

# UK Biobank Ethics and Governance Council Forty-fifth Meeting

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

Monday 7 December 2015 at 10.30am

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## Agenda

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1. **Apologies**
2. **Minutes** of the forty-fourth meeting held on 8 September 2015
3. **Matters arising**
  - (i) Tracking of requests to UK Biobank
  - (ii) Implementation of the EGC review outcomes
  - (iii) Revision of the EGF
  - (iv) Access (input required from the EGC on future reporting)
  - (v) Stored tumour tissue
  - (vi) Feedback report
4. **Closed discussion on topics to discuss under item 5**
5. **General update from UK Biobank** (Professor Rory Collins, Chief Executive Officer)
  - (i) Report on access applications
  - (ii) Review of the access process and access reporting to the EGC
  - (iii) Imaging update
  - (iv) Other enhancements (genotyping, web questionnaires etc.)
  - (v) Health outcome linkage and adjudication biannual report
  - (vi) IT and data security biannual report
  - (vii) Any other developments and outstanding recommendations from EGC44
6. **Implementation of the EGC review outcomes**
7. **Revision of the EGF**
8. **Introductions and discussion with the incoming EGC Chair and Vice Chair**
9. **Closed discussion of matters arising under item 5**
10. **Expenditure report 2014/2015 and approved budget 2015/2016**
11. **Report on meetings attended and upcoming activities**
  - (i) Taiwan Biobank EGC conference, Taipei 06-08/11/15
  - (ii) UK Biobank participants' meeting, Nottingham 12/11/15
12. **Any other business**
13. **Date of next meeting** 11 April, Wellcome Trust (tbc)

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

**7 December 2015  
Wellcome Trust, London**

Present: Professor Roger Brownsword (Chair), Dr Sheelagh McGuinness, Dr Jonathan Hewitt, Professor Søren Holm, Professor Nils Hoppe, Dr Susan Wallace and Mr David Walker.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Dr Jon Fistein and Dr Katie Finch (Medical Research Council) and Ms Katherine Littler (Wellcome Trust) for the whole meeting. Baroness Helene Hayman (incoming Chair) for items 8-13. Dr Eric Meslin (incoming Vice Chair) for item 8 (by Skype).

Speaker from UK Biobank: Professor Rory Collins (Principal Investigator and Chief Executive, UK Biobank) for items 5-7.

1. Apologies

There were no apologies.

2. Minutes of the forty-fourth meeting held on 8 September 2015

The Council approved the circulated minutes.

3. Matters arising

*Tracking of requests to UK Biobank*

Members noted the outstanding matters.

*Implementation of the EGC review outcomes*

Members noted a draft report of a UK Biobank, funder and EGC meeting at which the review outcomes were discussed, including the proposal for an Annual General Meeting (AGM) and revision of the EGF and Memorandum of Understanding.

At that earlier meeting it was agreed that it would be sensible for the EGF audit (against metrics) and the access audit (from the EGC's three strand oversight model) to be performed as part of the funders' existing audit of UK Biobank. As agreed at that meeting the funders reported back on the frequency of the audits; these normally take place every 5 years and one was performed about a year ago. It was

agreed that this frequency does not fit the access audit model; the funders will re-consider the options.

The EGC Review Panel recommended that the funders should investigate the possibility of creating a body to advise all UK cohort studies (the EGC had proposed to take on a more outward facing role in future but this was not supported by the review). The funders advised that there is no appetite to establish a new body to take on this role but instead the funders are considering how existing bodies might be involved. These discussions are ongoing.

#### *Revision of the EGF*

In light of the discussion at the review outcomes meeting, Mr Jonathan Sellors, UK Biobank's Company Secretary, prepared a revised version of the feedback section of the EGF. Members discussed the revised draft section under this item and with Professor Rory Collins under item 7.

#### *Access (input required from the EGC on future reporting)*

A year into the new access oversight scheme, members reflected that the standard reporting has been working well (i.e. the high-level summary of the numbers and types of applications received to date, summary details of each application in the adjudication pipeline and each project that is underway). Going forward, there is an opportunity to further revise and refine the access reporting; UK Biobank plans to make adjustments to its access systems and these changes should facilitate the reporting process.

The question of reporting novel or precedent setting applications was raised and discussed with Professor Collins under item 5.

#### *Stored tumour tissue*

At its September meeting the EGC offered to provide UK Biobank with advice on the question of the extent to which stored tumour tissue can be considered part of a participant's 'health-related record' (in terms of the consent given at recruitment). Members noted a draft response that had been developed by a subgroup of the EGC. The Chair proposed to further revise and re-circulate the paper.

#### *Feedback report*

Members noted the finalised EGC discussion paper 'Feedback of health related findings: foreground principles and background perspectives', which will be published on the EGC website shortly.

4. Closed discussion on topics to discuss under item 5

No further issues were raised.

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

*Report on access applications*

UK Biobank has witnessed a substantial increase in non-UK applications, including requests from the USA. The latter could in part be a result of an event that was held at the American Society of Human Genetics conference at which the availability of the resource was promoted; the event was very well attended.

A number of applications have been received from commercial organisations but these are coming in very slowly.

Members discussed with Professor Collins a few applications that they considered to be novel or precedent setting but which had not been the subject of an alert or reported as being salient. While the EGC would like to be made aware of these types of applications, it does not want to create any disproportionate burden on UK Biobank.

The EGC gleans much of its information on the 'difficult' cases from the Minutes of UK Biobank's Access Sub-Committee (ASC). Generally, the ASC Minutes are received shortly in advance of the quarterly meetings, often several months after the ASC meeting took place. It was agreed that early sight of the Minutes would allow the EGC to keep more up to date on the ASC's discussion and should help all parties develop a shared understanding of the types of applications that should fall in the 'salient and reportable' category and which should be the subject of an alert. Professor Collins agreed to put a request to the ASC for the circulation of its Minutes to the EGC as soon as possible after the ASC meeting.

Considering the issue of adjudication more broadly, the EGC recalled that in the early days of access the ASC indicated that it would set out a system of precedents and principles in a single document. The paper could describe the types of applications that are uncontentious and easily adjudicated and other types of applications that have presented difficulties. Professor Collins agreed that such a document would be useful.

*Imaging update*

UK Biobank's main phase imaging submission was considered by a Review Panel in September. UK Biobank has received the Panel's report which will inform the Wellcome Trust and MRC's funding decision.

UK Biobank's main phase imaging submission proposed the continuation of the piloted approach to the feedback of potentially significant incidental findings (PSIFs)<sup>1</sup>, as opposed to the systematic radiologist review which was undertaken on

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<sup>1</sup> Under the terms of the pilot protocol, PSIFs are fed back when they are observed initially by radiographers during the imaging visit and subsequently confirmed by radiologists (or other appropriate specialists).

the first 1,000 scans. Informed by the estimates of false positive rates during the pilot, and the social science research that assessed the impact of receiving feedback, UK Biobank concluded that the systematic radiologist review approach is not viable in a study of this nature and scale given the impact of generating a large number of false positives on the participants and their GPs (and the healthcare system).

The proposed approach was endorsed by the Review Panel, in light of the pilot's findings. As part of the ongoing funding review process, the Panel asked UK Biobank to seek an updated legal opinion on a number of questions around the feedback protocol and to provide a paper on the reputational risk issues related to the protocol (e.g. where an intervention resulting from feedback causes harm or cases where the radiographer did not pick up an issue that later presents clinically).

The funders advised that the review papers will be made available to the EGC after the funding decision.

Practically, if funded, two new imaging centres should open in July 2016 – in Newcastle and Reading. Installation is currently being considered and is under discussion with Siemens. UK Biobank is also giving consideration to the recruitment and retention of imaging staff, including issues of salary, training and career development.

*Other enhancements (genotyping, web questionnaires etc.)*

Professor Collins provided an update on the following enhancements:

Genotyping data: Data for 150,000 participants have already been released and are being used in research. Release of the full data set for all 500,000 participants (both genotyped and imputed) will take place mid-2016. The genotyping data have been re-quality controlled by Affymetrix and are also being quality controlled by the Wellcome Trust Centre for Human Genetics in Oxford and imputed genotypes will then be derived using an updated algorithm.

Centralised preparation of genotype/phenotype tabulations: The International Scientific Advisory Board (ISAB) met in November and discussed whether UK Biobank could prepare tabulations of genotypic variations against phenotype and make these available to researchers in a searchable system. Publication of the associations could provide a service to the research community and be preferable to this work being done in a piecemeal fashion by third party researchers. While the ISAB strongly supported this centralised approach the matter has not yet been discussed by UK Biobank's Board and ASC.

Biomarkers: Urinary, HbA1c and some serum biomarker assays will be released in the second quarter of 2016. All remaining biomarker data should be made available by the end of 2016.

Activity monitor: 100,000 participants have now returned the accelerometer. The activity data are being extracted and will be released soon.

Web questionnaires: Administration of the cognitive function and occupational history web questionnaires is now complete. A mental health questionnaire is being developed and will be sent to participants in 2016 by email.

#### *Health outcome linkage and adjudication biannual report*

Members noted this biannual report and, in particular:

Death and cancer: After prolonged negotiations UK Biobank's data-sharing agreement with the Health and Social Care Information Centre (HSCIC) has been renewed and the provision of death and cancer data has been re-established.

Primary care: The process for acquiring access to primary care records has been protracted, in part because of the lack of a comprehensive, national source of electronic, coded data. However, substantial progress has recently been made. Coverage of general practices in Wales has increased to 15,000 (70% of Welsh participants), coverage of general practices in Scotland increased to 30,000 (80% of Scottish participants) and UK Biobank has signed a data-sharing contract with a major English GP systems supplier for around 150,000 (30% of English participants).

#### *IT and data security biannual report*

The biannual report on IT and data security was noted.

#### *Any other developments and outstanding recommendations from EGC44*

No further matters were raised.

### 6. Implementation of the EGC review outcomes

Professor Collins reported that the AGM will be a discussion at the next UK Biobank Steering Committee meeting, including what might be included on the agenda. Also, the Board of Directors will review the current Memorandum of Understanding at its December meeting and discuss how the document might be revised.

### 7. Revision of the EGF

Members discussed with Professor Collins the draft revised feedback section of the EGF. The EGC considered that the language could be simplified and that the agreed approach (of embedding update boxes within the original text) may make the EGF difficult to read when applied across the whole document and especially so as multiple boxes are applied over time during future revisions. Professor Collins considered the approach to work well but agreed to discuss the EGC's feedback – especially around language – with Mr Sellors with a view to preparing a further revised draft.

## 8. Introductions and discussion with the incoming EGC Chair and Vice Chair

The funders have appointed a new EGC Chair, Baroness Helene Hayman, and EGC Vice Chair, Dr Eric Meslin. Baroness Hayman and Dr Meslin will take up their roles on 1 January 2016. The Appointments Committee recognised a strategic opportunity to bring authority and knowledge to the EGC via Baroness Hayman's and Dr Meslin's different and complementary experience and expertise. The funders fully endorsed the Committee's recommendation.

Baroness Hayman and Dr Meslin joined the meeting and expressed their delight at having been appointed to the EGC. Discussion focused on what the current members considered to be the current and future issues facing UK Biobank and the EGC and on how the governance arrangements have changed over time. The discussion touched on issues of access and the EGC's three strand oversight model, the imaging sub-study and the management of PSIFs, implementation of the outcomes of the EGC review and how the EGC interprets its role as a 'critical friend'.

## 9. Closed discussion of matters arising under item 5

No further matters were raised.

## 10. Expenditure report 2014/2015 and approved budget 2015/2016

Total expenditure for 2014/2015 was £137,386, 95% of the budget. This figure is higher than the usual annual expenditure as it includes the costs associated with the EGC's 10-year anniversary conference.

The funders have approved a budget of £122,920 for 2015/2016. The Secretary noted that costs associated with an audit of UK Biobank's access process (the third strand of the EGC's access oversight model) have been removed from the budget in light of the Review Panel's recommendation that the EGC should not undertake audits directly (see item 3).

## 11. Report on meetings attended and upcoming activities

### *Taiwan Biobank EGC conference, Taipei 06-08/11/15*

The EGC Chair and Secretary spoke at Taiwan Biobank's 10-year anniversary conference in November at the invitation of the project's Ethics and Governance Committee.

### *UK Biobank participants' meeting, Nottingham 12/11/15*

Members noted a report from Mr Andrew Russell who attended and spoke at UK Biobank's participants' meeting in Nottingham.

## 12. Any other business

The funders advised that the core renewal process for UK Biobank has been initiated and an outline submission is expected in early 2016.

The Chair gave thanks to Dr Jonathan Hewitt who steps down from the EGC in February 2016 having served 7 years. Dr Hewitt has made a considerable contribution to the EGC – as both member and more recently as Vice Chair. In particular his input during the biomarker discussion was essential to the EGC's understanding of what the biomarkers signified and their continuing health relevance for participants.

The funders offered their thanks to Professor Roger Brownsword for chairing the EGC so successfully over the last 5 years. Professor Brownsword's open and collaborative style has benefitted the EGC greatly and served to enhance the EGC's relationship with UK Biobank.

## 13. Date of next meeting

11 April, Wellcome Trust (tbc)<sup>2</sup>

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<sup>2</sup> Post meeting note: This meeting date was subsequently changed to 27 April.