UK Biobank Ethics and Governance Council
Thirtieth Meeting

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

Monday 5 March 2012 at 10.30am

Agenda

1. Apologies

2. Minutes of twenty ninth meeting held on 12 December 2011

3. Matters arising
   (i) Tracking of requests to UK Biobank
   (ii) Imaging application and feedback protocol
   (iii) Subgroup reporting as necessary
   (iv) Wellcome Trust and MRC initiative on feedback of clinically relevant findings

4. Biomarker assays by UK Biobank

5. Closed discussion on topics to discuss under item 6

6. Update from UK Biobank (Professor Rory Collins, Chief Executive Officer, UK Biobank)
   (i) Access issues and demonstration of the access application and reporting systems
   (ii) Funding application for imaging of participants
   (iii) Biannual report on longitudinal follow-up of participants
   (iv) Any other developments and outstanding recommendations from EGC29

7. Closed discussion of matters arising under item 6

8. The EGC and the access phase – operational aspects

9. The role of the EGC – advising on the interests of participants and the public

10. Communications activities
    (i) External speaking opportunities
    (ii) External enquiries to the EGC

11. Report on meetings attended
    (i) Board of Directors meeting 16/12/11
    (ii) Meeting with Professor Susan Wolf 19/12/11
    (iii) Meeting with a Japanese delegation on personalised medicine 10/01/12
    (iv) Funders meeting on UK Biobank 26/01/12
    (v) Nuffield Council on Bioethics workshop ‘Genomics, health records, database linkage and privacy’ 22/02/12

12. Any other business

13. Date of next meeting 21 May 2012 - Council meeting, London
UK Biobank Ethics and Governance Council
Thirtieth Meeting

5 March 2012
Wellcome Trust, London

Present: Professor Roger Brownsword (Chair), Professor Martin Richards, Dr Roger Moore, Dr Jonathan Hewitt, Professor Paolo Vineis, Mr Andrew Russell, Ms Tracey Phillips, Professor Heather Widdows and Professor Søren Holm.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Ms Katherine Littler (Wellcome Trust) for the whole day.

Speakers: Professor Rory Collins (Principal Investigator and Chief Executive, UK Biobank), Mr Jonathan Sellors (Company Secretary, UK Biobank) and Mr Steve Garrett (Business Analyst, UK Biobank) for item 6.

1. Apologies

Apologies were received from Mrs Margaret Shotter, Dr Sheelagh McGuinness, Professor Kate Hunt and Dr Catherine Moody.

2. Minutes

of twenty ninth meeting held on 12 December 2011

The Council approved the circulated minutes with one spelling correction.

3. Matters arising

Tracking of requests to UK Biobank

The EGC has previously requested the right to observe meetings of UK Biobank’s Access Sub-Committee (AC) on reasonable request on a case-by-case basis. Members noted that this request will be considered by the AC, which meets for the first time on the 16 March.

A list of proposed revisions to the Ethics and Governance Framework (EGF) has been provided to UK Biobank. The EGC Chair and Professor Rory Collins met recently and agreed that revision of the EGF should take place from Autumn 2012, after access has been launched.

Imaging application and feedback protocol

Members noted a report of a recent EGC, UK Biobank and funders meeting regarding UK Biobank’s imaging application and feedback approach.
Subgroup reporting as necessary

Feedback: A subgroup of the EGC continues to review the literature and practice of providing feedback of health information to research participants. The subgroup is preparing a report of its findings which will be presented at a future Council meeting. Two related initiatives were noted: first, the EGC is investigating the possibility of visiting the Framingham Heart Study to discuss their feedback policy. Second, the EGC has been formally approached by the Principal Investigator of the 1958 Birth Cohort and asked to assist in the consideration of the project’s feedback policy (in particular in relation to genetic findings).

Members also noted that Dr Anna Middleton, from the Wellcome Trust Sanger Institute, is co-ordinating a programme of work aimed at ascertaining attitudes towards receiving feedback of genetic research findings. Opinions are being sought via an online questionnaire.\(^1\)

Wellcome Trust and MRC initiative on feedback of clinically relevant findings

Ms Katherine Littler provided an update on the Wellcome Trust and MRC initiative on feedback of clinically relevant findings. The public engagement element of this initiative is well underway: Phase 1 utilised focus groups and in depth interviews to explore feedback preferences, including attitudes to feedback of different types of findings (e.g. varying degrees of significance of the disease and treatability etc) and conditions that might influence a feedback policy (e.g. if to provide feedback would be such a burden on resources that the research would have to stop). This first phase is complete. Phase 2 has involved questionnaires being completed by 1200 people; this consultation has now closed and the results are being analysed.

The findings of the commissioned qualitative and quantitative research will be launched in April while the overall findings of the project – a set of principles to be considered in the development of any feedback policy – will be published towards the end of the year.

4. Biomarker assays by UK Biobank

UK Biobank has developed a grant application proposing that a wide range of biochemical markers are measured in samples collected at baseline from all 500,000 of its participants.

In the context of the Council’s general review of the literature and practice of feedback, and noting that the EGF provides that there will be no feedback of information arising from sample analysis (whether the limited haematology performed by UK Biobank before samples are stored, or later analysis as a result of research use), a provisional discussion took place.

\(^1\) www.genomethics.org
5. Closed discussion on topics to discuss under item 6

The Council noted the five new members of the Board and the constitution of the Board’s new Access Sub-Committee (AC). The Council agreed to warmly invite the new Chair of the Board, Sir Mike Rawlins, to attend part of the 21 May Council meeting. Members are keen to meet with Sir Mike and to discuss with him his vision for UK Biobank. Further, allowing some time for all parties to gain experience of the access process, the EGC agreed to invite members of the AC to attend part of the 3 September EGC meeting.

Members agreed on other points to raise with UK Biobank under item 6.

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

**Access issues and demonstration of the access application and reporting systems**

Access to the resource will be launched at the end of March 2012. Members received a demonstration of the data showcase and access systems, which are in the final stages of development.

The AC, which will be Chaired by Ms Tara Camm, is expected to meet before the Board meetings, but it could communicate between meetings if guidance is needed. The AC will use its first meeting – on 16 March – to review the access application and reporting systems and to discuss how it wants to work as a committee.

The Council asked whether UK Biobank planned to announce the opening of the resource to its participants. Mr Andrew Trehearne is arranging the communications surrounding the launch including a press briefing to be held at the Wellcome Trust.

**Funding application for imaging of participants**

The imaging application is undergoing the final stages of revision. A near final draft will be considered by the Board at its 16 March meeting with a view to submitting the application to the funders at the end of March.

The Council welcomed the update on the imaging application and was re-assured to learn that the costings now include provision for research on participants’ attitudes to feedback, for follow-up of the clinical outcomes of receiving feedback and for the involvement of a health economist during the pilot to help evaluate costs to the NHS.

**Biannual report on longitudinal follow-up of participants**

UK Biobank’s focus at present is on setting in place cohort-wide flagging for deaths and cancers, and cohort-wide linkages both to coded hospital episode data and primary care data. The project aims to have in place during Q2 2012 a comprehensive system for receiving data on deaths and cancers for all participants in England, Wales and Scotland and to have cohort-wide hospital episode data available during Q2-Q3 2012. Work is ongoing by Professor Ronan Lyons and his
group in Wales, and by Professor Frank Sullivan and his group in Scotland, to link to and obtain coded data from Welsh and Scottish participants’ general practice records. In England, the General Practice Extraction Service (GPES) is working with UK Biobank to develop appropriate methods for defining and extracting coded data from English general practices. The project hopes to receive at least some primary care data from Wales, Scotland and England during 2012, and aims for cohort-wide linkage to primary care data during 2013.

The Council welcomed the update on these activities and appreciated being offered sight of a summary paper prepared by Dr Cathie Sudlow (UK Biobank’s Chief Scientist) for GPES.

Members were interested to learn that UK Biobank is developing a web questionnaire to obtain directly from participants information relevant to conditions that are not readily picked up through hospital or primary care coded data (such as mental health and musculoskeletal disorders). A questionnaire on mental health will be developed in the first instance; it is anticipated that an email notification will be sent to participants in both Spring and Autumn this year inviting them to complete the questionnaire. The Council asked whether the questionnaire will also be available to participants who have not provided email addresses to the project. Dr John Gallagher is leading the development of the questionnaire and is investigating the possibility of producing a paper version for participants who have no internet access. However, such paper questionnaires are more limited in scope and less interactive than online versions.

UK Biobank is working with experts to assess what level of adjudication will be needed to confirm diagnoses from participants’ health record data. Four UK Biobank funded studies are underway or about to start to pilot methods for ascertainment, confirmation and subclassification of cancer, diabetes, heart disease and stroke.

The Council noted that depending on the extent of the adjudication involved it is possible that this process could uncover misdiagnosis of disease for some participants. Professor Collins confirmed that misdiagnoses might come to light but that data on a participant’s health condition and treatment may be inaccurate for a number of reasons and UK Biobank may not know what condition the participant is being treated for. As such it is unlikely to be constructive to offer feedback in this context; UK Biobank’s ‘no feedback’ policy will apply.

Any other developments and outstanding recommendations from EGC29

(i) Activity monitors: The Research Ethics Committee (REC) responsible for UK Biobank having previously approved asking participants to wear activity monitors to obtain direct measures of activity (as part of a set of enhancements of the baseline assessment), UK Biobank now intends to clear the written materials (inviting participation) with the REC.

The activity monitor that is to be used is a watch-like device that is worn on the wrist. It records information about the duration, frequency and intensity of all kinds of activity. Participants will be invited to wear the monitor 24 hours a day for a week. A pilot is proposed which, if it runs smoothly, will be continued to a main phase.
(ii) Repeat assessments: The REC responsible for UK Biobank having previously approved repeat assessment visits (as part of the original protocol), UK Biobank now intends to clear the written materials with the REC.

The repeat assessment visits will involve 20-25,000 participants and will be identical to the initial baseline assessment (including the enhancements introduced in the latter stages of recruitment). The visit will take place at the UK Biobank co-ordinating centre in Cheadle, where participants will have the opportunity to visit the project’s laboratories and sample archive. UK Biobank anticipates having capacity to assess 60 participants per day.

If funded, the biomarker assays will be performed on the blood samples taken during the initial assessment visit for all 500,000 participants and also on the blood samples from those participating in the repeat assessment visit. The baseline samples would be assayed first; this is expected to take about a year.

7. Closed discussion of matters arising under item 6

Biomarker assays

The Council considered the clinical applications and meaning of the different biomarkers that UK Biobank has selected for assay. It was noted that, given the passage of time since the samples were taken (up to 6 years for some participants), some of these tests might have lost their practical clinical significance.

Following further discussion, it was agreed that the proposed assays were appropriately covered by UK Biobank’s ‘no feedback’ policy.

Access

The Council welcomed the update on access including the demonstration of the access management and reporting systems. It is understood that the intention is for UK Biobank to gain experience of access and to modify the systems and processes accordingly.

Members were pleased to be offered sight of the ‘Comment’ piece that the Lancet has agreed to publish (coinciding with the launch of access).

Application forms and guidance for researchers

The EGC would like to re-iterate its previous recommendation that UK Biobank could usefully articulate its interpretation of ‘in the public interest’ in the application forms. The forms should be drafted in such a way that they encourage the researcher to reflect on the fact that the ‘public interest’ is not merely the scientific interest and that in some cases public interests may conflict (e.g. a scientifically sound proposal but in an area which is potentially controversial and unlikely to receive public support).
More broadly, the EGC has discussed with UK Biobank the need for ‘Guidance for researchers’. Such guidance could articulate what types of research would be considered to meet the purpose of UK Biobank, including public interest considerations. The document could include other aspects such as a description of when UK Biobank might be ‘ready’ for certain disease research (i.e. the disease timetable); an explanation of how UK Biobank will manage research applications which seek to address similar goals (i.e. how collaboration between users will be initiated and encouraged); an explanation of how the depletability of samples will be managed and articulation of the check-list of access criteria.

**EGC access to information**

In response to the EGC’s request that it should have routine access to the methodology section of applications, UK Biobank has responded that the intention is that the lay summaries should be structured in such a way as to provide sufficient information about the study (including its methodology) to enable the EGC to carry out its oversight function. Reflecting on the latest demonstration of the access application and reporting systems, the Council agreed that it was not yet clear whether a 200-word lay summary would suffice for its oversight purposes.

Further, it was confirmed during the demonstration that the access system is able to record a detailed decision of the AC (e.g. if approval is given with caveats). However, at this stage the EGC will only be able to see the AC’s ‘Yes/No’ decision and will not be able to access the detailed information.

It was agreed that the adequacy of these arrangements would need to be kept under review as experience with the access procedures was gained.

**Ethox Centre**

In order for the EGC to better understand the relationship between UK Biobank and the Ethox Centre, and what the Ethox Centre is tasked to do, the EGC agreed to request sight of the contract that formalises this relationship.

**Re-contacts**

It is clear that a number of participant re-contacts are planned for the year ahead including the repeat assessments in 20-25,000 participants, the invitation to wear an accelerometer and the invitation to complete new questionnaires (e.g. on cognitive function). The Council was reassured by Professor Collins’s comment (in relation to the new questionnaires) that UK Biobank will assess the impact of these re-contacts and that an assessment will be made to establish whether these data could be derived by other means.

Section I.B.5 of the EGF notes that decisions on whether re-contact is appropriate for particular proposals will be made by UK Biobank with advice from the EGC and subject to REC approval. The EGC interprets this broadly to include both re-contact proposed by researchers in their access applications and also re-contacts proposed by UK Biobank for its own purpose. To this end the Council was pleased to be
offered sight of the proposed materials for the baseline re-assessment visit, the accelerometer invitation and the new questionnaires.

Members noted an action from the draft September 2011 Steering Committee Minutes concerning the generation of a report on UK Biobank’s frequency of contact with participants. The EGC would be interested to learn whether such a report was prepared and, if it was, would be interested to have sight of the document. It seems essential that UK Biobank keeps an active and ongoing overview of the frequency and reasons for which participants are being re-contacted, including at the individual level.

*Repeat assessment for 20-25,000 participants*

The EGC understands that participants will not be asked to provide formal written consent for the repeat assessment visit as such. The EGC considers it to be imperative that the information materials provided for REC approval refer back to the original consent and to the terms of that consent (e.g. re-iterating the no feedback policy). The EGC looks forward to receiving the information materials for the re-assessment visit in due course.

8. The EGC and the access phase – operational aspects

The EGC access subgroup will meet late April/early May to, amongst other things, review the applications received by UK Biobank.

9. The role of the EGC – advising on the interests of participants and the public

The 2010 review of the Council’s activities resulted in a number of recommendations including: that the third point of the EGC’s remit requires clarification by the funders²; that the EGC need not place as much emphasis on public engagement in future and it should not carry out an advocacy role with the public on behalf of UK Biobank; and that public engagement and communication with participants should primarily be a role for UK Biobank.

The funders are considering how the third point of the EGC’s remit should be revised and asked for the Council’s input. During the discussion it was agreed that, as per the review recommendations, it is for UK Biobank, not the EGC, to ascertain the interests of participants e.g. through targeted engagement work. It is for the Council to advise UK Biobank on such activities.

Once the immediate priorities of the launch of access and submission of the enhancement proposals have been addressed, the EGC would welcome a discussion with UK Biobank and the funders regarding the need for, and possible approaches to, engagement with participants and the public. Ideally any such work would have a defined purpose and objectives and measurable outcomes. For example, if funded, UK Biobank could consider undertaking an engagement exercise

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² ‘to advise more generally on the interests of research participants and the general public in relation to UK Biobank’
around the imaging visit in order to raise participants’ awareness and interest in this new element of the project.

ACTION: The Secretary will write a paper to articulate the EGC’s understanding of what it means ‘to advise on the interests of participants and the general public’.

10. Communications activities

The EGC Chair, Vice Chair and Secretary have been invited to observe a meeting of the ALSPAC Ethics and Law Committee (at a date to be arranged).

11. Report on meetings attended

Board of Directors meeting 16/12/11

The EGC Chair observed the December meeting of the Board at which UK Biobank’s imaging application was discussed.

Having come to the end of his term of office, Sir Alan Langlands has stepped down from his position of Chair of the Board of Directors. The EGC Chair conveyed a message from Sir Alan thanking the EGC for its valuable input.

Meeting with Professor Susan Wolf 19/12/11

The EGC Chair, Vice Chair and Secretary met with Professor Susan Wolf to discuss policies on the feedback of health information to participants. Professor Wolf has published extensively in this area and is a member of a new consortium of US National Institutes of Health grantees on return of results and incidental findings that has just been formed by the National Human Genome Research Institute.

Meeting with a Japanese delegation on personalised medicine 10/01/12

The EGC Chair and Secretary met with a delegation from Japan that had a primary interest in the regulation and implementation of personalised medicine.

Funders meeting on UK Biobank 26/01/12

The EGC Chair observed a funders meeting, the purpose of which was to raise awareness of UK Biobank and its enhancement proposals (e.g. MRI, biomarker assay etc) amongst a range of funding organisations.

Nuffield Council on Bioethics workshop ‘Genomics, health records, database linkage and privacy’ 22/02/12

The EGC Vice Chair attended a scoping meeting on ‘Genomics, health records, database linkage and privacy’.
12. Any other business

**Expert Advisory Group on Data Access**

A new Expert Advisory Group on Data Access (EAGDA) is being formed by the Wellcome Trust, Medical Research Council, Economic and Social Research Council and Cancer Research UK. The Group has a dual role: it will serve to provide expert advice to the partner funders on key strategic issues in relation to data access, and it will support current and future study Data Access Committees across the biomedical and social sciences landscape, including the fields of genetics, epidemiology and the social sciences – helping to identify best practice and encourage consistency in decision-making based on clear, common principles. A number of EGC members – and the Secretary – have been invited to participate in a stakeholder workshop to help formulate the EAGDA’s work plan.

**Access procedures**

Throughout the development of the access procedures the EGC advised UK Biobank that its confidentiality commitments should be robust but realistic. Attention having been drawn to the final version of the procedures, it was agreed that the Council should remain mindful of how confidentiality commitments are drafted.

13. Date of next meeting 21 May 2012 - Council meeting, London