UK Biobank Ethics and Governance Council

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UK BIOBANK ETHICS AND GOVERNANCE COUNCIL: AN EXERCISE IN ADDED VALUE

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INTRODUCTION

The purpose of UK Biobank is ‘to establish and operate a resource for research with the aim of improving the prevention, diagnosis and treatment of illness and promoting health throughout society for public benefit’. Recruitment of participants is currently underway and on completion in 2010 the resource is expected to contain health and lifestyle data and biological samples from some 500,000 people from the UK who were aged 40-69 at the time of recruitment. During the planning of the project, and in parallel with the development of the scientific protocol, an Interim Advisory Group (IAG) was established to make recommendations to the funders about an ethics and governance framework for the project. Two key recommendations to emerge from the deliberations of the IAG were, first, that UK Biobank should adopt an Ethics and Governance Framework which lays out explicitly the commitments of UK Biobank to its participants, the public and other stakeholders, and, second, that a permanent and independent Ethics and Governance Council should be established to oversee the project and to monitor and advise on its operation. As a result, a permanent Ethics and Governance Council (EGC) was formed in 2004. This was set up by the principal funders of UK Biobank (the Medical Research Council and the Wellcome Trust) to act as an independent guardian of the UK Biobank Ethics and Governance Framework (EGF), to advise on its revision, to monitor and report publicly on conformity of the project with the EGF and, more generally, on the interests of research participants and the general public in relation to UK Biobank. In this paper we will discuss the reasons why it was thought necessary to create this body, additional to the other institutions and processes for the regulation and ethics governance of research, and we will comment on the practice and work of the EGC in light of our experiences of working on the Council. But first we will provide a little more detail about the UK Biobank itself.

UK Biobank

UK Biobank is a charitable company limited by guarantee which is the legal owner and steward of the database and sample collection. Once recruitment is complete

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4 See www.ukbiobank.ac.uk for further information.
(expected in 2010) the resource will be available to medical and health researchers in both the public and private sectors, subject to successful application and appropriate approval processes. UK Biobank itself will not carry out research but has the responsibility to create and maintain the resource and regulate access to this by those who wish to use it for medical and health-related research purposes, being the broad purpose of project.

Recruitment to UK Biobank is being organised via a series of assessment centres, each operating for about six months in a chosen location. Those in the locality of the assessment centre and in the relevant age group are invited to join the project by letter. The letter includes a provisional appointment which can be accepted, changed for a more convenient time or simply ignored. Initial contact information about potential participants is obtained through National Health Service Records and this process has received relevant ethical approval and involves only the minimum amount of personal details needed to contact eligible persons. According to the EGF: ‘UK Biobank will seek to recruit as widely generalisable a population sample as is practicable so that the research may ultimately benefit a wide diversity of people’.5 It has been reported by UK Biobank that the proportion of those written to who are recruited to the project varies in general between 6-12% between assessment centres but is about 9% overall.6 A high attendance rate of 20% has been reported for Bristol.7 At the time of writing (September 2008) over 187,000 people have been recruited.

At each assessment centre would-be participants are given further details of what involvement in the project entails and a general description of the kinds of diseases that may be the focus of future research carried out using the resource. It is made clear that consent is being given ‘to participate in UK Biobank’ with its broad purpose to create a resource for health-related research. A clear guarantee is also given that only anonymised data or samples will be used for these purposes.

During the 90 minutes or so of the assessment, participants provide information about health, lifestyle, memory, work and family history through a touch screen questionnaire and health interview, undergo some physical measurements (including blood pressure, pulse rate, height, weight and bone density) and provide biological samples (blood and urine). Participants receive some details of their own physical measurements but are told that thereafter there will be no further feedback of any individual information (for example the results of research conducted on the resource). At some assessment centres there is a nurse provided by the British Heart Foundation with whom participants can discuss their cardiac assessments.

Further data on each participant will be collected from their NHS records and other health-related records (for example the National Cancer Registry) and there may be future re-contact to make further assessments from some or all of those enrolled. From the outset UK Biobank has been envisaged as a long-term project which will continue to collect information about participants and which is expected to hold data and samples over many decades. Information about the progress of the project and results of research carried out using the resource will be made available to participants and society in general, largely via the UK Biobank website and through the publication of research findings.

**Research Governance and Regulation**

As with any research project involving human participants, UK Biobank is subject to our national framework of research governance and regulation. It falls within national legislation, for instance, the Human Tissue Act 2004 and Data Protection Act 1998, common law duties of care and confidentiality, and is also under the watchful eyes of a number of regulators, such as the Human Tissue Authority, the Information Commissioner’s Office, the Charity Commission and Companies House. Other relevant governance mechanisms include the UK National Health Service which acts as a data controller with respect to information about participants and the system of Research Ethics Committees which will review relevant research projects involving UK Biobank, as well as the organisation of the UK Biobank itself. Professional ethics

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8 A participant has described her experiences of recruitment in a paper which also includes a commentary by a bio-ethicist. Minnie Sample and Richard Tutton, ‘Biobank as biographical disruption: conversations on some first person reflections’ (2008) 3 Medical Sociology Online 15.
and guidelines (e.g. the Medical Research Council) are also involved and, last, but not least, there is the freely-given consent of all participants. Notwithstanding, early in the planning of the project because of the size (both the number of participants and the amount of data and biological material, including DNA, to be held on each) and complexity of the project, and the need to foster and maintain public trust in the project, it was decided that an ethical framework for the project should be created in parallel with the development of the scientific protocol and in addition to the pre-existing governmental regulations to which the project would also be subject. This was done with widespread consultation with health and science professionals, experts in ethics and law and members of the public. An Interim Advisory Group on Ethics and Governance was set up by the funders. This activity resulted in the development, publication of, and consultation on an Ethics and Governance Framework (EGF).

The EGF establishes that consent will be sought to participate in UK Biobank. This will be based on an explanation and understanding of a number of features of participation (such as the kinds of information and samples that will be collected at enrolment and the possibility of being re-contacted in the future by UK Biobank). There is also a general description of the potential research uses of the data and samples, but broadly UK Biobank will encourage use of the resource for health-related research. The EGF affirms the right to withdraw at any time and makes a commitment to protecting the confidentiality of both samples and data. UK Biobank is confirmed as steward of the resource and legal owner of the database and sample collection. The principles which govern access to the resource by researchers are described. The framework goes on to outline the benefit-sharing that will be required which includes the obligatory publication of findings and accessible archiving of research findings in UK Biobank for future use. Finally, it describes the arrangements for management and accountability. These include the creation of an Ethics and Governance Council (EGC) which monitors UK Biobank’s conformance with the

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9 See http://www.ukbiobank.ac.uk/ethics/consult.php for further information.
10 The membership of the Interim Advisory Group was: Dr William Lowrance (Chair), Professor Alastair Campbell, Professor Erica Haimes, Dr Graeme Laurie, Professor Chris Mathew, Professor Jean McHale, Mrs Helen Millar, The Baroness O’Neill of Bengarve, and Mrs Madeleine Wang.
11 See http://www.ukbiobank.ac.uk/ethics/egf.php for the latest version.
EGF, advises on revisions to the EGF and, more broadly, on the interests of participants and the public in relation to the UK Biobank project.

**The Ethics and Governance Council**

We might begin by asking why the funders set up an independent EGC; why not simply rely on the ethics governance processes that cover all UK research? The consultations that were carried out in the process of formulating the EGF and on the draft document itself strongly supported the setting up of an independent body. It was a particular recommendation from the Interim Advisory Group that there should be a body to monitor UK Biobank’s conformance with the EGF.\(^{12}\)

There are a number of features of UK Biobank which led to this recommendation. UK Biobank has adopted a broad model of consent from participants. As with all such biobanks the future uses of the resource cannot be foreseen at the point at which a participant is recruited. So, key roles of an EGC are to monitor that UK Biobank is always managed in conformity with the original consent of its participants and to keep under review applications for access to the resources with regards to the interests of UK Biobank participants. In advising on the participants’ interest in the future, for example, the Council might ask itself if a ‘reasonable participant’ would have expected the proposed use of his or her data or samples at the point at which they gave their consent. We might note in parentheses that a number of current members of the EGC have happened to live in locations where UK Biobank has been recruiting and have accepted the invitation to take part in the project.\(^{13}\)

UK Biobank is a long-term project which will evolve over time. This raises challenges for existing regulatory mechanisms because traditional research ethics committee (REC) approval – required of all research involving human subjects - is a one-off event; active and on-going monitoring of a project’s progress is not generally

\(^{12}\) Indeed, during the early development of UK Biobank a Government White Paper envisaged the Council not only as an advisory body but as a committee that has ‘the power to veto uses of the data or samples that it considers to be against the interests of the participants or likely to damage the reputation of the study’. Department of Health *Our inheritance our future. Realising the potential of genetics in the NHS* (2003) <http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4006538> at 22 September 2008.
within a REC’s brief. This is where a body such as the EGC can add value to a governance model by actively monitoring and developing alongside the scientific project. Of course, UK Biobank is not unique for being a long-term project. For example, Britain has a series of birth cohort follow-up studies which recruited a week’s births in 1948, 1956 and 1970 which continue to follow these children – and indeed their descendants - today. These, like UK Biobank, have also relied on broad consent (of the mothers, in the first instance). They have also, more recently, collected DNA from participants. This is a feature of UK Biobank that has led to some anxieties about privacy, etc amongst some commentators. However, despite these similarities with UK Biobank none of these cohort studies has its own independent ethics and governance bodies. UK Biobank is, of course, larger in terms of participant numbers and it will be ten times the number of participants of the other birth cohort studies. Moreover, UK Biobank was set up at a time in history when social attitudes towards medical research and concerns about the protection of personal interests were different to those which existed previously. Notably, public attitudes about what it means to be a research participant and which principles and parameters should govern issues such as data protection and access have led to a changing social context – and thus, it might be argued, have necessitated a governance structure that can reflect and respond to such change. An important reason for the establishment of an independent EGC was to foster and maintain public trust in the UK Biobank project through its advisory and monitoring roles. A report from one consultation, ‘Biobank UK: A Question of Trust: consultations exploring and addressing questions of public trust (2002)’ recommended that ‘some form of oversight body should be established and that the body should be capable of acting independently of the user and sponsors.’ Any such body ‘should ensure that standards of behaviour and ethics are maintained and continued to reflect the public mood as the

13 During the consultation there was wide support for the idea that participants should be represented on the EGC though membership does not expressly include participant representatives. The EGC was initially set up before recruitment began.
public consensus changes but within the original terms of consent given by volunteers.’

A later consultation on the draft EGF was more specific. An oversight body was seen to be critically important and should be composed of ‘professional people, who knew what is going on’ as well as lay and participant representation with recruitment following open and transparent procedures. As we have indicated, the Ethics and Governance Council was established in November 2004.

In Practice: The EGC and its Work

Members of the EGC are appointed through processes in keeping with the Nolan Principles on Standards in Public Life, after public invitation of applications and on the basis of their backgrounds and abilities to further the purposes of the Council. The EGC is an independent body which ‘speaks about UK Biobank, not for UK Biobank’.

The currently-constituted Council is a multi-disciplinary group including expertise in law, ethics, biomedical sciences, policy, social science and consumer issues. It has 10 members and meets four times a year. In addition, it has one or more public meetings per year. Recently, these have been in localities where UK Biobank is recruiting. These meetings have attracted very mixed groups including some who have been recruited to UK Biobank, as well as others who had declined the invitation to take part.

When advising, reviewing and reporting on UK Biobank’s activities, the EGC serves as a mirror for UK Biobank, providing critical and constructive advice. As stated in the Ethics and Governance Framework ‘normally the Council will communicate its reflections and criticisms informally. If the Council is not satisfied with UK Biobank’s response, it could make a formal statement of concern (e.g. to the Board or

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16 ibid 4.
18 Details about membership of the Council, minutes of its meetings and other information can be found on its website http://www.egcukbiobank.org.uk. It is independent from UK Biobank though is funded by the UK Biobank funders who also approve appointment of members.
funders) or, if necessary, make a public statement that certain actions should or should not be taken. 19

The Principal Investigator of UK Biobank generally attends for part of each Council meeting and reports on current progress, etc. Papers may be requested or received from UK Biobank on particular issues or future plans. Other UK Biobank officers may attend to describe and discuss their aspects of the project. For example, the officer responsible for information technology security has provided a detailed description of the architecture of the data storage system and its security, and how it has met tests to assess its robustness in the face of trial attempts to gain access to information. The Council has also seen aspects of the work first hand, visiting an assessment centre and sample processing and storage facilities, for example.

In carrying out its work we should also note what the Council does not do. It does not assume responsibility for the ethical management of the resource – that remains the responsibility of UK Biobank itself. Nor does it own or develop the EGF and associated policies. As we have indicated – the mantra of the Council is clear: It does not speak on behalf of UK Biobank, rather the Council speaks about UK Biobank.

The EGC was established at a time when UK Biobank was developing its protocol and establishing its procedures. Today the project is recruiting approximately 600 people per day, 6 days a week at 7 dedicated assessment centres throughout the UK. During this period the EGC has been both reactive and proactive to the project’s stage of development. As such there has been a change in the focus of the EGC’s work over the last three years as different aspects of its remit come to the fore.

Initially the Council engaged predominantly with its advisory function. This included advising on revisions to the EGF itself and to the policies and procedures that flow from the framework. For example, the Council has advised on the standard operating procedures for the management of incidental findings at the assessment centres and for judging a potential participant’s capacity to consent. The Council also reviewed and advised extensively on the project’s participant information leaflet and consent form in order to assure itself that the elements of consent described in the EGF were

19 UK Biobank, UK Biobank Ethics and Governance Framework, Version 3, Section III.A.2 (October
conveyed in these materials. (For example informing participants explicitly of the range of potential researchers who might use the resource including researchers from other countries and those with commercial links.) During this period the Council also advised on the standard operating procedures for the handling of complaints and enquiries received by the project. In reviewing and advising on these materials the Council wishes to assure itself that UK Biobank has effective mechanisms in place to deal with participants’ complaints and enquiries promptly and efficiently.

Over the last year (2007-8), the Council has started to engage more with the monitoring aspect of its remit. For example, it has moved from providing advice regarding the standard operating procedures for complaints and enquiries handling to monitor the actual complaints and enquiries received by the project. These are monitored through biannual reports prepared by UK Biobank. The reports outline the number and types of enquiry and complaint and also detail the reasons given for participant withdrawals. The Council is interested in monitoring both the reason for, and trends in, the complaints and enquiries received by the project. These could provide an indication of how happy, or unhappy, individuals are with certain aspects of UK Biobank – whether that be the practical aspect of the assessment centre operation (e.g. waiting times or people having difficulty with some of the questions in the questionnaire) or about certain policies that are found to be unacceptable (e.g. the feedback policy). In the longer term the Council will look at the trends in the complaints and enquiries to see if certain concerns or opinions shift with time – possibly indicating a shift in concerns and opinions in society more broadly (for example regarding possible future uses of the resource if certain types of research become more or less publicly acceptable over time).20

The last function we would like to mention, in addition to the advisory and monitoring role, is a foresight role. In the early days of the Council its role was more reactive, reviewing and advising on procedures and policies that UK Biobank was developing. Over the last year the Council has started to be more proactive about identifying and investigating issues which it thinks warrants further consideration

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20 For more on the importance of being responsive to shifting in wider values and interests, see Graeme Laurie, Ann Bruce and Catherine Lyall, “The roles of values and interests in the governance of the life...
(either by UK Biobank or by the Council itself). A notable example is the challenges yet to come with respect to access to the resource and the management of any intellectual property that is generated from that access. While access is not anticipated before recruitment completes in 2010, the Council has none the less established a sub-group to anticipate and examine issues likely to arise.

Another method by which the EGC goes about identifying and investigating issues is through commissioning research.

In 2006 the Council commissioned a scoping study of public attitude surveys regarding biobanking related issues. This scoping study, which is available on the EGC website, identified a gap in the literature regarding public attitudes to certain aspects of access including opinions regarding commercialisation and benefit-sharing. The Council has since commissioned a further study to investigate actual public attitudes with respect to these areas and in the context of current UK Biobank policy. This study will help to test the Council’s own understanding of these issues and will in turn help the Council in formulating its advice to UK Biobank regarding the further development of its access policy.

In addition to research regarding public attitudes, the Council has commissioned a study to provide a conceptual analysis of the terms the ‘public interest’ and the ‘public good’. These terms are often used in the context of UK Biobank, including the early drafts of the project’s Access and Intellectual Property policy which describe UK Biobank as being ‘a managed resource for the public good’. However, as a Council we felt that the application of these terms to the management of resources like UK Biobank is unclear.

In commissioning this research the EGC wanted to inform itself of how these phrases might be interpreted in the context of UK Biobank and how they might apply to whole sciences: learning lessons from the “Ethics+” approach of UK Biobank’ in C Lyall (ed), XXXX, forthcoming, 2009.


access decision-making. Ultimately the EGC would like to develop a framework of principles to guide its future advice and decision-making with respect to access requests to the UK Biobank resource. The conceptual analysis was commissioned in order to inform, and provide a theoretical base for, the development of this framework.

This piece of work was reported to us in 2007 and is available on the EGC website. In order to extract the most value from the report, and in keeping with its commitment to transparency of advice and decision-making, the EGC has produced a document which summarises the findings of the report in the context of their application to the EGC’s activities. This is also available on the EGC’s website. The summary is a ‘living’ document and will be revised over time to take account of new thinking by the Council on its interpretations of ‘public interest’ and ‘public good’ (e.g. in response to other commissioned work or future experiences).

Finally, there are two additional areas where the Council has, and is, in the process of advising on issues that were either not foreseen or areas that are actively being developed. We believe these further demonstrate how a body like the EGC adds value and complements existing governance and regulatory mechanisms.

The first example relates to the method by which a participant can withdraw from the project. Three levels of withdrawal are offered. These range from ‘No further contact’ which means that UK Biobank would no longer contact the participant directly, but would still have their permission to use information and samples provided previously and to obtain further information from their health-relevant records; ‘No further access’ which means that UK Biobank would no longer contact the participant or obtain further information from their health-relevant records in the future, but would still have their permission to use the information and samples provided previously and ‘No Further Use’ which is described in the EGF as follows:

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‘In addition to no longer contacting the participant or obtaining further information, UK Biobank will delete all of their health-related information and samples collected previously (although the participant would be told that it may not be possible to trace and destroy all distributed anonymised sample remnants). Only some administrative details (such as their signed consent and withdrawal) would be kept as a record of their wishes. Such a withdrawal would prevent information about them from contributing to further analyses, but it would not be feasible to remove their data from analyses that had already been done.’ (emphasis added)

In June 2007 Professor Collins, the Principal Investigator for UK Biobank, sought the Council’s advice regarding this option of withdrawal because it had come to light that it is not possible for UK Biobank to destroy all of a participant’s health-related information due to the project’s data back-up and audit system. Importantly, however, UK Biobank can still guarantee the main principle behind this option, i.e. that there will be no further use of the data by researchers.

Following initial discussions the Council requested and received a briefing note from UK Biobank describing in detail the technical problem surrounding the withdrawal of data from the resource. Also, UK Biobank’s Systems Architect attended a Council meeting to provide an update on the project’s Information Technology and Data Management Strategy and to describe the technical and physical procedures involved when a participant withdraws from the project.

After further discussion the Council concluded that it considered that the fundamental guarantee described in the EGF is that there will be no further use of the data by researchers. This guarantee has not changed. The Council subsequently made several recommendations to UK Biobank that resulted in the following actions:

- The EGF and participant information leaflet were revised to describe the ‘No further use’ withdrawal option as follows:

  ‘This means that, in addition to no longer contacting you or obtaining further information about you, any information and samples collected previously would no longer be available to researchers. UK Biobank would destroy your samples (although it may not be possible to trace all distributed sample remnants) and would only hold your information for archival audit purposes. Your signed consent and...”
withdrawal would be kept as a record of your wishes. Such a withdrawal would prevent information about you from contributing to further analyses, but it would not be possible to remove your data from analyses that had already been done.’ (emphasis added)

- Additional text was inserted into the EGF describing UK Biobank’s commitment to keeping participants informed about important developments with the project.

- A new page was added to UK Biobank and the EGC’s website and information about this change was posted on both sites. Further, these pages will be updated with any such policy or procedure changes in the future.

This example illustrates the likelihood that issues will arise that have not been anticipated but that require ethical consideration. In this example the Council tried to consider the situation in terms of the participants’ expectations and in so doing aimed to provide UK Biobank with an appropriate and proportionate response that is acceptable to participants and the public.

Our final example relates to an area of ongoing discussion between UK Biobank and the EGC: the policy on providing participants with feedback of health information resulting from their participation in the project. During the developmental stages of the project the Council reviewed and advised UK Biobank on its policy and standard operating procedures in relation to this topic. Currently feedback is provided for a number of measures taken at the assessment centre but no feedback is provided on information that is derived about a participant after the assessment centre visit. So, at present, participants only receive information about blood pressure, weight, height, heel bone ultrasound, lung function amongst other things. These individual measures are reported with reference to population standards (thus avoiding individual interpretation and hopefully therefore staying true to the fact that UK Biobank is a research project, rather than a clinical encounter).

When UK Biobank’s funding was being considered an international scientific advisory board was convened by the funders to peer review the project’s protocol. The board endorsed UK Biobank’s protocol and in addition made a series of
recommendations. One recommendation was that UK Biobank could increase the value of the resource by collecting additional data on a subset of the cohort.

In response to this recommendation UK Biobank convened a sub group to look at the types of measures and questions that could be added to enhance the baseline measures and questions that are already administered to all participants. The conclusions of this sub group informed a proposal that has recently been put forward to the funders and the EGC for initial consideration.

The new measures range from additional questions and measures regarding exercise, diet and exposures to new measures regarding hearing and sight through to magnetic resonance imaging of the body. We will not go into a great deal of detail about these new measures because they are only at the proposal stage. However, the proposals have raised certain issues which UK Biobank and the Council will be considering in the coming months. In particular, the implications of the proposals in relation to UK Biobank’s current policy on providing – or not providing – feedback of health information to its participants will be considered.

This example shows that certain policies cannot be taken for granted. That is, it cannot be assumed that a current policy will necessarily be appropriate as a study develops. The EGC intends to go back and review its original advice to UK Biobank and to re-assess the principles that underlie the current policy on feedback. In due course we hope to provide consistent, informed advice back to UK Biobank about the further development of its protocol.

CONCLUSIONS

In conclusion, the Council was established in order to build and maintain public trust and in direct response to the broad model of consent adopted by UK Biobank and to the long term nature of the resource. The Ethics and Governance Framework (EGF) and the Council are intended to provide an extra safeguard for participants and the public and both are intended to provide a foundation for trust.

The Council aims to build this trust through its advisory and monitoring role and through the public reporting of its own activities and of UK Biobank’s conformance with the Ethics and Governance Framework. The monitoring aspect of the Council’s
remit is of particular importance as a compliment to traditional research ethics committees which do not offer a complete monitoring role. Through its work the Council hopes to advise on the public interest in relation to the project as it may change over time and to assure itself that UK Biobank is operating in the terms of the EGF and the participants’ consent.

As projects like UK Biobank develop there will be changes – both foreseen and unforeseen – that will require consideration. A body like the Council is able to provide a consistent, informed view on these situations, acting in the public interest and keeping key principles at the heart of its decisions. Through its work a body like the Council can promote and facilitate good governance and good science in the public interest.