

UK Biobank Ethics and Governance Council Eighteenth Meeting

Meeting at Wellcome Trust
215 Euston Road, London, NW1 2BE

Monday 16 March 2009 at 10.30am

Agenda

1. **Introductions**
2. **Apologies**
3. **Minutes** of seventeenth meeting held on 8 December 2008
4. **Matters arising**
 - (i) Summary of decisions and recommendations from seventeenth meeting held on 8 December 2008
 - (ii) Tracking of requests to UK Biobank
 - (iii) Paper 'Advising on the public interest and the public good'
 - (iv) Information Security subgroup
 - (v) Access and IP subgroup
 - (vi) Communications subgroup
 - (vii) Outcomes of the EGC review
5. **Proposal for enhanced phenotyping of participants** (closed discussion)
6. **Proposal for enhanced phenotyping of participants: MRI and feedback** (Professor Paul Griffiths and Dr Nigel Hoggard, University of Sheffield)
7. **Proposal for enhanced phenotyping of participants** (Professor Rory Collins, Chief Executive Officer, UK Biobank)
8. **Update from UK Biobank** (Professor Rory Collins, Chief Executive Officer, UK Biobank)
 - (i) General update from UK Biobank
 - (ii) Update regarding recommendations from EGC17
 - (iii) Update: Development of UK Biobank's access and intellectual property procedures
 - (iv) Biannual report on longitudinal follow-up of participants
9. **Proposal for enhanced phenotyping of participants** (closed discussion)
10. **Communications activities**
 - (i) External speaking opportunities
 - (ii) External enquiries to the EGC
 - (iii) Public meeting feedback
 - (iv) New member required for the EGC communications subgroup
11. **Report on meetings attended**
 - (i) National Cancer Research Institute workshop 07/01/09
12. **Any other business**
13. **Date of next meetings**
14. **Dates for 2010**

**UK Biobank Ethics and Governance Council
Eighteenth Meeting**

**16 March 2009
Wellcome Trust, London**

Present: Professor Graeme Laurie (Chair), Professor Ian Hughes, Ms Andrea Cook, Dr Heather Widdows, Professor Erica Haimes, Dr Roger Moore, Professor Roger Higgs, Professor Martin Richards, Mrs Margaret Shotter, Ms Tracey Phillips, Dr Jonathan Hewitt and Mr Andrew Russell.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Ms Katherine Littler (Wellcome Trust) for the whole day. Dr Catherine Elliott for the morning only and Dr Catherine Moody for the afternoon only (Medical Research Council).

Speakers: Professor Rory Collins (Principal Investigator and Chief Executive, UK Biobank) and Mr Jonathan Sellors (Company Secretary, UK Biobank) for items 6, 7 and 8 only. Professor Paul Griffiths and Dr Nigel Hoggard, University of Sheffield, for item 6 only.

1. Introductions

The Chair welcomed new member Dr Jonathan Hewitt, a Consultant Geriatrician at Portsmouth NHS Trust.

2. Apologies

Apologies were received from Professor Paolo Vineis.

3. Minutes of the last meeting held on 8 December 2008

The Council approved the circulated minutes.

4. Matters arising

Summary of decisions and recommendations from seventeenth meeting held on 8 December 2008

The Council approved the circulated summary of decisions and recommendations.

Tracking of requests to UK Biobank

The Council noted the requests for further information, the majority of which will be addressed by UK Biobank under agenda items 7 and 8. The request for additional information to be included in UK Biobank's biannual report on enquiries and complaints will be addressed in the next report.

EGC paper: 'Advising on the public interest and the public good'

The paper 'Advising on the public interest and the public good' has been revised in light of members' comments. Members approved the document with two minor changes.

ACTION: The paper will be revised and published on the Council's website. [AH]

Information Security subgroup

Two meetings of the new Information Security subgroup have taken place since the Council's last meeting. At its first meeting the subgroup discussed its remit and work programme and agreed to produce a lay person's guide to UK Biobank's data security measures. The subgroup's second meeting took place at the UK Biobank co-ordinating centre in Cheadle and involved UK Biobank representatives Dr Tim Sprosen, Mr Andy Harris and Mr Charles McCulloch. Mr Harris explained the processes of data management and provided an update on the project's progress in relation to ISO 27001 accreditation. The subgroup found the meeting to be very encouraging while also agreeing on a number of areas that require further clarification from UK Biobank (including the nature of its relationship with the Clinical Trial Service Unit). These aspects are currently being followed-up with UK Biobank.

Access and IP subgroup

The Access and IP (AIP) subgroup met with Mr Jonathan Sellors in January to discuss the development of the AIP procedures. It was agreed that the subgroup and Mr Sellors should aim to meet on a regular basis (e.g. every two months) and that it would be advantageous to concentrate on specific issues. To this end a further meeting is planned for late March at which the issue of reverse identifiability of participants will be discussed.

Members of the subgroup consider the task of writing the AIP procedures to be a considerable challenge because it is both complicated and sensitive. Mr Sellors' paper (submitted under item 8 (iii)) describes that UK Biobank intends to prepare the draft procedures by December 2009 with a view to finalising the materials by the end of recruitment (Summer 2010). Subgroup members expressed the view that ideally the materials should be available to participants sooner, not least because UK Biobank's model of 'broad consent' is only legitimate in the wider framework of the trust model and part of the trust model relates to how AIP is managed.

The question of timing was raised with Mr Sellors subsequent to the January meeting along with the offer of further support from the EGC. Mr Sellors remained confident that the timetable is reasonable and achievable. While encouraged by the

ongoing dialogue with UK Biobank, members expressed some concern over a degree of slippage from the previously advised timetable for drafting procedures and noted that it may take more time than currently anticipated. Members agreed that UK Biobank might benefit from additional resources (for example, hiring an expert consultant to provide input from an ethics and social science perspective to expedite the research and drafting process). The Council considered that it may wish to communicate its observations regarding the timetable to the Board of Directors but agreed to await the outcomes of UK Biobank's update under item 8 and of the AIP subgroup meeting with Mr Sellors in March.

The Council previously compiled a list of questions that it recommends UK Biobank address during the development of its AIP procedures. Members agreed that the document should be posted on the EGC website as an indication of its thinking in relation to the key elements of the procedures. The document might also be of use to other biobanks that are in the process of developing their procedures.

ACTION: The list of questions will be posted on the EGC website. [AH]

Communications subgroup

The Communications subgroup met recently and discussed the possibility of attending the Manchester Science Festival and the methods of engagement that might be employed. The subgroup agreed that the Festival would ideally involve UK Biobank showcasing the science of the project with input from the EGC. The Secretary has provisionally discussed this with Mr Andrew Trehearne, UK Biobank's Head of Communications, and is currently awaiting his response as to whether or not UK Biobank would be interested in such an initiative.

The subgroup also discussed the Council's public meetings and agreed that they should take place in locations where UK Biobank is actively recruiting. Given this, the subgroup agreed that the September 2009 public meeting should take place in Liverpool (where recruitment begins in Spring 2009 and is expected to continue through to 2010).

Outcomes of the EGC review

An EGC workplan for 2009-2010 has been developed in response to the Council's recent review by the Wellcome Trust and Medical Research Council. The workplan includes a proposal for a workshop on the pros and cons of seeking to achieve participant representation in biobanking activities. Members discussed the proposal and agreed that it should be developed further.

ACTION: The proposal will be developed and presented to the Council at its next meeting. [AH]

5. Proposal for enhanced phenotyping of participants (closed discussion)

UK Biobank's enhancement proposal will be considered at an expert peer review meeting convened by the funders on 11 May 2009. The proposal was recently

discussed at the UK Biobank Board of Directors meeting, at which the EGC Chair was present. He reported that UK Biobank has received legal advice which suggests that in certain circumstances a legal duty of care will likely require feedback to participants of serious incidental findings resulting from MR imaging.

The Council discussed and agreed on the key aspects to be raised with UK Biobank under item 7.

A member requested a revision to the internal minute of the Council's previous discussion of the enhancements proposal.

ACTION: The internal minute will be revised. [AH]

6. Proposal for enhanced phenotyping of participants: MRI and feedback (Professor Paul Griffiths and Dr Nigel Hoggard, University of Sheffield)

The Chair welcomed two guest speakers, expert radiologists Professor Paul Griffiths and Dr Nigel Hoggard. Professor Griffiths and Dr Hoggard work in an Academic Unit of Radiology that is based in a Teaching Hospital environment in Sheffield. Their Unit undertakes a combination of 'blue sky' and clinically-based research with a large number of clinical and non-clinical collaborators. The majority of the research involves brain magnetic resonance (MR) imaging. Professor Griffiths and Dr Hoggard were invited to the meeting to give an independent, expert view on the issue of providing feedback of incidental findings resulting from imaging research.

Professor Griffiths presented the findings of a paper which he and his colleagues had recently published in the *Journal of Medical Ethics*¹. The paper reports that of 525 different individuals scanned as normal volunteers, 46 had definite significant abnormalities (8.8%) with the percentage risk of an incidental finding increasing with age. Within their Unit it is current practice to inform the research participant of the finding, to counsel them and to inform their primary care physician about the finding.

The paper concludes that it is advisable for researchers utilising MR imaging of the brain to have access to trained neuroradiologists, a protocol should be in place to deal with incidental findings and consent should be obtained in a way that allows the participant to understand the possibility and implications of an abnormal finding (not only for the health of the individual but also financially, with implications for driving licences, insurance eligibility and borrowing).

Dr Hoggard presented responses to a number of questions put to Professor Griffiths and himself ahead of the meeting:

- Do you know of any research projects which involve MRI and are comparable to UK Biobank in terms of scale and the prospective nature of the study?

¹ N Hoggard, G Darwent, D Capener, I D Wilkinson and P D Griffiths 'The high incidence and bioethics of findings on magnetic resonance brain imaging of normal volunteers for neuroscience research' *Journal of Medical Ethics*. 2009 35:194-199

Dr Hoggard commented that they do not know of any comparable projects and that UK Biobank appears to them to be by far the largest.

- Are you able to quote any values for the frequency with which false positive and false negative incidental findings are made during research involving MRI of brain, heart and whole body? For each figure could you indicate how many studies these figures are based on and any other information that you consider relevant when considering the implications of these figures for UK Biobank's proposal (e.g. the age range of the study participants if the likelihood of making an incidental finding increases with the participants' age).

Dr Hoggard reported that equivocal findings do arise and some participants require further investigation but because of the conservative approach used by the team this uncertainty is communicated to the participant. Features which could represent serious pathology but on further investigation prove not to be so have arisen in a hand full of cases, giving a prevalence rate of less than 1% of all healthy volunteer participants. They have not had a case where a participant has been told that they have a particular pathology and then further testing has shown this not to be the case. They do not know what the false negative rate is but most groups report very similar rates of pathology. Of 151 retrospective studies of adults incidental findings requiring referral occurred in 6.6% of subjects.

- Is there a standard practice within the field of research involving MRI for whether or not, and in what circumstances, feedback should be provided (in relation to incidental findings)? Are there standard protocols within the field for how this information is fed-back and to whom (participant and/or GP)?

Standard practice has not yet emerged in this area although a consensus is emerging. In 2005 there was a meeting of Institutes of the National Institutes of Health (the National Institute on Neurologic Disorders and Stroke, the National Institute on Drug Abuse, the National Institute on Biomedical Imaging and Bioengineering, the National Institute on Aging, and the National Institute on Mental Health) and Stanford University held a workshop that focused on five areas:

- (1) detection of incidental findings
- (2) Institutional Review Board/Research Ethics Committee involvement
- (3) communicating with subjects
- (4) research protocols, the scanning environment, and training of personnel
- (5) subject selection

Dr Hoggard's Unit takes GP details at the time consent is sought and the participant is informed that their GP will be contacted in the event that there is a serious finding. Every potential participant needs to agree to feedback to their GP before they can be enrolled in a study. Dr Hoggard's Unit has adopted a policy of informing a participant's GP because this allows further discussion and access to required services. However, feedback to an individual's GP is not an essential part of the emerging consensus. One key aspect of the emerging consensus is that MR brain scans of healthy volunteers for neuroscience research should be reviewed and that review has to be by an expert clinical opinion.

- For research studies which are undertaken outside a clinical setting and where none of the researchers has clinical experience in the interpretation of scans, what might be the most appropriate process for checking that an incidental finding really warrants more investigation as a serious and potentially treatable condition?

In the view of Dr Hoggard and his colleagues, an MRI brain scan requires review by an experienced consultant neuroradiologist and other MRI scans are likely to require an equivalent level of skill. The better and more experienced the reviewer, hopefully the fewer false positives will be found and the more informed the decision of whether recall is in the best interest of the participant. Dr Hoggard recommended the use of protocols which could describe, amongst other things, which diagnoses need further investigation or treatment. Such protocols might promote consistency, in particular if images are evaluated by a group of expert reviewers (which might be a reasonable approach for UK Biobank given the scale of the proposed operation).

- In what circumstances, if any, would it be appropriate for researchers to release the scan itself (possibly stripped of personal identifiers) to facilitate obtaining an expert clinical opinion?

Dr Hoggard described that in their view, and as their own protocol dictates, all MRI brain scans with pseudo-anonymisation of imaging data ought to be routinely reviewed by a clinical expert. Using an expert clinical reviewer in this way allows further clinical expert opinion to be introduced in the most appropriate way.

- At what point in time during this process would you suggest informing the research subject and/or their GP that there is an incidental finding?

Under their current protocol the participant is to be contacted after the review of the imaging (which is done on a weekly basis) via the Principal Investigator for disclosure of findings and counselling. The GP is then written to with details of the discussions. Dr Hoggard commented that any recall of participants for disclosure of potentially serious findings has to be prompt (1 to 2 weeks). Further, once contact has been made with the participant there should be minimal delay between contact and opportunity for disclosure and counselling (about 1 week).

- Could you comment on your understanding about the current ease or problems of access for the general public (presumably via their GP) to the enhanced procedures being considered, if the participant were to request it? (The member who asked this thinks that these procedures might be hard for every GP to obtain if the participant were to be made anxious about the tests, and there might be considerable delay and possibly unnecessary cost borne by the NHS if feedback were to be provided and if follow-up was required.)

Dr Hoggard informed the Council that GPs in the Sheffield area have direct and timely access to ultrasound of the abdomen and pelvis, electrocardiograms and echocardiography and chest Xray. GPs in the Sheffield area do not have any direct access to CT scanning of head or body or MRI of any kind. However, there are numerous variations in local practice that do give access to CT and MR imaging directly, usually under agreed protocols. Dr Hoggard also noted that the public has

access to whole body CT scanning already, for example through commercial initiatives such as “Life scan”.

In conclusion Dr Hoggard commented that incidental findings are both predictable and inevitable. In their opinion consent is not fully informed if a discussion of incidental findings is omitted from the consent process.

Discussion

Dr Hoggard and Professor Griffiths were asked to comment on the amount of extra time and work required if they make an incidental finding. In such cases participants are informed of the finding and invited back for a clinical MRI. Once the image has been reviewed the individual is then debriefed in a consultation lasting 30-40 minutes. It is expected that this process of image evaluation, re-contact and counselling would take one or two weeks. If, under an alternative model, a participant’s GP is informed and then further MRIs occur through the routine NHS procedures, there would likely be an 18 week patient pathway.

Professor Collins noted that the Journal of Medical Ethics paper suggests a cost of £30 for expert radiologist review of an MR image in a single body area. UK Biobank plans to scan 3 body areas in 100,000 people. Even with a 50% discount in costs (that may be applicable given the scale of the project) this cost would equate to nearly 5 million pounds (50% of the technical costs of carrying out the MR imaging). Professor Collins asked if it would be feasible for a radiologist to only review those images found by the radiographer to have suspect incidental findings. Professor Griffiths confirmed that the study could be set up in any number of ways but that in his opinion best practice in terms of his work in Sheffield involves all images being reviewed by a radiologist.

The Chair thanked Professor Griffiths and Dr Hoggard for their insights and their informative presentation.

7. Proposal for enhanced phenotyping of participants (Professor Rory Collins, Chief Executive Officer, UK Biobank)

Professor Collins updated the Council on UK Biobank’s current thinking in terms of feedback of incidental findings for MR imaging and reported that the recent legal advice was that there may be found to be an irreducible duty of care as between the radiographer and the participant and that, as a consequence of this, a limited feedback protocol for reporting serious and modifiable incidental findings should be developed. Professor Collins considers this to be consistent with UK Biobank’s current procedure for managing incidental findings.

UK Biobank will now move to develop a draft protocol by which scans would be reviewed and incidental findings considered serious and modifiable might then be reported to participants. The Council and Professor Collins agreed that there is a need for clarity regarding what constitutes ‘serious’ and ‘modifiable’. UK Biobank intends to seek guidance from experts as to how this should be addressed.

Subject to a positive funding decision, UK Biobank plans to investigate the practicalities of the imaging visit during the second half of 2010, including how the measures will be performed and an assessment of the participants' expectations of the re-assessment visit. A pilot of the imaging re-assessment visit is planned for 2011.

During the lunch break Professor Collins had discussed with Dr Hoggard the possibility of training the radiographers to review the scans for abnormalities which are possibly indicative of serious and modifiable conditions. The identified scans could then be passed to a radiologist for expert review (rather than all scans being reviewed by a radiologist). The Council recommended that the different models by which incidental findings might be identified could be assessed during the 2011 pilot phase (e.g. escalation of findings from a radiographer to a radiologist or routine assessment of all images by a radiologist).

Given the cost of consultant radiologists reviewing scans of the proposed 100,000 participants, a member asked if UK Biobank had considered performing less scans and providing more feedback. Professor Collins commented that the resource will be scientifically less valuable if fewer people are scanned although this may be an option that the funders or the EGC might want to consider.

At its last meeting the Council had identified five options related to the imaging enhancements which appeared in an internal minute for further consideration by Council:

1. Do not collect these data at all.
2. Collect the data but provide full clinical feedback (a position recognised to have potentially significant ethical, economic and legal liability implications).
3. Consider how different MR imaging incidental findings are from UK Biobank's current Standard Operating Procedure on managing baseline assessment incidental findings (e.g. skin discolouration suggestive of melanoma).
4. Allow participants to decide themselves whether or not to receive feedback.
5. UK Biobank's earlier proposal to provide no feedback from the MR imaging and to have an explicit consent process (a position which was being explored prior to receiving legal advice). This rests on the autonomy of consent and of the individual. While agreeing that this form of consent is necessary the Council did not consider it sufficient in the context of what was proposed.

Professor Collins and Mr Sellors confirmed that number 5 is no longer an option as a blanket rule given the recent legal advice and decision of the Board of Directors. With regards to option 1, Professor Collins re-iterated that while the MR imaging does present a number of challenges it has the potential to be an incredibly valuable source of information. The Board is enthusiastic about this potential and to the value of moving to a pilot phase. The Board would, however, consider the results of any such pilot before making a decision regarding the full-scale launch of the re-assessment visits.

Clarification was sought over the distinction between points 2 and 3. The former would involve systematic clinical feedback on all images while point 3 would involve feedback for only those images which contain a potentially serious and modifiable incidental finding. Mr Sellors commented that option 2 has been ruled out by the

Board of Directors. To provide clinical feedback routinely would be a significant change in the project leading to clear liability issues as a consequence of the creation of a clinician/patient relationship (e.g. relating to the finding of a false positive or if UK Biobank does not find an abnormality which later manifests as a disease). UK Biobank does not intend to carry out a whole set of analyses on the images; the images will instead be stored for many years for future analyses by researchers.

Options 3 and 4 remain under consideration by UK Biobank. A member suggested that there may now be a sixth category. For example, if UK Biobank intends to look systematically for certain incidental findings in the images, are these findings still incidental? The Council agreed to bear this in mind during its further deliberations.

In the coming weeks UK Biobank will prepare a draft protocol describing how feedback of incidental findings will be managed. Mr Sellors indicated that it would be useful to have the EGC comment on the protocol and the Chair confirmed that the Council would be willing to offer its advice in this regard.

The Council, Professor Collins and Mr Sellors moved on to discuss the enhancement proposal more broadly, including the enhancements to the baseline assessment visit (e.g. eye-related measures) and those that will comprise the re-assessment visit (e.g. imaging and ECG). All parties agreed on the need for a consistent policy for the full suite of proposed enhancements in terms of the way in which incidental findings will be managed and which measures will be routinely fed back to participants (e.g. as with the routine reporting of blood pressure at the end of the current baseline assessment visit).

The enhancement proposal was discussed further by the Council in closed session under agenda item 9.

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

General update from UK Biobank

Professor Collins reported that 260,000 participants have been recruited to date. The original protocol envisaged that 35 assessment centres would operate throughout the UK, each recruiting 10,000-15,000 participants. In practice some centres have successfully recruited double the anticipated numbers and it is, therefore, likely that UK Biobank will reach its target of 500,000 participants by recruiting at only 20-24 assessment centres. The centres have been grouped so that a small number of future re-assessment centres could be located close to a number of the original centres. Six areas are being planned for the proposed re-assessment enhancement visit, involving three centres which will all move once during the 5 year period.

UK Biobank tries to close and transfer its assessment centres in such a way that staff can transfer between nearby cities if they wish. For example:

- The Bury centre closed at the beginning of the year and has been re-located to Liverpool. (Despite being a very good location in terms of high population and

accessible location of the centre, the attendance rate in Liverpool has been low.)

- The Newcastle centre will close at the end of March and will transfer to Middlesbrough.
- The Reading centre will close in May and will transfer to Hounslow.
- The Leeds centre will close in July/August and will transfer to Sheffield.
- The Bristol centre will close in August and will transfer to Swansea.
- The St Bartholomew's Hospital centre will close in September/October and will transfer to East London.
- The Nottingham centre will close in October and will transfer to Birmingham.

Enhancements

UK Biobank's final proposal for extra-cost enhancements was submitted to the funders on 2 February 2009. Two modifications from previous draft versions of the proposal were noted. First, UK Biobank proposes to write to those participants recruited prior to the introduction of the baseline enhancements to ask if they would be prepared to wear an activity monitor for a number of days before returning the monitor to UK Biobank for analysis. Second, participants who are invited to the re-assessment visit, and who were initially recruited prior to the introduction of the baseline enhancements, would be asked to undergo the enhanced baseline measurements as part of the re-assessment visit.

In addition to the extra-cost enhancements, UK Biobank hopes to introduce a number of no-cost enhancements to the baseline assessment visit at the start of May 2009. The Multi-centre Research Ethics Committee has indicated that the no-cost enhancements can be considered as an amendment to the current protocol rather than as a full new protocol.

Subject to a favourable funding decision in mid-2009, UK Biobank hopes to introduce the extra-cost baseline enhancements by August 2009 (including eye-related measurements and saliva collection). In turn, the proposed extra-cost re-assessment imaging visit would be piloted in 2011 and, if subsequently funded, would continue through to the main phase from 2011- 2016.

Equality and diversity

When asked about participation of individuals from ethnic minority groups, Professor Collins informed the Council that recruitment of such groups depends to a large extent on the location of the assessment centres. Having recently recruited a Communications assistant, UK Biobank can now dedicate more time to raising awareness about the project in 'hard to reach' groups. Professor Collins re-iterated, however, that UK Biobank aims to be generalisable rather than representative of any particular population. Minority groups would need to be over-represented to a very substantial extent in order to provide scientifically meaningful numbers of individuals and it was not intended for UK Biobank to do this.

Professor Collins advised that UK Biobank has not undertaken an equality and diversity impact assessment of its recruitment process. The Council considers that such an assessment would assist UK Biobank in identifying the barriers and

enablers to participation. In turn this knowledge would help the project to focus its efforts on setting the right conditions to enable participation of as diverse a group of individuals as possible.

The Council returned to this topic in closed session later in the day and agreed to recommend that UK Biobank should undertake an equality and diversity impact assessment of its activities. It is not being recommended that UK Biobank should over-represent certain groups in order to provide scientifically meaningful numbers, but instead the Council considers it important that everyone who is invited by UK Biobank should have an equal opportunity to participate.

ACTION: A recommendation will be drafted and the Council will provide UK Biobank with contact details of people who can help with such an assessment. [TP and AC respectively]

Re-contact

The first large-scale re-contact of participants will likely be in relation to the proposed enhancements. There are a number of aspects of the re-contact procedures on which the Council considers that it might advise (including the content of the information materials). Professor Collins confirmed that the Council would have sight of such documents ahead of any future re-contact.

Update regarding recommendations from EGC17

Post-visit survey

Professor Collins assured the Council that Dr Sprosen is working on a new survey, further to the Council's previous recommendation.

'Health-related' or 'health-relevant'

At its last meeting the Council highlighted a discrepancy between the Ethics and Governance Framework and the participant materials which describe, respectively, that UK Biobank will link to participants' 'health-relevant' and 'health-related' records. Professor Collins confirmed that the Framework will be revised to be consistent with the participant materials.

Roll-out timetable

Further to the Council's recommendation at its last meeting, Professor Collins informed members that, for practical reasons, UK Biobank will not be opening an assessment centre in Northern Ireland.

Update: Development of UK Biobank's access and intellectual property procedures

Mr Sellors reported that he has sought input and advice from a number of sources including senior members of the UK Biobank Steering Committee, the National Institutes of Health and projects comparable to UK Biobank (such as the Wellcome Trust Case Control Consortium and the Avon Longitudinal Study of Parents and

Children). His objective is to be able to draw up a set of detailed procedures (and ancillary documentation such as material transfer and data transfer agreements) by the end of 2009 with a view to finalising the documents by mid-2010.

The Chair informed Mr Sellors and Professor Collins that the EGC's list of questions regarding the access and IP procedures will be posted on its website in due course.

ACTION: The Council returned to this topic in closed session later in the day and agreed that the Chair should discuss the timetable with Mr Sellors at the March Access and IP subgroup meeting. [GTL]

Biannual report on longitudinal follow-up of participants

Towards the end of 2008, UK Biobank obtained approval from the NHS Information Centre for UK-wide linkage to death and cancer registration for all UK Biobank participants. This linkage will commence around the middle of 2009.

Different approaches to follow-up will be required in each of England, Scotland and Wales to reflect their different pace of migration to electronic medical records and differences in the design of the systems being implemented. At a recent meeting of the UK Biobank Steering Committee, the plans for exemplar pilots in around 10,000 participants in Scotland and Wales were approved. In relation to the exemplar pilot in England, it was recognised that the current plans for the initial implementation of the GP Extraction Service in April 2010 would mean that the pilot in England should be deferred until this time and that UK Biobank should continue to assist Connecting for Health in defining the user requirements for the GP Extraction Service to support the needs of UK Biobank and similar research.

UK Biobank has also submitted a proposal at the request of the Connecting for Health Research Capability Programme to undertake a pilot in around 10,000 UK Biobank participants to link to the electronic dental record both retrospectively (going back at least 10 years using the legacy system developed by the Dental Services Board) and prospectively (using the new systems being developed by Connecting for Health). This pilot is expected to commence by the middle of 2009.

9. Proposal for enhanced phenotyping of participants (closed discussion)

The Council discussed UK Biobank's proposal for enhanced phenotyping of participants in light of the day's presentations and discussions.

ACTION: A recommendation will be drafted incorporating the key elements of the discussion under this and previous agenda items (see annex 1). The recommendation will be sent to members for comment before being sent to UK Biobank and to the funders. [GTL, AH]

10. Communications activities

External speaking opportunities

The Council has been invite to present its work at a workshop convened by the Tiss.EU project in June 2009.

ACTION: Members should contact the Secretary if they are interested in representing the Council at this workshop. [Members]

External enquiries to the EGC

Members discussed a letter from an attendee of the Cardiff public meeting which expresses concern over the UK Biobank project.

ACTION: A response will be drafted and sent to members for comment. [AH]

Public meeting feedback

A new format was adopted for the Cardiff meeting held on 12 February 2009. The introductory presentations were followed by small group discussions with two Council members in each group to facilitate the discussion. Nearly all attendees completed a feedback form and were positive about the event, although numbers for the event were lower than previous meetings and the attendees were predominantly from related disciplines (e.g. scientists or research ethics committee members) rather than interested members of the public.

In relation to the poor attendance, it was noted that recruitment in Cardiff ended in Summer 2008 so participants could not be invited to the meeting through the assessment centre. The Council agreed that it is important to be able to target participants directly and that future meetings should be held in cities where UK Biobank is actively recruiting. Further, in light of the new format used in Cardiff, the Council agreed to review the format of future meetings while also re-visiting the meetings' history and purpose.

ACTION: The history, purpose and format of the public meetings will be reviewed with a view to informing the nature of future events. [AH and Communications subgroup]

ACTION: The Council will carry out an equality and diversity impact assessment of its own activities, including its public meetings. [AH]

New member required for the EGC communications subgroup

It was agreed that Mr Andrew Russell will join Professor Martin Richards and Dr Roger Moore on the EGC's Communications subgroup.

11. Report on meetings attended

National Cancer Research Institute workshop 07/01/09

The Chair recently presented a paper on the work of the EGC at a workshop on the 'Ethics and Governance in Cancer Biobanking'. Mrs Margaret Shotter also attended the event.

12. Any other business

Annual Review

The EGC 2008 Annual Review will be available for distribution shortly.

Resignation

Ms Andrea Cook has resigned from the Council with effect from March 2009. The Chair thanked Ms Cook for her contribution to the Council and in particular for having Chaired the Communications subgroup over the previous four years. The Council wished Ms Cook well for the future.

13. Date of next meetings

8 June 2009	–	Council meeting (London)
7 & 8 September 2009	–	Public & Council meeting respectively (Liverpool) ²

14. Dates for 2010

15 & 16 March	-	Evening public & Council meeting respectively (tbc)
7 June	-	Council (London)
27 September	-	Council (London)
6 December	-	Council (London)

² Subsequent to this meeting the 7 September public meeting has been cancelled. The Council meeting will now take place on 7 September in London.

Annex 1

Proposed Category 3 imaging enhancements: UK Biobank's feedback policy

Introduction

This document outlines recommendations from the UK Biobank Ethics and Governance Council in light of discussions at EGC18 at which the Council was informed that UK Biobank is now likely to consider feedback of incidental findings arising from enhancement measurements and the development of suitable Standard Operating Procedures (SOPs) with respect thereto.

Three initial points should be noted:

First, the Council recommends that UK Biobank should consider how its current policy on feedback at baseline will apply to any enhancement measurements, i.e., which measurements will be routinely relayed to participants arising from any enhancement procedure (including those measures that UK Biobank proposes to add to the baseline assessment and those measures that comprise the re-assessment visit).

Secondly, the Council recommends that UK Biobank should consider how its current policy on feedback of incidental findings will apply to any enhancement measurements (including those measures that UK Biobank proposes to add to the baseline assessment and those measures comprising the re-assessment visit).³

Thirdly, irrespective of whether enhancements proceed, the Council recommends that UK Biobank revisit the terms of its current SOP on incidental findings at baseline in light of the comments below.

Recommendation on Enhancements and Incidental Findings

1. The Ethics and Governance Council (EGC) would begin by re-iterating the fundamental purpose of UK Biobank which is to create a research resource for the benefit of future generations. It is not to provide a mechanism for giving participants routine health information nor to provide them with a health check. This is made perfectly clear both in the Ethics and Governance Framework and all participant information materials.
2. The EGC considers that a number of issues, detailed below, should be tested during any pilot phase for enhancements and reserves its position on whether or not any or all enhancement data should ultimately be collected, for example, because feedback proves to be unworkable and/or because no acceptable mechanism can be developed.
3. The starting premise for this recommendation with respect to a pilot phase is to ask whether UK Biobank's existing policy on feedback of incidental findings

³ With reference to the proposed MRI this document proceeds on the understanding that measurements and any procedures involving feedback of incidental findings would involve a radiographer and a radiologist (who might have a role in verifying findings and deciding on whether feedback should be given).

at baseline can be applied to the proposed enhancements; more specifically, the EGC would expect more detail to appear in any pilot SOPs across the range of enhancements and with respect to the following details:

- a. Which criteria will be applied to determine the “seriousness” of any suspected underlying condition or finding, for example, will these be by reference to established clinical guidelines? If none exist, what will be used?
 - b. What role, if any, should “treatability” play in the determination of whether or not feedback should be given? It may be useful to consider the reasons why a participant may wish to receive feedback of information on a condition which is not treatable, for example, to allow the individual to prepare for the onset of disease emotionally, socially, financially etc.
 - c. To whom would feedback be given, for example, only to the individual or to the individual and his/her GP and/or to any other party?
 - d. Will UK Biobank make provision to allow for an individual’s “right not to know”, that is to allow a participant to refuse all feedback? Would UK Biobank allow a participant to refuse to allow feedback to be passed on to their GP while receiving it him or herself?
4. What is the overall balance of “harms”, e.g., for the individual, for GPs, for the NHS, for families etc, and how do these compare with the “benefits” of conducting the enhancements in the first place?
5. The Council strongly believes that any move to adopt enhancements and to institute SOPs for incidental findings must proceed on the basis of a sound evidence-base. This should include:
- a. Satisfactory evidence of the scientific merits of carrying out the enhancements at all;
 - b. Evidence of the full range of potential harms associated with enhancements *and* of any particular feedback policy that is adopted (see above);
 - c. Evidence of procedures and processes that can be satisfactorily adopted to reduce/minimise said harms;
 - d. Evidence of robust mechanisms to respond to incidental findings, for example, clarity of relationships between the professional making the initial observation of potential incidental findings and the appropriate clinical specialist, clarity and acceptability of criteria for escalation within this relationship, clarity and acceptability of circumstances and format in which information will be given to an individual (and his/her GP or other party, if relevant), clarity and acceptability of the timescales involved with respect to the above;
 - e. Evidence of robust information materials. Given that this will be the first experience of re-contact for many participants the information materials will need to clearly address issues such as why a particular individual has been chosen, what the new involvement may entail and what they are consenting to and clarity about such issues as the implications (or

lack of them) that declining a re-assessment may have on their continued engagement with UK Biobank.

The materials might also address the possibility that incidental findings may be made (1) at the point at which the data are collected or (2) later, as a result of researchers analysing the images. The materials might indicate that the implications of any incidental finding may be uncertain (and for whom). In order to illustrate the likelihood and relevance of making an incidental finding in case (2), the materials could usefully include an indication of how the new data are likely to be used (e.g. that data will not be systematically analysed at the point of collection but will be used on a case-control basis) and the implications of this type of use (e.g. that analysis of the measurements or images will only occur many years after collection, that any incidental finding made at this stage will likely be less relevant to an individual than if the analysis had been performed at the point of collection and that any such analysis will relate only to a proportion of the whole population).

- f. Evidence that there will be appropriate training of the professionals involved in the measurement and feedback processes, including potential issues of counselling individuals receiving feedback;
 - g. The pilot should include *both* quantitative and qualitative evidence, for example, quantitative figures about the levels of incidental findings, false positives etc, as well as qualitative findings about the experiences of professionals and participants in any feedback procedures. On this last point, the Council recommends that the input of a sociologist should be sought.
6. Finally, and with respect to the design of the pilot, the Council recommends that UK Biobank be prepared to consider the full range of issues related to participation in enhancement, for example, the contents of an invitation letter, the likely impact or expectations of receiving such a letter, and the management of participants' expectations more generally. Furthermore, the pilot might be used to test differing approaches to feedback, for example, comparing (a) always involving an appropriate clinical specialist (e.g. a radiologist for MRIs), as opposed to (b) training the professional making the initial observation of potential incidental findings to escalate cases of concern to a clinical specialist (e.g. in the case of MRI the radiographers escalating cases of concern to a radiologist).