

UK Biobank Ethics and Governance Council Fifteenth Meeting

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

Monday 9 June 2008 at 10.30am

Agenda

1. **Apologies**
2. **Minutes** of fourteenth meeting held on 17 March 2008
3. **Matters arising**
 - (i) Summary of decisions and recommendations from fourteenth meeting held on 17 March 2008
 - (ii) Tracking of requests to UK Biobank
 - (iii) Update: EGC recruitment process
 - (iv) Confirmed guest speaker: further suggestions welcome
 - (v) Update: Commissioned public attitudes report
4. **Update from UK Biobank** (Professor Rory Collins, Chief Executive Officer, UK Biobank)
 - (i) General update from UK Biobank
 - (ii) Update regarding recommendations from EGC14
 - (iii) Development of UK Biobank's access and intellectual property policies
 - (iv) UK Biobank's IT and data management strategy
 - (v) UK Biobank's biannual report on enquiries and complaints
5. **UK Biobank's outline of proposals for enhanced phenotyping of participants**
(Professor Rory Collins, Chief Executive Officer, UK Biobank)
6. **Communications activities**
 - (i) Public meeting on 1 July 2008
 - (ii) External speaking opportunities
 - (iii) Governing genetic databases conference (24-26/06/08)
 - (iv) External enquiries to the EGC
7. **Report on meetings attended and other outreach activities**
 - (i) House of Lords, Sci and Tech Select Committee: Inquiry into Genomic Medicine (19/03/08)
 - (ii) NEURON workshop 'Future perspectives, benefits, bottlenecks and costs of Neuro-biobanks' (10/04/08)
 - (iii) Governing genetic databases law workshop (20/05/08)
 - (iv) P3G meeting (30-31/05/08)
 - (v) Update on OECD consultation: Guidelines on biobanks
8. **Any other business**
9. **Date of next meetings**

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

**9 June 2008
Wellcome Trust, London**

Present: Professor Graeme Laurie (Chair), Professor Ian Hughes, Professor Anneke Lucassen, Dr Heather Widdows, Professor Erica Haines, Professor Chris Wild, Professor Roger Higgs, Dr Roger Moore and Professor Martin Richards.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Dr Alan Doyle (Wellcome Trust) for items 4 – 9 only. Dr Catherine Elliott (Medical Research Council) for items 3 – 5 only.

Speakers: Professor Rory Collins (Principal Investigator and Chief Executive, UK Biobank) for items 4 and 5 only.

The Chair informed members that Dr Catherine Elliott and Dr Catherine Moody from the Medical Research Council have taken on responsibility for liaising with the Council, including observing at its meeting, while Dr Caroline Stone is on maternity leave.

1. Apologies

Apologies were received from Ms Andrea Cook.

2. Minutes of the last meeting held on 17 March 2008

The Council approved the circulated minutes subject to a clarification regarding the percentage correlation between data generated through web based diet assessments and data from diet diaries (page 6 of the minutes).

3. Matters arising

Summary of decisions and recommendations from fourteenth meeting held on 17 March 2008

The Council approved the circulated summary of decisions and recommendations.

Tracking of requests to UK Biobank

Two requests for further information were made to UK Biobank subsequent to the last meeting: First, the Council requested information regarding UK Biobank's proposal for enhanced phenotyping of participants. A paper on this topic will be considered under agenda item 5. Second, the Council plans to hold a public meeting in Wales on 12 February 2009, preferably in a town where UK Biobank is actively

recruiting. The Secretary requested information from UK Biobank regarding its plans to open a new assessment centres in Wales and was informed that UK Biobank has not yet scheduled the next centre in Wales. Cardiff was recommended as a potential location, where recruitment is currently ongoing but due to end in May 2008.

Update: EGC recruitment process

The advert for new members will be posted in the Guardian on 3 September 2008. The Council agreed that a diverse range of candidates should be sought and that the full extent of commitments of Council membership be clearly spelt out in appointment letters. The desire for a diverse range of applicants could be addressed through distribution of the advert to a wide and varied audience (including lobby forums, Islamic forums, think tanks, the Policy, Ethics and Life Sciences Research Centre contact list, General Medical Council patient and public involvement group and the EGC website).

ACTION: Members were asked to contact the Secretary with suggestions of how the advert might be disseminated. [All] The Secretary will investigate and compile a list of dissemination methods and will requests that the advert be posted on UK Biobank's website and in its assessment centres. [AH]

Confirmed guest speaker: further suggestions welcome

Professor Ruth Chadwick, Distinguished Research Professor at Cardiff University and Director of CESAGen, has agreed to join the Council at its December meeting to talk in and around the Council's commissioned reports on the public good and benefit sharing.

ACTION: Members were asked to contact the Secretary with suggestions of further guest speakers. [All]

Update: Commissioned public attitudes report

The Council reviewed the revised report from Professor Webster and his team 'Public attitudes to third party access and benefit sharing: their application to UK Biobank' (27 May 2008). The report takes account of members' comments from the last EGC meeting and includes enhanced results for the telephone questionnaire survey (the number of surveyed individuals from the younger age group having been increased from 50 to 151).

Members agreed that the report had been usefully re-structured and revised to reflect current UK Biobank policies. The Council agreed a further and final list of specific points to feedback to Professor Webster. Notably the feedback included the point that the report points to differences in the data but it is not always clear which of these differences are statistically significant (for example the differences between the two age groups). It was recommended that the report be reviewed for statistical significance throughout, that a note is made of whether a difference has statistical significance or not and that where significance is found a statistical test should be offered. Both significant and non-significant findings are of interest to the Council.

A decision regarding publication will follow after the final iteration of revisions. In the event of publication the Council will develop a preface for the report which will include an indication of how it intends to take forward the report's findings.

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

General update from UK Biobank

Marking the first year anniversary of the launch of the project, the 100 000th participant was recruited on the 14 April 2008. By the end of that month 2 million invites had been sent out with a response rate of 25%. The attendance rate is on average 9%, varying from 6 – 12% depending on the location. As of 9 June, 131 166 participants had been recruited, one quarter of the target cohort size of 500 000.

During the first year of recruitment UK Biobank has increased the number of assessment centres that operate concurrently. This has been as high as 7 but is currently 6. Up to 700 – 800 participants have been recruited per day for 6 days per week. UK Biobank aims to continue to recruit at least 100 people per day per centre. It is possible to maintain this level of throughput as a result of UK Biobank receiving approval to access potential participants contact details centrally. This approval is critical to the smooth running of recruitment and essential for the study to come in on budget.

The following assessment centres have now closed or will be closing soon:

Assessment centre	Number of participants recruited	Closing date (2008)
Glasgow	17 981	19 April
Cardiff	18 647	31 May
Edinburgh	17 295	7 June
Stoke	14 920 (expected to increase to 16 000 by the closing date)	26 July

The following assessment centres have just opened or will be opening soon:

Assessment centre	Opening date
Reading	14 May 2008
Bristol	9 July 2008
Nottingham	30 July 2008
London (at Professor Mark Caulfield's laboratory at St Bartholomew's)	27 August 2008
Sheffield	4 March 2009

In addition to the above, UK Biobank continues to recruit in Newcastle (including Sunderland), Manchester (located in Bury), and Leeds (including Bradford). The break in opening new centre between August 2008 and March 2009 reflects the fact

that recruitment will be ongoing in several of the above major cities well into next year.

Regarding the laboratory operations of UK Biobank, final acceptance testing work is taking place on the automated store. It is expected that the system will go live in June 2008 and thereafter that samples will be moved to the store. Assessment centre samples will be processed and added to the store during the day while samples which have been collected previously will be relocated from liquid nitrogen to the automated store at night.

Discussion

The Chair asked Professor Collins for an indication of UK Biobank's approach to recruiting individuals from ethnic minority groups. Professor Collins commented that beyond the strategic placing of the assessment centres there has been no targeting of ethnic minority groups to date. The work of UK Biobank's Head of Communications has so far focused on the regional, monthly launch of UK Biobank in different cities throughout the UK. Given that there will be a break in the cycle of opening new centres between August 2008 and March 2009, the focus can turn to other communications activities including approaches for targeting individuals from ethnic minority groups.

Professor Collins informed the Council that the overall numbers of participants in UK Biobank from ethnic minority groups are representative of numbers in the general population but are unlikely to be scientifically informative in a low number ethnic minority groups. He further commented that it is unlikely that UK Biobank can be used to look reliably at minorities on its own. Instead, collaboration with other studies will be key – including, for example, studies taking place in China, India and Mexico – where specific ethnic groups are the majority, not the minority. A member noted that to date the Council has focussed on potential risks of international collaboration and data sharing but that maybe the Council should also convey the very positive role of collaboration, as a means to more statistically powerful research.

Professor Collins was asked to confirm whether or not UK Biobank plans to immortalise white blood cells. He confirmed that blood is being stored in such a way that they can be immortalised in future. Pilot work has been undertaken by Professor Bill Ollier (Manchester University) and has been published in a special supplement of the International Journal of Epidemiology. The Council recalled that, acting on its advice, UK Biobank has include information about the immortalisation of white blood cells in its participant 'Further Information Leaflet'.

Update regarding recommendations from EGC14

Recommendations from EGC14 were addressed by Professor Collins in his general update and under the items that follow.

Development of UK Biobank's access and intellectual property policies

The Chair and Secretary recently attended a P3G meeting at which access issues were discussed. The Chair suggested sharing a paper with UK Biobank which was

prepare by Dr Jane Kaye for this meeting. The paper details a number of access strategies and might be useful to Mr Jonathan Sellors during the development of UK Biobank's policies.

ACTION: The Secretary will ask Dr Jane Kaye if the paper can be shared with UK Biobank and, if so, pass the paper on to Mr Sellors and Professor Collins. [AH]

There was a sense at the P3G meeting that it would be good to see iterations of draft policies and procedures being developed by its member biobanks. Professor Collins pointed to the fact that UK Biobank's policy on access is described in the publicly available Ethics and Governance Framework. The policy will be developed into procedures in the next document. When asked when such a document might be made public, Professor Collins informed the Council that Mr Sellors has prepared a tentative timetable for the development of the access and intellectual property procedures and offered to give the Council sight of this timetable.

ACTION: The Secretary will follow-up this offer and request sight of the timetable. [AH]

UK Biobank's IT and data management strategy

The Council was re-assured to read a report on the outcomes of penetration testing of the UK Biobank network at Cheadle and the Manchester assessment centre. It was recommended that information about the external testing could be made available on UK Biobank's website, thereby also providing re-assurance to participants and the public.

Professor Collins informed the Council that additional information about data security has been posted on UK Biobank's website, partly in response to the increasing number of questions on this topic that have been escalated from the Participant Resource Centre. Broadly, people are reassured about the measures in place once they have had the opportunity to discuss their concerns.

Implementation of UK Biobank's IT and data management strategy will be review by the Council at its December meeting and on an annual basis thereafter. In addition, urgent issues will be addressed throughout the year, if and when they arise.

UK Biobank's biannual report on enquiries and complaints

The Council welcomed UK Biobank's second biannual report on complaints and enquiries and was grateful that its earlier suggested additions to the report had been incorporated. On reviewing the report the Council congratulated UK Biobank on the low numbers of complaints and enquiries it has received.

The following observations were made with respect to the report:

- Statistics were provided of categories of enquiry or complaint that had to be escalated to a senior member of the study team. Very few escalated enquiries or complaints related to UK Biobank's policy on providing feedback of health information to participants (19 out of 625 escalated enquiries or complaints). Professor Collins commented that this subject is raised by potential

participants but, as that the Participant Resource Centre staff have become increasingly experienced to deal with the subject, fewer enquiries or complaints have had to be escalated to a senior member of the study team.

- The reported figures are not a reflection of 'public' attitudes towards UK Biobank but the concern of those who are thinking and/or willing to participate in the project. (i.e. If people have significant concerns they may simply decide not to participate rather raise their concern with the project team.)

The following requests were made with respect to future reports:

- The report as submitted was helpful in detailing escalated queries but it would also be helpful to have some reporting on the more standard enquiries and complaints that are raised at the assessment centres. The Council requested some reporting of these standard enquiries and complaints in future reports (categorised, for example, by different aspects of the visit 'language problem', 'waiting times', 'staff behaviour' etc.).
- The Council is interested to learn how many of the people who enquire or complain about an aspect of the study actually go on to participate. For example, the report cites this figure for the subject of commercial use of the resource, where 30 – 40% of those who raise this concern do not go on to participate. The Council requested that this figure is provided for all categories in the table of escalated enquiries or complaints in future reports.
- UK Biobank has received 110 requests to be withdrawn from the project during the 6-monthly reporting period and 146 in total during the first year of recruitment. Given that 100 000 participants were recruited in the first year, one member commented that this figure seems reassuringly low.

The Council is interested to learn how soon during or after recruitment participants withdraw. The Council requested a breakdown listing the number of participant withdrawals set against duration of time from the assessment centre visit.

- The 'miscellaneous' category contains 151 responses (a significant proportion of the total 625 escalated complaints and enquiries). The Council asked if this category can be broken down any further. Professor Collins reported that there are generally only one or two complaints or enquiries in each subcategory of this category and this is why they are reported together. Professor Collins offered to review this category to see if there are any significant subcategories that should be reported separately and agreed to show the Council the breakdown nonetheless.
- The Council recommended the use of a participant satisfaction survey and was interested to learn that UK Biobank plans to conduct a post-visit survey, one of the aims of which will be to assess participant satisfaction. A similar survey was used during the pilot phase of the project, the results of which led to refinements of the participant information leaflet and assessment centre operations. Professor Collins also highlighted that participants are able to leave anonymous comment cards at the assessment centre. He proposed

that UK Biobank could provide, and the Council agreed that it would welcome, a summary of the key messages arising through these report cards to be part of future complaints and enquiries reports.

ACTION: The Secretary will contact UK Biobank regarding the above requests and recommendations. [AH]

Professor Collins was questioned about the staffing of assessment centres. UK Biobank works with one recruitment agency, which identifies a cohort of candidate employees. This cohort is interviewed by UK Biobank's Training and Monitoring Team. Generally employees are agency staff and so are happy with the short term contracts. However, staff do tend to want to work a high number of hours, something which needs to be managed. UK Biobank has experienced some problems, particularly in the South of England, recruiting staff with sufficient spoken English skills to conduct the interviews with participants and answer questions regarding the touch-screen questionnaire.

Centres are generally open for six months before closing, when the equipment is moved to a new location. Largely new staff are recruited for each assessment centre, but some staff do move between centres. UK Biobank aims to transfer the centre managers between assessment centres but this is not always possible. New assessment centre managers visit operating assessment centres as part of their training. The Council noted that the main consistent factor between assessment centres is the Training and Monitoring Team itself and the advice it provides to new staff.

A member informed the Council and Professor Collins of an academic paper by an ethicist and a sociologist in which they describe and comment on an experience of being recruited to UK Biobank. The paper, which is soon to be published, highlights two particular issues, first that people may experience difficulty in the way in which questions are asked and subsequent difficulty in knowing how to provide answers. Second, the authors raise the subject of expectations and of being surprised at what happens at the assessment centre. Professor Collins commented that the project has received some responses from participants saying that some of the questionnaire is difficult to understand and therefore answer (e.g. questions about physical activity). UK Biobank has added a note to its touch-screen questionnaire to say that it recognises that the questions are difficult but that it would appreciate it if people would try to provide a response. Also, assessment centre staff are available to assist participants if they have difficulty answering the questionnaire.

ACTION: The member will provide details of the academic paper for reference.

5. UK Biobank's outline of proposals for enhanced phenotyping of participants (Professor Rory Collins, Chief Executive Officer, UK Biobank)

UK Biobank has developed a proposal for enhanced phenotyping of participants which will be submitted to the Funders for approval later in the year and which remains confidential in the interim. Professor Collins presented the proposal, seeking

the Council's view both generally and specifically on the implications of the proposal for the project's policy on the feedback of health information to participants.

Three categories of enhancement are proposed:

1. Enhancements feasible within available budget with minimal impact on throughput and assessment centre processes (e.g. additional measures of cognitive function and psychological status on the touch-screen and assessment of hearing on the touch-screen). If approved, these enhancements could be implemented early in 2009 and be incorporated in the baseline assessment visit of the 300 000 participants to be recruited from then until the end of recruitment in 2010.
2. Enhancements that require extra funding and modifications to the assessment centre process or layout (e.g. additional questions about residential and occupational history in the interviewer-administered questionnaire, fitness assessment with heart rate monitoring and collection of saliva sample). If approved, these enhancements could be implemented mid-2009 and be incorporated in the baseline assessment visit of the 200 000 participants to be recruited from then until the end of recruitment in 2010.
3. Enhancements that require a radically different approach from the current baseline assessment visits and significant extra cost (e.g. magnetic resonance imaging of brain and heart and electrocardiogram). These enhancements would be decoupled from the initial assessment centre visit and would involve participants agreeing to attend an additional visit of 90 -120 minutes. If approved the proposal will undergo piloting (including to test participant acceptability of the measures). Subject to the outcomes of the pilot, these enhancements could be implemented in 2011.

At present UK Biobank provides feedback to participants on a number of measurements taken during the assessment centre visit (blood pressure, weight, height, body mass index, lung function). Participants are not provided with individual feedback of analyses made after the assessment centre visit. The Council and Professor Collins discussed the proposed enhancements in broad terms and with a particular focus on UK Biobank's current policy on feedback. The discussion included:

- The suggestion that the category 1 and 2 measurements are probably comparable to measurements already taken during the assessment visit, whereas the category 3 measurements could be considered different due to their more intrusive nature. Therefore the category 3 proposal may require further consideration in terms of acceptability and the feedback policy.
- At present certain measures from the baseline assessment centre visit are reported to participants against population standard ranges in order to give the participant an indication of how 'normal' their measurement is. Certain questions arise from this: If feedback were to be provided for some of the proposed new baseline assessment measurements, do population standard ranges exist for these new measurements? If not, what, if anything, should be fed-back?
- The nature of some of the proposed category 3 measurements may give rise to different expectations among participants regarding feedback (e.g. imaging of *my* brain and heart and information being generated that *my* General Practitioner nor the NHS have hold of).

- The relevance of the fact that UK Biobank does not intend to analyse the proposed new measurements immediately but will instead store them for future analysis (the cost of analysing each measure would mean, for example, that no imaging would be possible because these costs would be prohibitive). Further, there is the consideration that the work would be carried out by technicians, rather than clinical staff.
- The predictive nature of the proposed measurements outside of a clinical setting (and issues surrounding false positive and false negative findings).
- The nature of the legal and ethical arguments surrounding feedback, the lack of legal precedent, and the fact that attitudes and other factors might change over time.
- If it is appropriate to provide feedback to participants, does this obligation also extend to the participant's first degree relatives or others, such as spouses?
- The implications of purchasing costly equipment that may be superseded within a relatively short timescale.
- Whether or not any of the proponents of the specific new technologies proposed to be included in the enhanced phenotyping have a commercial interest in those technologies. (The Council requested confirmation of this point as it wishes to be fully aware of any potential conflicts of interest in relation to adoption of specific approaches in the proposed additional parts of the study.)

As a result of the discussion a framework was devised within which to consider the implications of the proposal for UK Biobank's policy on feedback. It was recognised that the proposals for enhancement, which were developed over an 18 month period, have been driven by the science. The Council proposed that UK Biobank should now develop a paper on the legal and ethical implications of its enhancement proposals on the feedback policy, informed by the devised framework, to be considered by the Council at its September meeting. The Council will consider the issue further, and offered to review and provide input on UK Biobank's paper as it is developed over the summer.

Framework of considerations:

- 1) Re-affirm the basis of the original advice to UK Biobank regarding feedback.
- 2) From what is being proposed, what falls within the existing policy?
- 3) What, if anything, is ethically or legally different about what is proposed?
- 4) What is being done elsewhere (in other biobanks) and what is comparable to UK Biobank?
- 5) What, if anything, has changed?
- 6) What, if anything, should change?

In the longer term, if the proposals are funded, the Council would hope to review and provide input on certain operational aspects involved with the adoption of the new measures and questionnaires (e.g. the consent form, information leaflet, issues surrounding gender privacy etc).

6. Communications activities

Public meeting on 1 July 2008

Professor Sarah Cunningham-Burley will Chair the EGC public meeting in Edinburgh on 1 July 2008. Presentations will be made by Professor Anneke Lucassen, Professor Graeme Laurie and Professor Rory Collins.

External speaking opportunities

The Council agreed to be aware of, and where appropriate seek, opportunities to present its work at external meetings and events. The Council and Professor Collins agreed that it may sometimes be appropriate to conduct a joint EGC and UK Biobank presentation. Professor Haines proposed one such opportunity, a Café Scientifique in Newcastle, on the subject of biobanks.

ACTION: The Secretary will maintain a list of opportunities and will bring the list to each Council meeting for consideration. [AH]

ACTION: The Secretary will circulate a standard presentation and speaking notes to members for future reference. [AH]

Governing Genetic Databases conference (24-26/06/08)

Members were informed that the Chair, Vice Chair and Secretary will be attending the Governing Genetic Databases conference on 24-26/06/08. The Vice Chair, Professor Martin Richards, will present a paper on the added value of the EGC, with a focus on the monitoring aspect of the EGC's remit. The paper will also address some of the changes that have taken place since UK Biobank was set up, including unforeseen issues that the EGC has addressed.

External enquiries to the EGC

A number of external enquiries have recently been received by the Council concerning UK Biobank's policies. The Secretary reported on two such enquiries, one questioning UK Biobank's consent model and conformance with the Data Protection Act, the second seeking clarification regarding possible uses and users of the resource.

It was agreed that all enquiries received by the EGC relating to UK Biobank policy should be sent to UK Biobank for information and/or comment (including where the enquiry relates to the Council's opinion only). The Secretary will only pass the enquirer's contact details and actual email to UK Biobank with the enquirer's permission. If there is no permission the Secretary will only include an outline of their query along with the full EGC response.

7. Report on meetings attended and other outreach activities

House of Lords, Science and Technology Select Committee: Inquiry into Genomic Medicine (19/03/08)

The Chair was recently invited to give evidence at the House of Lords, Science and Technology Select Committee inquiry into Genomic Medicine. His talk addressed the legitimacy of broad consent, confidentiality versus security and commercialisation.

NEURON workshop 'Future perspectives, benefits, bottlenecks and costs of Neuro-biobanks' (10/04/08)

Ms Andrea Cook was recently invited to present at a workshop organised by the 'Network of European Funding for Neuroscience Research'. Her talk was entitled 'Biobanking harmonization – ethical and legal challenges'.

Governing Genetic Databases law workshop (20/05/08)

The Chair recently attended a law workshop organised by the 'Governing Genetic Databases' project team. Much of the discussion focused on whether or not feedback of health information should be provided to participants.

P3G meeting (30-31/05/08)

The Chair and Secretary attended a recent P3G meeting at which the subjects of governance, access and material transfer agreements were discussed.

Update on OECD consultation: Guidelines on biobanks

The consultation by the Organisation for Economic Co-operation and Development of its draft 'Guidelines for Human Biobanks and Genetic Research Database' has now closed.

Visitors from South Korean Biobank

The Secretary recently received two visitors from the South Korean biobank. Their project started recruitment in 2001 and hopes to have recruited 150 000 participants by the end of 2008. They are hoping to expand the project to include 300 000 participants, though this is subject to budget allocation. The visitors were interested to learn more about UK Biobank's model of consent, about how the EGC maintains its independence, how the EGC engages with participants and the public, the powers of the EGC and the relationship between the various stakeholders and organisations (e.g. RECs, the EGC, funders, UK Biobank Board of Directors).

8. Any other business

Pattern of Council meeting dates

Council meetings currently take place on a Monday. One member, for whom this day is not convenient, requested that an alternative day be considered in future. Other members agreed to this change providing sufficient notice is given. Dates for 2009 have already been agreed and so this change will be considered for the 2010 meeting schedule.

EGC review

The EGC review is expected to take place in 2009. Dr Alan Doyle suggested that the Funders would require from the Council, in time for the September EGC meeting, a document outlining how it has met its remit. This document will be circulated to members before being submitted to the Funders.

ACTION: The Secretary will develop the review document with input from the members.

Resignation from the Council

Professor Chris Wild resigned from the Council in light of his election as Director of the International Agency for Research on Cancer, the specialised cancer agency of the WHO located in Lyon, France. The Chair thanked Professor Wild for his commitment and input to the EGC.

9. Date of next meetings

1 July 2008	Public meeting
15 September 2008	Council meeting