UK Biobank Ethics and Governance Council
Fortieth Meeting

Meeting at Macdonald Manchester
London Road, Manchester, M1 2PG

Tuesday 9 September 2014 at 9.30am

Agenda

1. **Apologies**

2. **Minutes** of thirty-ninth meeting held on 2 June 2014

3. **Matters arising**
(i) Tracking of requests to UK Biobank
(ii) Subgroup reporting: Feedback
(iii) Subgroup reporting: EGC access oversight role
(iv) Re-contact applications

4. **Closed discussion on topics to discuss under item 5**

5. **Update from UK Biobank** (Professor Rory Collins, Chief Executive Officer)
(i) Report on applications
(ii) Review of the access process
(iii) Receiving and incorporating research results into the resource
(iv) Imaging pilot
(v) EGF revisions
(vi) Any other developments and outstanding recommendations from EGC39

6. **Closed discussion of matters arising under item 5**

7. **Funders' review of the EGC**

8. **EGC subgroups**

9. **Communications activities**

10. **Report on meetings attended**
(i) UK Biobank Frontier meeting 26/06/14
(ii) Workshop on residual newborn blood spots 30/06/14

11. **Any other business**

12. **Date of next meeting** 8 December 2014 – Medical Research Council, London

UK Biobank Ethics and Governance Council
Fortieth Meeting

9 September 2014
Macdonald Manchester Hotel, Manchester

Present: Professor Roger Brownsword (Chair), Mr Andrew Russell, Ms Tracey Phillips, Professor Nils Hoppe, Dr Sheelagh McGuinness, Professor Søren Holm, Mrs Margaret Shotter, Dr Jonathan Hewitt, Dr Susan Wallace and Mr David Walker.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Ms Katherine Littler (Wellcome Trust) and Dr Jon Fistein (Medical Research Council).

Speakers: Professor Rory Collins (Principal Investigator and Chief Executive, UK Biobank) for item 5.

1. Apologies

Apologies were received from Professor Kate Hunt and Mr Jonathan Sellors.

2. Minutes of thirty-ninth meeting held on 2 June 2014

The Council approved the circulated minutes (with one correction).

3. Matters arising

Tracking of requests to UK Biobank

Members noted the outstanding requests to UK Biobank.

Subgroup reporting: Feedback

The EGC Chair, Vice Chair and Secretary met with Professor Rory Collins, Mr Jonathan Sellors and Ms Katherine Littler on 5 June for the second in a series of meetings on feedback. Members noted a draft minute of the meeting and the proposed next steps; UK Biobank will produce a note, aimed at participants and intended for publication on the UK Biobank website later on this year. This note will reiterate UK Biobank's feedback policy (including relating it to the recent enhancements which are not explicitly addressed in the Ethics and Governance Framework).

The EGC Chair reported that he recently met with Mr Sellors to discuss the legal advice received by UK Biobank in relation to the imaging feedback protocol.

Subgroup reporting: EGC access oversight role

On the 8 September a number of EGC members visited the UK Biobank Co-ordinating Centre to discuss the access process with Dr Tim Peakman (Deputy Chief Executive Officer), Mrs Lorraine Gillions (Research Access Administration Manager) and Ms Erin Scobie (Access Administrator). This informative meeting gave members a good sense of how the access process has been working and developing over recent months. The visit was undertaken in advance of the EGC moving over to a proposed new access oversight governance model in January 2015.

The proposed new model contains three strands (i) alerting, (ii) reporting, and (iii) auditing. Members discussed a drafted Memorandum of Understanding (MoU) that elaborates on the details of the model. The EGC Chair explained that the onus would be on UK Biobank to alert the EGC to certain kinds of application; the EGC Secretary would no longer review the access database in real time and no longer provide updates to Council. In terms of the reporting strand, members already receive high level reports from UK Biobank and agreed to consider the content of these reports in the context of the new model.

Members agreed that the MoU should provide further clarification regarding the audit strand. The view was expressed that auditors should be brought in to undertake the work (i.e. the audit should not be conducted by the EGC) and that the MoU should make clear who will take commissioning and financial responsibility for the work.

It was initially envisaged that the audit would take place 12 months after adoption of the model i.e. January 2016. However, while UK Biobank is reviewing its access process, and will be introducing streamlining measures, members agreed it might be prudent to conduct the audit after 18 months, giving time for the streamlining measures to bed down. It is important, however, for the timing not to be put back too far as audit is a necessary element of the new oversight model.

A revised MoU will be prepared for the December EGC meeting, and will be shared with Professor Collins and Mr Sellors. Once finalised the three strand model will be published.

The EGC Chair proposed that he and the Secretary could meet with Mrs Gillions and colleagues in the New Year to discuss what type of applications would be the subject of an alert and the content of the standard reports.

Re-contact applications

Under the terms of the Ethics and Governance Framework, the EGC is required to advise on applications that request re-contact with participants. Members ratified the EGC's preliminary advice in relation to three recently escalated applications; the applications will be considered by UK Biobank's Access Sub-Committee (ASC) on September 12.

4. Closed discussion on topics to discuss under item 5

Members agreed on a number of matters to raise with Professor Collins.

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

Report on applications

Three general issues are currently under consideration at the ASC, in particular concerning: (i) re-contact in order to invite participants into a separate study where inclusion criteria might constitute feedback to participants; (ii) more broadly, the use of UK Biobank by researchers who want to identify people to invite into a separate study and (iii) how to manage and judge applications that request depletable samples.

On the latter, UK Biobank has received very few sample requests to date. There is a need for UK Biobank to develop a strategy for making samples available to researchers and to define the criteria to be used to judge these requests. Currently, requests for samples are subject to scientific review by UK Biobank, judged against the criteria set out in the access procedures and, ultimately, the ASC considers the opportunity costs of using the samples for the proposed research.

As part of its sample management strategy, UK Biobank is considering issuing calls on specific diseases, the timetable for which would be based on the number of cases accrued in the cohort. Under this model, UK Biobank would coordinate and perform the assays in its own laboratory, or commission a third party laboratory. If the assay is very specialised, and can only be performed at the applicant's laboratory, UK Biobank would provide the samples only and would require the return of the assay data before any UK Biobank data were released.

Review of the access process

At its June meeting the ASC discussed in detail the upcoming access process review. While a timetable was not formulated at that stage, the ASC will return to this discussion at its September meeting. Mr Steve Garrett will coordinate the implementation of the required systems changes, for example, it is possible that the Preliminary and Main Applications could be combined, in particular for non-contentious uses. When agreed, the new access process will be made public.

Receiving and incorporating research results into the resource

The Council received UK Biobank's 'Guidance Note for Approved Projects: Return of Results Data' for information.

Imaging pilot

Up to 15 participants are being imaged per day. The process is working well but the neuro-imaging takes 5 minutes too long. An IT alteration will be implemented and should reduce the imaging time by changing the way the image is measured (but not

what is measured). Once this change has been implemented, the throughput will be increased to 18 participants per day.

The Imaging Review Panel suggested that UK Biobank should repeat a number of the baseline measures during the imaging assessment visit (all but the eye and fitness test are incorporated). The time and cost of incorporating these measures is being evaluated during the current pilot phase; it is possible that fewer samples will be collected during any main phase imaging visit as this is a costly element.

Members asked if UK Biobank could encourage participation from older and disabled participants. Professor Collins responded that UK Biobank aims to encourage participation through its transport policy (e.g. if a participant is registered as disabled they can be reimbursed for the travel expenses of a companion). If fewer older and disabled participants attend, this may limit heterogeneity of the sample but it should not bias the sample in terms of who goes on to develop disease and who does not.

UK Biobank's imaging proposal requires a 20% attendance rate. While this has been achieved to date, recruitment so far has focused on participants who live close to the assessment centre. UK Biobank does not yet know how participants will respond when asked to travel greater distances. The assessment centres are open from 8.00am – 9.30pm; local people will be offered the early and late appointments while those living at a distance will be offered midday appointments.

The EGC will provide input when UK Biobank comes to consider the outcomes of the pilot and the implications for the main phase. In order to gain a better sense of when this might be, the EGC agreed to ask UK Biobank to provide a timeline for the imaging.

Imaging incidental findings protocol

The EGC Chair recently met with UK Biobank and funder colleagues to discuss the imaging feedback protocol. Under the terms of this protocol, potentially serious incidental findings are fed back when they are observed initially by radiographers during the imaging visit and subsequently confirmed by radiologists (or other appropriate specialists). A high proportion of the radiographer escalated findings have subsequently been found, by the radiologist, to be non-serious (i.e. false positives).

The incidental findings protocol is running in parallel to a separate process whereby the first 1,000 scans are being systematically reviewed by a Panel of radiologists. The purpose of this process is to evaluate the standard protocol by assessing the number of false positives and false negatives (i.e. where a potentially serious finding has been missed by the radiographers). These two processes are blinded to each other.

Approximately 20% of the scanned participants have received feedback relating to at least one imaging modality as a result of the systematic review; some participants have received feedback on more than one modality. The radiographers receive guidance from UK Biobank indicating what it considers to be potentially serious findings. The radiologists are reporting additional findings that they consider to be

potentially serious. It is anticipated that the majority of findings will, on further investigation, be false positives.

By the end of September, 1,000 participants will have been imaged and approximately 200 will have received feedback. Participants will be asked to complete a questionnaire on the impact of that feedback after 6 weeks and 6 months. All of the 6 week questionnaires should be complete towards the end of this year and the 6 month questionnaires should conclude in March/April 2015. Accordingly, the results could be reported in June 2015 as part of UK Biobank's main phase submission.

UK Biobank plans to add a GP questionnaire 3 or 4 months after the feedback has been given, in order to see what action, if any, has been taken. The results of this questionnaire will feed into the qualitative assessment at 6 months.

The social science research will continue throughout the pilot phase, with further data being gathered after the main phase submission. A member asked whether the raw data from the social science research will be deposited in the UK Data Archive. Professor Collins advised that the research will be published and raw data from the pilot will be archived by UK Biobank and accessible to researchers.

EGF revisions

In the context of the feedback meetings (see item 3), the funders have asked UK Biobank to clarify its plans for making non-material changes to the EGF (e.g. the Framework could usefully describe how the feedback policy relates to the recent enhancements, including the imaging and genotyping work).

Any other developments and outstanding recommendations from EGC39

Genotyping: The first tranche of genotyping data will be available this year and all data should be available by the third quarter of 2015. The Wellcome Trust Centre for Human Genetics will undertake imputation work involving the 820,000 measured markers; at least 12 million markers can be imputed.

Infectious disease biomarkers: Professor Adrian Hill is working on a funding application that proposes to measure approximately 50/70 infectious disease biomarkers across the whole cohort. The markers will relate to cancer in particular but also to other diseases.

Marketing the availability of the resource: UK Biobank's recent Frontiers meeting attracted a few hundred people. The audience was largely from academia but a few commercial groups were also present. UK Biobank colleagues, and their affiliates, have presented at a number of scientific meetings (nationally and internationally) and have a number of publications pending (for example, PLOS Medicine will soon publish a paper by Dr Cathie Sudlow that describes the resource). Researchers commonly misunderstand the nature of the resource and believe that they must collaborate with UK Biobank in order to gain access. Professor Collins hopes that this will change as the genotyping data become available; UK Biobank aims to make

genotyping data for 150,000 participants available by the end of the year to stimulate use of the resource.

6. Closed discussion of matters arising under item 5

The Council agreed to initiate a meeting with UK Biobank to discuss the issue of linkage to other resources and revision of the EGF.

7. Funders' review of the EGC

A quinnquennial review of the EGC's activities will commence in the New Year. The funders provided a letter detailing the review timetable and what evidence will be required. The draft Terms of Reference of the Review Panel were also provided, along with details of the Panel's composition:

- Dr Eric Meslin (Chair)
- Professor Martin Bobrow
- Dr Jonathan Montgomery
- Dr Jennifer Harris
- Dr Debbie Lawlor

The Review Panel will meet once to consider the evidence: (i) the EGC's submission, (ii) UK Biobank's submission, (iii) the outcomes of interviews with other cohorts (the cohorts are being asked what they know about the EGC and its role) and (iv) the outcomes of a consultation with participants. (Mindful that the EGC is required to comment on all re-contacts, members confirmed that they considered this a reasonable use and, indeed, a positive step in that it sets a precedent for consulting on governance issues. The funders indicated that the participant questionnaire will be circulated to Council for comment.)

The EGC submission will be in three parts: (i) An account of the activities undertaken in 2010-2014 (ii) Operational aspects (iii) A work plan for 2015-2020. Members discussed a draft of Part 1 and agreed on points to include in Parts 2 and 3.

A revised draft of the full submission will be circulated for comment and a further draft will be considered at the December meeting.

8. EGC subgroups

The Council reviewed the remit and membership of its subgroups, agreeing the following:

Subgroup	**Membership**	**Role**
Access	Margaret Shotter, Susan Wallace, Roger Brownsword and Søren Holm (Sheelagh McGuinness will step down)	To take responsibility for drafting the EGC's response to escalated applications and any matters relating to the new 3-strand access governance model.

Feedback	Roger Brownsword, Sheelagh McGuinness, Jonathan Hewitt and Kate Hunt	To be involved during the further development of the imaging feedback protocol, as the implications of the pilot phase and social science research are considered.
IT and data security	David Walker and Tracey Phillips	To consider issues of (i) data management and security during the development and management of UK Biobank's IT systems and (ii) data protection, confidentiality, identifiability and linkage as they relate to enhancement of the resource and proposed uses of the resource.
Communications	Andrew Russell, David Walker, Jonathan Hewitt and Margaret Shotter	To advise on engagement by UK Biobank and to consider the EGC's work to engage a wider stakeholder group.
EGF revisions	Tracey Phillips, Nils Hoppe and Sheelagh McGuinness	This new group will work to encourage and assist UK Biobank with the next revision of the EGF.

9. Communications activities

Registration is now open for the EGC's 10-year anniversary public lecture and conference, to be held at the Wellcome Trust on 3-5 November.

10. Report on meetings attended

UK Biobank Frontier meeting 26/06/14

The EGC Secretary attended UK Biobank's Frontiers meeting.

Workshop on residual newborn blood spots 30/06/14

The EGC Chair attended a workshop on the ethical and legal aspects relating to the retention and use of newborn blood spots.

11. Any other business

There was no other business.

12. Date of next meeting

8 December 2014 – Medical Research Council, London