the test has been assessed by a panel of experts and approved by Government – a list of approved tests can be accessed at www.dh.gov.uk and www.abi.org.uk. This list should be made available to applicants on request; and*
*iii. the insurer asks the customer to disclose the information."*

The panel noted and welcomed the continued moratorium on genetics and insurance.

## 9. Consultation on proposals to transfer functions from the Human Fertilisation and Embryology Authority and the Human Tissue Authority

Received for Information Only:

- Fertility and Human Tissue Regulators Consultation document

A copy of the consultation, accompanying consultation impact assessment and consultation equality analysis can be found at: http://www.dh.gov.uk/health/2012/06/consultation-regulators/

The Department of Health has published a consultation on proposals to transfer functions from the Human Fertilisation and Embryology Authority (HFEA) and the Human Tissue Authority (HTA) as part of the Government's drive to streamline regulation and to deliver effective and efficient services.

The consultation runs for 13 weeks and closes on 28th September. The Department of Health welcomes views from the organisations directly affected and from patients, the wider public, health professionals and organisations regulated by the HFEA and HTA. The consultation seeks views on whether:

- all functions should transfer to the CQC except the HFEA functions relating to research that would pass to the Health Research Authority; and the HFEA and HTA be abolished
- all functions should transfer, as set out above, but a limited number of functions would transfer to organisations other than the CQC
- the HFEA and HTA should retain their functions but deliver further savings

The consultation runs until 28 September. Any person, business or organisation with an interest is encouraged to respond.

The consultation documents can be downloaded from these links:

- Download the fertility and human tissue regulators consultation document (PDF, 339K)
- Download the consultation questionnaire form (DOC, 34K)
- Download the Equality analysis (PDF, 98K)
- Download the Impact Assessment (PDF, 2684K)

The panel noted the consultation and some comments were made which would be fed back to the HRA Board for consideration.

## 10. **NREA-Hosted Chairs network Meetings - Minutes**

Received for information:

- Minutes of the South Central NREA-Hosted Chairs' Network Meeting held on 17th May 2012*
- Minutes of the East of England NREA-Hosted Chairs' Network Meeting held on 20th June 2012

JB noted that the minutes of the East of England chairs meeting contained reference to researchers being invited back into the meeting following the committee's discussion of the research and their being given an informal indication of the REC opinion. JB wondered what the NRES policy was on this practice. CC said that he would follow this up.

**Post Meeting Note:** This practice is at least partially supported by Operational Management E-Mail Alert 31 dated 11th October 2010[6]:

> "6. Notification of a REC decision.
>
> We have recently received informal feedback from an investigator who telephoned the REC office to ask about the decision on his application and the Co-ordinator said they were unable to provide this over the phone. Whilst OMEA9-1 indicated that any informal contact with the CI should be via e-mail to provide an audit trail of advice given, *it is acceptable to give a CI a verbal indication of the decision of the Committee and any broad areas of concern which exist with a proviso that the formal decision of the Committee will be set out fully in the opinion letter which will be provided with 10 working days of the meeting*."

## 11. **Any Other Business**

### 11.1 **Gene Therapy Advisory Committee (GTAC)**

[6] http://www.nres.nhs.uk/home/hra-extranet/operational-email-alerts/?entryid61=83555&p=3

AG informed the panel that he had taken over as Chair of the Gene Therapy Advisory Committee on an interim basis the six months.

### 11.2 **NHS Clinical Excellence Awards**

PH raised the issue of the acknowledgement of NHS staff undertaking voluntary work within HRA/NRES in relation to NHS clinical excellence awards. Clinical Excellence Awards recognise and regard NHS consultants and academic GPs who perform 'over and above' the standard expected of their role. Awards are given for quality and excellence, acknowledging exceptional personal contributions. He noted that awards can be made both locally and nationally and stated that the system worked well at a local level but less well at the national level.

He noted that currently NHS consultants within the HRA/NRES might seek a citation from the HRA Chief Executive in support of an application for a national level clinical excellence award, but that he felt that this process should be made more formal. There are a number of national nominating bodies[7] able to nominate people for these awards and he suggested that the HRA might be strongly encouraged to register to be such a body. PH noted that current NHS consultants who were in the REC system could be nominated by their health authority or other body at a local level but he was concerned more with those who were performing 'over and above' the standard expected of their role at a national level and he pointed out that there would be only a small number of individuals within the REC community contributing at that level and that senior management including JW, Joan Kirkbride and David Neal would be well aware of them and would be well placed to comment upon their suitability for such an award. PH stated that if the HRA is to be a successful institution then it needed to provide encouragement to people who contribute to its work and that this was an important way to do that.

AG noted that these awards were only open to NHS consultants and academic GPs and similar recognition and encouragement was not afforded to people in the REC system who were not members of either of these groups. JB agreed and wondered how the HRA could encourage and reward non-clinicians. Such rewards did not necessarily need to be financial but there needed to be some thought about how to appropriately recognise and reward exceptional service by non-clinicians within RECs. SiWo agreed that there needed to be a system of rewarding those who were not eligible for NHS rewards so that all members felt that their efforts were acknowledged and valued.

JS sympathised with the lack of possible routes for the recognition of non-clinicians efforts but reminded the panel that this particular issue was one of the terms and conditions of NHS consultants. Not to say that they were more valuable than other REC members but that was the current system and mechanism for reward of these individuals. PH stated that of course it was not feasible to compare the contribution of an NHS consultant with that of a lay member as it was like comparing "apples and oranges". However, what was important was "fairness" in the current system so that NHS consultants who go above and beyond in their contributions to the HRA/NRES should be eligible to receive the same recognition afforded to other NHS consultants who direct their efforts into other areas within the NHS.

RT agreed that the HRA should be encouraged to become a nominating body. He also stated that he believed the Chief scientific Officer would like to see higher grade scientists treated in the same manner as NHS consultants. He hoped that mechanisms for rewarding such scientists would become clearer over the forthcoming year.

PH felt that now was a good time to look at the bigger picture including how all REC members contributions could be recognised, including lay members, some of whom have done incredible work and who deserved encouragement and recognition of that commitment and effort.

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7 http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_097007.pdf

**Agreed:** the panel encouraged the HRA to address the issue of how to appropriately recognise and acknowledge the contribution of all REC members that have given exceptional service.

### 11.3 **Guidance: Whole Genome Analysis**

NT informed the panel that he and HD were currently developing guidelines on the issue of genomic analysis which would be brought to the panel in due course. This was in response to a question raised by a REC chair on this issue.

### 11.4 **Final NREAP meeting before appointment of new NREAs**

Appointments are currently being sought for new NREAs to join the panel and this meeting was, therefore, the last with the current membership. AG thanked all of the past and present members of the panel for their contribution over the past 2 1/2 years and wished them all well for the future.

## 12. **Date of Next Meeting:**

TBC