NHS
National Research Ethics Service
NRES Committee North West - Haydock
North West Centre for Research Ethics Committees
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17 June 2011

Dr Tim Peakman
UK Biobank Limited
1-3 Spectrum Way
Adswood
Stockport SK3 0SA

Dear Dr Peakman

Title of the Research Tissue Bank:	**UK Biobank: a large scale prospective epidemiological resource of 500,000 people aged 40-69 from around the UK**
REC reference:	**11/NW/0382**
Designated Individual:	**Dr Tim Peakman**

The Research Ethics Committee reviewed the above application at the meeting held on 14 June 2011. Thank you for attending to discuss the application.

Ethical opinion

Discussion

The Committee reviewed the application and made the following comments:-

The Committee welcomed the new application from UK Biobank to formally establish the resource as a Research Tissue Bank (RTB) as Members were very much aware that the REC had reviewed and approved the earlier stages of the project.

The REC agreed that the RTB was compliant with the Human Tissue Act, and had an excellent infrastructure and very robust well considered governance arrangements in place.

The Committee agreed that this was both an excellent study and a model application of its type, and Members could identify no major ethical difficulties.

The REC had raised no ethical issues with the proposed application, however, it was acknowledged that the research team had travelled some considerable distance in order to answer any queries in person and it therefore agreed that it would be courteous to speak to the researcher's in order to inform them that overall the Committee were satisfied with the application.

Discussion with the researcher's

The Chair welcomed Dr Tim Peakman (Designated Individual), Professor Sir Rory Collins and Mr Jonathan Sellors to the meeting.

The Committee informed the research team that they had identified no ethical issues with the proposed application and wished the researcher's every success with their research.

The Chair asked the research team if they had any questions for the Committee.

The research team had no questions and left the meeting.

Decision

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation.

The Committee has also confirmed that the favourable ethical opinion applies to all research projects conducted in the UK using tissue or data supplied by the tissue bank, provided that the release of the tissue or data complies with the attached conditions. It will not be necessary for these researchers to make project-based applications for ethical approval. They will be deemed to have ethical approval from this committee. You should provide the researcher with a copy of this letter as confirmation of this. The Committee should be notified of all projects receiving tissue and data from the tissue bank by means of an annual report.

Duration of ethical opinion

The favourable opinion is given for a period of five years from the date of this letter and provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully. The opinion may be renewed for a further period of up to five years on receipt of a fresh application. It is suggested that the fresh application is made 3-6 months before the 5 years expires, to ensure continuous approval for the research tissue bank.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
REC application	3.1	31 May 2011
Protocol for Management of the Tissue Bank - Access Procedures: Application and review procedures for access to the UK Biobank Resource		31 May 2011
Assessment Centre Participant Withdrawal Form	3.3	22 June 2009
Human Tissue Authority Licence - Designated Individual: Dr Tim Peakman		26 July 2010
UK Biobank Ethics and Governance Framework	3.0	October 2007
UK Biobank: Past progress and future plans for 2010-2015 renewal application		19 April 2010
UK Biobank: Protocol for a large-scale prospective epidemiological resource		21 March 2007

Licence from the Human Tissue Authority

Thank you for providing a copy of the above licence.

Research governance

Under the Research Governance Framework (RGF), there is no requirement for NHS research permission for the establishment of research tissue banks in the NHS. Applications to NHS R&D offices through IRAS are not required as all NHS organisations are expected to have included management review in the process of establishing the research tissue bank.

Research permission is also not required by collaborators at tissue collection centres (TCCs) who provide tissue or data under the terms of a supply agreement between the organisation and the research tissue bank. TCCs are not research sites for the purposes of the RGF.

Research tissue bank managers are advised to provide R&D offices at all TCCs with a copy of the REC application for information, together with a copy of the favourable opinion letter when available. All TCCs should be listed in Part C of the REC application.

NHS researchers undertaking specific research projects using tissue or data supplied by the research tissue bank must apply for permission to R&D offices at all organisations where the research is conducted, whether or not the research tissue bank has ethical approval.

Site-specific assessment (SSA) is not a requirement for ethical review of research tissue banks. There is no need to inform Local Research Ethics Committees.

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Dr Tim Sprosen declared an interest on the basis that he was the former Chief Scientific Officer for UK Biobank and still retained a role in the governance arrangements for UK Biobank.

Dr Sprosen left the meeting room and did not participate in the discussion of the application.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

Here you will find links to the following:

a) Providing feedback. You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.
b) Annual Reports. Please refer to the attached conditions of approval.
c) Amendments. Please refer to the attached conditions of approval.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email:-

referencegroup@nres.npsa.nhs.uk

11/NW/0382	Please quote this number on all correspondence

Yours sincerely

P.P. **Professor Ravi S Gulati**
Chair

E-mail: noel.graham@northwest.nhs.uk

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

Standard approval conditions

NRES Committee North West - Haydock

Attendance at Committee meeting on 14 June 2011

Present:

Name	*Profession*	*Capacity*
Mrs Linda Ashcroft	Medical Statistician	Expert
Dr Caroline Carlisle	Visiting Professor to the Department of General Practice and Primary Care– The University of Glasgow	Expert
Mr Stephen Edgar	Designer	Lay Plus
Dr Michael U Eshiett	Consultant Physician in Neurological Rehabilitation	Expert
Professor Ravi S Gulati	Consultant Physician	Expert
Ms Pat Harvey	Hospital Chaplain	Lay Plus
Mrs Chris Haywood	Nurse and Head of Hospice Services	Expert
Dr Ben Johnson	Consultant Psychiatrist	Expert
Mr Charles Otim	Research Support Officer	Lay Plus
Dr David Pilling	Consultant Radiologist	Expert
Mr Alan Rigby	Medical Statistician	Expert
Dr Tim S Sprosen	Chief Scientific Officer	Expert

Also in attendance:

Name	Position (or reason for attending)
Mr Noel Graham	Committee Co-ordinator
Miss Helen Penistone	Assistant Committee Co-ordinator

CONDITIONS OF ETHICAL APPROVAL

Research Ethics Committee:	**NRES Committee North West - Haydock**
Research Tissue Bank:	**UK Biobank: a large scale prospective epidemiological resource of 500,000 people aged 40-69 from around the UK**
REC reference number:	**11/NW/0382**
Name of applicant:	**Dr Tim Peakman**
Date of approval:	**14 June 2011**

Ethical approval is given to the Research Tissue Bank ("the Bank") by the Research Ethics Committee ("the Committee") subject to the following conditions.

1. Further communications with the Committee

1.1 Further communications with the Committee are the personal responsibility of the applicant.

2. Duration of approval

2.1 Approval is given for a period of 5 years, which may be renewed on consideration of a new application by the Committee, taking account of developments in legislation, policy and guidance in the interim. New applications should include relevant changes of policy or practice made by the Bank since the original approval together with any proposed new developments.

3. Licensing

3.1 A copy of the Licence from the Human Tissue Authority (HTA) should be provided when available (if not already submitted).

3.2 The Committee should be notified if the Authority renews the licence, varies the licensing conditions or revokes the Licence, or of any change of Designated Individual. If the Licence is revoked, ethical approval would be terminated.

4. Generic ethical approval for projects receiving tissue

4.1 Samples of human tissue or other biological material may be supplied and used in research projects to be conducted within the establishment responsible for the Bank *and/or* by researchers and research institutions external to the Bank within the UK and in other countries in accordance with the following conditions.

4.1.1 The research project should be within the fields of medical or biomedical research described in the approved application form.

4.1.2 The Bank should be satisfied that the research has been subject to scientific critique, is appropriately designed in relation to its objectives and (with the exception of student research below doctoral level) is likely to add something useful to existing knowledge.

4.1.3 Where tissue samples have been donated with informed consent for use in future research ("broad consent"), the Bank should be satisfied that the use of the samples complies with the terms of the donor consent.

4.1.4 All samples and any associated clinical information must be non-identifiable to the researcher at the point of release (i.e. anonymised or linked anonymised).

4.1.5 Samples will not be released to any project requiring further data or tissue from donors or involving any other research procedures. Any contact with donors must be confined to ethically approved arrangements for the feedback of clinically significant information.

4.1.6 A supply agreement must be in place with the researcher to ensure storage, use and disposal of the samples in accordance with the HTA Codes of Practice, the terms of the ethical approval and any other conditions required by the Bank.

4.2 A research project in the UK using tissue provided by a Bank in accordance with these conditions will be considered to have ethical approval from the Committee under the terms of this approval. In England, Wales and Northern Ireland this means that the researcher will not require a licence from the Human Tissue Authority for storage of the tissue for use in relation to this project.

4.3 The Bank may require any researcher to seek specific ethical approval for their project. Such applications should normally be made to the Committee and booked via the NRES Central Allocation System.

4.4 A Notice of Amendment form should be submitted to seek the Committee's agreement to change the conditions of generic approval.

5. Records

5.1 The Bank should maintain a record of all research projects to which tissue has been supplied. The record should contain at least the full title of the project, a summary of its purpose, the name of the Chief Investigator, the sponsor, the location of the research, the date on which the project was approved by the Bank, details of the tissue released and any relevant reference numbers.

5.2 The Committee may request access to these records at any time.

6. Annual reports

6.1 An annual report should be provided to the Committee listing all projects for which tissue has been released in the previous year. The list should give the full title of each project, the name of the Chief Investigator, the sponsor, the location of the research and the date of approval by the Bank. The report is due on the anniversary of the date on which ethical approval for the Bank was given.

6.2 The Committee may request additional reports on the management of the Bank at any time.

7. Substantial amendments

7.1 Substantial amendments should be notified to the Committee and ethical approval sought before implementing the amendment. A substantial amendment generally means any significant change to the arrangements for the management of the Bank as described in the application to the Committee and supporting documentation.

7.2 The NRES Notice of Amendment form should be used to seek approval. The form is available at:-

http://www.nres.npsa.nhs.uk/applicants/after-ethical-review/amendments/#Noticesofsubstantialamendment.

7.3 The following changes should always be notified as substantial amendments:

7.3.1 Any significant change to the policy for use of the tissue in research, including changes to the types of research to be undertaken or supported by the Bank.

7.3.2 Any significant change to the types of biological material to be collected and stored, or the circumstances of collection.

7.3.3 Any significant change to informed consent arrangements, including new/modified information sheets and consent forms.

7.3.4 A change to the conditions of generic approval.

7.3.5 Any other significant change to the governance of the RTB.

8. Serious adverse events

8.1 The Committee should be notified as soon as possible of any serious adverse event or reaction, any serious breach of security or confidentiality, or any other incident that could undermine public confidence in the ethical management of the tissue. The criteria for notifying the Committee will be the same as those for notifying the Human Tissue Authority in the case of research tissue banks in England, Wales and Northern Ireland.

9. Other information to be notified

9.1 The Committee should be notified of any change in the contact details for the applicant or where the applicant hands over responsibility for communication with the Committee to another person at the establishment.

10. Closure of the Bank

10.1 Any plans to close the Bank should be notified to the Committee as early as possible and at least two months before closure. The Committee should be informed what arrangements are to be made for disposal of the tissue or transfer to another research tissue bank.

10.2 Where tissue is transferred to another research tissue bank, the ethical approval for the Bank is not transferable. Where the second bank is ethically approved, it should notify the responsible Research Ethics Committee. The terms of its own ethical approval would apply to any tissue it receives.

11. Breaches of approval conditions

11.1 The Committee should be notified as soon as possible of any breach of these approval conditions.

11.2 Where serious breaches occur, the Committee may review its ethical approval and may, exceptionally, suspend or terminate the approval.

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please enter a short title for this project (maximum 70 characters)
UK Biobank: a large scale prospective epidemiological resource

1. Is your project research?

(•) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product
( ) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial or clinical investigation
( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples, other human biological samples and/or data *(specific project only)*
(•) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

3. In which country of the United Kingdom is the bank established?

(•) England
( ) Scotland
( ) Wales
( ) Northern Ireland

3a. In which countries of the United Kingdom will centres collecting and/or supplying tissue and data to the bank be located? *(tick all that apply)*

[x] England
[x] Wales
[x] Scotland
[ ] Northern Ireland

4. Which review bodies are you applying to?

[x] Research Ethics Committee

☐ National Information Governance Board for Health and Social Care (NIGB)
☐ National Offender Management Service (NOMS) (Prisons & Probation)

6. Do you plan to include any participants who are children?

○ Yes ◉ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

○ Yes ◉ No

Answer Yes if you plan to recruit participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the NIGB Ethics and Confidentiality Committee to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the clinical care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

RESEARCH TISSUE BANK

NHS
National Patient Safety Agency
National Research Ethics Service

Application to Research Ethics Committee

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
UK Biobank: a large scale prospective epidemiological resource

Please complete these details after you have booked the REC application for review.

REC Name:
NRES Committee North West - Haydock

REC Reference Number:
11/NW/0382

Submission date:
31/05/2011

Preliminary checklist:

Please tick all activities to be undertaken by or within the establishment *(i.e. the legal entity with control of the tissue/data):*

- [x] Existing holding of stored tissue (any "relevant material" as defined by the Human Tissue Act and held prior to 1 September 2006)
- [x] Removal, collection and storage of new tissue from the living
- [x] Collection and storage of residual tissue from the living
- [ ] Removal of organs or tissue from the deceased
- [ ] Collection and storage of organs or tissue from the deceased
- [x] Collection and storage of DNA
- [x] Collection and storage of other biological material
- [x] Arranging the collection of new tissue samples or other biological material by collaborator(s)
- [x] Collection of new data from the living
- [x] Collection of clinical data from patient records
- [x] Other research procedures involving contact with participants (e.g. questionnaires)
- [x] Conducting research projects using the tissue samples or data
- [x] Releasing tissue samples or data to other researchers with no involvement of the establishment in conducting the research
- [ ] Collection and storage of tissue, other biological material or data from adults unable to consent for themselves due to physical or mental incapacity
- [ ] Collection and storage of tissue, other biological material or data from children without the capacity to consent for themselves

Part A: Core Information

Administrative information

1. Title of the tissue bank

UK Biobank: a large scale prospective epidemiological resource of 500,000 people aged 40-69 from around the UK

2. Name and address of the establishment responsible for management of the research tissue bank

Organisation	UK Biobank Limited
Address	1-3 Spectrum Way
	Adswood
	Stockport
PostCode	SK3 0SA
Telephone	01614755360
Fax	01614755361

Please give details of the locations at which tissue will be stored:
1-3 Spectrum Way, Adswood, Stockport SK3 0SA

3. Contact point within this organisation for purposes of the application

	Title	Forename/Initials	Surname
	Dr	Tim	Peakman
Address	UK Biobank Limited		
	1-3 Spectrum Way		
	Adswood, Stockport		
PostCode	SK3 0SA		
E-mail	tim.peakman@ukbiobank.ac.uk		
Telephone	01614755360		
Mobile	07786682081		
Fax	01614755361		

4. Name and address of the establishment responsible for storage of any relevant material under the Human Tissue Act

	Title	Forename/Initials	Surname
	Dr	Tim	Peakman
Address	1-3 Spectrum Way		
	Adswood		
	Stockport		
PostCode	SK3 0SA		
E-mail	tim.peakman@ukbiobank.ac.uk		
Telephone	0164755360		
Mobile	07786682081		
Fax	0161475536		

5. Does this establishment hold a licence from the Human Tissue Authority to store tissue for research? *Please enclose copy of licence if available.*

(●) Yes ( ) No ( ) Licence application pending

Further details:Licence number: 12002

6. Please give the name of the "designated individual" for purposes of licensing by the Human Tissue Authority:

	Title	Forename/Initials	Surname
	Dr	Tim	Peakman
Address	UK Biobank Limited		
	1-3 Spectrum Way		
	Adswood, Stockport		
PostCode	SK3 0SA		
E-mail	tim.peakman@ukbiobank.ac.uk		
Telephone	01614755360		
Mobile	07786682081		
Fax	01614755361		

7. Has this tissue bank (or any part of the bank) previously been the subject of an application for ethical review?

(●) Yes ( ) No

If Yes, was the application approved?

(●) Yes ( ) No

Name of Research Ethics Committee:	North West MREC
Date of decision:	16/12/2006
REC reference number:	06/MRE08/65

Purpose of the Bank

8. Please describe the types of tissue samples or other biological material to be collected/stored from the living.

Blood, urine and saliva

9. Please describe the types of tissue samples or other biological material to be collected from the deceased.

None

10-1. Please describe the data to be collected and linked with the samples. *Indicate whether any personal identifiers will be held and explain why this is necessary.*

During 2007-2010,UK Biobank conducted its recruitment phase and recruited 500,000 men and women from the UK population, who were aged 40-69 at the date of their baseline assessment visit.

UK Biobank's baseline assessment involved an extensive range of questions and measures, as well as the collection of biological samples (blood, saliva and urine) that allow many different types of assay. With the consent of participants, these data are being linked to each participant's health-related records (in such a way that their anonymity is preserved) so that the baseline information can be used in conjunction with the data on health outcomes.

Baseline data: By mid-2011, the database contained data collected from participants during their Baseline Assessment visit, which includes various different types of information:

♦ Questionnaire and physical measurement data (about 2,000 variables per participant); and

♦ Numbers of blood (with haematological assay results), urine and saliva samples.

♦ Additional baseline related data: As they become available, further data are to be added to the database, including:

♦ Data collected by remote methods, such as web-based questionnaires (e.g. on diet) and by devices (e.g. activity, environment);

♦ Specific assays conducted on biological samples from particular participants;

♦ Repeats of the baseline visits every 2-3 years in samples of 20-25,000 participants (Reassessment data); and

♦ Extra measurements that may be conducted at a second assessment visit for a sample of 100,000 participants (Enhancement data).

Health-related data: By mid-2011, the Resource only held data about the health of participants that was based on self reports made at the Baseline Assessment visit. Subsequent linkage to health outcomes data from an increasingly wide range of records systems allows participants' past medical history to be characterised more fully and, most importantly, allows the identification of incident disease that develops during follow-up. The data that are to be added to the database from linkage to medical and other health-related systems include:

♦ Death and cancer registry data;

♦ Hospital discharge diagnosis data;

♦ General practitioner data; and

♦ Other medical (e.g. prescriptions, pathology reports, imaging reports, screening) and health-related data (e.g. employment, benefits and other socio-economic records).

11. How is it intended to make beneficial use of the samples or data in research? *Please summarise the overall policy of the bank/establishment for use of the samples or data, including release to other researchers or research organisations*

UK Biobank's overriding objective is to ensure that the UK Biobank Resource is used extensively and appropriately for health-related research that is in the public interest, while at the same time maintaining the underlying agreement made with the participants regarding the confidentiality of their data and samples.

When UK Biobank was established, a detailed Ethics and Governance Framework (EGF) was drafted (see attached document reference: Version 3.0 October 2007). The EGF sets out the governance structure for UK Biobank and describes UK Biobank's purpose as to: ”build a major resource that can support a diverse range of research intended to improve the prevention, diagnosis and treatment of illness and the promotion of health throughout society”. The EGF also outlines UK Biobank's Access Policy.

UK Biobank's Access Procedures document (see attached document reference: Access Procedures 31 May 2011) details the application and review process for ensuring appropriate use of the Resource.

12-1. How have you actively involved, or will you involve, patients, service users, or members of the public in establishing the tissue bank and its policies?

There has been extensive consultation with stakeholders, members of the public and the scientific community throughout the life of UK Biobank, with rigorous review of its procedures.

UK Biobank began a preliminary feasibility phase in 2000 and 2001. This ultimately led to a pilot study which took place between March and June 2006, recruiting 4,000 participants from South Manchester. Key findings from this work allowed UK Biobank to refine and improve its recruitment processes. The UK Biobank protocol (see attached document reference: Protocol Number: UKBB-PROT-09-06 (Main Phase) 21 March 2007) was the subject of peer review, which led to approval of the funding by the MRC and Wellcome Trust (and other funding bodies).

An independent Ethics and Governance Council (EGC) was formed in November 2004 to help guide UK Biobank. This 11 person expert group is currently chaired by Roger Brownsword, Honorary Professor in Law at the University of Sheffield. Further details can be found at www.egcukbiobank.org.uk

Following successful recruitment of the planned 500,000 participants to UK Biobank during 2006 - 2010, the plans for the next 5 year phase of the project were the subject of peer review and continued funders approval. (See attached renewal application reference: 19 April 2010)

From 01 June 2011 to the 06 July 2011, UK Biobank will complete a public consultation on its Access procedures. The purpose of this consultation is to obtain the views of participants, scientists, members of the public and other interested parties on the draft procedures for allowing access to the UK Biobank Resource. Input from this consultation will be used to refine the Access Procedures and a revised draft will be put on the UK Biobank website

(www.ukbiobank.ac.uk) prior to initiating the access systems (which is intended to occur by the end of July 2011). As experience is gained with reviewing and approving applications, UK Biobank expects to update the procedures.

Use of samples or data in future research

Questions 13 - 21 apply where the bank/establishment will be conducting its own research using the samples or data. Answer in relation to this research programme.

Questions 22 - 32 apply where the bank will be releasing its own tissue and data to other researchers.)

13. Do you wish to seek generic ethical approval for research projects conducted by the bank/establishment using the stored tissue/data, under conditions agreed with the REC, without requirement for the researchers to apply individually to the REC for approval?

(●) Yes ( ) No

If Yes, questions 14 - 21 will be enabled.
If No, questions 14 - 21 will be disabled. Researchers will be required to apply individually to obtain ethical approval using the project-based application form.

14. What types of research will be undertaken and in what field(s) of biomedicine?

UK Biobank aims to encourage the widest possible use of the Resource to help develop improvements in the treatment and prevention of many different diseases. Bona fide researchers working in countries around the world will be able to apply to use the Resource for all types of health-related research that is in the public interest.

The main purpose of the UK Biobank resource is to assess the relevance of different exposures assessed at the baseline visit to health outcomes that occur during long-term follow-up. This can be done most cost-effectively by comparing the answers, measurements and samples collected at baseline from participants who develop some particular disease with those from apparently similar non-diseased controls selected from within the same cohort. This "nested" case-control (or case-cohort) strategy has the advantage that there are largely predictable timelines when the resource is likely to become mature for studying particular conditions based on their differing incidence rates, which allows, a coordinated approach to the use of the resource.

Even in a cohort of 500,000 individuals, it will take some years of follow-up before sufficient numbers have developed any particular disease to allow reliable statistical analyses of incident cases. Hence, the main uses of the resource in the next few years are likely to involve cross-sectional analyses of the baseline data and limited assays of samples (given their depletable nature) that are intended chiefly for assessing associations between potential risk factors and prevalent disease.

Researchers in universities, charities and other non-profit organisations, as well as in the pharmaceutical industry and other commercial organisations, will be able to use the Resource for any health-related research that is in the public interest. All approved researchers will be contractually obliged to put all of their data and findings back in to the Resource so that other approved researchers can use them.

15. What types of test or analysis will be carried out on the samples or data?

Due to UK Biobank being a prospective longitudinal study, it is difficult to be precise about what types of test or analysis will be completed (see answer to question 14). However, UK Biobank anticipates at least some of the following assays will be used on the samples:

♦ Large-scale technical analysis of the whole genome (e.g. GWAS, whole genome sequencing)

♦ Analyses of whole proteome (Mass Spectrometry or NMR)

♦ Analyses of metabonome (Mass Spectrometry or NMR)

♦ Measurement of individual or groups of specific markers using biochemical assays, immuno-assays, cell-based functional assays.

These are likely to change as new technologies become available over the course of the study.

16. Will the research involve the analysis of human DNA in the samples?

◉ Yes ○ No

17. Is it possible that the research could produce findings of direct clinical significance for individuals? *(This may include relatives as well as donors.)*

◉ Yes ○ No

18. Where research findings are clinically significant for individuals, will arrangements be made to notify the individuals concerned?

○ Yes ◉ No

If No, please justify. If Yes, say what arrangements will be made and give details of the support or counselling service.
UK Biobank participants were notified during the consent procedures that they (and their doctors) would not receive the results of any tests that UK Biobank completed. However, participants will be able to view the results of research conducted (on the UK Biobank resource) by visiting the UK Biobank website at www.ukbiobank.ac.uk.

19. Will the samples be used in animal research?

○ Yes ◉ No

20. Will the samples be used in research into termination of pregnancy or reproductive cloning?

○ Yes ◉ No

21. What arrangements will be made to consider applications from researchers for use of the tissue or data?

Please refer to UK Biobank's Access Procedures document (see attached document reference: Access Procedures 31 May 2011) for full details.

Questions 22 - 32 apply where the bank will be releasing tissue and data to other researchers.

22. Do you wish to seek generic ethical approval on behalf of external researchers who will be using tissue or data supplied by the bank, under conditions agreed with the REC, without requirement for researchers to apply individually to the REC for approval?

◉ Yes ○ No

If Yes, questions 23 - 32 will be enabled
If No, questions 23 - 32 will be disabled. Researchers receiving tissue or data will be required to apply individually to the REC to obtain ethical approval using the REC project-based application form.

23. What types of research will be undertaken by other individuals/organisations using the samples or data and in what field(s) of biomedicine? *Name any research organisations or units you plan to collaborate with at this stage.*

Please refer to the answer given to Questions 14 & 15 previously.

24. Will any types of research or research organisation be excluded from receiving tissue or data?

◉ Yes ○ No

If Yes, please give details:
The UK Biobank Resource has been established for only health-related research that is in the public interest. Any attempts to use it for other purposes will be resisted. So, for example, insurance companies and employers will not be

allowed to access the Resource to look at information, samples or test results for any identifiable participants. Nor will UK Biobank allow access by the police, security services or other law enforcement agencies, unless it is forced to do so by the courts. UK Biobank is prepared to take all necessary actions, including (where appropriate) recourse to legal proceedings in order to prevent such attempted access.

25. Will tissue samples be released for use in animal research?

○ Yes ◉ No

26. Will the samples be used in research into termination of pregnancy or reproductive cloning?

○ Yes ◉ No

27. What arrangements will be made to consider applications from researchers for use of the tissue or data?

Full details of UK Biobank's Access application and review procedures are contained within UK Biobank's Access Procedures document (see attached document reference: Access Procedures 31 May 2011)

28. Will tissue or data be released:

In fully anonymised form? *(link to stored tissue or data is broken)*
○ Yes ◉ No

In linked anonymised form? *(linked to stored tissue and data but donor not identifiable to the researcher)*
◉ Yes ○ No

In a form in which the donor could be identifiable to the researcher?
○ Yes ◉ No

29. Will tissue or data be released to individuals/organisations conducting research outside the UK?

◉ Yes ○ No

If Yes, please give details:
Use by researchers from overseas

As stated in the consent materials, bona fide researchers working in countries around the world will be able to apply to use the Resource for health-related research that is in the public interest. Restricting its use to UK researchers would prevent many other good scientists from using the data and samples to improve public health. Researchers from overseas may also 'add value' to the Resource by funding analyses of the biological samples which will then be available for UK scientists to use for their own health-related research in the public interest.

30. What will your policy be for requiring feedback of research findings specific to the donor to be linked with the stored tissue/data?

Research applicants will be required (in accordance with the Material Transfer Agreement) to provide UK Biobank with a copy of their results in a form and format as required by UK Biobank, along with the raw data behind the results.

31. Where research findings are clinically significant for individuals, will arrangements be made to notify the individuals concerned?

○ Yes ◉ No

If No, indicate clearly the reasons why data will not be notified to the subjects or their healthcare professionals
Please refer to the answer given previously to question 18.

32. What arrangements will be made with researchers for return or disposal of samples when studies are completed?

Successful research applicants will be required to sign a Material Transfer Agreement and in accordance with the terms of the Material Transfer Agreement, the researcher will confirm that, upon completion of the research project, they will destroy or return all samples provided by UK Biobank and confirm in writing that this has been done.

Sample collection and informed consent arrangements

Questions 33 - 34 apply only to the bank's existing collections of stored tissue/data:

33. Has informed consent already been given for use of tissue/data in research?

(●) Yes ( ) No ( ) Not applicable

If Yes, for what purposes has consent been given?
UK Biobank's participants were required to provide their written consent to a series of statements (see attached document reference: UK Biobank: Past progress and future plans for 2010 - 2015 renewal appplcation. Annex A2 - A2.4). This included the following statements regarding health-related research:

"I give permission for access to my medical and other health-related records, and for long-term storage and use of this and other inforamtion about me, for health-related research purposes (even after my incapacity or death).

I give permission for long-term storage and use of my blood and urine samples for health-related research purposes (even after my incapacity or death) and relinquish all rights to these samples which I am donating to UK Biobank"

Please enclose a copy of the information sheet and consent form used (if available).

34. If informed consent has not been given, is it proposed to seek consent for future use of tissue/data in research?

( ) Yes ( ) No (●) Not applicable

Application should be made to the National Information Governance Board for Health and Social Care (NIGB) to process the identifiable data of living donors without consent in England and Wales – see guidance notes.

Question 35 applies to collections from the deceased only:

35. What arrangements will be made to seek appropriate consent? *Please describe the involvement of collaborators.*

Not applicable

Please enclose copy of information sheet(s) and consent form(s).

Questions 36 - 39 apply to prospective collection of tissue samples, other biological material or data from the living:

36-1. How and by whom will donors be identified? *Please describe the involvement of collaborators.*

People to invite to take part in the study were identified from National Health Service (NHS) records. The only information UK Biobank used, in confidence, for this purpose was the person's name, address, sex, date of birth, NHS/CHI number and general practice. These details were processed centrally on behalf of the NHS in accordance with the Data Protection Act.

36-2. Will this involve reviewing or screening identifiable personal information of potential donors?

(●) Yes ( ) No

36-4. Will individuals other than the direct healthcare team have access to identifiable personal information of potential

donors for this purpose?

○ Yes ◉ No

37. How and by whom will donors first be approached? Indicate whether this will be in the course of healthcare provision or whether additional procedures will be involved?

UK Biobank approached potential participants direct via a posted invitation pack, which included an invitation letter (with a pre-booked appointment time) together with an information leaflet providing further details about the study.
In the case of additional procedures, what burdens could arise for participants?

38. Will there be any further contact with donors to collect additional samples or data following the initial donation?

◉ Yes ○ No

If Yes, please give details:
From time to time, UK Biobank may contact participants again to seek new information or to ask participants if health researchers can contact them to discuss possible involvement in a study that requires new information. UK Biobank will also seek consent for any proposed new uses that do not fall within the existing consent. UK Biobank intends to restrict the level of re-contact with participants (so that they are not approached too often), and will make contacts on behalf of other researchers (so that participants' anonymity is protected). Separate ethics approval will be required for such re-contact and the advice of the Ethics & Governance Council will also be sought. Participants are under no obligation to provide further information and, if they prefer, can request no further contact with UK Biobank.

Repeats of the baseline visits every 2-3 years in samples of 20-25,000 participants (Re-assessment data)are included in the approved protocol for UK Biobank.

With ethics committee approval, UK Biobank also plans to collect further data by remote methods, such as web-based questionnaires (e.g. on diet) and by devices (e.g. activity, environment).

An application for extra measurements that may be conducted at a second assessment visit for a sample of 100,000 participants (Enhancement data) is currently being developed.

39. Will you obtain informed consent to use tissue and data in research?

◉ Yes ○ No

If you will be obtaining consent from adult donors, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos or interactive material).
Participants gave their consent at the start of the assessment visit and this was overseen by trained assessment staff.

The consent process was completed on computer, with the participant confirming their agreement to each of a number of statements and signing their consent using an electronic pad. Each participant received a paper copy of their signed consent form at the end of the assessment visit.
Arrangements for adults unable to consent for themselves should be described separately in Part B Section 1, and for children in Part B Section 2. If you plan to seek informed consent from other vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

If you will not be obtaining informed consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

Questions 41-42 apply in all cases where consent is to be sought:

41. Will you record informed consent in writing?

◉ Yes ○ No ○ N/A

42-1. What arrangements have been made for persons who might not adequately understand verbal explanations or

written information in English, or who have special communication needs? *(e.g. translations, use of interpreters)*

UK Biobank provided interpreting and assistance services for participants with disabilities. For non-English speakers, UK Biobank encouraged participants to be accompanied by a relative or friend to interpret on their behalf.

42-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to data subjects in Wales?

Participant invitation literature, including instructions regarding the consent process were available in Welsh.

Questions 43 - 44 apply to all applications

43. Will any financial or other incentives be offered to donors?

○ Yes ◉ No

44. What steps will be taken where donors or relatives subsequently withdraw consent to the use of tissue/data?

As part of the recruitment process, persons invited to take part in the study were provided with detailed information about UK Biobank, so that they could make an informed decision as to whether or not to take part. However, an equally important part of the information provided was the detail on how a participant might withdraw from the study, should they change their mind at a later date.

UK Biobank defined 3 levels of withdrawal:

No Further Contact (“NFC”): This means that UK Biobank would no longer contact the participant directly, but would still have permission to use information and samples provided previously and to obtain further information from their health-relevant records.

No Further Access (“NFA”): This means that UK Biobank would no longer contact the participant or obtain information from their health-relevant records, but would still have permission to use the information and samples provided previously.

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

Whilst accepting that withdrawals would inevitably occur, UK Biobank sought to minimise the number of withdrawals by providing participants with detailed information at the outset. A dedicated Participant Resource Centre was established to handle individual queries and concerns (received by telephone) and a “Frequently Asked Questions” section was included on the UK Biobank website. Participants were also actively encouraged to discuss any final queries or questions that they might have, with assessment centre staff prior to consenting to participate in the study.

However, as indicated above, a withdrawal process was defined and the Information Leaflet (which formed part of the invitation pack) advised participants that they would be required to provide written confirmation of any request to withdraw. A withdrawal form (see attached document reference: DOC No: CLI24_A Version 3.3) was used for this purpose.

Documented withdrawal procedures were also a specific requirement of the Human Tissue Authority who audited UK Biobank's processes in October 2010.

Part C: Tissue Collection Centres

6. Please enter details of the organisations (NHS or other) in the UK that will act as tissue collection centres for this research tissue bank.

Tissue collection centre	Local collaborator

Part D: Declarations

D1. Declaration by the applicant:

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. If the application is approved I undertake to adhere to the terms of the application of which the REC has given a favourable opinion and any conditions set out by the REC in giving its opinion.
3. I undertake to seek an ethical opinion before implementing substantial amendments to the terms of the application of which the REC has given a favourable opinion.
4. I undertake to submit annual progress reports to the REC.
5. I understand that the information contained in this application, any supporting documentation and all correspondence with NHS Research Ethics Committees or their operational managers relating to the application:
    - Will be held by the main REC indefinitely (or until 3 years after the closure of the tissue bank).
    - May be disclosed to the operational managers or the appointing body for the REC in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed by the National Research Ethics Service to undertake accreditation of the REC.
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to the establishment and other research units and collaborators would be removed.

Signature of the applicant named at A3: .....

Name: Tim Peakman
Date: 31/05/2011

D2. Declaration by the Designated Individual

I confirm that the information in this form is true and accurate to the best of my knowledge and I support the application.

Signature of the Designated Individual: .....

Name: Tim Peakman
Date: 31/05/2011