

UK Biobank Ethics and Governance Council Twenty Second Meeting

Meeting at Cutler's Hotel
George Street, Sheffield, S1 2PF

Monday 22 March 2010 at 10.30am

Agenda

1. **Apologies**
2. **Minutes** of twenty first meeting held on 7 December 2009
3. **Matters arising**
 - (i) Summary of decisions and recommendations from twenty first meeting held on 7 December 2009
 - (ii) Tracking of requests to UK Biobank
 - (iii) Subgroup reporting as necessary
 - (iv) Discussion: Draft workshop report and outcomes
 - (v) EGC review
4. **Funder proposal for participant re-contact**
5. **Closed discussion on topics to discuss under item 6**
6. **Update from UK Biobank** (Dr Tim Sprosen and Mr Jonathan Sellors, UK Biobank)
 - (i) General update on developments and recommendations from EGC21
 - (ii) Access and intellectual property procedures
 - (iii) Information systems development, CTSU audit and ISO 27001 stage 1 assessment
 - (iv) Imaging visit and incidental findings protocol
 - (v) Biannual report on longitudinal follow-up of participants
 - (vi) UK Biobank equality audit
7. **Closed discussion of matters arising under item 6**
8. **Communications activities**
 - (i) External speaking opportunities
 - (ii) External enquiries to the EGC
 - (iii) EGC members' MRI paper
9. **Report on meetings attended**
 - (i) Meeting with researchers working for the Mitsubishi Research Institute, Japan 16/12/09
 - (ii) Meeting with researchers of the film 'Golden Genes' 06/01/10
 - (iii) Meeting with Dr Chekar from Cardiff University working for BBMRI 11/01/10
 - (iv) HGC/AHRC seminar 'Understanding genetic discrimination' 28/01/10
 - (v) HGC meeting 'Personal genetic profiling: the next 10 years' 09/02/10
 - (vi) Institute for Cancer and Immunology, 'Techniques in Cancer Genomics Symposium' 25/02/10
10. **Any other business**
11. **Date of next meeting** 7 June 2010 - Council meeting, London
12. **Dates for 2011** 14 March, 13 June, 26 September, 12 December

**UK Biobank Ethics and Governance Council
Twenty Second Meeting**

**22 March 2010
Cutler's Hotel, Sheffield**

Present: Professor Graeme Laurie (Chair), Professor Ian Hughes, Professor Paolo Vineis, Dr Roger Moore, Professor Roger Higgs, Mrs Margaret Shotter, Ms Tracey Phillips, Dr Jonathan Hewitt and Mr Andrew Russell.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Ms Katherine Littler (Wellcome Trust) and Dr Catherine Moody (Medical Research Council) for the whole day. Dr Teri Manolio (Director of the Office of Population Genomics, National Human Genome Research Institute) for items 6 – 12 only.

Speakers: Mr Jonathan Sellors (Company Secretary, UK Biobank) and Dr Tim Sprosen (Chief Scientific Officer, UK Biobank) for item 6 only.

1. Apologies

Apologies were received from Professor Martin Richards, Professor Heather Widdows and Professor Rory Collins.

2. Minutes of twenty first meeting held on 7 December 2009

The Council approved the circulated minutes.

3. Matters arising

Summary of decisions and recommendations from twenty first meeting held on 7 December 2009

The Council approved the circulated summary of decisions and recommendations.

Tracking of requests to UK Biobank

Members reviewed the list of requests which will be raised with UK Biobank later in the day.

Subgroup reporting as necessary

The subgroups have not met since the last Council meeting, however, the following was noted:

- *Access and IP (AIP)* – At its last meeting the Council offered advice on the draft skeleton procedures. UK Biobank has indicated that the revised draft procedures will be sent to the Council in April.
- *Information Security* – The Council has had sight of the terms of reference for an audit of those IT systems and procedures within the Clinical Trial Service Unit (CTSU) that relate to UK Biobank. An update is expected later in the meeting.
- *Communications* – UK Biobank intends to conduct a public review of its AIP procedures towards the end of 2010. The Council reiterated that the primary responsibility for public consultation on the procedures rests with UK Biobank. The Council may conduct an AIP engagement exercise in the future, depending on the nature, scope and outcomes of UK Biobank’s review.

Discussion: Draft workshop report and outcomes

Members discussed and agreed revisions to a draft report of its 8 December 2009 workshop ‘Involving publics in biobank research and governance’. The report will be revised to:

- a. Emphasis that there can be good reasons for undertaking public involvement initiatives and that such activities have clearly gained in popularity in recent years. However, tokenism should be avoided and there need to be clear benefits and public interest reasons for carrying out such initiatives.
- b. Highlight that public involvement can serve a number of purposes e.g. to give people a voice and to receive input into decision-making processes; to keep participants involved and engaged and so promote the success of the project by mitigating the possibility of people withdrawing; to manage risk and to raise awareness. It is essential, however, to understand that there is no such thing as a one-size-fits-all model and any engagement exercise must be very clear in its purpose and also reflect the nature and the needs of the project.
- c. Identify opportunities and challenges of involvement for UK Biobank, through the use of specific examples:
 - i. Cloning
 - ii. Re-contact
 - iii. Broader equality issues
- d. Address in turn the specific models of involvement and highlight the pros and cons associated with each.

The EGC’s Modus Operandi details that ‘the Council may, in due course, choose to include up to two UK Biobank participants in its membership’. The Council will return, at a future date, to the question of whether future recruitment processes should specifically target participants.

ACTION: The draft report will be revised and published in due course. [AH]

EGC review

People Science and Policy (PSP) Ltd has been commissioned by the EGC's funders to carry out a stakeholder survey and a literature review of the EGC's activities to date. The findings will be reported to the funders in April 2010 and will inform the discussion of the independent EGC Review Panel with whom Professor Laurie will meet in May. The EGC will be given the opportunity to respond to PSP's findings.

4. Funder proposal for participant re-contact

As part of the EGC review the funders plan to commission PSP to undertake focus group consultation work with a selection of UK Biobank participants. Section I.B.5 of the Ethics and Governance Framework (EGF) states that 'decisions on whether re-contact is appropriate for particular proposals will be made by UK Biobank with advice from the EGC and will be subject to Research Ethics Committee approval'.

At the funders request the Council discussed:

- the appropriateness of their draft re-contact proposal, in light of the provisions of the EGF and the expectations and consent of UK Biobank participants;
- how UK Biobank and the funders should address issues around re-contact for the purpose of reviews of this nature in the future;
- the draft proposal overview (including objectives, methodology and associated invite materials) and whether the review should be considered audit or research.

ACTION: The Secretary will compile a list of conclusions and recommendations to be circulated to the funders and UK Biobank. [AH] (see Annex A).

5. Closed discussion on topics to discuss under item 6

Members raised questions to be discussed under the following item.

6. Update from UK Biobank (Dr Tim Sprosen and Mr Jonathan Sellors, UK Biobank)

The Chair welcomed Dr Teri Manolio as an observer at the meeting. Dr Manolio is a physician and Director of the Office of Population Genomics, National Human Genome Research Institute (NHGRI), USA and a member of UK Biobank's International Scientific Advisory Board. The NHGRI led the participation of the National Institutes of Health (NIH) in the International Human Genome Project. Dr Manolio is visiting the UK to look at the scientific, operational and governance arrangements that have been adopted for UK Biobank to inform the NIH as it assesses the feasibility of establishing a similar cohort. She explained that one of the first steps is to look at the possibility of establishing an American Ethics and Governance Framework.

General update on developments and recommendations from EGC21

442,000 people have agreed to participate in UK Biobank and recruitment is expected to complete by the end of June/early July, six months ahead of schedule. The final six assessment centres will stay open until the end of recruitment (with the exception of Liverpool which will close in April):

Assessment centre	Numbers recruited so far
Liverpool	31,000
Hounslow	19,500
Sheffield	17,000
Croydon	13,000
Birmingham	8,000
Swansea	300

A mobile assessment centre was recently launched in Swansea by the Welsh Health Minister and Swansea Lord Mayor. Funded by the Welsh Government, the centre accommodates approximately 40 participants per day for a visit length of 2 hours (including all of the standard elements of the baseline visit except the fitness test).

Enhancements

All of the baseline enhancements have now been added to the assessment visit of all assessment centres (including a fitness assessment and photographs of the eye).

A prototype watch-style activity monitor has been developed and will be available for use by the project at the end of 2010. UK Biobank plans to re-contact and ask participants to wear the device for 7 days before returning it to the project.

Over 40,000 participants have completed the web-based diet questionnaire as part of their baseline assessment visit. Taking 15 minutes to complete, the questionnaire captures a diet history of the participant's previous day. Given the need for repeat measurements UK Biobank intends to re-contact participants by email approximately 4/5 times in a 12 month period, requesting that they complete the questionnaire at home (60 – 70% of participants provide email addresses). A piloted of this re-contact will take place in the next few weeks to assess what proportion of sent email requests are delivered and if and when participants respond. This information will help UK Biobank to optimise the timing of requests and to manage the subsequent flow of traffic to the questionnaire website.

UK Biobank's International Scientific Advisory Board (ISAB) met recently to review the project's progress with recruitment, the core funding proposal and the imaging protocols for the proposed re-assessment visit. On the latter point the ISAB discussed what additional measures might be incorporated into the re-assessment visit to make it even more valuable. For example, an enhanced phenotype might be gained (e.g. of blood pressure) through the use of more sophisticated measures than those used at baseline.

UK Biobank review

UK Biobank will submit a funding renewal proposal to the funders in April with a decision expected in September 2010. The proposal covers the next 5 years of operation and includes details of the following:

- Maintenance of the resource (e.g. the co-ordinating centre).
- Use of the mobile centre to repeat the baseline assessment in 20/25,000 participants every 3/4 years.
- Development of the IT systems to integrate various data types (e.g. assessment centre, sample-related and follow-up data) and to manage the access process (including the provision of an interface for research users to access the resource).
- Follow-up of participants through their health-related records (including record linkage and outcomes validation). Arguably a potential weakness of large scale population studies is poor phenotyping of health outcomes compared to baseline exposures. By improving the quality and detail of the information on health outcomes UK Biobank aims to maximise the scientific value of the resource. In terms of statistical power, specificity is much more important than sensitivity (that is, it is less important that all myocardial infarctions are captured but very important that captured myocardial infarctions are validated and subject to detailed classification). An Outcomes Working Group has been convened to advise UK Biobank on the processes for validation of disease outcomes among participants. UK Biobank aims to have the outcomes reviewed and validated in time for the first nested case-control research access requests (which are expected in 3/4 years time).
- The project's website will be redesigned so it can be used to keep participants informed about progress and to engage researcher and public communities.
- UK Biobank's proposed imaging re-assessment visit is described in the renewal proposal although it is not the subject of the application. It is intended to submit the application for the re-assessment visit for initial review by the ISAB in October and then for funder review by the end of 2010, with initial funding for a pilot study involving approximately 4,000 participants and thereafter for the full 100,000 participant study. Two expert meetings are planned for May 2010 to consider (1) the proposed cardiac and whole body protocols and (2) the proposed brain protocol. A technical discussion of the project's proposal is ongoing via a Google Docs page, the details of which Dr Sprosen offered to share with the Council after the meeting. UK Biobank will revisit and review the imaging incidental findings protocol and will circulate this to the Council for its review and input in advance of the funding application.

Access and intellectual property procedures

UK Biobank's ISAB and Steering Committee have reviewed the project's skeleton access and intellectual property (AIP) procedures, the further development of which depends on progress in three key areas: (1) the process of ethical review of access applications (i.e. the decision on whether or not UK Biobank will seek Research Tissue Bank approval); (2) development of the IT systems and (3) follow-up of participants through health-related records (including what data will be accessed and how it will be validated). UK Biobank is actively considering each of these areas.

Procedures for cross-sectional access requests will be produced in the first instance and should be finalised in the first quarter of 2011. Procedures for case-control access requests will be developed at a later date.

ACTION: A meeting between UK Biobank and the EGC AIP subgroup was proposed for mid/late May 2010 prior to the next EGC meeting in early June. It is hoped that it would be possible to discuss the draft procedures at this time. [AH]

The funders have advised UK Biobank to take a rigorous and cautious approach in the early phase of access and recommend that the Access Committee (AC) has the opportunity to view all applications. The Council has previously recommended the use of an interim AC which would serve during the development and early access phase. Such a body might help to navigate the route to access and to lay down the application filtering process. Ultimately the work of such a body might cease, or be replaced by a permanent AC, but in the first six months the body could usefully review all access applications. Ultimately it is a matter for the Board of Directors to decide the remit of the AC.

UK Biobank is open to proposals for access and envisages that initial review will be based on a summary proposal, rather than a long form scientifically justified application being submitted in the first instance. The website will be key to providing information to researchers about the types of data held by the resource and to give advanced notice about when the resource will become useful for particular diseases.

Information systems development, CTSU audit and ISO 27001 stage 1 assessment

UK Biobank has identified aspects of the IT system that require further development including an extension of the systems by CTSU to allow them to be used for future repeat assessment visits and development of UK Biobank's laboratory database. In addition a number of applications will need to be developed, including:

- Access management tool (an online application that is able to track applications)
- Data management and integration tool
- Events validation tool

The likely costs of development will be included in the funding renewal proposal. While funding has not yet been secured, no parties have been commissioned to undertake this work. It may be the case that certain developments, such as the events validation tool, will be put out to external tender. In relation to events validation, UK Biobank is consulting with a number of academic groups and experts who work at the forefront for specific diseases, including members of the Outcomes Working Group.

At its December meeting the Council was reassured to learn that an audit of the IT systems and procedures within CTSU that relate to UK Biobank would be commissioned and would report in early 2010. The Council understands – and agrees – that the initial audit quote was prohibitively expensive and that the scope of the review has subsequently been revised, and the cost decreased accordingly. Despite the decreased cost, members were informed that UK Biobank cannot

commission the audit in the short term due to budgetary constraints. UK Biobank is committed to carrying out the audit as soon as finances are made available. (See closed discussion under item 7.)

UK Biobank successfully passed the ISO 27001 stage 1 assessment and a related inspection of the Sheffield assessment centre. Dr Sprosen offered to provide further information after the meeting regarding the outcomes of the stage 1 assessment and an update on UK Biobank's progress through the accreditation process.

Mr Sellors proposed that UK Biobank prepare a short presentation for the Council's 7 June meeting, outlining the project's plans and progress in relation to the IT systems development. Members were grateful for this suggestion.

Imaging visit and incidental findings protocol¹

UK Biobank's ISAB will meet in October 2010 to review the project's detailed MRI proposal. UK Biobank's proposal will also be sent to the Council for review at that time.

Biannual report on longitudinal follow-up of participants

The overall strategies for longitudinal follow-up will be the same across the UK, but the detailed approach for record linkage will necessarily be different in Scotland, Wales and England:

- Scotland: The current pilot involves linkage to a number of national and primary care level records for 20,000 Glasgow-based participants including death/cancer (Information & Statistics Division), hospitalisation (Scottish Morbidity Record) and primary care data (including pharmacy, laboratory and imaging) (Scottish Enhanced Functionality). UK Biobank has received the agreement of the Privacy Advisory Committee for this linkage. In order to facilitate the linkage to primary care data, a Read code will be inserted into the participants' record and the GP note to flag their involvement in UK Biobank.
- Wales: A pilot is planned for Wales involving 18,000 Cardiff-based participants and linkage to death/cancer (Health Solutions Wales (HSW)), hospitalisation (Patient Episodes Database for Wales) and primary care records. HSW acts as an honest broker service by holding individual identifiers through which linkages can be made to anonymised medical and health-related records held by the Health Information Research Unit (HIRU). UK Biobank has provided HSW with the NHS number, name, address and an anonymised linking code for those participants involved in the pilot. HSW will in turn provide HIRU with an anonymised linking variable to facilitate linkage to the anonymised records after which the data will be sent to UK Biobank.

¹ This subject was covered in the general update.

- England: UK Biobank has received approval from the NHS Information Centre to centrally upload death and cancer records (for both England and Wales). Having recently tested the process with dummy data, the participants' records will be uploaded shortly in batches of 50,000. Once uploaded, UK Biobank will receive monthly notification of deaths in each of England and Wales (with notification including those participants who were recruited in Scotland if they die or develop cancer whilst living in England or Wales). Linkage to hospitalisation records (Hospital Episodic Statistics) is expected to take place towards the end of 2010 while linkage to primary care data, through the GP extraction service (GPES)², should take place in the first 6 months of 2011.

UK Biobank plans to establish links with NHS health records before considering which records might fall under the wider interpretation of 'health-related'. Expert views will be sought (e.g. from social scientists) to inform the decision of which other records to access (e.g. occupational health). It is likely that any such linkage would occur via an Honest Broker System.

Funder proposal for participant re-contact

The Chair updated UK Biobank colleagues on the morning's discussion and confirmed that the Council considers re-contact for this type of work – being a form of participant engagement for audit of governance – as appropriate in terms of the Ethics and Governance Framework. The Council emphasised the importance of managing this process with care since it is the first time that re-contact for this purpose has been contemplated. Members offered to review the revised proposal from the funders and to provide feedback as soon as required.

UK Biobank equality audit

UK Biobank has commissioned an independent equality consultant to analyse available data regarding participation in UK Biobank across the 'equality strands' (ethnicity, gender, sexual orientation, transgender, disability, faith and belief, age (within the 40- 69 age band), and socio-economic position). Considering each of the functions of UK Biobank, the report recommends actions to increase participation among groups that, on the available evidence, are less likely to participate.

Dr Sprosen commented that in the context of UK Biobank the project goes to great lengths to facilitate participation by all those who receive an invitation. Some shortcomings in the recruitment process are recognised, however. For example, the touch-screen questionnaire may present a barrier to individuals who are visually impaired and, while core consent materials have been translated into several languages, the touch-screen questionnaire has not.

The following was discussed:

The report concludes that it was not possible, from the available data, to establish whether UK Biobank includes a representative proportion of disabled people. Given

² GPES is a new service which is expected to deliver at the end of 2010. Its primary purpose is to access information in electronic patient records held in general practice clinical computer systems to help inform and deliver improvements in healthcare. UK Biobank will be one of the first research users of this service.

the high morbidity for long-term disabled individuals, members enquired if anything could be done during the final recruitment phase to promote their participation. Disabled people would generally be recruited through home visits, which is something that has not been possible for UK Biobank to date but is not precluded for the future (if a scientific rationale could be put forward as part of a funding request).

The data shows that people in the lowest Social Economic Status tertile have been less likely to participate in UK Biobank. Also, a comparison of the ethnicity of UK Biobank participants with UK statistics shows that there is a lower percentage of Asian and black people participating in the project compared to the demography of the country. Although the pattern of response for both groups varies across each of the centres, the overall impact has been that there are proportionately fewer participants in this tertile and from these ethnic groups compared to their number of in the general population. UK Biobank is addressing this issue through the location of its assessment centres and hopes to have redressed the balance through the placement of the remaining centres. (The report's findings relate to the first 250,000 participants and so the overall profile of the current 442,000-participant cohort could vary significantly from these findings.)

Biocentre

Mr Sellors offered to provide further background and information, at the Council's 7 June meeting, regarding UK Biobank's plans to establish a Biocentre to act as a storage and retrieval service for other research initiatives.

7. Closed discussion of matters arising under item 6³

Members reflected on the discussion with colleagues from UK Biobank and agreed the following:

Information systems development

While assured that UK Biobank remains committed to the CTSU audit, members were disappointed that the audit is being postponed at this stage. The Council recommends that the audit be progressed as soon as feasible in order to provide an assurance to UK Biobank and its stakeholders about CTSU's security provisions.

ACTION: The Council will ask UK Biobank to address a list of specific questions and issues as part of its proposed presentation on the development of the project's IT systems. The questions will be bound by the EGC's remit. [AH and Information Security subgroup to develop the list.]

³ Separate to the formal aspect of the meeting, the Chair proposed that the Secretary pull together all the changes that are required to the EGF (in light of the re-contact discussion and the recent enhancements etc) and suggest to UK Biobank that these be addressed once the renewed funding bid has been submitted.

UK Biobank equality audit

The Council was pleased to have sight of the Equity Report regarding participation in UK Biobank. While understanding that UK Biobank's scientific objective is to collect generalisable and not representative data and samples, the Council considers it important from a prudential and political viewpoint that UK Biobank aims to be as inclusive as possible. Therefore, it is recommended that UK Biobank demonstrates further serious attempts to overcome barriers to participation for those individuals identified by the audit report as having been under-recruited, or for which no data was available but under-recruitment is likely (e.g. Asian and black people and those with disabilities). Further, it is recommended that the project make every effort to address the outcomes of the audit. UK Biobank might find it useful to contact local organisations and individuals for advice on how to reach particular groups e.g. the Local Authority Adult Services, Equality and Diversity officers etc.

ACTION: The Secretary will compile and circulate previous Council discussions regarding the representativeness / generalisability of the UK Biobank cohort. [AH]

8. Communications activities

External speaking opportunities

Professor Richards will speak at the King's Health Partners Information Governance Conference in May.

External enquiries to the EGC

Members were informed about a recent complaint regarding the accessibility of participation in UK Biobank for visually impaired individuals. Having sought approval from the complainant, the Council addressed a number of questions to UK Biobank and shared with them the letter of complaint. UK Biobank's response was subsequently provided to the complainant. The correspondence concluded with a request from the complainant to be sent a copy of UK Biobank's Equity Report. The Council has passed this request on to UK Biobank.

EGC members' MRI paper

A number of EGC members have written a paper that draws together the Council's analysis and discussion regarding the ethical implications of MRI imaging in a biobanking context. Members agreed that:

- The paper should address the main ethical considerations which are likely to arise for any biobank project that includes MRI, rather than focus on UK Biobank's proposal (the details of which are under development).
- The paper should most likely be submitted for publication on behalf of the Council, rather than by the members acting in their individual capacity. The final draft will be circulated to the Council shortly for endorsement.
- The paper offers the EGC an opportunity to share its deliberations with a wider audience and to contribute to broader debates through its work.

9. Report on meetings attended

*Meeting with researchers working for the Mitsubishi Research Institute, Japan
16/12/09*

The Chair, Professor Richards and the Secretary met with researchers working for the Mitsubishi Research Institute (MRI), Japan. MRI is conducting research for the Japanese government regarding the management of ethics and the operation of ethics committees in relation to a number of areas of research.

Meeting with researchers of the film 'Golden Genes' 06/01/10

Professor Richards, Professor Ian Hughes and the Secretary met with film makers from Vienna who were undertaking research for their new film project 'Golden Genes'. The documentary is intended as a full feature film of 90 minutes dealing with the topic of biotechnological and genetic research and the role of biobanks (including plant, animal and human resources).

Meeting with Dr Chekar from Cardiff University working for BBMRI 11/01/10

The Secretary met with Dr Choon Key Chekar, a researcher from Cardiff University who works on the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) ELSI Work Package. Dr Chekar was interested to learn about the Council's workshop on public involvement.

HGC/AHRC seminar 'Understanding genetic discrimination' 28/01/10

Ms Tracey Phillips attended the Human Genetics Commission (HGC)/Arts and Humanities Research Council's (AHRC) seminar 'Understanding Genetic Discrimination'. The seminar aimed to develop the HGC/AHRC's understanding of what 'genetic discrimination' means today, by analysing the historical, philosophical, legal and social dimensions of unfair discrimination and exploring how this relates to genetic difference.

HGC meeting 'Personal genetic profiling: the next 10 years' 09/02/10

Mr Andrew Russell and Professor Richards attended the HGC's annual 'forward look' meeting on the subject 'Personal genetic profiling - the next 10 years'. Speakers addressed the anticipated advances in this field, their applications, and their implications for individuals and society. The meeting was intended to inform preliminary HGC advice to government ministers.

*Institute for Cancer and Immunology, 'Techniques in Cancer Genomics Symposium'
25/02/10*

Professor Laurie gave a presentation at a recent symposium of the Institute for Cancer and Immunology entitled 'Ethics and Privacy in Genome Research'.

10. Any other business

A member proposed that the Council might write a paper on the topic of representativeness and population biobanks. The Council agreed to return to this proposal at its next meeting.

Members discussed the details of the evening's public meeting.

11. Date of next meeting

7 June 2010 - Council meeting, London

12. Dates for 2011

14 March, 13 June, 26 September, 12 December.

Annex A Funder proposal for participant re-contact

Broad aspects of re-contact

Conclusions

- Re-contact for this type of work – being a form of participant engagement for audit of governance – is appropriate in view of the consent and expectations of UK Biobank participants and in terms of the Ethics and Governance Framework (EGF). While participants consent for their data and samples to be used for 'health-related research', they provide consent to be re-contacted by UK Biobank for a wider variety of reasons, including the possibility of being asked to consent to research that falls outside of their original consent.
- It is a reasonable interpretation of EGF Section I.B.5 (as it stands) that UK Biobank is the principal decision-maker on the appropriateness of re-contact, with advice from the EGC and subject to REC approval.
- The Council is hopeful that it will not be necessary to go back to the REC in every single circumstance of research for audit (either by the funders or UK Biobank). UK Biobank is advised to seek clarification from the REC regarding its duties to report and seek approval for re-contacts of this nature (see recommendations below).

Recommendations

- The Council recommends that the EGF section I.B.5 be revised to incorporate provision for quality control, audit and regulatory inspection. In particular the re-wording should clarify:
 - whether or not all proposals for research for audit require REC approval.

A literal interpretation of section I.B.5 of the EGF would suggest that every individual proposal for re-contact requires separate REC approval. Under a less literal interpretation the phrase 'particular proposals' might encompass a category of proposals (e.g. research for audit purposes).

The Council recommends that UK Biobank seek the REC's view on whether the current proposal should be considered as research or audit. Further, UK Biobank should seek clarification regarding whether or not REC approval is necessary for every case of this type of work (conducted by the funders or UK Biobank).

- that the provisions in the EGF should not present a barrier to legitimate audit by the funders.

The Council recommends that the following text be added as a second sentence to the final paragraph of section I.B.5 'These provisions will not preclude the project's funders from carrying out legitimate audit of UK Biobank or its governance structures'.

- The Council recommends that UK Biobank address the issues of quality control, audit and regulatory inspection in the draft Access and IP procedures and policy.

The draft proposal for re-contact

Conclusions

- It is appropriate and right for UK Biobank to approach this proposal with care given that this is the first time that participants are being re-contacted and invited by UK Biobank to take part in face-to-face sessions. This needs to be done correctly and be seen to be done correctly applying appropriate standards. As part of those appropriate standards the participants need to be reassured that their data are being handled confidentially and told why they were selected by UK Biobank.
- It is appropriate that REC approval is sought for the current proposal.
- On the audit and research distinction, *audit* was understood to be a means of assessing standards and processes while *research* was considered to encompass the creation of generalisable knowledge and to address a hypothesis. Given that the proposal involves ascertaining opinions on the governance of UK Biobank and the current and possible future roles of the EGC, members considered the proposal to be more akin to research, albeit for audit purposes. Further, if the funders plan to publish the focus group findings this moves the proposal closer to research. The REC should be consulted for its view on this distinction in relation to the current proposal.

Recommendations

- The focus groups will investigate the EGC in the context of UK Biobank's governance more broadly. It is entirely appropriate that the EGC is not represented during the focus group work. Further, in order not to inhibit or potentially bias the discussion the Council recommends that the provision of accurate written material and an independent observer (with background in social research and who is knowledgeable about UK Biobank) would be preferable to having an observer from UK Biobank. The presence of a funder representative at the focus group meeting was considered appropriate and unproblematic.

The draft proposal materials

Conclusions

- The current materials produced by PSP are not sufficient for the EGC to provide a proper review of the proposal. More information is required on how the focus groups will be conducted. PSP's tightly-timed agenda and written note regarding UK Biobank and the EGC should be sent to both UK Biobank and the (Chair of) EGC as soon as possible. It is noted that such materials will be needed for an application to the REC.
- The Council is ready to comment, and provide feedback, on the detailed proposal as soon as required.

Recommendations

- The invitation letter should re-assure participants that no-one other than UK Biobank has any access to identifiable data (that should be explained in clear lay language).
- The invitation should indicate that a random selection has been made by UK Biobank of participants who live close to the proposed venue for the focus groups.
- The invitation should explain that PSP will only ever know information provided on the Reply Form if a participant decides to put their name forward for the focus group session.
- The letter of invitation could be re-worded to be more 'lay language' (for example paragraphs 2 and 3 are too high level with mention of public policy etc.) Paragraph 2 should be the place where they are invited to join a focus group and are re-assured about selection criteria and data confidentiality. Then the purpose of the focus/discussion group can be outlined, again in lay language.
- The Reply Form heading "UK Biobank Review" could be misleading and intimidating. This is not a review of UK Biobank but of the EGC. Maybe "Meeting for UK Biobank Participants" (or similar) would be better.

- On the Reply Form: It is important to think very carefully about the sentence "I understand that the information I provide will not be used for any other purpose than to help the funders of UK Biobank in their review of UK Biobank" First, it is not a review of UK Biobank itself but of an element of its governance structures; more importantly, this sentence is too restrictive. The funders ought to be able to disseminate a report via public presentations or on websites provided no personally-identifiable views or other details are included. It is strongly in the interests of transparency that the funders be able to do so.