# *UK BIOBANK Ethics and Governance Framework: Summary of comments on Version 1.0*

May 2004

## Acknowledgements

The UK Biobank funders (the Department of Health, Medical Research Council and The Wellcome Trust) would like to thank the individuals and organisations who generously gave up their time to comment on this version of the UK Biobank Ethics and Governance Framework.

## Table of Contents

## Executive Summary

The first public draft Ethics and Governance Framework (EGF) was prepared by the UK Biobank funders – the Department of Health, the Medical Research Council, and the Wellcome Trust – with the advice of an Interim Advisory Group on Ethics and Governance (IAG).

Copies of the EGF and EGF response template were sent to over 100 stakeholders and made publicly available on the UK Biobank and Wellcome Trust websites between 24 September 2003 and 24 October 2003. The total number of responses to the exercise was 29. Of these 12 were personal responses and 17 represented the views of groups or organisations.

On the whole, respondents found the EGF a useful framework, in that it described the general structure and properties of the UK Biobank well. It was, however, seen by most respondents as being at '*an early stage in its evolution*', with many areas lacking in detail.

The Framework's treatment of recruitment received a mixed response from respondents. Whilst, the majority of respondents were content with the general principles, respondents raised a number of concerns around the selection and approach of participants, these included:

- selection bias of recruitment processes;
- whether GP participation was guaranteed; and
- data protection and clarity of data required from participants.

Most respondents found the Framework's proposals around consent acceptable. However, respondents highlighted the need for a clear explanation of what consenting to participate in UK Biobank will entail. The importance of establishing genuine consent and ensuring that participants retain and understand what they are consenting to and the need to find an approach suitable for the many years UK Biobank will operate were also noted.

There were a number issues raised concerning the requirements, restrictions and ownership of data that is to be collected by UK Biobank, including:

- who would have access to the full patient records (e.g. UK Biobank staff, UK Biobank researchers, UK-only researchers, researchers across the world);
- if records were to be anonymised, who would carry out the anonymisation process;
- what types of information would be collected and from which records data would be accessed.

A number of respondents requested a more detailed explanation of UK Biobank's policy on what information resulting from UK Biobank would be fed back to individual participants.

Some respondents noted that participants may expect information of relevance to their health to be fed back to them in some way. However, respondents differed on the stages at which such information should be provided (e.g. at enrolment or following the initial analyses on all participants' samples) and whether this information should be fed back to the participant or their GP.

Respondents found the Framework's proposals around ongoing engagement with participants and the public, and participants' expectations of recontact or personal financial gain, broadly acceptable.

Most respondents thought the Framework's treatment of confidentiality was acceptable. However, there were concerns around access, anonymisation and security of the data.

A number of respondents indicated that they were concerned about permission being granted for specific types of research, particularly medical market research and insurance industry research. A particular concern was access being granted for police use, and there were calls for a clarification of the law in this area.

The majority of respondents found the three management and accountability structures (Board of Directors, Science Committee, Ethics and Governance Council) acceptable. Although, a number of respondents felt that the governance structure as a whole lacked clarity.

Whilst there was a view that the Ethics and Governance Council was acceptable, a number of respondents commented that its powers might not be sufficient in relation to individual uses of the resource, investigation of compliance, and procedures for addressing concerns.

Respondents welcomed the embedding of the external governance of UK Biobank within existing research and professional governance structures in the UK, but had concerns around:

- how MRECs would be used;
- the involvement of GPs and local healthcare organisations;
- conflicts of interest;
- the role as 'sponsor' of research; and
- the legislative framework within which UK Biobank will operate.

There were mixed views on the Framework's proposals around benefit sharing particularly the relationship between UK Biobank and the biotechnology and pharmaceutical sector. Similarly, respondents had divergent views on the Framework's proposals around the transfer of assets or closure of UK Biobank, most respondents requesting more information to allow them to make a more informed judgement on this issue.

# 1 Background and methodology

## 1.1 Background to UK Biobank Ethics and Governance Framework

1. The first public draft Ethics and Governance Framework (EGF) was prepared by the UK Biobank funders – the Department of Health, the Medical Research Council, and the Wellcome Trust – with the advice of an Interim Advisory Group on Ethics and Governance (IAG).

2. The Group includes experts in research ethics, philosophy, law, science and social science, and consumer representation, and is chaired by Dr. William Lowrance, a consultant in health policy and ethics. (More information on the IAG, including terms of reference and biographies of members, is available on the UK Biobank website).

3. The IAG met three times between February and July 2003. The Group's deliberations were informed by a number of consultations, including an ethics consultation workshop held in April 2002 and two consultation exercises, undertaken in May 2003 on an early draft of the EGF, in which members of the public, health-care professionals, and a wide-ranging group of experts and stakeholders participated.

4. Version 1.0 of the EGF was published in September 2003.

5. This report was considered by the IAG at their final meeting in April 2004.

## 1.2 Methodology

6. Hard copies of Version 1.0 of the EGF were sent to over 100 stakeholders, including all those who had previously taken part in consultation events to develop the EGF, directly requesting their comments. The EGF and EGF response template were also made publicly available on the UK Biobank and Wellcome Trust websites between 24 September 2003 and 24 October 2003.

7. Not all respondents used the template to respond, some outlined their thoughts on the EGF in letter format. None of the questions contained in the template about the acceptability of the EGF were compulsory, and some respondents completed only those where they had specialist knowledge.

## 1.3 Respondent characteristics

8. The total number of written responses was 29. Of these 12 were personal responses and 17 represented the views of groups or organisations.

## 1.4 Structure of this report

9. This report reviews the comments received on the EGF. Overall comments are reviewed first, followed by comments on the individual sections of the report. Tables showing raw

data from the satisfaction/acceptability scales are given in Annex A (note - not all respondents completed all questions). Illustrative quotes used in this report are labelled [O] for organisation/group responses or [P] for personal/individual responses.

## 2 Overall acceptability of EGF

### 2.1 Introduction

10. Respondents were asked how acceptable the UK Biobank EGF was overall. This section describes their responses to this question.

11. On the whole, respondents found the EGF a useful framework, in that it described the general structure and properties of the UK Biobank well. It was, however, noted by some respondents as being at '*an early stage in its evolution*', with many areas lacking in detail. This meant that some respondents felt that full consideration of the acceptability of proposals was not yet possible.

### 2.2 *'More acceptable than unacceptable'*

12. In general, the EGF was seen as a useful foundation on which further work clarifying issues of concern could be built (**Box 1**), with 67% of respondents finding it acceptable. A common theme from responses was the need for the EGF to comprehensively tackle all ethical and legal issues, as this would ensure public trust and participation.

**Box 1. The importance of the EGF**

*'The project, in principle, is worthwhile. We would like to support it but before doing so we need to be reassured that there will be sufficient public trust in the organisation to operate effectively and to act responsibly and ethically with the medical information that it collects and retains. We are not convinced, from what we have read in the consultation document, that the organisation has reached that position. We would expect to see some significant developments before our concerns are allayed.' [O]*

*'We believe that the draft Framework is an excellent basis for the development of acceptable policies for the operation of Biobank and an essential element of this important project to identify the links between genomics, environment and health outcomes.' [O]*

*'More acceptable than unacceptable, though there are still important issues to clarify.' [P]*

*'A number of ethical and legal issues have been raised in these comments and there are issues still to be resolved, however, the general approach is acceptable.' [P]*

*'UK Biobank is likely to be subject to understandably high levels of public scrutiny. For this, and other, reasons it is important that its Ethics and Governance Framework should be 'Gold Standard'.' [P]*

*'UK Biobank funders will be aware of the importance of ensuring that the Ethics and Governance Framework is appropriate and properly followed to ensure the success of UK Biobank.' [P]*

### 2.3 Main concerns

13. A number of concerns were raised by respondents, these included the need for greater clarity on the:

- relationship of UK Biobank with participants and society, particularly the project's aims and the expectations the project has of participants;
- the value of biobanks;
- plans for income generation and handling of property rights; and
- level of and controls on commercial access.

14. Respondents called for the remit, roles and potential impact of UK Biobank to be clearly explained to all stakeholders, particularly participants.

> *'Nowhere in the document is there a statement of either the expected benefits or the potential harms of the Biobank project both for participants and for the wider society. Such a statement is essential to meaningful public consultation.' [O]*

15. The role of biobanks was questioned by one respondent, as were the risks involved in such projects:

> *'There is considerable controversy regarding whether or not UK Biobank can generate scientifically valid and useful results (see eg. The Lancet, Vol 361, p1734-1738). Concerns include both the broader issue of the relevance of this type of study to reducing the incidence of common diseases and the narrower issue of whether the biobank is optimally designed to minimise the chances of making spurious and misleading conclusions about the role of genes in health. It is wrong to imply to participants that long-term participation will lead to health benefits until these issues have been democratically debated and resolved. Arguments in favour of participating are critically dependent on the claimed benefits of the project (see eg. John Harris, 2003, Ethical Biobanking, HGC03/19 Annex B).' [O]*

> *'We would, however, be interested in hearing about whether or not a risk analysis has been conducted for the overall project. If so, and in line with the recent recommendations by the House of Commons Science and Technology Committee on openness and transparency, we would support publication of such analyses, and indeed the overall business plan, to allow wider scrutiny.' [O]*

16. Access to the data contained in the UK Biobank was also a concern:

> *'I would still be a bit concerned about the short, throw-away sentence about access by the police or the state as a whole. There has been considerable concern about this in other countries with databases of this type and I am not sure whether this statement will be reassuring enough. I think many members of the public will be worried that this is simply a back-door way into the widely discussed concept of a broad national DNA database and it seems to me that a database which is being held purely for medical research should be better protected than this.' [P]*

17. There was conflicting opinion about the value of commercial involvement, with a number of respondents requesting further information about the possible nature of UK Biobank's relationships with commercial entities, some noting that it may endanger individuals' willingness to participate (**Box 2**).

**Box 2. Commercial involvement**

*'Concerns raised in past consultations (particularly regarding the science, poor prospects for health benefits and lack of controls on commercial access) have not been addressed.' [O]*

*'The vision of a user community that, in principle, includes commercial entities is to be warmly welcomed and strongly supported. Such diversity of eventual use promises maximal returns from UK Biobank in terms of scientific discovery and improved healthcare, both in the UK and globally.' [O]*

*'Our main concern is that the great utility of Biobank for UK researchers might be undermined by the possibility that it will be of use to pharmaceutical and biotechnology companies. We think its very*

*important for participants to know clearly that this isn't just a resource that will serve to promote medical knowledge, but will also be a useful tool for companies to make profits.' [P]*

## 2.4 The need for continued dialogue

18. A number of respondents noted that they were unclear as to how the EGF would be further developed. Clarity about the form and level of consultation that would occur with stakeholders in the future was also requested (**Box 3**).

19. One respondent also called for an independent review of the outcomes of the pilot stages of UK Biobank.

**Box 3. The need for continued dialogue**

*'Further extensive and interactive dialogue over such plans is strongly to be counselled.' [O]*

*'The public and all professional organisations need to be kept fully informed of new developments at every stage of the project' [O]*

*'There are certain issues which need to be carefully and appropriately addressed if the project is to be a success.' [O]*

*'The current consultation is also inadequate to ensure that the project is acceptable to the public and participants (as opposed to the board).' [O]*

*'I just wonder whether a brief external review after the pilot stage by a body which is completely dissociated from the whole thing would not be a sensible way forward.' [P]*

# 3 Relationship with participants

## 3.1 Introduction

20. This section outlines respondents' views on aspects of the EGF concerning UK Biobank's relationship with participants, namely:
    - Recruitment;
    - Understandings and consent; and
    - Confidentiality.

## 3.2 Recruitment

21. The Framework's treatment of recruitment received a mixed response from respondents. The majority of respondents were 'very satisfied' or 'satisfied' with the general principles (n=16, 80%). However, in relation to the selection and approach of participants, 5 respondents (25%) were 'very unsatisfied' or 'unsatisfied', with only 8 respondents (40%) being 'satisfied'. Enrolment was thought to be 'very satisfactory' or 'satisfactory' by 11 respondents (55%). Many respondents believed further development and clarification of concerns was needed in the EGF around issues relating to recruitment.

22. Concerns around the selection, approach and enrolment of participants into the UK Biobank included:
    - selection bias of recruitment processes (**Box 4**);
    - whether GP participation was guaranteed (**Box 5**); and
    - data protection and clarity of data required from participants (**Box 6**).

23. The recruitment of volunteers to UK Biobank was thought to be an area needing more explanation (**Box 4**). Many respondents were concerned about how UK Biobank would achieve a representative sample of the population and asked for further information on the methodologies that might be used to identify participants. There was praise and support for the outlined efforts to reduce barriers to participation. However, there were still concerns over how UK Biobank would ensure inclusion of under-represented groups in society. This included concern that more information was needed on how people's capacity to consent would be judged, so that claims of coercion or discrimination could be avoided.

**Box 4. Selection bias**

*'Reflecting specifically on the details of recruitment, we would look for further information as to procedures to avoid an ascertainment bias favouring the more health conscious individual' [O]*

*'...researchers should not approach people directly (as this would constitute a breach of confidentiality) and [we] would like consideration to be given to the idea of selecting participants via a different sampling frame. However, other possible sources (e.g. electoral register) are notoriously incomplete and use of these could lead to serious under-representation of certain groups. We would like more detail about how UK Biobank plans to recruit potentially under-represented groups (e.g. travelling people and the homeless). If this aspect is not addressed the most under-researched groups in terms of disease levels and health needs will be even more disadvantaged.' [O]*

*'It will be important to ensure that the framework addresses the issue of subjects with a variety of disabilities. Understanding health issues for these members of society is also very important.' [O]*

*'Our preferred option is recruitment via letters from general practitioners to all of their patients in the relevant age groups. This would need to make clear that a large number of patients are being approached rather than an individual patient being "singled out" which might imply some pressure to accept the invitation. [O]*

*'Enrolment consultations should be held at convenient times to participants to avoid bias in the sample eg if held in the day, a disproportionate sample of non-working people.' [O]*

*'We would welcome clarification of what 'representative' means in the context of the UK Biobank sample population. Our understanding is that the sample will not be randomly selected from a population register, nor will there be purposive sampling according to quotas in particular categories. From the information provided, it seems that this will be a convenience sample with selection at the level of GPs and individual patients. In what sense, then, will this be representative? Also how the target population is to be defined (e.g. UK citizens, UK residents or people who actually live in the UK (e.g. to include assylum seekers, illegal immigrants etc)). UK Biobank needs to have proper policies in place to ensure that non-English speakers are as actively recruited as English speakers.' [P]*

*'UK Biobank indicates it will "work to reduce barriers to participation such as ethnicity, employment and language". It would be useful to provide the reader with some tentative overall strategies or some indications of how this will be approached because it is a delicate and difficult issue.' [O]*

*'Piloting will be crucial to establish best means of recruitment, not just to ensure high, representative enrolment rates but also that participation is with fully informed consent.' [P]*

*'In relation to the selection and approach to participants, we strongly support the efforts to reduce barriers to participation. There are, however, a couple of additional barriers to participation that you may need to consider in order to make this project as inclusive as possible. The first concerns literacy levels given 1 in 5 of the general population are functionally illiterate. This could affect inclusion in the study in a number of ways. For example, it is self evident that an initial approach made by a letter may not reap the results you want, or that some participants may need some help with filling in questionnaires.' [O]*

*'The protocol used for judging potential participants' capacity to give consent will need to be agreed by an MREC (in addition to the Ethics and Governance Council) to avoid claims of coercion or discrimination, particularly against those where English may not be the first language.' [O]*

24. Although several respondents expressed a strong preference that participants should be recruited via their general practitioner, a few respondents noted that the involvement of general practitioners could not be guaranteed and that the recruitment process should ensure that this does not create a biased sample of the population (**Box 5**).

**Box 5. GP involvement**

*'Selection raises scientific issues regarding whether or not the biobank is representative and these need to be openly considered. Recruitment via either GPs or PCTs implies their endorsement of the biobank as a valid and useful approach to improving health and their satsfaction with the safeguards for participants. It is difficult to envisage how this could occur without more transparency and involvement of health professionals in the debate, including on issues of concern of particular relevance to them (eg the validity of medical records for follow up, and the ethics of commercial access to such records).' [O]*

*'The selection approach will have to be clarified. Certainly the Icelandic experience shows that GP participation cannot be taken for granted.' [P]*

*'[Another] barrier concerns GPs who may not as yet have computerised all their records, and what effect this may have on recruitment as well as the following up of medical histories. The Biobank recruitment and follow-up will be taking place in parallel with major additional investment in common NHS IT programmes that will affect the storage of medical records.' [O]*

25. Respondents requested more details of how patient data would be accessed; what patient data might be collected; how it would be stored; and, how it might be used in research projects. A small number of organisations requested that they be consulted again when more detail was available on recruitment and enrolment.

**Box 6. Data requirements, uses and protection**

*'Our view, is that it is not appropriate for researchers to be given the names of potential research participants, since this would constitute a breach of confidentiality. We receive a steady stream of complaints from patients and doctors when patients have received unsolicited letters from researchers about participation in a project, since it is clear that their personal details have been passed to an individual unconnected with their care without their consent. Some patients also feel pressure to agree if they are approached directly by the researchers.' [O]*

*'In terms of compliance with the Data Protection Act 1998, the basis on which individuals are enrolled into the project will be a key issue. In so far as involvement in the project will lead to records about living, identifiable individuals being kept, the data protection principles will need to be complied with. This means that individuals must be properly informed of the identity of the body keeping information about them, of the purposes for which information about them is to be processed, and any other information necessary to make the processing of the information fair. The latter requirement may mean telling individuals about the disclosure of information about them, or whether the research results will be exploited commercially. In particular, the research body must ensure that no one is deceived or misled whilst being enrolled into the project. The objective here is transparency, and there is no reason why this should not be achieved given clear, truthful enrollment procedures.' [O]*

*'We are not entirely sure how, precisely, researchers will make initial contact with volunteers. From a data protection perspective, a good solution would be for the doctor him or herself or the NHS Trust to select patients fitting the research criteria, and for the doctor or Trust to issue invitations for participation in the project. This would avoid any unconsented disclosure of confidential personal information about patients. An unconsented disclosure of confidential personal data could constitute a breach of the 1st data protection principle. Doctors and other record holders involved in the research project should also be mindful of the relevant professional rules, for example those issued by the General Medical Council.' [O]*

*'Little thought seems to have been given to explaining to participants about the use of their genetic information, even if anonymised, by commercial firms. Exactly what will be done about the patient who refuses, as I myself would do, on the grounds that an altruistically-based NHS should not be supporting commercial research.' [P]*

26. A number of respondents noted activities that if undertaken might support the recruitment process and enable greater participation (**Box 7**).

**Box 7. Ensuring participation**

*'UK Biobank could consider providing potential participants with examples of how a better understanding of disease and disease processes has resulted in significant reductions in morbidity and mortality (eg understanding infectious diseases paved the way for strategies to combat infections, including therapeutic interventions).' [O]*

*'The UK Biobank project needs to be very high profile in the media to ensure that potential participants know the background and aims of the project when approached.' [O]*

*'…mass participation is unlikely to be achieved or trust maintained unless the main issues of public concern are first resolved by involving the public in drawing up the ground rules for participation. One major issue of concern that has been raised in all the consultations to date is the role of commercial companies - it is therefore particularly disappointing that the public has not been involved in considering commercial conflicts-of-interest or intellectual property rights.' [O]*

## 3.3 Understandings and consent

27. Many respondents, whilst noting a number of concerns and areas where further development was needed, welcomed the framework for consent outlined by the EGF, for example:

*'This seems to represent a genuine attempt to ensure that all participants who give consent are fully informed.' [O]*

*'Broadly, however, we welcome the lead provided by UK Biobank over such issues. Again we await further detail and anticipate the extra clarity and benefits dialogue with stakeholders will bring.' [O]*

*'The mechanisms for gaining consent from individuals for participation in the project appear to be very thorough and well thought out.' [O]*

### 3.3.1 Consent

28. Most respondents found the EGF's proposals around consent 'very acceptable' or 'acceptable' (n=11, 58%). Respondents highlighted the following (examples in **Box 8**):
    - The need for a clearer explanation of what consenting to participate in UK Biobank will entail, including the following issues:
        - what exactly participants will be asked to do;
        - whether consent will be required for each type of patient record accessed;
        - what will happen to their data and samples; and
        - what ongoing rights or information participants will have.
    - The need for transparency concerning the activities that consent allows and how decisions on access to the resource will be made;
    - The importance of genuine consent and establishing that participants retain and understand what they are consenting to; and
    - The need to find a suitable ethical and legal approach to consent appropriate for the many years UK Biobank will operate.

**Box 8. Consent**

*'A much clearer prior assessment is needed of what data is likely to be accessed…' [P]*

*'Exactly what individuals are consenting to seems rather unclear other than it will be to 'participate in UK Biobank'. I think that this is too broad to be useful.' [P]*

*'Rather than responding to the detailed questions in the draft, we would like to draw your attention to the discussion and recommendations in the 1995 [Nuffield Council on Bioethics] report, Human Tissue: ethical and legal issues, regarding consent: "The ethically significant requirement is not that consent be complete, but that it be genuine. Ensuring that consent is genuine is mainly a matter of care in detecting and eliminating lack of consent… Obtaining genuine consent requires medical*

*practitioners to do their best to communicate accurately as much as patients, volunteers or relatives can understand about procedures and risks, and to respect the limits of their understanding, and of their capacities to deal with difficult information. If all reasonable care is exercised, adequate and genuine consent may be established, although it will necessarily fall short of fully informed consent. (Paragraphs 6.20 – 6.21)". [O]*

*'[we] maintain that all participation in sample repositories designed to support genetic research should be entirely voluntary in nature. Supporting policy should dictate and guarantee genuine independence of individual choice as to participation in DNA collection for genetic research. Clearly respecting such independence of choice includes avoidance of undue inducement to participate in genetic research. We would expressly caution that the success of such a complex consent process in achieving its purpose relies entirely upon understanding and retention of its content. Experience in the field would predict that such comprehension and retention may be unexpectedly low. Experimental testing and verification of the effectiveness of proposed vehicles for communication around the issue of establishing consent is much to be desired.' [O]*

*'There seems some tension between the open consent envisaged in the framework, which is oriented towards overall goals and purposes rather than specific uses of UK Biobank, and the suggestion that further consent would be sought in the future for research that falls outside of the original consent. It is not clear what is meant by this -- does this mean that potentially in the future the UK Biobank's purposes could change and be used for different purposes other than 'enchancing other people's health'? To my mind this is not clear. Also I feel that participants should be informed as part of the consent process about what would happen regarding the transfer of assets or closure arrangements. The framework states that participants will be told but it is not clear whether this is part of the consent process or not. ' [P]*

29. In terms of what giving consent entails, one respondent argued that there was a need to obtain separate consent for each (medical) record system, both now and in the future. Another respondent said that it would be hard to achieve truly informed consent as the procedure was complicated and participants may not understand the details of their consensual agreement:

    *'Patients should perhaps be asked to give separate, explicit consent for access to past records and a link to records in the future. Similarly, patients should perhaps give separate consent for each record system. If consent to participate covers all these options, this must be explicit before consent is sought.' [O]*

    *'This is a complicated consent procedure; therefore it is going to be difficult to get truly informed consent from many people, which is likely to bias your sample. I don't think that obtaining broad consent to gathering information from several different types of record at some date in the future is very satisfactory. People giving consent will often not realise the extent of the personal information held in some of their records. I may give my GP very confidential information that will be entered in my medical records, but I may have forgotten that some years before I gave permission for any 'data' to be accessed whenever needed by Biobank.' [P]*

30. One respondent suggested that UK Biobank should try to demonstrate 'continuing consent':

    *'There are concerns about the ethical and legal basis of blanket consent over the many years proposed for UK Biobank. Regular reconsenting would be expensive and 'drop out through non-response' may threaten the viability of UK Biobank. However, the need to follow accepted professional and legal standards for consent is essential e.g. Data Protection Act 1998, Human Rights Act 1998. Opt-out should be acceptable approach to demonstrating continuing consent provided adequate measures are in place for ensuring participants are aware that they are still part of UK Biobank e.g. through the regular newsletters proposed and there are easy opt-out procedures.' [P]*

31. One respondent advised that the system for obtaining consent should be modelled on having a more general "authorisation for biobank", akin to a license to operate:

> *'There is a school of thought that we should be informing individuals about the conditions of use rather than the specific use as required by informed consent. Arnason and Greely suggest that we should have an authorisation for biobanks rather than informed consent. We then don't dilute the principle so (sic) informed consent but acknowledge that biobanks create different issues. There is a need to develop a conceptual clarity about the type of consent or permission that individuals are being asked to agree to.' [P]*

32. Another respondent argued that it would be useful to have some evaluation of the consent process:

> *'Evaluation of the consent process is essential and we feel that Biobank should be strongly encouraged to carry out such an evaluation. This could be of tremendous benefit to anyone considering setting up a large scale sample collection. It would also be very helpful if the circumstances under which a new piece of research activity would be considered to have fallen outside the current existing consent could be clarified.' [O]*

33. The importance of briefing participants about the potential risks of being involved in UK Biobank was stressed. Risks identified included not only the accidental release of UK Biobank information into the public domain, but also the physical risk from giving a blood sample.

> *'The potential informational risk from release of information collected by UK BioBank and the physical risk taking a blood sample should be described in the consent process.' [O]*

34. A number of respondents recommended that UK Biobank could gain from investigating how other guidelines on consent operate. In particular, references were made to the following:
    - The Roche Charter on Genetics (1999);
    - The World Medical Association Declaration of Helsinki; and
    - European Patent Directive (in particular Recital 26).

### 3.3.2 Collection of data from medical records

35. Most respondents found the EGF's proposals around the collection of data from medical records 'very acceptable' or 'acceptable' (n=13, 69%). There were a number issues raised concerning the requirements, restrictions and ownership of data that is to be collected by UK Biobank. Issues raised include:
    - Who will have access to the full patient records (e.g. UK Biobank staff, UK Biobank researchers, UK-only researchers, researchers across the world)?
    - If the records are to be anonymised, who will carry out the anonymisation process?
    - What types of information will be collected and from which records will data be accessed? Is lifestyle data to be collected?
    - Will researchers be able to look at a participant's whole medical record at any one time?
    - Will data requirements need to be explained in 'layman's language' to participants?

36. A number of respondents found it unclear whether third parties would have access to data records themselves and requested clarity from UK Biobank on this issue.

*'Who will have access to the full patient records? If the records are to be anonymised, who will carry out the anonymisation process? Will participants give UK Biobank access to their medical records or a few named individuals?' [O]*

37. Another respondent asked for greater understanding of the types of linkage envisaged and how these would be managed:

*'Collection of data from medical records: whilst we realise that data collection and follow-up strategies for UK Biobank are still being piloted, we would welcome clarification of what is currently envisaged. Certainly we think that such clarification will be essential for those whose consent is actually being sought. For example, we imagine that for practical reasons follow-up will be through linkage to Primary Medical and Dental Care records (which include details of secondary care contact), cancer registries and death certificates. Are any other types of linkage currently envisaged? Furthermore, reference is made to GU medicine records and occupational health records. We are unclear as to the relevance of such records to UK Biobank. In any case would they contain any important information not held in Primary Care records?' [P]*

*'In our opinion, the list of records to which UK Biobank wants to have access for linkage should be limited. Although participants many very well grant a general consent to access these records, they should know what type of linkage is envisaged. For instance, access to the occupation health record might not be expected from participants unless it is explicitly mentioned. A participant may be comfortable granting access to certain records and not to others. ...and what about privately held records?' [O]*

38. In terms of sensitive data, one respondent asked if UK Biobank would seek medical records that are considered by participants to be highly sensitive:

*'The Framework document mentions that UK Biobank may decide not to seek access to some record systems (eg genito-urinary medical records). While such a view may be taken on the basis that some medical information is particularly sensitive, such exclusions risk severely compromising the value of UK Biobank for research (eg genito-urinary medical records would be valuable in examining infectious associations with cardiovascular disease). Attention should therefore focus on ensuring systems and procedures are in place to protect the confidentiality of the data rather than excluding certain data sets.' [O]*

39. Another respondent was concerned that despite UK Biobank's data being anonymised, there would still be the risk that individual identities might be deduced:

*'An assessment of the potential for deductive identification is therefore essential before safeguards and/or warnings can be put in place.'*

40. Many respondents asked if there were any policies that would govern access to UK Biobank data, in particular what types of organisations might be able to request or apply for access:

*'The purpose of the companies seeking access may vary and may be against the interests of participants or those they are seeking to help. The biotech, pharmacy, chemical, nuclear, food, insurance and tobacco industries have all been involved to varying extents in this type of research and their commercial interests may sometimes (and in some cases, often) conflict with public health.' [O]*

### 3.3.3 Provision of health information to participants

41. There were mixed views about the EGF's treatment of the provision of healthcare information to participants, with 12 respondents (63%) finding it 'very acceptable' or 'acceptable', 3 respondents (16%) finding it 'unacceptable' and 4 respondents (21%) finding it 'neither acceptable or unacceptable'.

42. A number of respondents requested a more detailed explanation of UK Biobank's policy on what information resulting from UK Biobank would be fed back to individual participants. For example, one respondent highlighted the need for a process to manage requests for results from early screenings:

> *'… you will have a lot of results that are way outside the normal range (sugar, Hb, BP etc. etc.). I agree that you must have a protocol for dealing with these results, but what is written is too vague to be able to comment on.' [P]*

43. Some respondents noted that participants may expect information of relevance to their health to be fed back to them in some way. However, respondents differed on the stages at which such information should be provided (e.g. at enrolment or following the initial analyses on all participants' samples) and whether this information should be fed back to the participant or their GP (**Box 9a**).

**Box 9a. Provision of healthcare information to participants**

*'Patients will expect that clinically relevant findings at enrolment or before samples are stored will be fed back in some way, even if through their GP. The different contractual status of research nurses as opposed to practice nurses are noted, but professional obligations still apply. Similarly, the difference in laboratory standards for research rather than clinical purposes is also noted. However, participants may not fully appreciate these differences, especially if recruitment is via the NHS and/or on NHS/GP premises. Earlier detection of preventable diseases will also benefit NHS health objectives. The implications for the NHS needs to be further considered. Piloting to examine patient expectations will be helpful in this.' [P]*

*'Participants are likely to expect provision of health information from initial screens eg blood pressure, blood sugar and cholesterol. We believe this information should be provided to the participant's GP as long as they have given consent for this to be done.' [O]*

*'In our opinion, results from the baseline analysis should be systematically provided to participants to avoid discretionary and perhaps contradictory practices. This would be consistent with the purpose enunciated on page 6: "UK Biobank will seek active engagement with participants". It is also consistent with the principle of solidarity and reciprocity. It is only fair to participants that information, which could be helpful to their health, be communicated. Such process could, for instance, be done by sending update letters to the physician which holds the medical records (These records will be regularly consulted by UK Biobank for on-going data collection). The physician would have to decide upon the best course of action based on the information received.' [O]*

*'In our view, the only individual health related information Biobank should consider feeding back should be that gathered from the enrolment meeting, such as blood pressure. Participants should then be encouraged to discuss the results with their GPs. If this information is fed back, then it should go to all participants as those collecting such information should not be expected to make clinical judgements about individuals health status. The reason for this position in relation to the feeding back of health information is that, in some cases, participants may be (falsely) reassured that their participation in this project would mean that would receive warning about any potential health problems.' [O]*

44. Some respondents found the exact 'duty of care' owed to participants to be unclear in the EGF and it was stressed that the provision of information would have to be with due care, as it might not meet mandated clinical laboratory standards for quality and accuracy, for example:

> *'A point of note is that research information may not meet mandated clinical laboratory standards for quality and accuracy. For example, research assays and methodologies may not be validated. Therefore even where the research produces information that may be of value for the healthcare management of the participant it must be provided in this context via the physician. UK BioBank should clearly outline the duty of care in this research context. For example, it is stated in the Framework document that should any health concerns arise, participants will be encouraged to contact their GPs. However UK BioBank should also consider if the duty of care in this research context should extend to communicating these findings to the GP directly as informing the participant alone may not be adequate. UK BioBank should clearly outline the duty of care in this research context. What will be the policy of UK BioBank where a participant applies under the Data Protection Act for access to their information?' [O]*

45. It was also recognised that a policy of duty of care may actually encourage participation, based on potential health knowledge gain. It was recognised that UK Biobank could carry implications for the NHS. **Box 9b** contains a number of respondents' views on the issue of provision of health information.

**Box 9b. Provision of healthcare information to participants**

*'Were some research derived from UK Biobank to discover that a number of participants were at particular risk of a condition, then this should be reported in the general feedback to all participants – and indeed to public and medical community at large – so that any individual who might be at risk could seek advice and help. ' [O]*

*'I agree that most results will only be interpretable at a population level, but some very clear and strong associations may have immediate individual implications. What to do about these, if any, needs careful thought--particularly whether there is an acceptable and effective treatment.' [P]*

*'From my own experience of population studies which have only set out to look at frequencies of single genetic disorders we have, from time to time, obtained unexpected information about the possibility of other diseases which may sometimes be relevant to the health of an individual. How will this information be handled? If it is of genuine importance to an individual's future health. (sic) Will it be fed back to their GP or to them or will "unexpected" findings be kept confidential to Biobank?' [P]*

*'…if a particular genetic test with clinical relevance was identified, participants should be offered the opportunity to be re-tested in a clinical setting as opposed to a research setting. We felt that the individuals who made the finding possible through participation in research should have access to any tests identified. However, we realise that this would raise issues concerning provision of the clinical setting and also that it may encourage people to enter into research because they think they may have better access to a test that may benefit them. We believe this needs further consideration.' [O]*

*'Earlier detection of preventable diseases will also benefit NHS health objectives. The implications for the NHS needs to be further considered. Piloting to examine patient expectations will be helpful in this.' [P]*

### 3.3.4 Ongoing engagement with participants and the public

46. Most respondents found the EGF's proposals around ongoing engagement with participants and the public 'very acceptable' or 'acceptable' (n=14, 74%). A few respondents stressed the importance of giving participants the opportunity to influence the conduct of UK Biobank, through the establishment of a 'participants' panel'. This is examined further in section 5.

> *'We note the recommendation in I(B)4 that the Biobank "may wish to establish a participant's panel". We would strongly encourage the establishment of such a panel.' [O]*

47. However, it was felt that in the current plans, the suggestion for such a panel is vague and does not seem to fit in with the current governance structure of UK Biobank, though other suggested methods of engagement were thought acceptable:

> *'The idea of a website, newsletters or meetings and the like are fine but the suggestion of a participants' panel is vague and does not seem to fit with the governance structure of Biobank.' [P]*

### 3.3.5 Expectation of recontact

48. The majority of respondents found the EGF's proposals around the expectation of recontact 'very acceptable' or 'acceptable' (n=15, 79%). However, respondents requested clarification of how follow-up strategies around consent for future activities would be established. One participant responding on behalf of a group noted:

> *'The group were divided about whether or not participants should have greater control over the research conducted via UK Biobank using their samples and information. The practical difficulties of gaining consent for each project were acknowledged but there was reluctance to simply accept that participants could have no input at all. Views here ranged from wanting all projects to get specific consent, to participants stipulating the kinds of research they would object to (racial difference studies, for example) to the participants having more actively to review whether they wished to continue to make their sample and information available.' [P]*

49. One respondent noted concerns about recontact of subsets of participants:

> *'In relation to the expectation of recontact (I(B)5), we endorse the comment that 'care will be taken' over the use of selection criteria. Clearly if a subset with a particular genetic variant were recontacted and were told why, this might reveal aspects their genetic status. However, we suggest this possibility should be explained in advance and the principle of general consent should then apply. For example, consent should be sought for a particular study of, say risks of heart disease, and they should be told what information and measurements would be collected. There should be the presumption that such research would involve some kind of comparison group and we do not feel individuals should be told which group they may be in.' [O]*

50. In terms of the frequency of recontact a range of views were expressed by respondents:

**Box 10. Frequency of recontact**

*'In the scientific protocol it may be necessary to stipulate recontact with participants to gain ongoing information on risk factors and life style by follow-up questionnaire (eg every 2 years). This recontact should be made clear to participants.' [O]*

*'Biobank has probably considerably underestimated the level of re-contact necessary in order to obtain the data needed to test the relevant hypotheses. An assessment of the likelihood of recontact is necessary before participants can be informed about it.' [O]*

*'It is unlikely that recontact will be a regular event, thus it would be feasible for the Ethics and Governance Council to be involved in and approve all decisions to recontact participants.' [P]*

*'We suggest that you indicate that consideration will be given to the possible "over-solicitation of a given sub-population" in decisions to recontact participants. A registry should be set to keep track to recontacts with any given individual.' [O]*

### 3.3.6 Right to withdraw

51. The majority of respondents found the EGF's proposals around the right to withdraw 'very acceptable' or 'acceptable' (n=14, 70%). The main issues concerning the right to withdraw were to what extent participants should be given the freedom to make decisions about continuing to be a participant in UK Biobank and how withdrawal would be operationalised. Examples of respondents' views are included in **Box 11**. The EGF proposed three possible options:
    - Complete withdrawal;
    - Discontinued participation; and/or
    - No further contact requested.

52. A number of respondents believed that all three levels of withdrawal should be available. However, it was recognised by respondents that the value of UK Biobank as a resource for research would be limited if many participants withdrew and chose to have their data removed from the database. Furthermore, it was highlighted that there could be difficulty in tracing and destroying distributed samples for anonymised data sets.

53. Despite its potentially limiting impact on the value of the resource, a number of respondents still felt that it was absolutely necessary to give participants the option of breaking the link with their medical record and having their identifiable information destroyed, as this was crucial to make the project "ethical". On the other hand, a number of respondents suggested that the most practical and acceptable way forward was discontinued participation.

**Box 11. Right to withdraw**

*'Ideally, we would like to see patients being given the option of the three levels of withdrawal. It would be a shame to lose the information already collected, and that available from maintaining an ongoing link, if the patient simply does not want to be contacted again. We believe it is essential, however, that the option of breaking the link with the medical record and of destroying identifiable information is available to all participants.' [O]*

*'A possible solution would be to offer participants who withdraw the choice of the three options outlined in the Framework document. However the Complete withdrawal option risks significantly limiting the value of UK BioBank for research if large numbers of participants take this option. Furthermore the fact that it may not be possible to trace and destroy all distributed sample remnants could cause difficulty. Therefore Discontinued participation may be the best practical option although this should be clearly stated in the original consent process.' [O]*

*'Since right to withdraw may not be feasible for at least some research using anonymised data sets, it is critically important that there is prior agreement on what types of research are publicly acceptable.' [O]*

*'We were concerned that opting out completely (either by not joining or withdrawing later) because of an objection to certain kinds of research (or even one particular project) seemed too blunt an instrument.' [P]*

*'Seen from one perspective, the right to withdraw overall has the potential to undermine the resource but the framework should be seeking to protect the interests of participants here. Also, the lack of recognition of familial interests in the samples and data provided could be problematic in terms of securing wider public trust in the project.' [P]*

### 3.3.7 Respect for incapacitated or deceased participants' wishes

54. Most respondents found the EGF's proposals around the respect for incapacitated or deceased participants 'very acceptable' or 'acceptable' (n=14, 74%). There were a number of issues around respecting the wishes of incapacitated or deceased participants:
    - the ethics of taking blood samples, and possibly carrying out other "invasive procedures" on people who have lost capacity;
    - lack of details on the role that family may have in deciding on what happens to the data or samples of deceased relatives or those that have lost their mental capacity, even though genetic information is "familial in nature"; and
    - the role that carers may potentially have in representing the best interests of their patients, following the implementation of the proposed Mental Incapacity Bill.

55. It was felt by many that the policy in the event of death of a participant was unclear and inconsistent:

    *'In the event of death etc: There is an inconsistency here. On the one hand participants will not be recruited if they do not want to continue after death, as it were, and on the other a policy will be developed for dealing with those who are participating and who decide that they do not want to continue after death. The policy should have been developed by now, and be included as part of this consultation so that it could be commented upon.' [P]*

56. In particular the proposal to reject applicants who say that they would like to have their data withdrawn at the time of their death or incapacitation was "flawed" according to one respondent:

    *'I find the reasoning behind the position that people would not be recruited who wanted to specify that they would like to have their samples and data withdrawn at the time of their death or incapacitation somewhat flawed. This seems to undermine individual choice. After all, once people have enrolled they can withdraw without giving any reason. Moreover, it is suggested that a policy will be developed to deal with people who do wish, once they are already enrolled, to be withdrawn when they die or become incapacitated. This seems rather confused to me: either people have a right to withdrawal that they can exercise at any time and under any circumstances or they don't at all.' [P]*

57. Another respondent noted that it should be made clear in the EGF that a person who has lost capacity cannot be entered into research that is outside the scope of their existing consent. The respondent also pointed out that the Draft Mental Incapacity Bill has implications for the extension of consent:

    *'The policy that family members will not be able to withdraw relatives who have lost capacity from the project may need to be reconsidered if the Draft Mental Incapacity Bill is introduced. This Bill proposes that both carers and professionals will have an equal general authority to act in the best interests of the person with dementia. Therefore, if a carer considers that it is not in the best interests*

*of a person with dementia to continue to participate in Biobank the Bill may allow them to withdraw that person. The holder of an PA [power of attorney] would also be able to withdraw a person from Biobank.' [O]*

58. This respondent also noted that the words and sentiments of incapacitated people must be respected when tests are being carried out, as discussed below:

*'We would also urge UK Biobank to include a clause in its guidance that states if a person who has lost capacity appears to object to any test or procedure, by words or actions, this should be taken as a request to withdraw from participation.' [O]*

### 3.3.8 Expectation of personal financial gain

59. The majority of respondents found the EGF's proposals around the expectation of personal financial gain 'very acceptable' or 'acceptable' (n=14, 74%). Respondents argued that it was important to outline to participants, from the outset, that there would be no financial or material gain from their involvement in UK Biobank.

*'In relation to the statement in the framework document "participants will not be offered any significant financial or material inducement to participate. . ." In our view it should be made clear that participants will not be offered any financial or material inducement "significant" or otherwise.' [O]*

60. One respondent felt that people were unlikely to get involved purely out of altruistic feelings and that other rewards or benefits needed to be considered:

*'Money and healthcare information might not be the right solution but other measures can be used for them to feel special.' [P]*

## 3.4 Confidentiality

61. This section explores respondents' comments and concerns about the EGF's treatment of confidentiality in relation to its:
    - commitment to maintaining confidentiality;
    - treatment of anonymisation;
    - policy on re-identification of samples and data.

62. Most respondents thought the Framework's treatment of confidentiality was 'very acceptable' or 'acceptable' (commitment to maintaining confidentiality: n = 15 [83%], treatment of anonymisation: n = 13 [72%], policy on re-identification: n = 13 [72%]).

63. A number of respondents commented that the proposed system, although not "foolproof" or fully outlined to date, was sound in principle:

*'In general, these principles are acceptable. They will never be foolproof, as if someone in a 'sensitive' position is determined to abuse the system, they will be able to. However, this is probably as effective a system as it can be.' [O]*

*'The steps that have been taken to ensure this seem to strike a balance between protecting the interests of participants and ensuring that the data actually are available for scientific analysis.' [O]*

*'Many of the procedures alluded [to] here remain to be established in detail. In general terms, however, we believe that, in addition to recognising corporate and individual obligations to abide by national and international research standards and applicable laws, researchers should voluntarily assume pre-eminent responsibility in preventing the misuse of genetic information obtained in the course of their research activities. As we understand it, such obligation mandates the use of optimal confidentiality. Misuse of genetic information should be deemed to include, but not be limited to, the support of discrimination against, or exploitation of, any individual or group of individuals. We recognise the assumption of such responsibility in the proposed elements of the Framework.' [O]*

64. A number of respondents, whilst not commenting on the detail of the framework, noted the importance of this issue:

*'Very strict measures are required to protect confidentiality in both directions. It is equally important that participants do not have access to information relating to them at a later stage.' [P]*

*'Strong safeguards need to be put in place to guarantee confidentiality on the part of researchers (those employed at the start of the project and also those recruited once the project is underway).' [O]*

65. Access, anonymisation and security of the data were a concern for a number of respondents, and there is a clear need for UK Biobank to be precise about the exact procedures that will be in place to protect participants:

*'The document states that identifying information will be removed from the data and sample 'at the earliest opportunity'. In a project as detailed as this one, such a vague term should be clarified more specifically ie 'immediately labelled with unique non-NHS number which can be only linked to any identifying information by using a secure code, held [by] a strictly limited number of people' or words to that effect.' [O]*

*'The type of person (ie seniority) who has access to the original identifiers should be defined. The use of dual key codes so that no one person has complete access without the use of a second person's code so that there is additional security should be considered. UK Biobank should define (eg roles and responsibilities) all those who have access to the key and ensure that the keyholders are publicly acceptable.' [O]*

*'Who will anonymise the records? In order to keep the number of people who see the complete patient records to a minimum, perhaps the same people who anonymise the data should perhaps be the same few who are able to re-identify data and samples.' [O]*

*'We assume that some form of encryption is proposed for the central data storage in order to safeguard the information although this is not mentioned in the text.' [O]*

*'The identifiers will be held in a centrally (sic) restricted-access database. However it is not clear who will be controlling access to this database. This would have to be made clear. This could be a role for the Ethics and Governance Committee who could authorize any linkage of identifiers and information.' [P]*

66. A number of respondents had concerns around re-identification of individuals in UK Biobank through deduction, for example:

*'Biobank has failed to address the important issue of 'deductive' identification from anonymised samples. Information on re-identification processes and safeguards is insufficient to determine whether or not these processes are likely to be adequate.' [O]*

*'The document says that the personal information and samples will be anonymised but what they actually mean is coded. The personal identifiers are removed and a code is allocated to an individual so that the data is not directly identifiable. This could still mean that a person may be indirectly identifiable from the detail of the information itself.' [P]*

*'Consideration needs to be given to how the "anonymised" database can be queried and what level of results can be obtained eg only return results with >10 subjects, only provide summary data etc.' [O]*

*'The issue of "re-identification" (i.e. the re-linking of participants' identifying information – name, address, birth date etc. – with data and samples) has the potential to cause serious harm if any errors are made. As such there needs to be verification that data have been matched correctly.' [O]*

67. Some respondents believed greater clarity and reassurance was needed on the personal information that enrolment centres would hold and how this would be protected, for example:

*'It is not clear what kind of security procedures will apply to the enrolment centres if they hold personal identifiers and information. All data would have to be handled by people under an obligation of confidentiality such as medical staff or administrative staff who have made this undertaking as part of their employment contract. The safest procedure would be to allow the recruitment centres to enter data but not be able to withdraw it so that data can only be fed in one way. It is only when it is in the main Biobank database that there should be the possibility of linking the identifiers to all the information and this should only be for re-contact purposes and adding extra information. All the removal and linking of identifiers should be carried out by an independent body.' [P]*

*'The information that enrolment centres need to hold has to be clearly defined. Re-identification - impossible to comment until I see the policy.' [P]*

68. A number of respondents recommended the use in the EGF of the terminology used by the European Medicine Evaluation Agency and US FDA, for example:

*'We note with regret the decision within the Framework not to employ the standards of sample encryption terminology, endorsed/issued by the both the European (EMEA, CPMP) and US (FDA) regulatory authorities, the pharmaceutical industry, and increasingly the scientific community at large (Spear et al. Pharmaco J 2001: 1; 101-103). According to such standards, the data handling processes described within Framework would most appropriately be represented using the term "coded", which indicates the most basic standard of data/sample encryption. In contrast, the term "anonymised" would be reserved to convey a destruction of the link between sample and subject identities, and thus excludes all forms of prospective research. We strongly deprecate the loss of this unique opportunity to support greater homogeneity of terminology and prevent confusion in future dialogue.' [O]*

69. Lastly, a number of respondents believed further consultation was needed on the issues surrounding confidentiality:

*'It is difficult to give a considered view of this given the limited information provided. We would be happy to comment on your detailed plans as they are being developed.' [O]*

*'The document seems somewhat inconsistent with respect to these issues at present and cannot be adequately commented upon.' [P]*

*'It would perhaps be best to go through this section thoroughly with the Information Commissioner.' [O]*

*'The Icelandic population collection demonstrates that all these broad ethical and governance requirements will be (sic) require further analysis once the details of the computer system are finalised. This can radically change all the security safeguards and the way that things will operate. It will also require greater clarity about the data pathways and who will be controlling and overseeing access and input.' [P]*

# 4 Relationship with research users

## 4.1 Introduction

70. This section explores the relationship of UK Biobank with research users, reporting respondents' views on proposed:
    - Stewardship of data and samples;
    - Research access to data and samples.

## 4.2 Stewardship of data and samples

71. Most respondents found the Framework's proposals for stewardship of data and samples 'very acceptable' or 'acceptable' (n=13; 65%). Respondents noted that:

> *'There seem to be no problem[s] in relation to this.' [O]*
>
> *'This is a very clear and considered part of the proposal.' [P]*
>
> *'The legal framework is to a certain extent imposed upon Biobank. It's pleasing to see that participants will be informed about the status of the samples they have given.' [P]*

72. Some thought that the stewardship model lacked safeguards for participants:

> *'…the document refers to the principle of stewardship of the resource of the genetic databank, but this seems a rather simplistic use of the term. The sense of (sic) which trusteeship is used as a very helpful model in the literature on patents and data banks is in the sense that the databank organisers hold the resource as trustees for the direct benefit of the patients, or, more widely, the NHS as a whole. There are insufficient safeguards in the proposals to make that (sic) the so-called stewardship model anything more than a figleaf, and patients should be told so.' [P]*

73. Various respondents felt strongly that UK Biobank should not 'own' or have the right to 'sell' participants samples:

> *'We all agreed that UK Biobank should not sell samples (or data from participants' medical records) under any circumstances.' [O]*
>
> *'That UK Biobank should retain the right to sell people's samples, in combination with limitations to the right to withdraws one's consent is very unacceptable. What happens in case of bankruptcy and why is it not specified what rights donors have in this type of situation? It might be that UK Biobank "Does not intend" to use it's right to sell, but keeping it for a case of emergency is not a comforting signal to send to the public!' [P]*
>
> *'UK Biobank should not have the right to 'sell' samples. They should be able to pass on to third party with an administrative fee attached, but selling is unethical.' [P]*
>
> *'Whereas the basis of UK scientific research using human tissue has always been one of informed and altruistic donation. (sic) That a institution such as UK Biobank should suggest that human tissues, or any constituents of such, are subject to considerations of property and ownership, (except in so much as their subsequent treatment embodies process of work and skill) may be seen as a departure from such principles. Nonetheless, we recognise the need to establish such legal competence as may be required to provide adequate stewardship of archived biological materials. It may be questioned as to*

*if competence to provide such stewardship could not equally well be achieved by adoption of a 'custodial' role for such materials, without implication of ownership.' [O]*

74. A number of respondents commented on UK Biobank's commitment to engage actively with participants and its relationship to the public trust in UK Biobank:

*'It's pleasing to see that participants will be informed about the status of the samples they have given.' [P]*

*'It should be noted that feedback to participants in anything but the most generic terms will prove to be easier said than done.' [O]*

*'I approve, however, of the idea of maintaining active communication with participants--but will that include information about new commercial uses or contracts concerning their samples? Only by providing such information will participants genuinely be allowed to exercise a right of conscience, on the same model as shareholders who have ethical objections to particular firms of (sic) practices.' [P]*

*'It is absolutely essential that the public are fully engaged. The adverse effects of public opinion cannot be under estimated. Adverse public opinion would have far reaching effects on other aspects of importance to the research community.' [P]*

## 4.3 Research access to data and samples

75. This section explores the relationship of UK Biobank with society, reporting respondents' views and concerns on the proposed framework for:
    - General principles of access;
    - Decisions on access and use;
    - Licenses for specific use; and
    - Sharing of data and findings.

76. There were mixed overall views from respondents about the Framework's proposals for research access to data and samples (9 (45%) responded 'acceptable', 4 (20%) responded 'unacceptable' or 'very unacceptable' and 7 (35%) responded 'neither acceptable or unacceptable'). A general view was expressed by several respondents that the policies and process for making decisions on access should be clearly explained to participants at recruitment:

*'The key issue here is to ensure that access issues are properly explained to individuals when seeking their initial consent for involvement in the project.' [O]*

*'It will be important to present to the public not only the intention of "augmenting the value of the resource" and "the greatest benefit" but to show the form of checks and balances that will ensure these intentions - and thus specify who will have influence on defining what actually constitutes benefit - for whom.' [P]*

77. Respondents noted the need for clarification on a number of issues concerning what samples would be collected, and how samples would be collected and treated:

*'When do the collectors of information cease to be collectors and become researchers? I have great difficulty with this as the collectors of the data and the users of the Biobank are potentially the same people. If you know people's name and identity because you have collected the data and then you use the data (even if it is part of Biobank) then will you be able to pick out Mr. X because he had such a unique translocation? I think that this is a potential flaw in the planning. Has this been an incentive to*

*get researchers to collect the information and be collaborators? There needs to be a separation of these responsiblities.' [P]*

*'As the samples become depleted, will research projects be prioritised? Have UK Biobank considered taking additional blood at a later stage in the overall project to replenish depleted samples or using cell lines?' [O]*

*'It is not clear if samples will be sent to researchers for analysis or if there will be "central" genotyping of the samples. The latter approach would help to ensure that genotyping was conducted with consistent methodology and that appropriate quality controls are in place. The concept of researchers conducting genotyping and sending the results back to UK Biobank is attractive in theory but has the major disadvantage that research could be based on sample handling procedures and genotype data of variable quality.' [O]*

78. A number of respondents raised concerns regarding the number of approval mechanisms involved in making decisions on access to the resource (MREC(s), UK Biobank, external peer review, and the Ethics and Governance Council). Further details were requested regarding how these bodies would operate, the timelines for decisions and the procedures for handling conflicting advice:

*'The use of different MRECs could give rise to inconsistencies, as research acceptable to one may be turned down by other. It would aid consistency if one MREC was used.' [O]*

*'The Scientific Research Ethics Committee [Ethics and Governance Council] is a double check on the MRECs. Is it essential to put researchers through two systems of authorization? Will this become an unnecessary duplication and frustrating for researchers? This will have to be very streamlined.' [P]*

*'The only thing that I am not clear about is the structure of the review process involved in assessing proposals to use Biobank. There seems to be 3 stages involved: peer review; ethical review by MREC and a review by an unspecified body of UK Biobank. I suppose this would be the Scientific Committee but what potential role might the Ethics and Governance Council play here? This system of both external and internal review looks like it would provide a good set of checks and balances and prevent Biobank from becoming a 'law unto itself'. However, some researchers may find the process laborious, involving duplication of paperwork. Also, how would Biobank deal with conflicting views? For example, if the MREC rejects a proposal but a body at the Biobank supports it?' [P]*

*'What about the timelines for decision making? Will there be regular meetings of selection committees, or will they be ad hoc?' [P]*

79. Respondents also commented on the need for further clarity on the purpose and implementation of a licensing system:

*'Though supporting UK Biobank through equitable licensing agreements is evidently critical, it is imperative that undue financial emphasis does not encumber the opportunity of UK Biobank to help deliver better healthcare and health care technologies on both a UK and global scale.' [O]*

*'What is the relevance of the licence? Will every user have to have a licence?' [P]*

80. Differential licence fees were considered acceptable by a number of respondents, recognising that some users might be expected to derive financial benefit from using the resource, but there was concern regarding the appropriate identification of such users:

*'We agree that organisations that might be expected to derive financial benefit might be charged higher fees. However, please note that academic institutions are also in this category along with industry particularly where the research contributes to a patentable invention of commercial interest.' [O]*

*'In relation to licences (II(B)3), we feel that more might need to be said about the level at which licence fees will be set, and how you will assess the possibility of future financial gain in setting fee levels. In addition, will there be the possibility of the retrospective collection of a licence fee if there is an unexpectedly large or unforeseen financial gain? The issue around financial arrangements is one that participants will need to be made aware of. We note the comments in relation to licences and intellectual property rights that a detailed policy is still being developed. We believe that such policies will benefit from proper dialogue with interested parties, including those with experience of genetic research in the commercial sector, academic researcher and patients. We would also be interested in considering the detailed policies on these matters in due course.' [O]*

*'Charges should be higher for organisations that are likely to derive financial benefit from the use of resources. Biobank must be careful not to be exploited by commercial organisations.' [P]*

81. Some respondents commented on the proposal that Regional Collaborating Centres would be permitted to use early data as part of the development of the resource:

*'I think it is right that the Regional Collaborating Centres should be permitted use of some early data to validate and improve their processes. [P]*

*'The use of early data and samples by the Regional Collaborating Centres to validate and improve methods of data collection and analysis should be considered in relation to the need for the consent process to refer to this use of the data and samples.' [O]*

82. A number of respondents noted that they were concerned about permission being granted for specific types of research, particularly medical market research and insurance industry research, and noted that participants should be clearly informed of UK Biobank's intentions in this regard:

*'Biobank should be prepared to rule out some uses at the outset, particularly where commercial conflicts of interest may arise. Public involvment mechanisms should be used to draw up the groundrules for access and types of research and research priorities (particularly as use of samples will have to be limited).' [O]*

*'The possibility that the database may be used for medical market research is something that participants need to know. The impression that Biobank creates is that it is a resource for UK medical researchers working towards public good and something that will be utilitised by drug companies for commercial reason. Certainly participants would want to know that market research firms may make use of the resource before agreeing to take part. Why is this being possibility listed here? Are there plans for allowing this resource to be used for medical marketing?' [P]*

*'There are obvious controversial areas of research that could be performed on UK Biobank, as well as other uses such as insurance and market research. At present the Ethics and Governance Framework states that none of these would be excluded. Decisions need to be made in advance of commencing recruitment as to whether any of these will be proscribed, and if so subjects should be informed accordingly. If UK Biobank wishes to leave these options open, then subjects must be explicitly told that such uses may be allowed with examples. Piloting should be used to test whether participants could reasonably predict various predicted uses with the information provided at recruitment.' [P]*

83. A particular concern was access being granted for police use, and there were calls for a clarification of the law in this area (**Box 12**):

**Box 12: Police access**

*'I would still be a bit concerned about the short, throw-away sentence about access by the police or the state as a whole. There has been considerable concern about this in other countries with databases of this type and I am not sure whether this statement will be reassuring enough. I think many members of the public will be worried that this is simply a back-door way into the widely discussed concept of a*

*broad national DNA database and it seems to me that a database which is being held purely for medical research should be better protected than this.' [P]*

*'UK Biobank should be pro-active about protecting confidentiality. In our view, the information contained within UK Biobank should be legally and absolutely privileged and efforts should be made to legislate for this in advance of putative court orders requiring access.' [P]*

*'The biobank should seek legal clarification of the circumstances under which the police may seek and be granted access - current legislation is too vague.' [O]*

*''access to the resource by the police or other law enforcement agencies will be acceded to only under court order'. We have been unable to identify precisely the conditions under which such court orders might be made available. In the current paranoid climate following September 11 2001, it is important to ensure that the access to the databank by the forces of law and order is agreed only under extraordinary circumstances which should be specified in advance.' [O]*

*'We have noted the comments regarding access to Biobank by the police or other law enforcement agencies (II(B)1). We welcome this, and the assurances given in the Genetics White Paper that such access requests are only likely to take place in exceptional circumstances. The [organisation] would like to see further reassurance that such access requests will not be conducted ex-parte and that the Biobank will seek to be represented in <u>all</u> circumstances. We also note, but have not fully explored, the powers contained in the Regulation of Investigatory Powers Act 2000 which include new, simplified, arrangements for the handing over of computer encryption materials. We understand that the Act's powers are to be underpinned by a Code of Practice, and we would urge Biobank to ensure that it is aware of these powers, and if necessary seek to have Biobank excluded from some of the routine access arrangements.' [O]*

84. Respondents were positive about the Framework's proposals for sharing of data and findings and made suggestions as to how data sharing could be best accomplished (**Box 13**). The intention to make the database as publicly accessible as possible while also allowing for legitimate use for drug discovery and development was variously commented upon.

85. Some respondents thought that research hypotheses or protocols should be published as well as results from research. Other respondents asked for further clarification of the licence terms in relation to data sharing, for example, regarding the limited period during which users would be able to seek to publish findings.

**Box 13: Data sharing**

*'The emphasis of the framework is on public accessibility. However, it is important to remember that in order to develop a useful product from this resource, confidentiality and patentability are required to access the commercial funding… …In addition, it is stated that results will be allowed to remain confidential for limited periods, but the definition of 'limited' is important, as this could potentially be a big problem for commercial researchers.' [O]*

*'We agree that research findings should be incorporated back into the resource, but it is also necessary that hypotheses are published and the outcomes of studies are tracked to ensure that negative results are also published and publication bias and 'rescue bias' are avoided - otherwise most findings may be false and therefore worthless or harmful.' [O]*

*'As stated in the Framework document it will be important for research results (positive and negative) to be placed in the public domain. The Framework document mentions that UK BioBank will explore strategies for disseminating negative findings (presumably because there is less chance of publication in a peer reviewed journal). However UK BioBank should guard against the publication of negative findings that are due to a technical issue rather than a "real" scientifically valid negative result. In this regard, it may be relatively rare that such results would not be published in a scientific journal. Nonetheless we urge UK BioBank to consider strategies for access to results via a "one stop shop" that*

*provides citations of publications and abstract information for scientifically valid negative results where publication has not been possible. This could be done in an annual report of (sic) via the UK BioBank website.' [O]*

*'…establishing an e-journal in which all findings of research using UK Biobank must be published.' [P]*

*'UK Biobank should publish all results at some point and protocols when accepted. UK Biobank will recognise that the issue of publication bias is particularly important in this context. Research teams should be given a finite period (say 2-3 years from completion of the project described in their protocol) to secure publication of their findings. Results of any analyses described, unpublished following this period, should be made available for publishing by UK Biobank.' [P]*

# 5 Relationship with society

## 5.1 Introduction

86. This section explores the relationship of UK Biobank with society, reporting respondents' views on proposed:
    - Management and accountability structures;
    - External governance arrangements;
    - Benefit sharing arrangements;
    - Transfer of assets, or closure arrangements.

## 5.2 Management and accountability

87. The majority of respondents found the three management and accountability structures to be 'very acceptable' or 'acceptable' as follows:
    - Board of Directors (n=14, 78%);
    - Science Committee (n=14, 78%);
    - Ethics and Governance Council (n=12, 63%).

88. However, a number of respondents felt that the governance structure as a whole lacked clarity, for example:

> *'The governance structure is not clear. There is very little opportunity for participants to be part of the management structure and there is a danger that the participants are the research guinea pigs rather than being partners in the research. The participants should have more opportunity to be involved in the agenda setting, the long term management of the resource as well as having powers to veto research. There is no body that has the power to investigate all parts of the biobank (including the spokes) to make sure that they are in compliance with the protocol and Biobank guidelines. How can the Biobank act as sponsor of some of the research as well as trying to fulfill its other responsibilities as the custodian of the resource?' [P]*

89. This section explores comments from respondents about each of these structures in turn.

## 5.3 Board of Directors

90. Few respondents commented on the Framework's proposals for the Board of Directors; those that did were concerned with the range of membership, e.g. corporate, lay or participant representation:

> *'The Board of Directors is listed under the title 'relationship with society' but it is astounding that there is no one from 'society' represented on the Board. If society consists of the funders then they are well represented. Why can't there be a lay member on the Board?' [P]*

> *'... I would strongly argue for the inclusion of representatives of participants on the Council and the Board of Directors. There is a trend towards greater public involvement in institutions such as the NHS and Biobank should recognise this trend. I appreciate that these democratising initiatives are not without their problems but the people who take part in UK Biobank should not just be viewed as the sources of samples and data but as potentially active participants who might have a lot to offer to its*

*governance and indeed overall success. Without doubt, participant representation and involvement are essential in this day and age.' [P]*

91. One respondent also noted that the Framework did not make it clear how conflicts of interest would be dealt with by the Board of Directors.

## 5.4 Science Committee

92. In addition to requesting more information on the role of the Science Committee, some respondents raised concerns about the membership and transparency of the Committee.

93. As with the Board of Directors, a few respondents noted that they would like to see lay or participant involvement, for example:

*'…the Science Committee – membership will consist of two Board members – (each who already represent the funders) and a further three nominees of the funders. I think that this is overrepresentation. Why couldn't this be more representation of the general scientific community, the patients and wider society. Or is there concern that the public are not able to understand the science?' [P]*

94. Respondents commented on the need to ensure the relevant expertise, broadly understood, was present on the Committee. This included the need to ensure that both the Science Committee and the Ethics and Governance Council included scientists and ethicists in their membership:

*'We note the arrangements for management and accountability of the Biobank, and for the appointment of a Science Committee. We have in the past commented on the need for a suitable range of scientific and medical disciplines, for example to include social scientists and geriatricians.' [O]*

*'Whilst the responsibilities of the Science Committee and Ethics and Governance Council are distinct, we believe that it will be important for cross fertilisation between them. The Science Committee should be aware of ethical issues and vice versa. Therefore the two groups should contain experts from the other discipline ie ethics on the Science Committee and vice versa.' [O]*

95. One respondent noted that the Committee's processes should be as open and transparent as possible:

*'…of the Science Committee, should be open in the same way as the HGC meetings are to reinforce its transparency and external scrutiny, at least by the wider academic community.' [O]*

## 5.5 Ethics and Governance Council

96. A number of respondents commented on their satisfaction with the Ethics and Governance Council's remit and selection procedures:

*'We are pleased that there is to be an independent council to govern the work of UK Biobank and to monitor its compliance with the ethics and governance framework, once agreed.' [O]*

*'[We] applaud the setting up of the Ethics and Governance Council, and the fact that appointments to it will pay full regard to the Nolan principles.' [O]*

*'The "Ethics and Governance Council" is truly an interesting model which takes into account the public's opinion and concern. It is a new and innovative approach, which should be encouraged. We*

*support the opinion that this entity should be given the powers necessary to really play a role in the governance scheme.' [O]*

97. Whilst there was a view that the Ethics and Governance Council was acceptable, a number of respondents commented that its powers might not be sufficient in relation to individual uses of the resource, investigation of compliance, and procedures for addressing concerns (**Box 14**).

**Box 14: Power of the Ethics and Governance Council**

*'We are not sure that the idea of an Ethics and Governance Council is sufficient as a mechanism for dealing with any ethical issues that might arise. Its role seems to be simply that of monitoring compliance.' [O]*

*'Currently, the framework document does not envisage that the Ethics and Governance Council could veto uses of UK Biobank. It is noted that this conflicts with the view expressed by the recent Government White Paper. I support the position that public confidence in the governance of UK Biobank will only be achieved if the Council has this kind of power to ensure that the ethical framework is adhered to.' [P]*

*'To see such a limited role for the ethics council is nonsense, if this is to have any impact on public trust. At least the council must be able to veto certain forms of research, and preferably it should also hold the right to influence how profit is used - that is, an ethics on positive terms influencing what type of research we do think is good, though not necessarily commercially feasible.' [P]*

*'The Ethics Council should have the power of veto - to be used only in exceptional circumstances.' [O]*

*'The Council should have greater powers - it is not enough that the ultimate power the Council has is that its members resign (presumably they could be replaced by the (sic) interested parties with members who do not object). It should have the power of veto.' [P]*

*'…the Council should have investigative powers to visit sites to see what is happening on the ground.' [P]*

*'There needs to be a formal and specific mechanism for dealing with any statements of concern that may be made by the Ethics and Governance Council to the Board.' [O]*

*'We question if the Ethics and Governance Council should not be more appropriately empowered as proxy for the participants in UK Biobank.' [O]*

*'Given the mandate of the Ethics Governance Council, we are of opinion that its discussions and deliberations shouldn't be communicated to the Board 'informally' as suggested in the document. To the contrary, this should be a more communicative and very transparent process since the Council is supposed to act as an "independent guardian of public interest". (4th paragraph, under 'Power') should be re-worded accordingly. This doesn't preclude the Ethics Governance Council to make informal intervention when it deems it necessary.' [O]*

*'This Council will act as an independent 'guardian'. I think that this body is basically a political one to be seen to be doing. If the body is going to carry out these functions then it should have sufficient sanctions to use if it sees that there are problems with the Biobank. It should have powers of investigation so that it can determine if the Biobank is being run as it has been told it would. The Council should be able to stop the research if it believes after investigation that the research is not been (sic) conducted as required by the Science Committee and the Board. Otherwise the role of this body is simply to be the public face of Biobank.' [P]*

98. However, a few respondents noted their satisfaction with the Framework with respect to the Council:

*'We believe that the proposed ultimate sanction of resignation of the Ethics and Governance Council is adequate as the only means of registering a serious difference of opinion with the UK Biobank board. We recommend arbitration through a three wise men process or via someone like the President of the Royal College of Physicians prior to resignation.' [O]*

99. A number of concerns were raised about the Council, including:

- Independence and transparency of appointments –

  *'We also welcome the use of the Nolan Principles of Public Life for appointment, provided that the vacancies are suitably advertised and the selection can be made independently from a pool of high quality applicants.' [O]*

- Continuity of funding -

  *'The funding of this group should be guaranteed for the life-time of UK Biobank.' [P]*

- Relationship to Board of Directors and Science Committee -

  *'I think that the framework lacks clarity about the governance structure, the role of the Board of Directors, the Science Committee (the remit of which is yet to be finalised anyway), and the Ethics and Governance Council and how they will interact.' [P]*

- Relationship with NHS Multi-centre Research Ethics Committee -

  *'… one important function of an oversight body, such as the EGC, …will be to consider the wider ethical issues and the implications of any proposed nested studies working with subsets of data from UK Biobank. If these are considered in isolation, for example by an MREC, they may raise no particular concerns. However, such studies may potentially raise difficulties over feedback and re-consent. They may also contribute to a gradual "mission-creep" of the UK Biobank into potentially controversial areas of study that were not envisaged by participants.' [O]*

- Members' expertise -

  *'…it will be important that the Science Committee are aware of ethical considerations and that the Ethics and Governance Council has an understanding of the science and the potential benefits of research. Therefore the Ethics and Governance Council should include scientific experts and the Science Committee should include recognised ethicists.' [O]*

- Greater participant involvement/inclusion on the Council -

  *'It is extremely difficult to see how the Ethics and Governance Council can ensure conformance with the interests of participants and the general public if the public has not been involved in advance in developing policies to address issues of concern.' [O]*

  *'There need to be many more statutory safeguards to ensure that the voice of participants and the voice of the Ethics and Governance Council are heard. There is an assumption that the project is beneficent but it may not be.' [O]*

## 5.6 External governance

100. The majority of respondents (n=14, 78%,) thought that the arrangements for external governance as laid out in the framework were 'acceptable'. Respondents welcomed the embedding of the external governance of UK Biobank within existing governance structures in the UK:

> *'We strongly support the employment of traditional and proven mechnisms of external oversight and governance to assure such privacy and informed consent. We consequently welcome the provison within the Framework of structures of external governance reflecting existing standards within UK constituent nations, thereby best to support the endeavours of UK Biobank.' [O]*

101. Respondents commented that a number of areas concerning external governance needed further clarification or caused concern. These included:

- How MRECs would be used –

> *'Which MREC? Will one be established specifically for this role, or will the various existing MRECs pick up the extra burden?' [P]*

- The involvement of GPs and local healthcare organisations –

> *'The framework puts certain responsibilities on participants' GPs and on primary care trusts and other healthcare organisations to be aware of the research being undertaken and to ensure that the arrangements for the research meet the governance standards. It is unclear, at this stage, what information will be provided to doctors to enable them to undertake this role. More information is therefore needed before we can say whether this is an acceptable expectation. GP involvement should also be both voluntary and properly resourced.' [O]*

> *'The involvement of the recruiting GPs in fully understanding the principles of research governance is very important, both for the project, and for capacity and capability building within the GP workforce.' [O]*

> *'How are local healthcare organisations going to be informed of research involving participants who are patients under their care?' [P]*

- Conflicts of interest –

> *'MREC review and RGFs do not generally cover important issues such as conflicts of interest or the scientific validity or usefulness of the research. These issues are currently covered (albeit inadequately) in other research studies by the process of informed consent and scientific peer review. Biobank's proposed governance processes appear to weaken these safeguards without putting alternative systems in their place. This is critically important because commercial conflicts of interest are particularly extensive in biomedical research, and because the majority of genetic association studies to date have given false or misleading results.' [O]*

- Equity of assessment processes –

> *'In assessing applications, all of them should be treated equitably ie those from academia and industry.' [O]*

- The role as 'sponsor' of research –

*'As UK Biobank will have the role of 'sponsors' of research , what indemnity arrangements are in place?' [P]*

*'When UK Biobank will act as a sponsor for a research project, are there any additional requirements or safeguards to ensure compliance with the legal and ethical framework? (Could be perceived as a sensitive issue since UK Biobank is also the key holder to personal data).' [O]*

- The legislative framework within which UK Biobank will operate –

*'Indicate what other audit/monitoring process will take place as required by law in England (besides the MREC). For instance: - The Charity Commission for England and Wales/The Data Privacy Commissioners.' [O]*

## 5.7 Benefit sharing

102. Respondents had mixed views on the EGF's treatment of benefit sharing, with 50% (n=9) of respondents finding the framework 'very acceptable' or 'acceptable', and 22% (n=4) finding the framework 'very unacceptable' or 'unacceptable'.

103. A number of comments were made by respondents concerning the dissemination of knowledge from UK Biobank, including:

*'Whilst these proposals are broadly acceptable, they must also include prior publication (for wide consultation and review) of research hypotheses and protocols (see above). Otherwise the dissemination of misinformation is much more likely than the dissemination of information.' [O]*

*'In addition, it is stated that results will be allowed to remain confidential for limited periods, but the definition of 'limited' is important, as this could potentially be a big problem for commercial researchers.' [O]*

104. Some respondents suggested that the Framework should go further than reinvesting income from fees in the resource, by acquiring and returning a share in any profits to the resource, or to the NHS:

*'We suggest that UK Biobank gains a share of any commercial benefit derived from research by researchers/commercial companies. We agree that such profits must be ploughed back into UK Biobank.' [P]*

*'Income should be reinvested in the NHS and not in Biobank, since it is from the NHS that patients are being recruited, through NHS facilities and doctors' time.' [P]*

*'Given the investment of tax payers' money and the altruistic involvement of participants, the public will expect that there is a proper return/reinvestment in UK Biobank and/or the NHS in terms of fees and/or profits from patents etc., especially when there is access from private companies or organisations from outside the UK.' [P]*

105. One respondent was concerned by the lack of detail in the EGF concerning income generation:

*'We note in general the lack of detail surrounding strategies within UK Biobank for income generation and would actively seek dialogue between stakeholders better to define such detail.' [O]*

106. A number of respondents commented on the relationship between UK Biobank and the intellectual property arising from use of UK Biobank:

**Box 15. Benefit sharing**

*'… we urge against any intellectual property rights being held by UK BioBank.' [O]*

*'IP and access policies that will be embodied in any legal agreements should ensure that biotechnology and pharmaceutical industries are not exploited improperly…It should be avoided that biotechnology and pharmaceutical industries are asked to sign agreements that would subject their inventions to pre-filing review by UK Biobank. The terms of licenses or material transfer agreements should not demand for rights to future inventions that might arise from experiments involving UK Biobank data or samples (i. e. reach-through rights).' [O]*

*'Should research using this resource contribute to a patentable invention, it is appropriate that any intellectual property obtained is owned by the institution making the invention.' [O]*

*'Academic institutions should be free to negotiate their own arrangements for intellectual property ownership and management. This would not be possible should UK BioBank retain some or all of the intellectual property rights. Therefore such provisions could inhibit collaborative research.' [O]*

*'The patentable products most likely to emerge from research in biobank are genetic tests, because of the nature of the research (attempting to link genes and environmental exposures with risk of disease). Patents for genetic tests commonly include claims for DNA sequences and are based on the discovery of an association between a gene and a disease (see eg. Thomas et al, 2002, Nature Biotechnology, Vol 20, 1185-1188). Such patents often also claim any future uses of the sequence or gene products and any therapeutics that may in future be derived from it. The benefit of such tests (outside a research context) is often highly questionable since the test itself is likely to lack both clinical validity and utility (most genetic associations are not replicated and for complex diseases risk predictions based on genetic tests are largely meaningless). Such patents are also morally objectionable to many people and may lock up whole areas of future research, slowing innovation. The patenting of gene sequences on the basis of associations identified in the biobank should therefore be prevented. Discussions on 'benefit sharing' miss the point as far as this type of patent is concerned as the benefit of the genetic test itself, outside of a research context, is likely to be limited, and its widespread use may even be misleading or harmful to health.' [O]*

107. There were a number of outstanding concerns about the relationship between UK Biobank and the biotechnology and pharmaceutical sector, and in particular the need to explain this relationship to participants:

*'The relationship between Biobank (which is a nationally funded resource) and commercial organisations needs to be very carefully documented.' [P]*

*'Legal agreements outlining the terms that will be charged for licenses should be disclosed to potential participants.' [O]*

*'We suggest that the development of intellectual property policies involve key stakeholders and potential users of the resource including industry.' [O]*

*'Improper exploitation requires clarification. Policy needs to be in place preventing approved access holders from passing on (part of) sample to third party.' [P]*

*'While it first appears to be a good thing that biotechnology and pharmaceutical companies will acquire access to sample and information in accordance with the protections provided by Biobank their involvement [at] all will be a cause for concern for many people. Consequently they do need to be fully informed about potential uses by commercial entities; this issue cannot be treated casually during the consent process. While medical records will be anonymised many people will still see this as being, in some sense, their information. They might be happier about Wellcome or MRC rseearchers accessing this than they are about those working for corporations. It's one thing to hand over a sample*

*and access to medical records to researchers who are working towards the common good and its another to do this for companies that are seeking to make a profit with work that may benefit the public in the future.' [P]*

## 5.8 Transfer of assets, or closure

108. Respondents had divergent views on the EGF's proposals for the transfer of UK Biobanks assets or closure, with 30% (n=5) of respondents finding the framework 'very acceptable' or 'acceptable' and 30% (n=5) finding the framework 'very unacceptable' or 'unacceptable'. Many respondents requested further details on the strategy to allow them to make a more informed judgement:

*'More details are required. For example, what will happen if UK BioBank becomes insolvent? Who will own the data? Will they be bound by the same terms.' [O]*

109. Many respondents believed that greater transparency will be needed regarding financing and ownership of the resource to ensure participation by the general public:

*'This is a particularly important consideration given the concerns evoked by the sale of the Icelandic database to a private company. Many people may be willing to provide samples, and allow access to their medical records for a public venture, but would feel less committed to a private company. It should be agreed that, in the event of any change in the ownership or control of the database, all participants will be informed of the change and given the option to withdraw.' [O]*

*'Financial transparency as to future revenue will ensure stakeholders and participants are best placed to adjudge the likelihood of closure or substantial transitions in sample holdings or control of such and (sic) must be assured.' [O]*

*'DNA samples and associated data are now of considerable commercial value. The majority of biobanks (existing or proposed) are also suffering financial difficulties and UK Biobank has not yet published a fully transparent budget or convincing evidence that it will be financially viable once it has been set up. This means there is a very real prospect of bankruptcy and receivorship. It is unclear whether in such circumstances the terms of consent ('soft law') would carry any weight in relation to the financial requirements which may necessitate sale of samples to the highest bidder. UK Biobank should provide transparent information both on its anticipated future budget and the legal situation should bankruptcy occur. The implications of a more gradual decline in financial viability should also be considered - eg. will the biobank need to compromise its ethical standards if it becomes increasingly dependent on commercial funders, and what safeguards could be developed to prevent this?' [O]*

110. Many respondents noted that they did not believe that the UK Biobank resource should ever be sold:

*'It was previously stated that DNA resource would not be sold. This is a principle which should be agreed and adhered to. Subjects have gifted the samples to UK Biobank and they should not be sold onto a third party.' [O]*

*'UK BioBank should consider whether a lack of intent to sell or make other substantial transitions in the holdings or control of the resource should be part of the consitution of UK BioBank.' [O]*

*'We all believed that under no circumstances should samples or data contained within UK Biobank be sold.' [P]*

111. Finally, a number of respondents suggested how the contents of the resource should be treated in the event of the UK Biobank's closure:

*‘We propose that the Department of Health should act as guarantors of the company to ensure safety of the participants and society at large by ensuring that sale of the DNA resource does not occur.’ [O]*

*‘They should be transferred to the NHS or similar. Our preference would be that they were not 'owned' in this sense in the first place (hence our concerns - above - about UK Biobank being a limited company). UK Biobank should be something akin to the National Trust.’ [P]*

*‘Is there the possibility that this could be underwritten by the government to ensure that this valuable collection remains a national resource and is not sold to a large company?’ [P]*

*‘Participants or their relatives should also have some involvement in such a decision and be consulted about any sale or transfer of assets.’ [P]*

# 6 Adoption, implementation and revision

## 6.1 Introduction

112. This section outlines respondents' views on the adoption, implementation and revision of the EGF.

## 6.2 Respondents' views

113. Most respondents found the EGF's treatment of adoption, implementation and revision acceptable (n=9, 64%). This was within the context that there would be further development of the framework alongside further opportunities to comment on the evolving framework.

> *'[We] both recognise the need for, and welcome the existence of, such plans relating to the adoption, implementation and revision of the ethics and governance framework We would await the communication of the details of such plans prior to offering further comment.' [O]*

114. Clarity was also requested about the process of, and involvement of stakeholders in, developing the EGF.

> *'Not clear whether the revised framework will be publicly available and whether the findings of this current consultative period will be published. I hope that they are.' [P]*

115. A number of respondents commented on the role of the Ethics and Governance Council in the adoption, implementation and revision of the EGF:

> *'We would expect any substantive change in direction or policy to be approved by the Ethics and Governance Council.' [O]*

> *'This is a minor complaint really, but because of the importance attached to governance shouldn't they [the Ethics and Governance Council] have the power to say how the thing should run? It's unlikely to compromise them seriously but it does look like there is a possibility that the Ethics and Governance Council could be toothless.' [P]*

116. One respondent also noted the need for ensuring industry participation:

> *'[We] would however like to see more emphasis on the potential high value of this database for the discovery of new therapeutics, diagnostics etc. An approach is needed that would encourage UK industrial participation - as well as the emphasis on public accessibility, commercial funding needs to be sought through confidentiality and patentability.' [O]*

## ANNEX A. RESPONSES TO SATISFACTION/ACCEPTABILITY SCALES

## I. RELATIONSHIP WITH PARTICIPANT

### A. RECRUITMENT (n=20)

**How satisfied are you that the Framework covers all the issues relevant to RECRUITMENT?**

| | Very satisfied | Satisfied | Neither satisfied nor unsatisfied | Unsatisfied | Very unsatisfied |
|---|---|---|---|---|---|
| General principles | 2 (10%) | 14 (70%) | 1 (5%) | 1 (5%) | 2 (10%) |
| Selection and approach | 0 (-%) | 8 (40%) | 7 (35%) | 2 (10%) | 3 (15%) |
| Enrolment | 2 (10%) | 9 (45%) | 6 (30%) | 2 (10%) | 1 (5%) |

### B. UNDERSTANDINGS AND CONSENT

**How acceptable are the following aspects of the Framework in relation to UNDERSTANDINGS AND CONSENT?**

| | Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|---|
| Consent (n=19) | 1 (5%) | 10 (53%) | 4 (21%) | 2 (11%) | 2 (11%) |
| Collection of data from medical records (n=19) | 2 (11%) | 11 (58%) | 2 (11%) | 3 (16%) | 1 (5%) |
| Provision of health information to participants (n=19) | 3 (16%) | 9 (47%) | 4 (21%) | 3 (16%) | 0 (-%) |
| Ongoing engagement with participants and the public (n=19) | 3 (16%) | 11 (58%) | 0 (-%) | 5 (26%) | 0 (-%) |
| Expectation of recontact (n=19) | 2 (11%) | 13 (68%) | 2 (11%) | 1 (5%) | 1 (5%) |
| Right to withdraw (n=20) | 1 (5%) | 13 (65%) | 1 (5%) | 3 (15%) | 2 (10%) |
| Respect for incapacitated or deceased participants' wishes (n=19) | 2 (11%) | 12 (63%) | 1 (5%) | 2 (11%) | 2 (11%) |
| Expectation of personal financial gain (n=19) | 3 (16%) | 11 (58%) | 3 (16%) | 1 (5%) | 1 (5%) |

### C. CONFIDENTIALITY (n=18)

**How acceptable are the following aspects of the Framework in relation to CONFIDENTIALITY?**

| | Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|---|
| Commitment to maintaining confidentially | 4 (22%) | 11 (61%) | 2 (11%) | 1 (6%) | 0 (-%) |
| Anonymisation | 2 (11%) | 11 (61%) | 3 (17%) | 1 (6%) | 1 (6%) |
| Re-identification | 2 (11%) | 11 (61%) | 5 (28%) | 0 (-%) | 0 (-%) |

II. RELATIONSHIP WITH RESEARCH USERS

## A. STEWARDSHIP OF DATA AND SAMPLES (n=20)

**How acceptable is the Framework in relation to the STEWARDSHIP OF DATA AND SAMPLES?**

| Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|
| 3 (15%) | 10 (50%) | 3 (15%) | 3 (15%) | 1 (5%) |

## B. RESEARCH ACCESS TO DATA AND SAMPLES (n=20)

**How acceptable are the arrangements for RESEARCH ACCESS TO DATA AND SAMPLES?**

| Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|
| 0 (-%) | 9 (45%) | 7 (35%) | 2 (10%) | 2 (10%) |

# III. RELATIONSHIP WITH SOCIETY

## A. MANAGEMENT AND ACCOUNTABILITY

**How acceptable are the following aspects of the Framework in relation to MANAGEMENT AND ACCOUNTABILITY?**

| | Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|---|
| Board of Directors (n=18) | 1 (6%) | 13 (72%) | 2 (11%) | 2 (11%) | 0 (-%) |
| Science Committee (n=18) | 1 (6%) | 13 (72%) | 2 (11%) | 1 (6%) | 1 (6%) |
| Ethics and Governance Council (n=19) | 0 (-%) | 12 (63%) | 1 (5%) | 3 (16%) | 3 (16%) |

## B. EXTERNAL GOVERNANCE (n=18)

**How acceptable are these arrangements for EXTERNAL GOVERNANCE?**

| Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|
| 1 (6%) | 13 (72%) | 2 (11%) | 1 (6%) | 1 (6%) |

## C. BENEFIT SHARING (n=18)

**How acceptable is the proposed approach to BENEFIT SHARING?**

| Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|
| 1 (6%) | 8 (44%) | 5 (28%) | 2 (11%) | 2 (11%) |

## D. TRANSFER OF ASSETS, OR CLOSURE (n=17)

**How acceptable is the Framework's approach to TRANSFER OF ASSETS AND CLOSURE of UK Biobank?**

| Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|
| 1 (6%) | 4 (24%) | 7 (41%) | 3 (18%) | 2 (12%) |

## IV. ADOPTION, IMPLEMENTATION AND REVISION (n=16)

**How acceptable are the arrangements for the ADOPTION, IMPLEMENTATION AND REVISION OF THE FRAMEWORK?**

| Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|
| 0 (-%) | 11 (69%) | 4 (25%) | 1 (6%) | 0 (-%) |

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## OVERALL ACCEPTABILITY (n=18)

**Overall how acceptable is the UK Biobank Ethics and Governance Framework?**

| Very acceptable | Acceptable | Neither acceptable nor unacceptable | Unacceptable | Very unacceptable |
|---|---|---|---|---|
| 0 (-%) | 12 (67%) | 2 (11%) | 3 17(%) | 1 (6%) |