

**Report: Public meeting of the UK Biobank Ethics and Governance Council
11th June 2007
Nowgen, Manchester**

Professor Graeme Laurie, Chair of the UK Biobank Ethics and Governance Council (EGC), opened the public meeting by welcoming everyone and introducing his co-speakers: Dr Bill Lowrance (independent consultant in health policy and ethics), Professor Rory Collins (Chief Executive Officer and Principle Investigator, UK Biobank) and Professor Martin Richards (EGC member).

Four presentations followed: an introduction to biobanking; background and progress regarding the UK Biobank project; an introduction to the EGC and its work and an overview of the EGC communications subgroup discussions.

1. Introduction to biobanking (Dr Bill Lowrance)

Dr Lowrance addressed the following questions:

- What are biobanks? How new are they?
- How diverse are health research biobanks?
- How does UK Biobank fit in the international scene?

1.1 What are biobanks? How new are they?

Originally, and often still now, the term 'biobanks' refers to collections of biospecimens which are available for some dispersive use (as compared with archival reference use). More recently the term has come to include collections of biospecimens along with related health and/or social information to be used in research. Often these biobanks are accumulated in the course of clinical care, and are often closely held by those who created the collection. The most robust contemporary definition of 'biobanks' is "rich collections of data plus biospecimens, specifically developed as resources for research".

Many data collections are gathering or linking to biospecimens, and conversely many biospecimen collections are gathering or linking to health data. Some biobank-like collections are being cast as "genebanks," and others as "genome-wide association databases."

1.2 How diverse are health research biobanks?

There are many population-based health research biobanks with diverse aims and designs. For example:

- Long-term cohorts (Avon Longitudinal Study of Parents and Children, ALSPAC; UK 1946, 1958, and other birth cohorts).
- Gene-disease association resources (US Genetic Association Information Network, Genetic Alliance BioBank, Wellcome Trust Case Control Consortium...).

- Some twin-study collections (genomEUtwin...).
- Some clinical trial collections.
- A defunct biobank: Tonga.
- Biobanks in operation: Iceland, Estonia, Japan, etc. (not all of these biobanks have full, high-quality data plus specimens, and several have suffered serious setbacks).
- Biobanks under development: CARTaGENE in Quebec, Western Australian Genome Health Project, Danubian Biobank Consortium, Karolinska Institute Biobank, Generation Scotland, and lots more.

1.3 How does UK Biobank fit in the international scene?

- It shares and compares its experience with others; but basically, it is developing in its own way.
- It is perhaps the most ambitious true biobank initiative – in its scientific scale and comprehensiveness, its *de novo* prospective design, and its tending to openness, ethics, and governance.
- Aspects of the Ethics and Governance Framework are being adopted by many others, and the concept of the EGC is widely admired.

Closing remarks:

- Core concerns with all banks are structure, security, return on investments (both the bank's and its clients'), stability, and trust.
- Inevitably, UK Biobank will have a very long startup lag-time and demand great patience on the part of its sponsors, managers, scientific partners, participants, the EGC, and everybody else.
- During this startup time it is important that we do not lose sight of the purpose of all this, to build resources for health research which aim to improve the health of future generations.

2. UK Biobank (Professor Rory Collins)

Professor Collins presented the design of UK Biobank, the process and scientific basis of the core elements of the assessment centre visit and the strategy for access to the resource.

2.1 Prospective study design

In 1951 Sir Richard Doll began a prospective study of smoking and health in British doctors. At the onset of the study, and periodically thereafter, 34,000 UK doctors were asked what they smoked. During the course of the study all deaths were recorded over a 50 year period (1951-2001). The study's main findings (for men born in the 20th Century) were that smokers lose, on average, 10 years of healthy life and that stopping smoking works (ex-smokers who stopped at age 35-44 gained 9 years).

UK Biobank is also a prospective study that, as compared with the 34,000 people involved in Sir Richard Doll's study, aims to involve 500,000 UK men and women

aged 40-69 years. Although it is not a novel concept in its own right, UK Biobank should generate a richness of data which sets it apart from other studies to date. The project will accumulate extensive baseline questions and physical measures along with stored blood and urine samples in order to allow many types of assay in the future. Repeat assessments will occur over time in subsets of the participants to allow for sources of variation (and the potential for other enhancements to the information that was initially collected). UK Biobank will seek broad consent from participants for follow-up through all health records and for all types of health research that fit the project's purpose. Over time participants will develop certain illnesses. The target participation rate of 500,000 is a sufficiently large number of people developing different conditions to assess reliably the causes of a wide range of different diseases.

2.2 Baseline assessment

There are three elements to the baseline assessment of participants: a questionnaire, physical measures and biological samples.

The strategy for questionnaire selection has been informed by the following:

- The public health importance of the relevant condition.
- The likely importance of factors for main effects, or as confounders and sources of bias.
- The reliability and validity of questionnaire measures.
- The lower threshold for inclusion on touch-screen than in interviewer questionnaire.
- The availability of alternate sources of information about the factor (e.g. previous medical and other health-related records; physical measurements; biological samples; internet diet/activity diaries).

The strategy for physical measures selection has been informed by the following:

- Whether or not previous studies have indicated that the measure was relevant (i.e. associated with important health outcomes).
- The chosen method should be reliable (e.g. calibration system; ease of training, use, monitoring and maintenance; direct data transfer to computer).
- The feasibility of conducting measures within about 20 minutes (given limitations of available resources).
- The opportunities for enhancement (such as intensive phenotyping in subsets of participants at baseline and/or at periodic re-assessments over time).

The strategy for sample collection and handling has been informed by the following:

- Blood and urine are being collected because of the wide range of possible assays and wide physiological coverage that these samples allow.
- There has been a careful choice of anticoagulants and preservatives to allow widest possible range of potential future uses.
- Detailed pilot studies have been undertaken to show that sample processing procedures allow very wide range of assays.

- Storage facilities (automated -80°C and back-up liquid nitrogen) provide physical security and reliable tracking of individual samples.

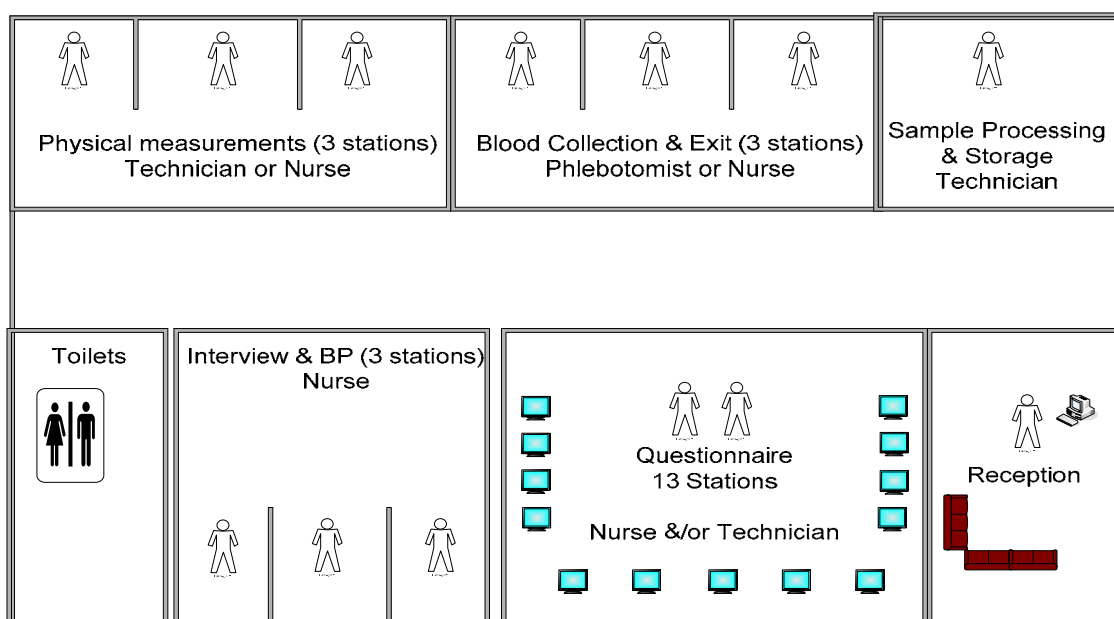
2.3 Invitation to participate and the assessment centre visit

UK Biobank generates invitations to participate by processing, in confidence, contact details from central registries. The project's central invitation and appointment system aids high throughput and smooth running of the assessment centres, and reduces costs. UK Biobank has the potential to over-sample particular groups (e.g. age, sex, deprivation) through the central invitation strategy and through selective location of assessment centres.

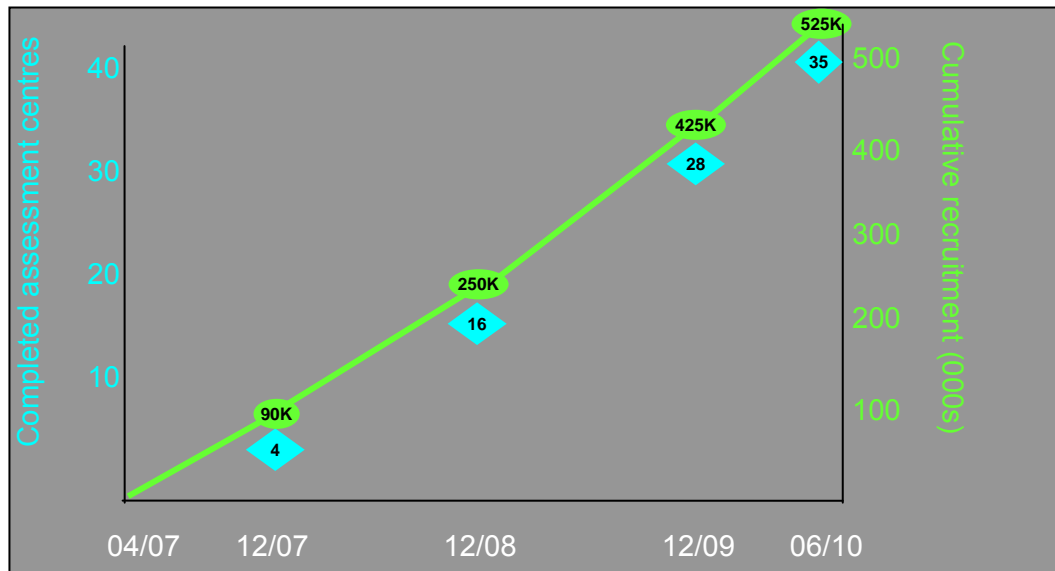
UK Biobank had recognised the potential sensitivity surrounding the project processing potential participants' contact details (albeit in confidence). As an indicator of potential participants' concerns regarding the project, those who chose to decline participation during the pilot phase of the project were requested to provide their reasons. Of the approximately 10,000 people who responded to the invitation letter by declining to participate, 70% provided their reason. Of the 7,000 people who provided their reason for declining participation only 56 people stated concerns over the invitation (e.g. an invasion of privacy). This represents 0.1% of all invited individuals, suggesting that the method of invitation is broadly acceptable to potential participants.

Strategies have been developed which aim to increase attendance rates. For example, a number of mailings are sent to potential participants subsequent to the initial invite (e.g. appointment confirmation, pre- and post-visit reminders). Also, the project aims to raise awareness about the project locally (e.g. through the local news stories or advertisements).

UK Biobank has created a streamlined assessment centre flow with the aim of accommodating approximately 110 people per day. The lay-out of the assessment centre is as follows:



Experience has shown that each person will take, on average, 90 minutes to complete their assessment centre visit. Once the project is fully operational there will be six assessment centres recruiting concurrently in different regions of the UK at any given time. Recruitment is expected to continue until mid-2010 during which time a total of 35 centres will have been in operation with a target recruitment total of approximately 500,000 people (see the table below).



2.4 Strategy for access to the resource for health-related research

It is anticipated that the UK Biobank resource will chiefly be used for a series of case-control studies of different outcomes within the cohort (using anonymised data sets and/or samples). A timetable will be developed to indicate when sufficient cases of each condition are likely to have occurred (which could be many years from now; e.g. 10 years). Based on this timetable, UK Biobank will coordinate calls for efficient use of the resource, allowing researchers to develop proposals against this indicative timetable. Disease-specific proposals will be reviewed by independent expert groups, while a national Access Committee will advise UK Biobank on prioritisation. The EGC will advise on, and monitor, the access process.

3. The Ethics and Governance Council (Professor Graeme Laurie)

Professor Laurie addressed the following questions:

- How and why was the Council formed?
- What is the purpose of the Council?
- What are the recent activities of the Council?

3.1 How and why was the Council formed?

The Council was established in November 2004 through a publicly-advertised, open appointments process in keeping with the Nolan Principles of Public Life. There are

currently twelve members who come from a number of disciplines including law, ethics, biomedical science, policy, consumer issues, and lay representation. The initial idea of the Council came about during early public consultation work regarding the proposed resource. The need for independent oversight was raised during the consultations as an important element of UK Biobank’s governance structure. The Council was subsequently established to act as the independent guardian of UK Biobank’s Ethics and Governance Framework (EGF). This Framework describes a series of standards to which UK Biobank will operate during the creation, maintenance and use of the resource. In addition, it elaborates on the commitments that are involved, not only to those participating in the project but also to researchers and the public more broadly. Three key areas which are identified in the EGF are the ‘3 C’s’: consent, confidentiality and commercialisation.

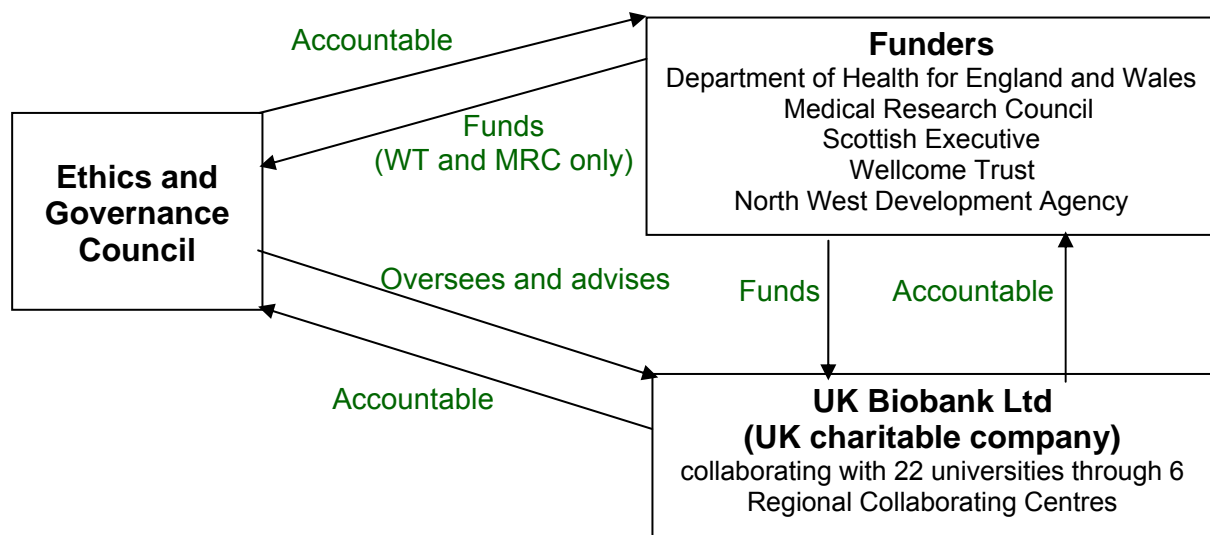
3.2 What is the purpose of the Council?

The remit of the EGC is:

- To act as an independent guardian of the EGF and advise on its revisions;
- To monitor and report publicly on the conformity of the UK Biobank project with the EGF;
- To advise more generally on the interests of research participants and the general public in relation to UK Biobank.

The Council is also charged to advise UK Biobank on any policies which relate to or flow from the EGF, for example those relating to recruitment, access to the resource or complaints handling.

The EGC’s relationship with UK Biobank and its Funder can be found below.



As the EGF states, in advising, reviewing and reporting on UK Biobank’s activities, the EGC will serve as a “mirror” for UK Biobank, providing critical and constructive advice. Normally the Council will communicate its reflections informally. If the Council is not satisfied with UK Biobank’s response, it could make a formal

statement of concern. It could escalate concerns, if necessary, by making a public statement that UK Biobank should or should not take certain action.

It should be noted that the EGC is independent of UK Biobank (i.e. it is not the project's internal ethics advisory body). As such, there are a number of activities and responsibilities which do not fall to the EGC but to UK Biobank itself. For example, the Council has not been established to:

- Assume responsibility for the ethical management of the resource;
- Speak on behalf of UK Biobank (instead the Council speaks *about* UK Biobank);
- Own and develop the EGF and associated policies.

3.3 What are the recent activities of the Council?

The Council has engaged in a number of recent activities including:

- Advised on the project's participant materials. UK Biobank has developed its participant materials over the last year and the Council has provided comment and advice throughout this period. Key points include the suggestion that, as per the requirements of the EGF, the materials should include the word 'commercial' before specifying that 'companies' are likely to apply for access to the resource. Stating only the word 'company' permits a possible ambiguity over who might apply (i.e. 'company' might be taken to mean a charitable company). In addition to being explicit about the possibility of commercial access the Council considered it important for potential participants to be informed that they will not financially benefit from their participation (beyond reasonable travel expenses). The Council therefore recommended that the consent form should state that participants 'will not benefit financially from taking part (for example, if research leads to *commercial* development of a new treatment)'.
- Advised on the project's standard operating procedures (SOPs). The Council has reviewed and advised on several of UK Biobank's SOPs, including how incidental findings (for example, significantly high blood pressure) made during the assessment visit will be managed by UK Biobank staff; how capacity of potential participants will be judged, and how complaints and enquiries will be handled.
- Commissioned work to inform the Council's advice giving. The Council has recently commissioned two studies; a scoping study of research conducted on public attitudes to biobank-related issues and a conceptual analysis of the 'public interest' and 'public good'.

The former study summarised the research that has already been conducted in this field and highlighted the main comments and concerns arising from this research. The study also identified gaps in the current literature, allowing the Council to then consider the need for further public attitude research. As a result of this scoping study the Council has recently sent out an invitation to

tender for an exploratory project to study opinions regarding the terms of 'third party' access to UK Biobank.

The analysis of the concepts of the 'public interest' and 'public good' is intended to inform the operation of the Council. For example, the Council's remit states that it will advise on the interest of the general public, but what does it mean to advise in this way? Further, the Access and Intellectual Property Policy of UK Biobank states that the resource will be managed as a resource for the public good. In order to monitor and advise UK Biobank on applications for access to the resource the Council intends to develop a clear understanding of what the public good might mean in this context.

- Established a subgroup to advise on the development of project's Access and Intellectual Property Policy (AIP policy). UK Biobank is currently revising its AIP policy with advice from the Council. A subgroup of EGC members has been established to provide advice (including between Council meetings) drawing on the expertise of particular members with knowledge of this field. One round of advice and revisions has been conducted so far with further round of revision expected in the future.
- Established a subgroup to develop the Council's communications strategy. A second subgroup has been established to discuss and develop the Council's communications strategy, the activities of which Martin Richards will describe in the next presentation.

Professor Laurie concluded by stating that the three key messages regarding the EGC are:

- Independence
- Scrutiny
- Acting in the public interest

4. EGC communications subgroup work (Professor Martin Richards)

Professor Richards described the activities of the EGC's communications subgroup.

The subgroup is a new initiative of the Council and has met on one occasion so far. The subgroup used this initial meeting to discuss a number of 'foundational' aspects to a possible strategy, including:

- The values which should underpin the communications strategy. These were determined to be accountable, consultative, independent (promoted by transparent methods of working) and multidisciplinary.
- The aims of the communications strategy: To inspire trust and confidence, inform and shape the EGC's decision-making; shape public debate and promote good practice (in relation to good ethics and governance). The subgroup proposed that the aims are not of equal priority. The first two aims were considered to be a higher priority than the third. The aims will be

achieved in part by the EGC providing information to, and gathering information from, its key audiences.

- The key audiences of the EGC. In order of priority these were considered to be the participants of UK Biobank, the broader public and interested parties and the EGC's peer group (including researchers, charities, other committees, for example the Human Genetics Commission and the Human Tissue Authority).
- Methods of communication which might be employed in the strategy. A number of methods are currently employed by the Council; a web presence (where reports of the Council's meetings are published), production of an annual report, public meetings and commissioned research. These current activities are being considered alongside other methods such as holding Council meetings in public and participant representation on the Council.

During general discussion the subgroup had noted that the EGC is an advisory, not a decision-making body in relation to UK Biobank. In providing its advice the EGC will not be acting as an advocate for individual participants or members of the public but instead acting to safeguard the collective interest for the common good.

In developing a strategy it will be important to maintain clarity about UK Biobank and the EGC's roles and responsibilities with respect to communications about the project. As the Ethics and Governance Framework states 'The Council will not speak "on behalf of" UK Biobank, as this will be the responsibility of the Board; instead it will speak "about" UK Biobank.' There should however be an interface between UK Biobank and the EGC's communications strategies whilst remaining mindful of the Council's independence.

5. Question and answer session

In the second half of the session the attendees were invited to share with the Council their concerns, ideas or suggestions. The issues raised were either discussed by attendees at the meeting and the Council or were addressed by UK Biobank's Chief Executive, Professor Rory Collins.

The questions and comments touched on issues such as:

- Longevity of the Council

Q: Bearing in mind the long term nature of the resource, how do you know that the Council will still exist when the bulk of applications for access will be made (10 or 20 years hence)?

A: The Council was established by the Wellcome Trust and the Medical Research Council with a specific role in review applications for access to UK Biobank. Although we can not say for sure that the Council will continue to operate for the next 20 years, it seems unlikely that it will cease to function before being able to fulfil one of the key purposes for which it was established.
[GL]

- Accountability of the Council

Q: If the public is not happy with the running of the Council how can this be expressed?

A: The Council has a complaints policy through which participants or members of the public can raise concerns with the Council directly. Alternatively, comments can be directed to the funders of the Council, the Wellcome Trust and the Medical Research Council. [GL]

- Links with external stakeholders

Q: Has the EGC established any links with charitable organisations which conduct research in specific disease areas? People with particular conditions will have opinions on how the resource should be used.

A: This a good suggestion and could be very informative for the Council and UK Biobank for future engagement activities. For example, recent work in Edinburgh has shown that members of patient interest groups are willing to accept the involvement of commercial organisations in the research process, more so than members of the general public. The experience of such groups could help shape the work of the EGC. [GL]

- Relationship between UK Biobank and participants

Q: What is the specific contract between participants and UK Biobank?

A: The information leaflet and consent form are the basis of the contract between UK Biobank and the participant. For example, individuals are asked to allow UK Biobank to store their health related information and samples for many years. In turn the information leaflet states UK Biobank's commitment to maintain the highest levels of confidentiality of all data and samples. [RC]

- UK Biobank security

Q: What processes are being employed to safeguard data? How many people will have access to the key which links identifiable and reversibly anonymised data?

A: A number of measure will be in place, for example, information that might identify individuals (such as name and address) will be kept separate in UK Biobank's databases from other information about participants; computer security is being employed to block unauthorised access (e.g. by "hackers") to the computers that hold personal information; data or samples provided to researchers will not include personal identifying details. Access to personal information and the key that links this to other data and samples is restricted within UK Biobank to only those staff members that need it to fulfil the purpose of their job. Further, all staff sign confidentiality agreements as part of their employment contracts. [RC]

- Police access

Q: How will UK Biobank resist requests for access to data by the police and other bodies of authority? What are the legal requirements in this regard?

A: UK Biobank will vigorously resist such access to the resource in all circumstances. Access by the police or other law enforcement agencies will be acceded to only under court order. The outcome of such a court order is hard to predict as there are few legal precedents. [RC]

UK Biobank is treated the same as any other research project or database: all are subject to potential police inspection so long as the correct legal procedures are followed. For example, in Scotland those making a case for having access would have to show that access is necessary. UK Biobank does not represent a special case. [GL]

- Consent

Q: How does UK Biobank assess an individual's mental capacity to provide consent?

A: An individual's capacity to consent is judged by the assessment centre nurse during the first part of the assessment visit. The nurse considers whether the potential participant understands what they are consenting to (e.g. storage of samples, linking to their medical records etc). Where there is doubt the nurse will escalate the matter to the assessment centre manager and, where doubt still exists, to a senior member of the scientific team. [RC]

Q: What happens if individuals are unable to read and/or unable to read English?

A: Information material and the consent form are being translated into a number of languages. In addition, UK Biobank will be sensitive to the positioning of its assessment centres. For example, if these are placed in areas where certain ethnic minority communities live, UK Biobank will seek to recruit nurses from these communities. [RC]

UK Biobank has received positive feedback from a blind individual who recently attended the assessment centre. In such circumstances a member of the individual's family or UK Biobank staff can assist the participant through the recruitment process. [RC]

Q: Is it possible for individuals to provide informed consent given the undefined future uses of the resource? How has the EGC deliberated on this issue?

A: The Council has deliberated extensively on this issue, concluding that it is important for UK Biobank to describe to potential participants the parameters of what they are being asked to consent to. As such, while an individual is not informed about the specific future uses of the resource they are informed

about the range of uses, the certainties and the uncertainties surrounding the project. [GL]

Potential participants will require different levels of information regarding the project, some will want to receive a lot of information, some not so much. When people consent to an open-ended project like UK Biobank they are putting their trust in the organisations involved. [BL]

It is the role of the Council to engender this trust. [GL]

Practically, UK Biobank is conducting a post-visit survey of participants to ask them about their experience at the assessment centre and to test their understanding of consent. Results of this survey have indicated that participants have a good understanding of what it means to participate in UK Biobank and the various elements of consent. [RC]

- Feedback of health information

Q: Will descendants of participants be provided with any health indications?

A: Participants are provided with limited feedback from the physical measures taken during their assessment centre visit (e.g. blood pressure, pulse rate, height, weight, body fat and grip strength). No further individual feedback will be provided to them or their relatives. General research results will be made available to the participants and the public via UK Biobank's website. [RC]

Professor Laurie concluded the session by thanking the participants for attending and by inviting everyone to continue the discussion over a post meeting drink.