

UK Biobank Ethics and Governance Council Forty-fourth Meeting

Meeting at Cotswold Lodge Hotel
66a Banbury Road, Oxford, OX2 6JP

Tuesday 8 September 2015 at 9.30am

Agenda

1. **Apologies**
2. **Minutes** of forty-third meeting held on 1 June 2015
3. **Matters arising**
 - (i) Tracking of requests to UK Biobank
 - (ii) Subgroup reporting: Access
 - (iii) Subgroup reporting: Feedback (report and imaging)
4. **Funders' review of the EGC**
5. **Closed discussion on topics to discuss under item 6 and 7**
6. **General update from UK Biobank** (Professor Rory Collins, Chief Executive Officer)
 - (i) Report on access applications
 - (ii) Review of the access process
 - (iii) Imaging update
 - (iv) Other enhancements (genotyping, web questionnaires etc.)
 - (v) Access to stored tumour tissue
 - (vi) Revision of the EGF
 - (vii) Any other developments and outstanding recommendations from EGC43
7. **UK Biobank communications** (Mr Andrew Trehearne, Head of Communications)
8. **Funders' review of the EGC** (discussion with Professor Collins and Mr Trehearne)
9. **Closed discussion of matters arising under item 6 and 7**
10. **Communications activities**
11. **Report on meetings attended**
 - (i) Board of Directors meeting 26/06/15
 - (ii) BioSHaRE conference: Latest tools and services for data sharing, Milan, Italy 28/07/15
 - (iii) WHO Consultation on Identifying Ebola Virus Disease (EVD) Biobanking Needs in West Africa, Freetown, Sierra Leone 6-7/08/15
12. **Any other business**
13. **Date of next meeting** 7 December, Wellcome Trust
14. **Tentative dates for 2016**

**UK Biobank Ethics and Governance Council
Forty-fourth Meeting**

**8 September 2015
Cotswold Lodge Hotel, Oxford**

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

In attendance from EGC Secretariat: Ms Adrienne Hunt.

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

Speakers from UK Biobank: Professor Rory Collins (Principal Investigator and Chief Executive, UK Biobank) and Mr Andrew Trehearne (Head of Communications, UK Biobank) for items 6 and 7.

1. Apologies

Apologies were received from Professor Nils Hoppe.

2. Minutes of forty-third meeting held on 1 June 2015

The Council approved the circulated minutes.

3. Matters arising

Tracking of requests to UK Biobank

Members noted the outstanding requests to UK Biobank.

Subgroup reporting: Access

At its last meeting the EGC discussed a re-contact application which was significant in that it would set a precedent for use of UK Biobank as a recruitment platform into third party studies. The Access Sub-Committee (ASC) had, at that stage, decided to approve the application on the understanding that: (i) the project will need to fit in with UK Biobank's own timetable of re-contacts; (ii) the study will serve as a pilot (the cost and resource implications for UK Biobank will be monitored and assessed, in addition to participant take-up); and (iii) the EGC does not raise any further concerns. After its last meeting the EGC provided advice to the ASC.

Members noted an update from Mrs Lorraine Gillions detailing the conditions under which the Main Application has been approved by the ASC.

Subgroup reporting: Feedback (report and imaging)

In June the EGC feedback report was sent to the funders and UK Biobank for consideration during the drafting of the imaging review submission. At the current meeting the Chair proposed that the report should be published on the EGC website; the funders confirmed their support for this proposal. The Chair will discuss this with Professor Rory Collins.

The EGC Chair attended the recent Imaging Review Panel meeting and presented the EGC's response to the incidental findings protocol. Amongst other things, the Panel discussed two key design points in relation to the protocol (i) the proposed approach whereby potentially significant incidental findings (PSIFs) that happen to be noticed by a radiographer will be escalated for radiological review versus routine radiological review of all scans and (ii) the policy for compulsory feedback of PSIFs.

The Review Panel recommendations will be considered by the respective Wellcome Trust and MRC funding committees with a decision expected towards the end of the year.

4. Funders' review of the EGC

The funders convened an Expert Review Panel to assist during the EGC's quinquennial funding review. Members received and discussed the Panel's report, which contained the following key recommendations:

- the introduction of an Annual General Meeting as a formal mechanism for public reporting, discussion and future planning of UK Biobank
- the need to initiate the process of revising the entire EGF soon and consideration of revisions periodically in future (at least every five years)
- the development of metrics against which the EGF can be assessed
- the development of a new Memorandum of Agreement that clarifies all aspects of the relationship between UK Biobank and the EGC, including the new responsibilities of the EGC as recommended by the Panel
- a reduction in EGC membership, meetings and secretariat support
- the funders to explore the idea of supporting the development of a national EGC that would interface with all UK biobanks and cohort studies.

5. Closed discussion on topics to discuss under item 6 and 7

No further issues were raised.

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

Report on access applications

Professor Collins reported on the application discussed under item 3 and offered to keep the EGC informed as the pilot progresses.

Review of the access process

A detailed report has been prepared for UK Biobank describing what a review of the access process might look like. This report is being distilled down into something that UK Biobank can go out to tender on. Most likely it will take about a year for the access systems changes to be implemented. In the meantime, UK Biobank has adopted a number of streamlining measures in light of the significant increase in applications.

UK Biobank is exploring options for how best to describe and visualize the data that it holds. While researchers can look at each variable in the Data Showcase and see what data are available, visualizing the data in a more user friendly way is a challenge.

UK Biobank's work on the development of a sample management protocol will commence shortly.

Imaging update

The Wellcome Trust has funded a research fellow to follow-up on the impact of the imaging incidental findings protocol (including an assessment of clinical outcomes). This work will relate to the first 5,000 participants who receive feedback of a PSIF. The results of the imaging pilot work on the impact of feedback, and this future work, will be published.

Both raw and derived data for the first 4-5,000 scans will be released in October; this will be announced on UK Biobank's website. In line with standard practice, masking of faces is taking place for the brain images.

Other enhancements (genotyping, web questionnaires etc.)

Genotyping data for 150,000 participants are now available (both measured and imputed); the process of sending these data to researchers is working well. Release of data for all participants was expected to take place at the end of the year but due to the scale of work involved in QC and imputation processes, release of the full set of data is now expected to take place mid-2016.

An application involving telomere assays was recently approved by the ASC. A QC process is currently underway and advice is being sought from colleagues who have already performed such assays as part of the Kaiser Permanente study. All data

resulting from this work will be returned to UK Biobank (as per the standard access requirements).

Approximately 140,000 participants have completed the cognitive function questionnaire and similar numbers have completed the employment questionnaire, which looks at the participants' full work history.

Access to stored tumour tissue

UK Biobank recently ran a pilot to assess access to stored tumour tissue. The pilot showed that UK Biobank could identify that there was a stored sample; the work has not been taken further. An underlying question is whether tumour tissue can be treated as a health record (in terms of the consent given by participants at enrolment). Late last year, when representatives from UK Biobank and the EGC met to discuss the revision of the EGF, it was agreed that the EGF might be augmented with a suitable protocol that would cover those cases where UK Biobank was contemplating a linkage (or some similar activity) that did not clearly fall within the literal wording of the participant consent / EGF. At the current meeting, it was agreed that access to tumour tissue provides an important exemplar of this kind of issue (when consideration should be given to the spirit, as well as the precise wording of what's written in the EGF). The EGC offered to provide advice on the question of the interpretation of the EGF in this case.

Revision of the EGF

The EGC Review Panel recommended that the process of revising the entire EGF should be initiated soon. Professor Collins has spoken with the Review Panel Chair, Professor Eric Meslin, regarding the Panel's recommendation. Revision of the EGF will be discussed at an upcoming UK Biobank management meeting and also at a series of UK Biobank, EGC and funder meetings.

Any other developments and outstanding recommendations from EGC43

At an earlier meeting, members sought confirmation as to whether UK Biobank might commission an external audit of the Cardiff University systems that deal with UK Biobank data. Professor Collins reported that UK Biobank has undertaken an internal audit of the relevant Cardiff University systems and offered to provide the report to the EGC.

At the end of last year, the UK Biobank, EGC and funder discussions on feedback resulted in a proposal from UK Biobank to write a note for participants. Professor Collins reported that a draft has been prepared but is on hold while UK Biobank awaits the outcomes of the imaging review. Professor Collins offered to share the draft note with the EGC.

Members asked whether UK Biobank has – or plans to have – a systematic approach to the assessment of a participant's capacity. Professor Collins advised that UK Biobank will act on the advice of family members and/or GPs and, to his knowledge, there have been no questions raised by participants in relation to

incapacity. Primary care data could provide a systematic way for UK Biobank to find out about a participant's incapacity, however, these data are not yet available for all participants.

Colleagues at UK Biobank are keenly aware that they are dealing with an aging population and that communications need to be tailored accordingly (e.g. in relation to the logistics of the participants' meetings and the format of online and printed material etc.).

7. UK Biobank communications (Mr Andrew Trehearne, Head of Communications)

UK Biobank's Head of Communications, Mr Andrew Trehearne, provided an update on UK Biobank's communications activities. The update and subsequently discussion included the following:

- Participants' meetings have taken place in Edinburgh and Manchester and future meetings are planned for Nottingham and Leicester. To date UK Biobank has invited participants via email but in future may also advertise the events in the local media. The last event was videoed and will appear on UK Biobank's website shortly; all future meetings will be recorded and made available. UK Biobank invited a representative from the EGC to speak at future participants' meetings.
- Alternative formats for the participants' meeting were discussed as a way to actively engage participants and to seek their views (rather than the focus being on information-giving). More time for Q&A and small group discussion was suggested, in addition to asking participants for their questions in advance of the meeting.
- Members asked whether UK Biobank could make use of the Wellcome Trust's provision for public engagement¹.
- UK Biobank's 5th annual newsletter has been distributed to participants and is available on UK Biobank's website.
- UK Biobank is working on its strategy for keeping up with – and disseminating information about – approved research. Recognising that this is time consuming work for a relatively small communications team, members asked whether UK Biobank had considered hiring an intern to help identify newsworthy research. Similarly, there may be value in someone going through the videos of the participants' events to pull out the key issues raised by participants – for example, this could be an interesting project for an MA student.
- A portfolio of videos is being developed, in which researchers explain how they are using the resource. The videos will be posted on a dedicated page on UK Biobank's website.
- A video piece on genomics is being prepared and will be used at the launch of the genotyping data next year. This work involves a participant interviewing scientists about their work; the aim is to make the piece simple and easy to

¹ <http://www.wellcome.ac.uk/Funding/Public-engagement/Engagement-with-your-research/Funding-within-research-grants/index.htm>

understand. A video featuring the UK Biobank Eye Consortium will also be prepared.

- Participants can be re-contacted by UK Biobank for a variety of reasons. The need for a re-contact monitoring report has been discussed at previous meetings as a way of tracking the number and frequency of re-contact requests. Responding to this, Mr Trehearne presented a summary paper describing re-contacts by UK Biobank (including the reason for re-contact and the numbers of participants involved). This summary will appear in all future communications updates. (In closed session members noted that the summary report does not include re-contact for third-party research. The Secretary will ask for this to be added to future reports.)

8. Funders' review of the EGC (discussion with Professor Collins and Mr Trehearne)

The EGC Chair updated Professor Collins and Mr Trehearne on the morning's discussion.

9. Closed discussion of matters arising under item 6 and 7

Members further discussed a number of matters that arose during the day, including (i) the key points to include in the EGC response to the Expert Review Panel report and (ii) the idea that the EGC could be represented at future UK Biobank participants' meetings (and the potential resource issues). This discussion formed the basis of an EGC response to the Review Panel report (see Annex A).

10. Communications activities

The EGC Chair and Secretary will speak at Taiwan Biobank's 10-year anniversary conference in November. The event is being organised by the Taiwan Biobank EGC.

11. Report on meetings attended

Board of Directors meeting 26/06/15

The EGC Chair attended the June Board meeting.

BioSHaRE conference: Latest tools and services for data sharing, Milan, Italy 28/07/15

Dr Susan Wallace attended the Biobank Standardisation and Harmonisation for research excellence in the European Union (BioSHaRE) conference. Taking place in the final year of the FP7-sponsored project, the conference presented and demonstrated the data sharing tools and services that have been developed by the BioSHaRE researchers.

WHO Consultation on Identifying Ebola Virus Disease (EVD) Biobanking Needs in West Africa, Freetown, Sierra Leone 6-7/08/15

Dr Susan Wallace spoke at a meeting convened by the WHO, the objective of which was to work toward consensus and implementation of a biobanking system for samples collected from West Africa during the Ebola outbreak as well as samples that may be collected in future epidemics of Ebola Viral Disease. The WHO asked for a presentation concerning the UK Biobank Ethics and Governance Framework and the role of the EGC as one example of a biobank governance model.

12. Any other business

Members agreed to seek clarification as to how 'adverse events' during the imaging sub-study are reported, logged and monitored.

13. Date of next meeting 7 December, Wellcome Trust

14. Tentative dates for 2016 11 April, 11 July and AGM to be confirmed

Annex A EGC response to the Report of the Expert Review Panel

The EGC welcomes this opportunity to respond to the recommendations of the Expert Review Panel. The points addressed below were raised and discussed by the EGC at its September 2015 meeting. While this document is primarily a summary of the EGC's discussion at that September meeting, it does to some extent also reflect the ongoing post-Review discussions with the funders and/or UK Biobank. This response follows the structure of the Review Panel Report.

Updating the Ethics and Governance Framework (EGF)

The EGC strongly endorses the Panel's recommendation that (i) the entire EGF should be revised, (ii) revisions should be considered periodically in future and (iii) 'triggers' be identified that would prompt and necessitate revisions to the EGF.

The Panel also recommended that 'metrics' should be developed in order to facilitate a more 'objective' assessment of UK Biobank's compliance with the EGF. The EGC is broadly supportive of this recommendation.

The Council is ready to input into further discussions concerning the articulation and implementation of these recommendations.

Updating the Role and Function of the EGC

The Panel highlighted a number of functions that it was 'convinced ... are not appropriate for the EGC to undertake going forward':

- 'Reviewing and offering advice on research protocols and submissions to the UK Biobank'.

There was some uncertainty on the Council as to whether this statement was intended to encompass all research applications (e.g. including re-contacts). Having discussed this with the funders, the EGC now understands that all re-contact and novel applications will continue to be escalated for advice (as per the three-strand access oversight model) but that the EGC's advice should in general relate to the associated policy issues and not necessarily to the specifics of the application (e.g. whether it has REC approval etc.).

- 'Monitoring active protocols and other projects, a responsibility that is most appropriately left to committees with authority and expertise to monitor ongoing projects'.

This has never been a function of the Council and, to the Council's knowledge, UK Biobank does not have a committee that routinely monitors active projects. A new committee might be required to fulfil this function if it is considered necessary.

- 'Auditing the activities of the UK Biobank to ensure compliance with the EGF a responsibility that is most appropriately left with the UK Biobank, for example under the auspices of an audit committee'.

The EGC's broad reading of this section – as demonstrated by this point in particular – is that the Panel recommends a move to a more light-touch approach and a shift from the EGC's direct role in monitoring compliance with the EGF to a more indirect role whereby the EGC relies on audits performed by – or on behalf of – UK Biobank. While the EGC assumes that such audits should (and would) be undertaken by an independent third party, it remains to be decided how frequently they should take place. Clarification of this latter point will be welcome as discussions take place regarding the implementation of the recommendations (including whether any new audits are required under the new scheme).

The new model of indirect oversight throws into question the third strand of the EGC's access oversight model. The audit element is a critical feature in this scheme; it was envisaged that the audit would be commissioned by the EGC to be shared and discussed with UK Biobank. Clearly, however, this direct role is now at odds with the recommended indirect monitoring. The

EGC welcomes further discussion as to how – and by whom – the access audit should be taken forward²; a clear protocol on access audit is essential.

- ‘Undertaking external engagement with UK Biobank participants’.

While this statement is clear, it seems to the Council to be slightly at odds with the later suggestion that ‘the EGC should be expert on the EGF so that any advice given to the UK Biobank reflects *current* expectations of participants’ (emphasis added). It is not clear to the Council how it can be knowledgeable as to the *current* expectation of participants if it cannot engage with them. In saying this the Council is not advocating that it should itself routinely undertake engagement work but it is querying the expectation that its advice can reflect participants’ current interests when there is no mechanism in place to communicate with the majority of the cohort.

The EGC can see a role for itself in recommending when it thinks engagement should take place (by UK Biobank) and an EGC subgroup could assist UK Biobank in the development of its participant engagement activities. There has been some discussion about the EGC becoming more actively involved in UK Biobank’s participants’ meetings; the EGC welcomes this as an opportunity to raise its profile amongst the cohort and to engage directly with at least a subset of participants.

This section concludes with two recommendations:

- ‘The EGC’s Remit should be amended to reflect its updated function to advise the UK Biobank on what the EGC deems to be those issues and topics the UK Biobank should *consider* in developing its own policy’ (emphasis added).
- ‘The EGC Remit be amended to reflect the practice that the *recommendations* it makes to UK Biobank should be seriously considered for adoption, with a mechanism available to the UK Biobank to indicate its intention to adopt or not adopt such recommendation’(emphasis added).

The EGC interprets this to mean that, in general, its role is to advise UK Biobank as to the relevant considerations during policy and protocol development; but that, in addition, as and when it might be appropriate and necessary, the EGC may formally recommend a particular approach (and in such cases that UK Biobank should formally respond to the recommendation).

Establishing a UK Biobank ‘Annual General Meeting’

The EGC supports the idea of an Annual General Meeting and welcomes further discussion on the following:

² After discussion with the funders, the access audit costs have been removed from the EGC 2015/16 budget.

- i. **Should the EGC or UK Biobank take primary responsibility for the event?** The Panel proposed that the EGC should take the lead but Professor Collins has queried whether UK Biobank should instead be responsible. The EGC is comfortable with either approach provided that the event is organized jointly.
- ii. **Who is the audience?** The AGM cannot be all things to all people. The funders have proposed that the audience could be similar to the EGC's November 2014 conference (i.e. other biobankers, policy makers, funders and academics with an interest in this field). This was suggested because UK Biobank already has in place a series of participants' meeting at which the participants' voice can be heard and the EGC has started to have an active role in these. While not the primary audience for the AGM, the EGC is of a view that some places should be reserved for participants.
- iii. **What length, structure and content would serve the purpose of the AGM most effectively?** It will be essential for the event to be organized in such a way that it provides substance and allows UK Biobank to demonstrate how it has complied with its commitments in the EGF. This is in contrast to an event that solely acts as a platform for UK Biobank to highlight its many achievements. Striking the right balance will be key.

While there may be challenges in relation to an event of this kind, the EGC welcomes the fact that the Panel's recommendations are, in general, in such a form that they invite interpretation. The EGC and UK Biobank have an opportunity to decide how best to take forward the AGM recommendations, with the funders' advice.

Building on the Current EGC/UK Biobank Relationship

The EGC fully supports the development of a new Memorandum of Agreement but is mindful that work on this can only begin in earnest once the various other aspects have been discussed and agreed (e.g. responsibilities in regards to the AGM, mechanisms for information sharing and briefing etc.). Responsibility for drafting the MoA needs to be agreed.

Operational and Budget Issues

Meetings: It has been recommended that the EGC should move from quarterly meetings to potentially two meetings a year, plus the AGM and in-camera session. There is a background concern that the new model is, in effect, asking the EGC to switch on and switch off over time, with fluctuating involvement as issues arise, rather than running regularly throughout the year. Critical aspects to resolve are:

- i. the quarterly meetings have always provided a regular opportunity and impetus for the sharing of information and relevant materials. With

fewer meetings how best can the EGC keep apprised of UK Biobank's activities and when, how and what will UK Biobank report to the EGC?³

- ii. will the proposed method of working require members to do more between the Council meetings (including more formalized EGC subgroup)? See also 'Members'.

Members: A smaller membership (e.g. 5-8)⁴ has been recommended, and a steer was provided as to the types of expertise that could be included (or not) on the EGC going forward:

- i. it is for discussion whether a reduced membership will provide the EGC with the necessary range of expertise and perspectives (see also the next point). Having discussed this with the funders, the EGC understands that members could be co-opted for subgroup work as necessary. However, there is a sense that such ad hoc membership would not aid the cohesion or 'memory' of the Council or its sense of collective responsibility.
- ii. the Report states that 'Continuing the practice of a single lay member (i.e. member of the general public, person without a specialised or professional interest) would not be an appropriate way to accommodate the issue of participant representation.' In fact, the EGC has never had a practice of having a single lay member and, in any event, would not equate lay membership with participant representation. (There are a number of members who might consider themselves lay in terms of the subject matter but they would not claim to represent participants.) The EGC has always considered a broad range of experiences to be a valuable feature of its make-up; our 'lay' members often bring a fresh and valuable perspective to discussions. It may be to the EGC's detriment to lose this input.
- iii. in recent years the EGC has worked effectively through a number of subgroups and responsibility for this work has been shared comfortably amongst the Council's 12 members. Sharing such responsibilities amongst a committee of 5-8 will likely require a higher degree of engagement by the members (if the same level of subgroup work is required in future). In addition, it has been proposed that a representative of the EGC could present at UK Biobank's participants' meetings (with one or two meetings planned per month). Again, this responsibility will be shared amongst the reduced membership. The Council suggests that the funders should err on the side of caution and recruit at the higher end of the recommended scale.⁵ Also, both the EGC and funders should keep membership and time commitment under review as the EGC moves into its new phase of operation.

³ At minimum, relevant papers prepared for the Board need to be available to the EGC. Beyond this both teleconferencing and face-to-face meetings will be options.

⁴ In practice, this is likely to be 8.

⁵ The funders have indicated their agreement to this.

Potential for Greater Impact

In its submission, the EGC proposed to adopt a more outward-facing role in future. There was enthusiasm on the EGC to develop in this way and so the Panel's lack of support for this proposal was met with some disappointment.

That said, if the EGC had anticipated that it might be recommended that the Secretary's time commitment should be significantly reduced, its submission would have been drafted in very different terms. Rather than proposing an enhanced role for the EGC, the emphasis would have been on damage limitation and the importance of maintaining the tripartite co-operative working relationship established between UK Biobank, the EGC, and the funders. In the event, the reduction of the Secretary's time commitment by 40% is by some distance the most significant change following the Review, pre-empting any possibility of the EGC developing an outward-facing role and placing serious questionmarks about its ability to discharge its inward-facing responsibilities.

Although the EGC will not develop an outward-facing role in the way proposed, it is very supportive of the recommendation that the funders should give serious consideration to the idea of forming a national body to advise all UK biobanks and cohort studies. If such a body is established, the EGC would be keen to establish close links; this could perhaps be achieved through overlapping membership. In this way the EGC could at least link indirectly with other biobanks and the array of longitudinal and cohort studies with whom the UK Biobank initiative shares a number of issues and challenges.