UK Biobank Ethics and Governance Council
Ninth Meeting

Meeting at Wellcome Trust
215 Euston Road London NW1 2BE

Monday 25 September 2006 at 10.30am

Agenda

1. **New Chair introduction** (Professor Mark Walport, Director, Wellcome Trust)

2. **Apologies**

3. **Minutes** of eighth meeting held on 12 June 2006

4. **Matters arising**
(i) Public report of eighth meeting held on 12 June 2006
(ii) Tracking of requests to UK Biobank
(iii) Update on consultations
(iv) EGC Memorandum of Understanding
(v) Update on process for recruitment of members

5. **Report on meetings attended**

6. **Feedback from the International Review Panel (IRP) meeting**
(i) Overview of IRP meeting and recommendations
(ii) IRP recommendation that UK Biobank should explore opportunities for surveying opinions and attitudes of cohort members: The role of the Council in this process

7. **Update from UK Biobank** (Professor Rory Collins, Chief Executive Officer, UK Biobank)
(i) Integrated pilot report
(ii) Progress update: From pilot phase to the main study
(iii) Progress update: Access policy

8. **Access to UK Biobank**
(i) Role of the EGC in guiding UK Biobank's access policy (the need for a subgroup?)
(ii) Access to participants for social science research
(iii) The role of the EGC in commissioning or facilitating research involving the resource

9. **Role of the EGC in facilitating broader research**

10. **Complaints handling**
(i) The EGC's role in monitoring the handling of complaints by UK Biobank
(ii) The handling of complaints received by the EGC

11. **Remuneration of Council members**

12. **Any other business**

13. **Date of next meetings**

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Ninth Meeting

25 September 2006
Wellcome Trust, London

Summary of meeting

New Chair of the EGC

Professor Graeme Laurie has been appointed as Chair of the UK Biobank Ethics and Governance Council with effect from 1 September 2006. Professor Mark Walport (Director of the Wellcome Trust) introduced Professor Laurie. He is Chair of Medical Jurisprudence at the University of Edinburgh and co-director of the Arts and Humanities Research Council Research Centre for Studies in Intellectual Property and Technology Law. He was a member of the Interim Advisory Group on Ethics and Governance for UK Biobank that advised the Wellcome Trust and the Medical Research Council on the development of the Ethics and Governance Framework. He is also Chair of the Privacy Advisory Committee for Scotland, a member of the NHS Central Register Governance Board and a member of the Scottish Executive Generation Scotland Advisory Board.

Professor Walport also took the opportunity to thank the Council for its work to date.

Professor Laurie thanked Professor Walport for his introduction and for his words of support.

Matters arising

Update on consultations

A scoping study, investigating the current literature regarding publics' attitudes to UK Biobank-related issues has been commissioned. This paper will be brought to the next Council meeting.

At its last meeting the Council agreed to commission an academic paper that provides a conceptual analysis of the 'public interest' and 'public good'. A Review Panel (consisting of two EGC members and one external, independent person) is currently considering the submissions that were received in response to the Council's Request for Proposal.

The value of the paper will be in assisting Council in its decision and advisory role towards UK Biobank. The report also has the potential to contribute to a wider debate, for example in relation to defining the 'public interest' in the context of the use of personal data in medical research. A recent report from the Academy of Medical Sciences has argued that it is both ethically and legally justifiable to use anonymised data without an individual's consent if the use is in the public interest. However, there is a lack of clarity or consensus regarding how to define, and what constitutes, the public interest.

EGC Memorandum of Understanding (MoU)

The Council approved the draft MoU (7 July 2006) on the understanding that: the document is an agreement describing how UK Biobank and the EGC work together with regards to the exchange of information (but does not supersede the Council's Terms of Reference nor the ability of the Council to report publicly on the broader issue of (non)conformity with the EGF); further consideration should be given to the need for, and possible form of, a dispute resolution process; further consideration should be given to articulating the operational relationship between UK Biobank and the EGC.

Action: The EGC Chair will contact the Chair of the Board of Directors regarding the Council's discussion. The EGC Chair will move to sign the MoU.

Update on the process for recruitment of members

Interviews for new EGC members will be taking place on the 16 and 17 November 2006. The Appointments Panel will consist of Dr Michael Wilks (Chair of Medical Ethics, British Medical Association), Dr Anthony Tomei (Director, Nuffield Foundation), Professor Martin Bobrow (Governor, Wellcome Trust) and Professor Genevra Richardson (Medical Research Council member).

Feedback from the International Review Panel (IRP) meeting

Overview of IRP meeting and recommendations

The Wellcome Trust and the Medical Research Council ('the Funders') recently convened an International Review Panel to assess the UK Biobank main study protocol (from both a scientific and ethical perspective). The Panel reviewed the main study protocol in terms of the outcomes of the pilot phase and the proposed main study budget. The Panel unanimously agreeing to endorse the protocol of UK Biobank and recommended to the Funders that full-scale recruitment of the cohort is launched. Agreement was based upon further consideration of a number of points. Dr Alan Doyle presented the main points to the Council:

- The overall value of UK Biobank would be enhanced by the collection of more detailed exposure data within one or more of the cohort subsets.

  (The main study protocol includes a proposal for more detailed phenotyping of a subsection of the cohort, although this is an additional element to the project and is not included in the current budget.)

- There should be further consultation on the core questionnaire and physical measures to gain additional expert opinion on the final study design.

  (UK Biobank is checking the final design of the project against further expert opinion (including the questionnaire design)).

- The Panel stressed the need to increase the response rate during recruitment, impacting on the potential cost-effectiveness and generalisability of the study.

- Heterogeneity of the study population must be monitored and if necessary, the recruitment strategy altered to achieve an improved balance of participants.
- There should be efforts to establish linkage to local sources of biopsy or any other relevant diagnostic or clinical information from participants.
- The scientific rationale for UK Biobank should include explanations about how the study may lead to identification of important causes of diseases, potentially leading to better prevention and treatment.
- There is the potential for UK Biobank to provide international leadership, acting as a model for other national studies. It has the capacity to contribute substantially to international collaborations.

  (UK Biobank is now a member of the Public Population Project in Genomics; the not-for-profit international consortium which aims to promote collaboration between researchers in the field of population genomics.)
- There is an urgent need to define the procedures and mechanisms for access to the resource and dissemination of data. Consideration must be given to the early productive use of cross-sectional data.
- The interrelationship between the component parts of the Ethics and Governance Framework must be well defined.
- UK Biobank should take the opportunity to survey opinions and attitudes of cohort members towards research as a result of participation.

  (Dr Doyle endorsed this recommendation stating that UK Biobank presents an opportunity to conduct social science research to ascertain the publics' attitudes to UK Biobank related issues.)

Council members highlighted two trends present in the reviewers' comments:

- reviewers noted that the ability of the cohort to provide data for subsets of the UK population, such as those from ethnic minority groups, has not been sufficiently demonstrated. Questions were therefore raised as to the generalisability of the cohort to minority groups.
- several individual reviewers and the IRP itself clearly indicated that the details of the Intellectual Property and Access Policy should be developed as a priority.

Action: The Council will continue to review UK Biobank's progress in relation to these matters.

IRP recommendation that UK Biobank should explore opportunities for surveying opinions and attitudes of cohort members: The role of the Council in this process

Professor Collins was asked to comment on UK Biobank's plans to address the IRP recommendation that UK Biobank should explore opportunities for surveying opinions and attitudes of cohort members. He was also asked whether UK Biobank has the financial resources to fund a robust social science research study. (The Council recognises that there is an opportunity to conduct a social science research

study which could inform a wider enquiry, investigating, for example, not only attitudes of cohort members but also reasons for non-participation.) Professor Collins commented that this would depend upon the recruitment process and whether UK Biobank is able to keep within budget for this phase. He commented that UK Biobank would be enthusiastic to collaborate with the EGC. The Council reflected on the fact that there is a need to differentiate between the roles of the EGC and UK Biobank with regards to conducting this kind of research.

UK Biobank is in the process of recruiting a communications person who will:

- provide information to the public about UK Biobank (e.g. raising awareness of the project within certain areas before individuals are invited to participate).
- seek to ascertain various stakeholder's views regarding UK Biobank. (This may include reviewing information from non-participants concerning their reasons for not participating in the project and reviewing the outcomes of the post-visit questionnaire.)
- be involved in monitoring the profile of those individuals who do, and do not, agree to participate in the study (e.g. in terms of socio-economic group, ethnicity etc) and will consider ways in which response rates may be influenced by targeted communications.

Update from UK Biobank (Professor Rory Collins, Chief Executive Officer, UK Biobank)

Professor Collins addressed a number of the issues raised by the International Review Panel (IRP).

Enhancing the phenotyping data

Two possible, complementary approaches may be adopted to enhance the phenotyping data available to the project. First, additional measure may be incorporated into the baseline assessment of between 100, 000 - 200, 000 participants to produce an intensively phenotyped sub-cohort. Adding an extra 10-15 minutes on to the assessment centre visit equates to an few extra million pounds for the study in staff costs. UK Biobank will consider the extent of extra phenotyping at baseline to be undertaken once recruitment has begun (taking into consideration budgetary limitation).

UK Biobank is conducting an international consultation on both the questionnaire and the physical measurements to be taken as part of the project (as standard at baseline and as proposed for further phenotyping). Through this consultation, advice is being sought regarding the additional measures that should be performed on the sub-cohort.

Secondly, in addition to the proposed extra measure occurring at baseline, phenotyping of the cohort as a whole may be enhanced through calibration against a random sample of 10, 000 or 20, 000 participants undergoing repeat assessment of

more precise measurements at some point in the future. This method would complement that of increased phenotyping of a sub-cohort at baseline.

Heterogeneity of the study population

The IRP recommended that UK Biobank should seek to monitor the heterogeneity of the study population and if necessary, alter the recruitment strategy to achieve an improved balance of participants. Professor Collins commented that, in the event that targeted recruitment is required, UK Biobank will be able to locate the assessment centres strategically in areas populated by under-recruited groups and direct the communications accordingly.

Response rate during recruitment

Some reviewers suggested that the recruitment response rate of around 10%, achieved during the integrated pilot, was disappointing. Professor Collins commented that this rate reflects the realities of recent studies. UK Biobank aims to increase the rate through awareness raising, by locating the assessment centres in convenient locations and by extending the assessment centre opening times.

Integrated pilot report

Referring to a report of the integrated pilot phase, Professor Collins highlighted a number of outcomes relating to the participants' experience of the invitation and assessment centre process:

- Very few of the 60,000 people approached had any issues with their contact details being used to invite them or with the inclusion of provisional appointments (as used routinely by NHS screening services). Moreover, after receiving further information (from UK Biobank call centre staff), the majority of those few who did raise such concerns then went on to attend the assessment centre.

  The Participant Information Leaflet has been revised to express more clearly the method of identification.

- The invitation letter has been altered to apologise in advance if the invitation has been received during difficult circumstances (e.g. if the participant is unwell).

- The post-visit survey indicated that the participants' understanding of the information leaflets was good and that the consent procedures used during the pilot worked well and, generally, there were high levels of comprehension about what taking part involves both during and after the assessment visit.

Professor Collins also highlighted a few findings in relation to the assessment centre process:

- The space available at the assessment centre was too cramped. In particular, more space was required to allow for reception and waiting areas between stations, to improve privacy (in particular for the touch-screen questionnaire and interview), and to include dedicated urine collection facilities.

- Thirteen staff are required to be on duty throughout each centre's opening hours to cover all of the visit stations, but the pilot found that high participant throughput was more readily achieved if an additional senior member of staff was present to ensure participants move smoothly through the visit, to direct staff to address short-term bottlenecks, and to conduct any of the stations when required during busy periods. Consequently, this 13+1 staffing level is planned for each assessment centre during the main phase of recruitment.

Progress update: From pilot phase to the main study

The main protocol for UK Biobank had been submitted to the North West MREC for review in October 2006.

During the pilot phase, the method of centralised identification and invitation was trialled, with contact details sought from four Primary Care Trusts (PCTs) surrounding the assessment centre in Altrincham. This method was allowed by the Department of Health on the understanding that UK Biobank had to demonstrate the effectiveness of the proposed approach to invitation and to assess the potential participants' reaction to a pre-booked appointment.

Access through the PCTs was variable (with two of the four PCTs having provided no data by the end of the pilot: i.e. within 4-6 months of the request being made). UK Biobank concluded that, in order to achieve the necessary high throughput during the main study (to remain within budget) the process should be streamlined by using just a few national points of access to contact details. As Professor Collins noted above, the results of the integrated pilot indicated that very few of the 60,000 people approached had any issues with their contact details being used to invite them or with the inclusion of provisional appointments.

These outcomes suggest the effectiveness, and acceptability, of the proposed method of identification and invitation. UK Biobank has been in discussions with the Department of Health regarding release of contact details for potential participants from a few central NHS sources for the main study. It is currently unclear whether the required information (e.g. name, title, address, sex, date of birth, NHS number and GP details) constitutes confidential patient information under Section 60 of the Health and Social Care Act 2001. UK Biobank is meeting with representatives of the Patient Information Advisory Group (PIAG) to discuss this matter shortly. The position in respect of the Scottish RCC is different and UK Biobank has had discussions with NHS Scotland in this regard.

The first main study assessment centre is due to open in Manchester in February 2007. (This date will depend on the outcome of the MREC submission and the discussions with PIAG.)

Discussion

A Council member commented that the Participant Information Leaflet seems to focus on obtaining future, rather than past, health information from participants'

medical records. Professor Collins clarified that UK Biobank will pursue retrospective health information insofar as this information is available in electronic format from the participants' medical records.

English may not be the first language of some potential participant. It was noted that the participant materials could be translated into any language necessary. UK Biobank is currently considering, however, whether it would be sufficient to translate the summary information material provided in the assessment centre and the consent form (since these relate to understanding what taking part involves), but not the questionnaire (which is more straightforward). A more difficult issue in terms of management arises if an individual has questions during their assessment centre visit that require the services of a translator. One option being considered is to recruit assessment centre staff who have the language skills present in the local community.

The requirements for conducting the recruitments in Wales will influence the strategy UK Biobank ought to adopt for other ethnic groups. Professor Collins informed the Council that the summary consent information and consent form used in the assessment centre would be translated into Welsh. In addition, Welsh-speaking staff are to be recruited. He agreed that there should be consistency in the approach across ethnic groups.

The Council asked Professor Collins if there had been any cases of incidental findings during the pilot phase and whether records of such findings have been (and for the main study, will be) kept. Professor Collins had received no reports on this matter from the Chief Scientific Officer. He commented that the report card, which is used to feedback baseline measurements taken at enrolment, has been modified to make the card more informative by reporting values against population ranges which reflect the individual's gender, height, age etc (as appropriate).

UK Biobank has received a request from the British Heart Foundation (BHF) for a BHF nurse to be placed in the assessment centres in order to provide information to participants. The Council endorsed this proposal providing that consultation with the nurse is not utilised as an incentive to participate and is an option for potential participants which is entirely separate from the recruitment process.

The Council re-iterated that it would be in UK Biobank's interest to develop the following Standard Operating Procedures (SOP) (with advice from the Council) before the assessment centres become operational. Professor Collins agreed that this would be done.

- SOP describing how an individual's capacity will be assessed
- SOP describing how incidental findings at the enrolment visit will be managed

During the Council's June 2006 meeting it was suggested that the Participant Information Leaflet should make reference to the values enshrined in the Human Rights Act 1998. It was agreed that UK Biobank should be described as a resource for the 'public good' (rather than a 'public resource', given that UK Biobank is a private resource, owned by a private company, to be used charitably for public benefit). The Council agreed that the section should state that UK Biobank will

respect participants' human rights (without specific mention of the Human Rights Act).

UK Biobank was advised to seek formal legal review of the main study participant materials (through either an in-house or external party).

Progress update: Access policy

UK Biobank will revise the Intellectual Property and Access Policy (IP and A Policy) in time for the Council's next meeting and prior to the February 2007 assessment centre launch.

UK Biobank is currently placing a greater emphasis on access, in the revised policy. The Council highlighted, however, that IP issues, including the potential for commercialisation of research results, continue to be an area of contention for many of UK Biobank's stakeholders and as such the project team should not lose sight of this aspect of the policy.

Access to UK Biobank

A number of initiatives are being undertaken by the Wellcome Trust and the Medical Research Council ('the Funders') investigating 'best practice' with respect to the management of population-based collections of data and materials. Guidelines are being developed with an aim of describing aspects of governance and access broadly. This work is being undertaken in order to promote consistency and mutuality of the projects funded by the respective bodies. The Funders also aim to bring together the interest of research (funding) organisations more broadly and promote the long term sustainability of population-based collections through national strategies and policies (e.g. through discussions with the UK Clinical Research Collaboration and the Economic and Social Research Council).

The Funders commissioned Dr Bill Lowrance to review various issues surrounding research access to population-based collections of data and materials in the UK. His final report, 'Access to collections of data and materials for health research', has informed the development of the guidelines for the governance of population-based collections.

The Funders anticipate that in the short term a set of high level principles and policies will be developed. In turn these principles and policies may be developed for use in certain types of collections and then developed more specifically for individual collections.

A number of initiatives are also being undertaken in the international arena. The Organisation for Economic Co-operation and Development is leading a work programme that aims to develop guidelines for the management of Human Genetic Research Databases (HGRDs). The programme will cover the management of HGRDs broadly whilst having a particular focus on access issues. The programme will reflect on UK Biobank's policies.

The Council asked how these initiatives will impact on UK Biobank. The Funders responded that UK Biobank is being established in a way that aims to demonstrate best practice and is consistent with the guidelines being developed. The experience of UK Biobank has informed the Funders' ideas of the principles of governance and access which are now being developed more broadly for other collections. Further, UK Biobank can be seen as setting the tone internationally, for example, through involvement in initiatives like the Public Population Project on Genomics.

Role of the EGC in guiding UK Biobank's access policy (the need for a subgroup?)

Recognising that access to the resource represents a major area of its future work and that UK Biobank and the EGC have distinct responsibilities with regards to the IP and A Policy, the Council agreed to establish an EGC subgroup to work in detail on issues surrounding applications for access to the resource.

Action: The role and constitution of the subgroup will be discussed at the next Council meeting with the new members.

The Council agreed that its role was to advise and monitor UK Biobank in relation to the IP and A Policy (rather than guiding or scrutinising UK Biobank's activities). It should be clear to the public and participants who is responsible for the management of access to the resource.

Access to participants for social science research

UK Biobank may receive applications for access to the resource for both science and social science research. Both types of research may require access to participants. In developing the project the Funders were concerned that participants should not be subjected to high frequencies of re-contact.

In the cases where access to participants has been requested, the EGC will review the application in advance of the Board of Directors making a decision on whether or not to approve access (as described in the IP and A Policy, 11 January 2005). The EGC will advise UK Biobank on such applications and will monitor the frequency of re-contact with participants. This monitoring role was seen as a key feature of the long-term management of the resource. (The Council was established within a research ethics committee (REC) system whereby protocols are initially reviewed by RECs, but not consistently monitored during the course of the research project. The role of the Council is complementary to this system but distinct in its own terms.)

The Funders had envisaged that the resource would be used for a range of research, including for example health-service research and social science research. In providing advice the Council will be guided by the purpose of UK Biobank and the scope of the participants' consent. The current participant materials seek consent to participate in a 'medical research project'. The Council was concerned that this description does not adequately describe the breadth of research that might be conducted and as such may give a false impression to participants about the scope of their participation (and the possible reasons for re-contact).

The Council agreed to advise UK Biobank that, if broader research use is envisaged, the materials (including the invitation, participant materials and consent form) should be reworded from the current formulation of 'medical research' to, for example, the broader term 'health-related research' (reflecting the language in the Ethics and Governance Framework).

Action: The Funders will contact UK Biobank and inform them of the Council's advice to re-word the materials.

A distinction was made between UK Biobank's responsibility to monitor the research conducted using the resource and the Council's responsibility to monitor the 'higher-level' issues surrounding the use of the resource, including issues regarding 'mission creep'.

In developing its role in relation to access applications, the Council will need to establish appropriate methods of working (both internally and with external parties). These processes should be elucidated in the IP and A Policy. The Council noted that its advice on applications for access to the resource will be better informed if the publics' attitudes to the resource have been explored. In addition, if consent is sought for 'health-related research' the Council should reflect on, and be robust in its understanding of, this phrase.

Role of the EGC in facilitating broader research

Members were invited to put forward work themes that the EGC might investigate as part of its future work programme (including proposals for consultations or commissions to support the programme). The need for public attitude surveys, and increased public engagement activities, was highlighted.

Three specific proposals were put forward;

- a paper that reflects on the nature and role of an advisory body
- a paper investigating the commercial potential for the uses of UK Biobank and publics' perceptions in relation to possible commercial exploitation of research conducted on the resource
- a research project involving focus group work with faith groups exploring their attitudes to UK Biobank.

The Council will return to this topic at the next meeting, where the discussion will be informed by the scoping study which will report on the current literature regarding the public's attitude to UK Biobank related issues.

The situation may arise where a member of the EGC offers a commission idea to the Council when they themselves, or their department, are in a position to submit a proposal to undertake the work. It was agreed that it would be acceptable for the Council to consider proposals from members providing that they are judged as part of a competitive, transparent tendering process.

Action: A paper describing the process of procuring consultancy services will be developed by the Secretary.

Complaints handling

The EGC's role in monitoring the handling of complaints by UK Biobank

The Council noted that UK Biobank does not currently have a Standard Operating Procedure (SOP) for the handling of complaints. The Council recommended that UK Biobank should develop this SOP. There should be scope for escalation within the SOP (i.e. if an individual is not satisfied with the way in which their complaint has been handled there should be recourse to a senior member of staff). There should also be scope for review within the SOP. It should also identify how UK Biobank will ensure consistency in how complaints are handled. The Council would want to have sight of this SOP once developed.

The Council has a role to play in reviewing UK Biobank's handling of complaints and enquiries to ensure that an appropriate and effective process is in place, and to monitor the pattern of, and reasons for, complaint. While the details of the frequency and level of reporting of complaints will need to be agreed with UK Biobank, biannual reporting from UK Biobank was endorsed by the Council as an adequate and appropriate frequency. The Council has not been established as a formal ombudsman (i.e. with a role in investigating complaints or acting as a mediator between parties).

The handling of complaints received by the EGC

The Council will handle complaints received regarding its own activities. Where the Council receives a complaint about UK Biobank this will be referred, with the complainant's permission, to UK Biobank. In both cases, if the complainant is not satisfied with the response, they may be referred to the Funders.

Remuneration of Council members

The Modus Operandi (MO) of the EGC states that a time commitment of no more than 1 day per month is anticipated for members. Within this allocation, members are expected to attend approximately 4 Council meetings per year. A meeting attendance allowance (£200 per diem) is payable to all members (other than the Chair and Vice Chairs).

It is envisaged that the future working of the EGC will require the establishment of subgroups. These subgroups will convene between full Council meetings and focus on specific elements of the Council's remit (e.g. a subgroup dealing with issues relating to access to the resource). It was agreed that additional payment for subgroup working would be appropriate if the time dedicated to such activities was in excess of the expected 12 days per year work commitment.

Action: The Secretary will investigate, with the Funders, the possibility of payment for meetings of formal EGC subgroups to be treated in the same way as attendance at a full Council meeting.

The EGC Modus Operandi MO will be revised in order to reflect and clarify any changes that are made to the payment policy.

Date of next meetings

4 December 2006 - London (tbc)

Appendix A

Present: Professor Graeme Laurie (Chair), Ms Clara Mackay, Ms Sally Smith QC, Professor Chris Wild, Professor Roger Higgs, Professor Ian Hughes, Professor Sandy Thomas (morning only), Ms Andrea Cook and Ms Jayam Dalal.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Dr Caroline Stone, Medical Research Council for the whole meeting. Dr Alan Doyle for the whole meeting and Ms Tara Camm for item 8 only, Wellcome Trust. Professor Mark Walport for item 1 only, Wellcome Trust.

Speakers: Professor Rory Collins (Chief Executive and Principal Investigator, UK Biobank) for agenda items 6 and 7 only.