UK BIOBANK ETHICS AND GOVERNANCE FRAMEWORK

Version 3.0 (October 2007)

UK BIOBANK

Purpose and overview

UK Biobank aims to build a major resource that can support a diverse range of research intended to improve the prevention, diagnosis, and treatment of illness and the promotion of health throughout society.

Lifestyle and environmental information, medical history, physical measurements, and biological samples are to be collected from about 500,000 people aged 40-69 at presentation and then, with consent, their health will be followed for many years through medical and other health-related records. The biological samples will be stored so that they can be used for a wide range of biochemical and genetic analyses in the future.

Scientists have known for many years that our risks of developing different diseases are due to the complex combination of different factors: our lifestyle and environment; our personal susceptibility (genes); and the play of chance (luck). Because UK Biobank will involve thousands of people who develop any particular disease, it will be able to show more reliably than ever before why some people develop that disease while others do not. This should help to find new ways to prevent death and disability from many different conditions.

UK Biobank will seek active engagement with participants, research users and society in general throughout the lifetime of the resource. Data and samples will only be used for ethically and scientifically approved research consistent with the above purpose. Safeguards will be maintained to ensure the confidentiality of the participants' data and samples.

Organisation and funding

Financial support for the core UK Biobank resource is being provided to UK Biobank Limited, which is a charitable company limited by guarantee, by the Medical Research Council, Wellcome Trust, Department of Health, Scottish Executive and North West Regional Development Agency (the Funders).

UK Biobank's Board of Directors, which is accountable to the Members of the Company (Medical Research Council and Wellcome Trust), will act as charity trustees under UK charity law and company directors under UK company law, and exercise management oversight of UK Biobank.

UK Biobank will serve as the legal custodian of the data and samples, and will operate through a Coordinating Centre hosted by the University of Manchester. It will also allocate some funds through a collaborative agreement with six Regional Collaborating Centres representing more than 20 UK universities, which will be involved through a Steering Committee in the scientific design of the resource.

An independent Ethics and Governance Council will advise the Board and Funders, and publish public reports on the conformance of UK Biobank with this Ethics and Governance Framework and with the interests of participants and the public.

I. RELATIONSHIP WITH PARTICIPANTS

A. RECRUITMENT

1. General principles

UK Biobank aims to recruit 500,000 people aged 40-69 from all around the UK. It is not intended to enroll people who are unable to give consent (for example, because of diminished mental capacity); those who are unable to take part in data collection (for example, because they are too ill); or those who are uncomfortable with any of the conditions of participation. Staff will be trained to judge each potential participant's capacity to give consent and to take part in data and sample collection.

Participation in UK Biobank is voluntary. All aspects of recruitment, from initial contact with potential participants through to enrolment at the baseline assessment visit, will be conducted in a way that preserves the voluntary nature of participation and respects cultural differences. In order to generate scientifically valid results, UK Biobank must also obtain agreement from participants for examination of the progress of their health, illness and incapacitation in depth and over time.

UK Biobank will act in accordance with the Data Protection Act and all other relevant legislation, and seek all necessary approvals that are required for the planned invitation, assessment and follow-up procedures (e.g. from relevant ethics committees, the Information Commissioner, Caldicott Guardians and other relevant bodies).

2. Selection and approach

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. UK Biobank will work to reduce barriers to participation (such as those relating to age, gender, ethnicity, social class, residence, employment, and language) through, among other things, the location and opening times of assessment centres and by translation of study materials.

UK Biobank will identify potential participants from contact details in NHS records (and other registers), without access to any medical information. These contact details will be processed in confidence by UK Biobank, in accordance with the Data Protection Act. Potential participants will then be sent information about the study and invited to attend a local UK Biobank Assessment Centre.

3. Enrolment

Potential participants will receive, by mail, information about UK Biobank and an invitation to attend a local study Assessment Centre. Further information will be available from UK Biobank through a free telephone service and website.
During the Assessment Centre visit, UK Biobank staff will answer questions, provide clarifications and explain the consent process. If an individual decides to take part, their

signed consent will then be sought and recorded before they are enrolled. Enrolment will involve completing a questionnaire about lifestyle (e.g. diet, exercise, smoking, alcohol) and other factors (such as mood, cognitive function, medical history), having baseline physical measurements (e.g. blood pressure, size, grip strength, lung function) and giving blood and urine.

B. UNDERSTANDINGS AND CONSENT

1. Consent

Consent will be sought to participate in UK Biobank. Participation will be presented as an opportunity to contribute to a resource that may, in the long term, help enhance other people's health. Because it will be impossible to anticipate all future research uses, consent will be sought for research in general that is consistent with UK Biobank's stated purpose (rather than for specific research).

Consent will be based on an explanation and understanding of, amongst other things:

- the purpose of UK Biobank, the fact that it is a long-term research resource (not a healthcare programme), and any risks and benefits of taking part
- the kinds of information and samples that will be collected at enrolment, which may include data that some participants consider especially sensitive (with options to avoid certain questions and measurements)
- the fact that there will be a link to the full record of medical and other health-relevant information (past and ongoing) and the need for participants to allow such linkage for as long as possible to maximise the value of UK Biobank as a research resource
- the fact that UK Biobank will be the legal owner of the database and the sample collection, and that participants will have no property rights in the samples
- the kinds of safeguards that will be maintained, including secure storage of data and samples in reversibly anonymised form (as explained in Section I.C.2), and severe restrictions on access to data and samples that are not anonymised
- the assurance that only research uses that have been approved by both UK Biobank and a relevant ethics committee will be allowed, and that data and samples will be anonymised before being provided to research users
- the expectation that commercial entities will apply to use UK Biobank
- the possibility of being re-contacted in future by UK Biobank and the purpose of such contacts
- the intention to continue to hold and allow research access to data and samples after participants lose mental capacity or die, as such data and samples are crucial for research on severe illnesses

- the right to withdraw at any time without having to give a reason and without penalty, and the meaning of different levels of withdrawal

- UK Biobank's commitment to maintaining active engagement with participants and society in general.

The points listed above are some elements of what it means "to participate in UK Biobank"; each is discussed in more detail later in this Framework document. These elements and other customary undertakings will be addressed in information provided to participants during the consent process.

UK Biobank will endeavour to make sure that participants understand what they are consenting to when they agree to take part. An evaluation has been conducted in preparation for the main phase of recruitment, which will provide further opportunities for assessment of the consent procedures.

The consent to participate in UK Biobank will apply throughout the lifetime of UK Biobank unless the participant withdraws. Further consent will be sought for any proposed activities that do not fall within the existing consent.

2. Collection of data from health-relevant records

The ability to accumulate data from health-relevant records will be essential for the success of UK Biobank. It must track health events, the development of disease, and the course of treatments, and so must aim to obtain such information as diagnostic codes and prescribing data. The range of different records that can be accessed will be determined by developments in health service electronic records systems.

UK Biobank will collect data from NHS record systems (e.g. GP, hospital, dental and prescription records) and other relevant record systems (such as disease registries or occupational health records). In the consent process, UK Biobank will explain to participants the kinds of record systems to which it will seek access, and will keep participants informed of progress with accessing different types of records.

UK Biobank will not be able to say in advance which data from these various records will be needed. Although, in general, only parts of these health-relevant records will be examined, consent will cover access to the full records. This will include past records, since these will help to characterise participants and to understand later health events more completely. The full records may also be required when it is necessary to verify the accuracy of data.

3. Provision of health information to participants

UK Biobank will aim to ensure that participants understand that enrolment does not provide them with a health check. In principle, it would be possible to provide participants with the results of some measurements or observations at any of three stages: at the initial assessment visit (e.g. blood pressure or incidental findings), in the

initial stage before samples are stored (e.g. white cell count), and much later as results arise from research studies (e.g. genetic or biochemical studies).

However, the value of such feedback is questionable because the data would be communicated outside of a clinical setting and would not have been evaluated in the context of the full medical record. As a consequence, the significance of the observations might not be clear and UK Biobank staff would not be in position to interpret their implications fully. Further, it is not likely to be constructive, and might even be harmful (including causing undue alarm and having potentially adverse effects on insurance and employment status), to provide information without prior counselling or support (which UK Biobank will not be able to provide: as explained below). For these reasons, UK Biobank will generally not provide health information to participants, and a clear explanation of this policy (and the few exceptions) will be provided in the participant information material.

Specifically, provision of health information at the three stages will be covered:

- **At the initial assessment visit:** It would be impractical and inappropriate to conceal from participants some of the measurements taken in their enrolment visit (i.e. blood pressure, height, weight, estimated amount of fat). Consequently, a printed report will be provided at the end of their visit as a means of feeding back such measurements. By reporting standard ranges, the participant should be provided with sufficient information to give meaning to the measurements taken, so that they may act on the results if necessary and arrange to see their general practitioner or other relevant health professional.

  The legal duty of care for staff conducting enrolment will be determined by the research context, and will apply mainly to safe and competent collection of questionnaire data, baseline measurements, and blood or other samples. They will not have the same duty of care that they would have in a clinical setting. However, even in this research context, there may be occasions when staff consider there to be a professional or ethical obligation to draw attention to abnormal measurements (such as elevated blood pressure) or incidental findings (such as possible melanoma). In such circumstances, participants will be encouraged to contact a relevant health professional.

- **Before samples are stored:** Prior to storage of samples, UK Biobank is planning to conduct routinely only those few investigations that cannot be done subsequently on stored samples (i.e. haematology). As is the case with other measurements that may be conducted on stored samples (see below), these baseline measurements are being conducted outside of a clinical setting without prior counselling and support. Moreover, all such analyses will be conducted on anonymised samples without other relevant medical information about the individual. Consequently, these individual results with personal identifying details will not be provided to a participant or to anyone else. A clear explanation of this policy will be included in the participant information material.

- **Later, as a result of research studies:** In normal healthcare settings, tests are conducted at the individual level immediately after sample collection; they search

for specific conditions or outcomes; and, in the case of genetic tests, pre- and post-test counselling is provided. But, given the lack of knowledge at recruitment about the tests that might be done in this research context (and, hence, the inability to provide specific counselling beforehand), UK Biobank will not provide participants with information (genetic or otherwise) about their own individual results derived from examination of the database or samples by research undertaken after enrolment. Instead, the overall findings and implications of results that derive from UK Biobank will be made available to participants and the wider community so that they can influence public health strategies (including, where appropriate, the introduction of screening for newly discovered risk factors).

4. Ongoing engagement with participants and the public

Regular communication will be important to inform participants of general findings from research based on the resource and to encourage continued participation. UK Biobank will, therefore, look for a variety of ways for communicating with (including listening to) participants, the general public, research users and the scientific community.

A variety of media, such as websites, helplines, newsletters, and public meetings will be used to inform participants about the development and use of the resource, and of ways to contact UK Biobank (including, for example, how to withdraw). Systems will be put in place to allow participants to indicate how, and whether, they would like to receive such information.

UK Biobank may also establish a participants' panel with a clear remit that is as representative as possible of the UK Biobank population and able to express views typical of the participants generally. UK Biobank will also maintain procedures for responding in a timely fashion to any enquiries or complaints.

5. Expectation of re-contact

It will be explained to participants that they may be re-contacted by UK Biobank for various reasons, including:

- To collect new information (such as questionnaire data, measures or samples) for the resource. It is anticipated that repeat assessment visits would be done every few years and would generally involve reasonably representative subsets of just a few tens of thousands of people, with different individuals selected for sequential repeat assessments. Invitations to provide additional information that do not require such visits (e.g. questionnaire data collected by mail or internet) might be sent to all participants at similar intervals during the study.

- To seek consent to proposed new uses that have passed scientific and ethics review but do not fall within the existing consent

- To ask participants whether they would be willing for researchers to contact them to discuss possible involvement in a study that requires new information or samples.

It will be emphasised that participation in all such re-assessments is entirely voluntary, and that any initial re-contact will be undertaken by UK Biobank.

Decisions on whether re-contact is appropriate for particular proposals will be made by UK Biobank with advice from the Ethics and Governance Council (see Section III.A.2), and will be subject to Research Ethics Committee approval. When re-contacting special sub-populations, care will be taken over the use of selection criteria (such as genetic make-up) that might inadvertently reveal information to participants about themselves of which they may not be aware.

6. Right to withdraw

Participants will be advised at enrolment that they have the right to withdraw from UK Biobank at any time without having to explain why and without penalty. This is essential to preserve and demonstrate the voluntary nature of participation. Should participants become incapacitated or die, they would no longer be able to withdraw themselves (see Section 7).

During enrolment, UK Biobank will provide information to participants about the options for withdrawal:

- **"No further contact":** 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":** 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.

- **"No further use":** In addition to no longer contacting the participant or obtaining further information about them, any information or samples collected previously would no longer be available to researchers. UK Biobank would destroy their samples (although it may not be possible to trace and destroy all distributed anonymised sample remnants) and would only hold their information for archival audit purposes. The participant's 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 possible to remove their data from analyses that had already been done.

(N.B. UK Biobank is completely committed to ensuring that participants are informed about important developments with the project. One such development to emerge during the establishment of the IT systems is that, although data from participants who choose the "No further use" withdrawal option can be made unusable, it is not possible to destroy it completely. This is due to the development of complex IT systems designed to protect the integrity and security of the data.)

If, having discussed their concerns and options, a participant decides to withdraw then UK Biobank would seek written confirmation of the level of withdrawal from the participant. UK Biobank will need to retain some minimal personal data for a number of reasons, which include: ensuring that participants who have withdrawn are not re-contacted; and assessing the determinants of withdrawal and any impact on research findings. Participants who withdraw will be assured that this administrative record will not be part of the main database that is available to others.

Despite UK Biobank's efforts to stay in touch with participants, it may well lose contact with some as they relocate, emigrate, or do not respond to communications. Where a participant has not actively withdrawn, UK Biobank will continue to use the samples and data and maintain linkages, although it will not be able to update some data (e.g. those collected by repeat questionnaire).

7. Respect for incapacitated or deceased participants' wishes

UK Biobank will not enrol potential participants who express the view that they would want to be withdrawn should they lose mental capacity or die because this would reduce the value of the resource for research. But, if a participant decides some time after enrolment that he or she would wish to be withdrawn in the event of mental incapacity or death then this request would be honoured. In such circumstances, the options for withdrawal would be discussed with the participant (see Section 6) and written confirmation of their preferred option sought to confirm their modified consent. UK Biobank would then withdraw that participant in accordance with their preferred option for withdrawal on becoming aware that he or she had lost capacity or died (e.g. through routine follow-up systems or by being notified by a family member or someone else able to act on behalf of the participant). Otherwise, participants will not be withdrawn if they lose mental capacity or die. In all events, UK Biobank will continue to safeguard the confidentiality and security of all participants' data and samples as long as it holds them, including after a person's mental incapacity or death.

8. Expectation of personal financial gain

Participants will not be offered any material financial or other inducement to contribute to UK Biobank, irrespective of whether the use of data or samples might ultimately lead to profit. Reasonable expenses incurred through participation (such as travel and parking) will be reimbursed as required by the participant.

As is explained in Section II.A "Stewardship of data and samples", participants will be told that their involvement will not create or confer any property rights in samples.

C. CONFIDENTIALITY

UK Biobank is committed to protecting the confidentiality of data and samples. Systems will be in place for secure data flow and for protecting confidentiality, (reversibly) anonymising data and samples, and enforcing security. These measures will

be explained to participants during the consent process. Some principles and comments on these matters follow in this section.

1. Commitment to maintaining confidentiality

UK Biobank will maintain strict measures to protect confidentiality, and will ensure that data and samples are (reversibly) anonymised, linked and stored to very high standards of security. The same protection will be extended under contract for any handling or analysis of data or samples by third parties engaged to provide services necessary for developing the resource. Research users will only be given access to anonymised data and samples.

2. Anonymisation

During enrolment, the assessment centre will need to hold identifying information (such as name, address, birth date, NHS number) together with information collected from the participant during the assessment visit, and this information will be encrypted for security. Following the assessment visit, these data will be transferred to the UK Biobank central system and removed from the assessment centre system. On arrival at the UK Biobank coordinating centre, all personal identifying information will be separated from participants' data and samples and only linked using a code that has no external meaning (e.g. not the NHS number).

All identifying information will be held centrally by UK Biobank in a restricted-access database that is controlled by senior UK Biobank staff. Only a few people within UK Biobank will have access to the "key" to the code for re-linking the participants' identifying information with their data and samples (i.e. "reversible anonymisation"). It is necessary to retain this link with identifying information to allow follow-up of participants' health; to eliminate redundant data (e.g. duplicate cases); to verify correctness and completeness of data against original records; to establish correct linkages among databases; and to find specific data or samples if participants withdraw.

3. Re-identification

Access to the key code will be restricted to only those UK Biobank staff who need it to allow proper linkage of follow-up data and for other necessary procedures. All UK Biobank staff will be required to sign confidentiality agreements as part of their contracts. Researchers will not be able to identify individual participants from the anonymised data or samples that are provided to them.

4. Security

A wide variety of measures will be taken to ensure the security of data, samples, the database and the information technology system in general. These include staff training and confidentiality pledges, physical and electronic controls on access to data, cyber-security, and physical security. This should prevent identifiable information from being

used – inadvertently or deliberately – for any purpose other than approved research (see Section II.B.1 below).

II. RELATIONSHIP WITH RESEARCH USERS

A. STEWARDSHIP OF DATA AND SAMPLES

UK Biobank Limited will be the legal owner of the database and the sample collection (see Section III.A.1). Such ownership conveys certain rights, such as the right to take legal action against unauthorised use or abuse of the database or samples, and the right to sell or destroy the samples. Participants will not have property rights in the samples.

UK Biobank does not intend to exercise all of these rights; for example, it will not sell samples. Rather, UK Biobank will serve as the steward of the resource, maintaining and building it for the public good in accordance with its purpose. This implies both the judicious protecting and sharing of the resource. It also extends to the careful management of any transfer of parts or all of the database or sample collection, as is addressed in Section III.D (Transfer of assets, or closure).

UK Biobank will explain the legal status of the database and sample collection to participants, and its committed role as steward of the resource. Even when this legal status is understood clearly, it is likely that many participants will continue to be interested to know how their data and samples are used; for this reason, among others, UK Biobank will inform participants about uses of the resource (see Section I.B.4) and will guarantee the right to withdraw from participation.

As well as respecting the commitments made to participants in the consent agreement, UK Biobank will strive to build a relationship of trust with participants and the wider public, in order to foster acceptance of the ways the resource is developed and used. A detailed Access Policy for use of the resource will be developed, with guidance from the Ethics and Governance Council, which will evolve in response to users, participants and the wider public.

B. RESEARCH ACCESS TO DATA AND SAMPLES

1. General principles of access

UK Biobank will retain full control of all access to, and uses of, the resource.
UK Biobank will not proscribe any medical or other health-related research uses at the outset. However, all proposals will be reviewed by UK Biobank to ensure they are consistent with the participants' consent and this Framework, and that they have relevant ethics approval. All users, whether employed by universities, government, charities or commercial companies, will be held to the same scientific and ethical standards.

Exclusive access to the fully developed resource will not be granted to any party. Use of the biological samples will have to be carefully coordinated and controlled because they are limited and depletable. While the resource is being developed, UK Biobank may use the early data and samples to validate and improve methods of data collection and analysis.

Access to the resource by the police or other law enforcement agencies will be acceded to only under court order, and UK Biobank will resist such access vigorously in all circumstances.

2. Decisions on access and use

The UK Biobank Board of Directors will have the overall decision-making authority over access to and use of the resource. In practice, the Board may delegate decisions on routine applications to suitable bodies or persons (such as an Access Committee or specially designated UK Biobank Working Groups).

UK Biobank will explain, to participants and the public, the policies and procedures for research access. An overall policy and detailed terms of access has been, and will continue to be, developed (i.e. the IP and Access Policy) which addresses fairness and transparency of decision-making, the handling of conflicts of interest and the prioritisation of use of samples.

The Ethics and Governance Council will keep use of the resource under review in order to advise on conformance with this Framework and the IP and Access Policy, and to assure itself, and others, that the resource is being used in the public interest.

3. Licences for specific uses

Access to data and/or samples will be granted under licence for scientifically and ethically approved research consistent with UK Biobank's purpose. Licences will be for specific uses under strict terms and conditions in standard access agreements, including compliance with the consent given, the provisions of this Framework and other policies.

Fees will be charged for licences, with the possibility of charges being higher for organisations that might be expected to derive financial benefit from use of the resource.

4. Sharing of data and findings

UK Biobank seeks to augment the value of the resource in order to ensure that the greatest potential benefit for public health may be realised from it.

All research users will be required to put results from all analyses made on participants' data and samples, and any relevant supporting information, in the UK Biobank database so that they are subsequently available to all researchers with appropriate scientific and ethics approval.

There will also be a requirement on all research users to place the findings (whether positive or negative) from all research based on UK Biobank in the public domain so that people can benefit from them. Publication should be in the peer-reviewed scientific literature whenever possible. UK Biobank will also explore further strategies for dissemination of findings (such as through accessible electronic archives).

Researchers will only be permitted to keep results based on UK Biobank confidential for a limited and reasonable period as described in the IP and Access Policy (for example, while they prepare papers for publication, file patent applications or otherwise pursue reasonable competitive advantage for their efforts). This policy will apply to all research users, whether non-commercial or commercial.

III. RELATIONSHIP WITH SOCIETY

A. MANAGEMENT AND ACCOUNTABILITY

1. Board of Directors

The Board of Directors of UK Biobank are company directors under UK company law, and charity trustees under UK charity law. They are accountable to the Members of the Company (Medical Research Council and Wellcome Trust), and to the Charity Commission for England and Wales, for the performance of their duties as directors and charity trustees, including the duty to act in the interests of UK Biobank.

Up to five Board members, including the Chair, will be jointly appointed by the Members of the Company. A further five members may be individually nominated by the Department of Health, the Medical Research Council, The Wellcome Trust, the Scottish Executive and the University of Manchester (which hosts the coordinating Centre). The Board will include persons with relevant scientific knowledge or other relevant expertise who will be selected for their ability to serve as directors and charity trustees of UK Biobank.

The Board will adopt this Ethics and Governance Framework and be responsible for making sure that all UK Biobank policies and activities conform to it. The Board will also be responsible for matters of corporate governance, including the management of conflicts of interest within UK Biobank. Potential conflicts of interest among members of the Board and the Chief Executive Officer/ Principal Investigator (CEO/PI) will be recorded. The Board retains overall responsibility for the direction, management and control of UK Biobank, but it delegates day-to-day management to the CEO/PI

2. Ethics and Governance Council

The UK Biobank Ethics and Governance Council has been established by the Medical Research Council and the Wellcome Trust in a way that enables it to operate independently of them and of UK Biobank. Terms of reference are attached as Annex 1.

The remit of this Council includes: acting as an independent guardian of the Ethics and Governance Framework and advising the Board on its revision; monitoring and reporting publicly on the conformity of the UK Biobank project with this Framework; and advising more generally on the interests of participants and the general public in relation to UK Biobank.

In pursuing its remit the Council will engage with, and render accounts to, a number of internal and external audiences. Internal dialogues will be with the Board of Directors, the CEO/PI and the funders. External dialogues could be with participants, regulatory or government bodies, other interested parties, and the general public. 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.

In order to be able to fulfil its remit, the Ethics and Governance Council will need to be appropriately knowledgeable about UK Biobank's continuing activities. It is hoped that effective communication will occur on the basis of mutual respect and co-operation. However, the Council will be able to require from parties involved in UK Biobank whatever information and discussion are necessary to fulfil its remit.

Normally the Council will communicate its reflections and criticism 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 funders) or, if necessary, make a public statement that certain actions should or should not be taken. In the extreme, members of the Council could resign in protest and announce this publicly.

The Ethics and Governance Council will work in an open and transparent fashion and report to participants and the public. This may be achieved in a variety of ways, such as through publishing reports of its reviews or discussions, occasionally meeting in public, or holding meetings with the public.

3. Steering Committee and International Scientific Advisory Board

The Steering Committee is responsible for advising the CEO/PI on the development of the scientific protocol, and on the direction and scientific objectives of UK Biobank. It is chaired by the CEO/PI, with the lead investigator from each Regional Collaborating Centre as members and UK Biobank's Executive Director and Chief Scientific Officer as observers. The CEO/PI, Board and funders will also receive independent scientific guidance from an International Scientific Advisory Board, which will meet annually to review UK Biobank's progress and future plans.

B. EXTERNAL GOVERNANCE

1. Ethics approval by relevant ethics committees

The core scientific protocol and operational procedures of the UK Biobank resource, as well as proposed uses of it, will have approval from appropriate ethics committees in accordance with guidance from relevant bodies (such as the Central Office of Research

Ethics) and with relevant provisions (such as the Research Governance Frameworks of England, Wales, and Scotland; Governance Arrangements and Supplementary Operational Guidelines for NHS Research Ethics Committees). Participants will be told that such independent ethics approval will be obtained.

2. Compliance with Research Governance Frameworks

With respect to the core protocol, UK Biobank will assume the responsibilities stipulated by the Research Governance Framework for Health and Social Care in England and the corresponding frameworks in Wales and Scotland.

In England, for example, at present these responsibilities are as follows:

- Sponsor is the Board of UK Biobank Limited: responsible for confirming that proper arrangements are in place for initiating, managing, monitoring and financing the project.

- Principal Investigator is the Chief Executive (CEO): responsible for the design of the project, seeking approvals from the MREC, managing activities in the Co-ordinating Centre, Regional Collaborating Centres and assessment centres, and liaising with researchers (and, in all of this, accountable to the Sponsor).

- Co-ordinating Centre: responsible for the day-to-day conduct of the project and ensuring it follows the protocol, and for training and monitoring of all staff involved in its conduct.

- Regional Collaborating Centres: responsible for scientific input to the development of the study protocol and procedures through the Steering Committee, and for carrying out key aspects of project delivery on behalf of the Co-ordinating Centre.

Typically, external researchers will act as the sponsor of particular research using the resource and will take on the relevant responsibilities. But, if UK Biobank acts as the sponsor of some research then it will take on these responsibilities.

As required under the Human Tissue Act 2004, UK Biobank will be licensed by the Human Tissue Authority to store biological samples for research.

C. BENEFIT SHARING

1. Dissemination of knowledge generally

The purpose of UK Biobank is to learn from the collective health experience of the participants over time, in order to generate and disseminate new knowledge to benefit the health of the public in the UK and elsewhere.

Knowledge derived from studies based on UK Biobank will be:

- Published in the world's scientific and medical literature;

- Communicated to UK Biobank participants, the NHS, and others (as appropriate);

- Accumulated and made available by UK Biobank as a resource for further research (e.g. via archives of the findings of studies).

Such knowledge may also be applied to the development or improvement of healthcare techniques, technologies, materials or routines.

2. Intellectual property, income generation and royalties

Intellectual property and access policies are being developed to help ensure that the UK Biobank resource is accessible to all *bona fide* research users, but is not exploited improperly or used in any way that inappropriately constrains use by others. Terms of access will be embodied in legal agreements that reflect UK Biobank's objectives.

UK Biobank is not expected in itself to lead to patentable inventions that return significant income either to researchers or UK Biobank, but it is expected to become a valuable common resource for research. Nevertheless, there is some chance that research conducted using the resource (which might be conducted by researchers in the public or commercial sector, as well as the academic and charity sector) will subsequently support the development of an invention that returns a profit.

The biotechnology and pharmaceutical industries can play an important role in realising health benefits in a practical sense by developing and improving the use of biomedical products. Commercial companies and other research endeavours that stand to make a profit will, therefore, be allowed access to UK Biobank if their proposal falls within the UK Biobank purpose and complies with the usual scientific and ethics requirements.

Any income that UK Biobank secures from access fees or intellectual property will be re-invested in the resource.

D. TRANSFER OF ASSETS, OR CLOSURE

A detailed strategy is being developed for handling contingencies in the event that the UK Biobank charitable company has to close or make other substantial transitions in the holdings or control of the resource. This will address the possibility of partial or full transfer of the resource, whether elective or as a result of insolvent liquidation.

The objective will be to ensure that the protection and respect for the rights of the participants provided by this Framework continue to be maintained, and that the Ethics and Governance Council is consulted by the Company on the proposed terms before any such transitions or transfers are made.

Information about such measures will be made available to participants.

IV. ADOPTION, IMPLEMENTATION AND REVISION

The Ethics and Governance Framework is a core reference document against which UK Biobank policies and activities will be judged.

A. ADOPTION

The Board of Directors has adopted this Framework and will be responsible for ensuring that all UK Biobank policies and activities conform to it.

B. IMPLEMENTATION

The Co-ordinating Centre, under the direction of the CEO/PI, will be responsible for implementing the Framework. Compliance with it will be a condition of continued funding of UK Biobank by the Funders.

C. REVISION

The Board of Directors, the Ethics and Governance Council, the Funders and other interested parties (including participants and members of the wider public) may propose amendments or revisions of the Framework. In particular, the Ethics and Governance Council will advise on outstanding issues, and may propose adjustments in response to new developments. Adoption of any amendment or revision will rest with the Board of Directors.

ANNEX: UK Biobank Ethics and Governance Council terms of reference

The UK Biobank Ethics and Governance Council (EGC) is an independent committee established by the Medical Research Council and the Wellcome Trust.

Remit

- To act as an independent guardian of the UK Biobank Ethics and Governance Framework (EGF) and advise on its revision;

- To monitor and report publicly on the conformity of the UK Biobank project ("UK Biobank") with the EGF;

- To advise more generally on the interests of research participants and the general public in relation to UK Biobank.

Functions

1. To keep the creation, maintenance and use of the resource under review in order to advise and report publicly on the conformity of UK Biobank's activities with the EGF;

2. To consider and advise on revisions to the EGF that may be required to respond to changes in the legislative or regulatory context, developments in ethics or advances in science or technology;

3. To advise on UK Biobank policies that relate to or flow from the EGF (such as those on recruitment, access, or complaints handling);

4. To keep under review applications for access to the resource with regard to the interests of research participants and in accordance with the Intellectual Property and Access Policy;

5. To approve any transfer of the resource (or substantial parts of it) to a third party, for example, in the event of a liquidation, as set out in the Memorandum and Articles of Association of UK Biobank Limited.