ACCESS PROCEDURES: Application and review procedures for access to the UK Biobank Resource

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SUMMARY

During 2007-2010, UK Biobank conducted its recruitment phase in which 500,000 participants gave their consent, answered questions, had measurements and gave biological samples at a baseline assessment visit. Follow-up of their health is now being conducted through medical and other health-related records.

The overriding objective of these Access Procedures is to encourage the extensive and appropriate use of the Resource. In particular, the intention is that the process for applying to use the Resource is simple and streamlined, without undue delays in providing access to data and samples for research.

The Access Procedures reflect the Access Policy which is outlined in UK Biobank’s Ethics & Governance Framework and the undertakings given to the participants when they agreed to take part. The procedures and processes that have been applied to access to the Resource derive from the following key principles:

- The Resource is available to all bona fide researchers for all types of health-related research that is in the public interest, without preferential or exclusive access for any person. All researchers, whether in universities, charities, government agencies or commercial companies, and whether based in the UK or abroad, will be subject to the same application process and approval criteria.

- Applications to use the Resource will be checked to ensure that research proposals are consistent with these Access Procedures, the Ethics & Governance Framework, and the consent that was provided by the participants (including having relevant scientific and ethics approval).

- Access to the biological samples that are limited and depletable will be carefully controlled and coordinated. The quantity of sample that is required will be judged against the potential benefits of the research project, with advice from appropriate experts as required.

- Safeguards will be maintained to help ensure the anonymity and confidentiality of participants’ data and samples. Researchers will enter a legal agreement with UK Biobank not to make any attempt to identify participants, and data and/or samples provided to researchers from the Resource will not identify any particular participant (i.e. they will be “anonymised”).

- Researchers will have to pay for access to the Resource on a cost-recovery basis for their proposed research, with a fixed charge for initiating the application review process and a variable charge depending on how many samples, tests and/or data are required for the research project.

- UK Biobank will remain the owner of the database and samples, but will have no claim over any inventions that are developed by researchers using the Resource (unless they are used to restrict health-related research or access to health-care unreasonably).

- Researchers granted access to the Resource will be required to publish their findings and return their results to UK Biobank so that they are available for other researchers to use for health-related research that is in the public interest.

- UK Biobank will seek active engagement with participants, researchers and society in general throughout the Resource’s lifetime (which is intended to be some decades), in particular regarding the research that is being conducted on it and the research findings that emerge.
A OVERVIEW OF THE ACCESS PROCEDURES

A1 The UK Biobank Resource

A1.1 UK Biobank has recruited 500,000 men and women from the UK population who were aged 40-69 at the time of their baseline assessment visit during 2007-2010. This assessment involved an extensive range of questions and measurements, as well as collection of biological samples that allow many different types of assay to be conducted.

A1.2 With the consent of each participant, these data are being linked to their health-related records (in such a way that the participant’s confidentiality is preserved) so that the baseline information can be used in conjunction with the information about health conditions that develop.

A1.3 The rationale for recruitment of a cohort of such large size was to allow reliable quantification of the relevance of a large number of risk factors (e.g. lifestyle, environment and genes), both separately and in combination, to a wide range of diseases developing during follow-up.

A2 UK Biobank’s Access Policy

A2.1 When UK Biobank was established, a detailed Ethics & Governance Framework (EGF) was drafted and adopted. The EGF sets out the governance structure for UK Biobank (including the role of its Board and an independent Ethics & Governance Council [EGC]) and provides the framework that UK Biobank operates within (including the Policy governing access to the UK Biobank Resource).

A2.2 UK Biobank’s purpose is described in the EGF 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”. This intent is paraphrased in the Consent Form and related information materials as being “health-related” and in the “public interest”. Researchers who apply to use the Resource will be required to explain explicitly how their research project supports this stated purpose.

A3 Objective of the Access Procedures

A3.1 The objective of these Access Procedures is to facilitate access to the samples and data so that they get the widest possible usage while ensuring that such access and usage is consistent with the undertaking given to the participants (see below) and the wider public interest (including being lawful and compatible with respect for human rights).

A3.2 At all times, decisions to grant access should maintain the undertakings made to participants when they consented to take part: (i) to help ensure that any uses of the resource are consistent with its stated aims; (ii) to protect participants’ anonymity and confidentiality; (iii) to ensure that research projects have relevant scientific and ethics approval, and (iv) to make information publicly available about the uses of the UK Biobank Resource.

A3.3 It is intended that these Access Procedures are clear and transparent and are implemented in a manner which is proportionate, accountable and fair. The Procedures provide a framework for addressing and determining access issues. They deliberately do not prescribe what will be done in each and every circumstance because UK Biobank cannot (and would be unwise to try to) predict the nature of access requests that it will receive over the long-term. Built into the Procedures is sufficient flexibility to address both the expected and the unexpected, including the ability to revise them in the light of practical experience.

A3.4 The functioning of these Procedures will be kept under review by the UK Biobank Principal Investigator (UKBPI), with UK Biobank’s Board and its Access Sub-Committee. Input from the participants, researchers, funders, EGC and other interested parties will be taken into account. UK Biobank’s Board will amend the Access Procedures as required on a periodic basis.
A4 Communication

A4.1 The EGF sets out the basis of the relationships that UK Biobank aims to foster with participants, researchers and the public at large. UK Biobank is committed to maintaining a dialogue with these different communities, and will keep them updated on the progress of UK Biobank and the research work which is carried out using the Resource.

A4.2 Summaries of approved applications and an indication of their status (e.g. approved/research in progress/completed/published) will be made available on UK Biobank’s website.

A4.3 Summaries of the research findings that derive from use of the Resource will also be provided on the website, with links to related publications.

A4.4 Contentious and/or ethically challenging issues related to proposed or approved uses of the Resource will be highlighted on the website. This will allow participants, and the wider public, to provide input on particular research uses and other issues.

A5 Access charges

A5.1 UK Biobank has carefully considered a variety of charging models and has decided to adopt the following approach:

A5.1.1 All researchers will be charged on the same cost-recovery basis;

A5.1.2 There is a fixed charge for each Application of £250 (plus VAT if applicable) to help cover UK Biobank’s initial costs for the administration of the Application. This charge is payable on submission of the Preliminary Application Form; and

A5.1.3 There is a variable component which depends on what is being accessed, calculated as a simple cost recovery of UK Biobank’s internal costs plus any third party costs incurred by UK Biobank. This component will include charges for administration, sample extraction, sample assays, any re-contact costs, data derivation and (for large data sets) extraction. It will be payable prior to the release of any data or samples.

A5.2 UK Biobank will keep this charging policy under review (including the possibility of different levels of charge for different types of researcher) to ensure that it continues to represent an equitable, balanced and pragmatic approach.
B FACTORS AFFECTING ACCESS

B1 Publicly available information

B1.1 Each person who agreed to join the UK Biobank project received a clear assurance that all of their personal information would be held in strict confidence with careful controls, and that identifiable information about them would not be available to anyone outside of UK Biobank.

B1.2 All technical and legal measures that are available to UK Biobank will be used to help ensure that each participant’s identity remains confidential. In particular, highly secure IT industry standard methods are used to protect the database from accidental access or intentional abuse.

B1.3 Identifying information is retained by UK Biobank to allow it to make contact with participants when required and to link with their health-related records. The level of access that is allowed to staff within UK Biobank is controlled by unique user names and passwords, and restricted on the basis of their need to carry out particular duties.

B1.4 UK Biobank aims to make as much data as possible publicly available on its website in grouped format (i.e. not at individual participant level), so that potential research users can evaluate what the Resource contains before applying to use it. This includes a list of the questionnaire and measurement data variables and the types of biological samples collected at the baseline assessment, along with the numbers of participants in various groupings of the data variables.

B1.5 UK Biobank requires researchers to make a formal application for data and/or samples relating to selected participants (e.g. based on information from the baseline assessment or subsequent follow-up of their health outcomes). UK Biobank will respond to questions about the Resource prior to submission of applications and during the course of considering them (Annex I).

B1.6 When data are provided to researchers, all practical steps will be taken to remove direct and indirect identifiers that might allow identification of individual participants (a process known as “reverse anonymisation”). The Material Transfer Agreement (MTA: Annex II) includes a strict prohibition on researchers trying to identify any participant. In the case of inadvertent identification, researchers are required to report this immediately to UK Biobank and not to disclose it further or make any attempt to contact the individual.

B2 No preferential or exclusive access

B2.1 UK Biobank’s aim is to provide fair, consistent and transparent access to the Resource in order to promote health-related research by bona-fide researchers that is in the public interest. No distinction will be made between Applicants on the basis of whether they are:

B2.1.1 From the UK or abroad; and/or

B2.1.2 Charitable, academic, governmental or commercial entities.

B2.2 UK Biobank will apply a standard set of criteria (subject to ongoing review and amendment by UK Biobank’s PI and Access Sub-Committee) to the assessment of all Applications, including the compatibility of the research project with the purposes of UK Biobank; the feasibility of the research project; and the facilities for managing data and/or samples (Annex I).

B2.3 The level of scrutiny used to assess Applications will be proportionate to the nature and scale of the research project, taking into account (by way of example) whether a significant amount of depletable sample is required, whether re-contact of participants is sought, and whether there are considered to be potentially contentious issues involved.

B2.4 UK Biobank wishes to encourage collaboration between prospective researchers in order to increase the efficient use of the Resource. For example, when their proposed research involves overlapping uses of the same set of depletable samples, UK Biobank may initiate contact (in confidence and with mutual consent) between them.
Researchers who provide funding to derive data from the Resource (e.g. assays of samples; analyses of images) will be allowed to use them for a limited period of time (e.g. to analyse the data and to prepare papers for publication) before these data will be made available for other researchers to use. There will be no restrictions on the number of researchers who can be provided with the same or overlapping data that are already contained within the Resource.

This approach is intended to encourage rapid reporting of findings and different approaches to the analysis and interpretation of the data, as well as allowing researchers to confirm or refute published findings based on the Resource (i.e. representing a robust form of peer review that is consistent with the aim of facilitating use by all bona fide researchers).

Data available in the Resource

If data alone are required from the Resource then there is not typically a requirement that the Research Proposal has undergone independent scientific review, although UK Biobank may still require it in certain circumstances (e.g. when the proposed use is potentially contentious or there are concerns about its value, whether for scientific, public health or other reasons).

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

- Questionnaire and 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 that are related to the baseline assessment of participants are to be added to the database, including:

- Data collected by remote methods, such as web-based questionnaires (e.g. on diet) and by various devices (e.g. activity, environment);
- Extra measurements that may be conducted at subsequent assessment visits among sub-sets of the participants (“Enhancement Data”);
- Repeats of the baseline assessment visit every few years in samples of 20-25,000 participants (“Re-assessment Data”); and
- Specific assays conducted on biological samples from particular participants.

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 will allow participants’ past medical history to be characterised more fully and, most importantly, will allow studies of incident disease that occurs 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).

Researchers are required to provide any data derived from use of the Resource to UK Biobank so that such data can be incorporated into the database for use by other researchers.
B4 Samples and assay data available in the Resource

B4.1 If samples are required from the Resource then there is a requirement that the research proposal has undergone appropriate independent scientific review (with “appropriate” depending on the nature of the proposed research and with peer-review by a recognised body typically considered sufficient); and the potential benefits of the project will be considered by UK Biobank in the context of the number and volume of samples required, the proposed location for conduct of the assays, and any overlapping studies.

B4.2 As UK Biobank has been established as a prospective resource, the participants’ samples are expected to be used chiefly (but not solely) to assess the relevance of different exposures assessed at baseline to the subsequent development of disease (rather than disease already present at the baseline visit). It is anticipated that this will typically be done by conducting case-control or case-cohort studies of particular health outcomes “nested” within the cohort.

B4.3 This approach has the advantage that the assays only need to be conducted on samples from relatively small subsets (e.g. a few thousand or tens of thousands) of “informative” participants who develop a particular disease and similar numbers of controls. Moreover, decisions about what assays to perform only need to be made when specific hypotheses are clearer (rather than at the time of sample collection), and the range of assays that can be conducted at reasonable cost is much wider. Consequently, assay costs are substantially reduced, depletion of limited samples is minimised, good quality control is facilitated, and scientific return is maximised.

B4.4 In the short-term, however, it is anticipated that researchers may want to assay the samples of people with disease already known to be present at the baseline assessment visit or in those with other particular characteristics (e.g. extreme values of questionnaire and/or measurement variables). Again, such studies would typically involve conducting assays only on relatively small subsets, with the advantages of reduced costs, minimised depletion and good quality control.

B4.5 Given the limited and depletable nature of the samples, their use is to be carefully controlled in order to optimise the informativeness of the Resource in the long-term. In particular, UK Biobank aims to co-ordinate the assays that are conducted so that sample depletion and costs for researchers are minimised, while quality control is maximised. It is anticipated that this will typically involve UK Biobank conducting or commissioning assays and distributing the sample assay data to researchers, rather than distributing the samples themselves.

B4.6 In those circumstances where UK Biobank does provide samples to researchers for specialised assays then it will aim to do so in such a manner (e.g. by providing anonymised samples without related data about disease status or other characteristics for each participant) that requires the researcher to return the assay data and related information (e.g. assay method; quality control) to UK Biobank before they are able to do any research involving those assay data. This is intended to help ensure that high quality assay data are available in the Resource for use by any subsequent researchers irrespective of whether the assays were done by UK Biobank, by third party laboratories or by previous researchers.

B5 Timetable for studies of incident disease

B5.1 Based on anticipated incidence rates for a range of different conditions and plausible estimates of relevant exposure associations, UK Biobank will develop a timetable (with guidance from its Access Sub-Committee, Steering Committee, International Scientific Advisory Board [ISAB] and other experts) indicating when the Resource is likely to be sufficiently mature to establish case-control collections for each condition (and the planned frequency of updating these collections).

B5.2 UK Biobank intends to use this timetable to guide calls for use of the Resource and to plan sample retrieval. This indicative timetable is to be made available on the UK Biobank website so that researchers can develop their proposals in accordance with it. Applications received in between these planned calls would typically use the most recently retrieved sample set (unless there was considered to be a strong case for updating the relevant sample set).
Such scheduling of access for each condition should help to ensure more efficient use of the Resource: for example, case-control sample sets can be established and updated in a planned way (rather than unduly frequently in response to separate requests). In addition, the wide range of assays required for many individually approved Applications can be conducted in a coordinated fashion at one or a few laboratories (rather than sending separate aliquots to a large number of different laboratories, with each doing a few assays).

Research requiring re-contact of participants

Participants have consented to be re-contacted, but UK Biobank will monitor carefully the level of, and rationale for, re-contact to ensure that participants are not over-burdened. Initial re-contact for an approved study would always be undertaken by UK Biobank.

Re-contact may be for a variety of reasons, including to collect new information or samples; to seek additional consent for uses that fall outside the existing consent; and to ask participants whether they are willing to be contacted directly by approved researchers (e.g. to provide new information or take part in another study).

Researchers are required to make it clear in their Application if it is proposed that participants be re-contacted. Decisions on whether re-contact is appropriate will be made by UK Biobank, with advice from the EGC, and such re-contact requires separate approval from a Research Ethics Committee (and UK Biobank will generally also require independent scientific review to help ensure that re-contact is warranted).

Provision of new information, samples or consent by participants would be entirely voluntary. When re-contacting special sub-populations, UK Biobank will take appropriate care to ensure that the use of selection criteria (such as genetic make-up) does not inadvertently reveal information to participants about themselves of which they are not aware.

Legal and ethics approval

UK Biobank has obtained Research Tissue Bank (RTB) approval from its governing Research Ethics Committee (REC), as recommended by the National Research Ethics Service (NRES). This approach should cover the great majority of proposed uses of the Resource, so that researchers do not typically need to obtain separate ethics approval.

This generic RTB approval applies to access to data and/or samples for renewable periods of 5 years. As a condition of obtaining generic RTB approval for use of both the data and samples, UK Biobank has made certain commitments to its governing REC. Consequently, UK Biobank requires equivalent commitments from all researchers in the MTA (Annex II).

Notwithstanding RTB approval, UK Biobank may still require a prospective researcher to obtain specific REC approval for a particular research project in the following circumstances:

Any research project involving the re-contact of participants;

Research uses (which are expected to be few) of the Resource that are not covered by RTB approval (such as research involving human reproductive technology); or

UK Biobank reasonably considers it appropriate to do so.

UK Biobank possesses a Human Tissue Authority (HTA) licence, so a separate HTA licence is not required by researchers who receive samples from the Resource, provided that:

Residual samples are destroyed or returned at the end of the Research Project; and

Applicants are not entitled to transfer the samples to third party premises without the specific approval of UK Biobank.

UK Biobank requires these commitments from all researchers in the MTA (Annex II).
**Intellectual Property Rights**

**B8.1** UK Biobank’s approach to Intellectual Property Rights (IPR) is structured on the basis that it seeks to encourage use of the Resource for health-related purposes by bona fide researchers. To this end, UK Biobank will retain ownership of its rights in the Resource (so that it is available to all other approved researchers), while at the same time facilitating the development of clinical advances (e.g. diagnostics and treatments) arising from its use.

**B8.2** UK Biobank is the owner of the property in the database and the samples (which will be added to, and updated, throughout the life of the Resource) and retains all the intrinsic IPRs in the data in the Resource (notably database rights and copyright).

**B8.3** Researchers are granted limited licences (but not any ownership rights) to use the data and samples to conduct the approved Research Project for a particular period of time. These rights are not assignable or transferable, and nor is there any ability to sub-license.

**B8.4** If a researcher creates separate datasets as a result of their use of the Resource, then IPRs in the researcher-generated datasets will be owned by the researchers and/or their institutions, subject to the requirement to grant a non-exclusive licence back to UK Biobank for its use on an irrevocable, perpetual, worldwide, fully paid-up, royalty-free, fully sublicensable basis. These datasets will, therefore, be available for use by other researchers who are granted access to use the Resource.

**B8.5** UK Biobank will have no claim over inventions and associated IPRs that are developed by researchers as a result of using the Resource, unless such IPRs are used to restrict health-related research and/or access to health-care unreasonably. UK Biobank does not intend to use this right to appropriate third party inventions, but (for example) would not expect naturally-occurring genetic sequences, biomarkers, proteins or biochemical processes to be made the exclusive preserve of one party. In this context, UK Biobank does not seek to restrict applications for the protection of IPRs, rather their use in an unreasonably restrictive manner.

**B8.6** In the event that conduct is considered unreasonably restrictive by UK Biobank, it reserves the right to require that a licence of such rights is granted back to UK Biobank on an irrevocable, perpetual, global, royalty-free, fully sub-licensable basis so that other researchers who are granted access to use the Resource can exercise such rights to the extent necessary to conduct their research project.

**B8.7** UK Biobank will keep this policy on IPRs under review to ensure that it continues to represent an equitable, balanced and pragmatic approach.
Stages in the application and review process (with the indicative timelines in parentheses); the roles of the different parties are described in Section C11.
C1  **Application review stages**

C1.1 The application process is entirely on-line via the UK Biobank website. The process is designed so that each potential user of the Resource only has to register once and then just confirms (or amends) their details for each application. All communications relating to each application will be retained so that there is a comprehensive file.

C1.2 There are 4 stages to the application process (see schematic on previous page):

- **Registration**: To confirm the identity of each person seeking to use the Resource and to check their bona fides before registering them as an approved researcher.

- **Preliminary application**: To allow approved researchers to determine: (i) whether their proposed research use is likely to be approved; (ii) whether the resource contains the data and/or samples required for their proposed research; and (iii) the indicative cost of obtaining such data and/or samples (e.g. in preparation for a funding application).

- **Main application**: To allow UK Biobank to assess: (i) whether the proposed research use meets the required criteria for access (including having relevant scientific and ethics approval); (ii) whether the amount of depletable sample required is scientifically justified; and (iii) the cost of providing such data and/or samples.

- **Material Transfer Agreement (MTA)**: For approved applications, the Material Transfer Agreement will need to be executed and access charges paid before release of data and/or samples to the approved researcher.

C1.3 **Timelines**: In order to facilitate access to the Resource, it is intended that each review stage will be conducted in accordance with an indicative timeline (although the need to seek further information or guidance on particular applications may lead to a more prolonged process). The intended timelines for each stage are:

- **Registration**: 2 weeks to check identity;

- **Preliminary application**: 4 weeks to review and respond;

- **Main application**: 4 weeks to review and respond;

- **Material Transfer Agreement**: 4 weeks to execute and process access fee; and

- **Release of data/samples**: Data will typically be released on a monthly basis, whereas samples will typically be released on a quarterly basis in order to provide opportunities to coordinate sample usage between separate studies and minimise duplicate usage.

C1.4 The review stages for Preliminary and Main applications of a research proposal are not likely to run immediately after each other (e.g. an approved Preliminary Application may first lead to an application for external funding, especially when costly sample assays are involved). But, if they do, the process from the start of the review of the Preliminary Application to execution of the Material Transfer Agreement may take up to about 3 months. There would then be a further period of time before data or samples (or related assays) would be ready for release.

C1.5 The process of reviewing applications will be managed by the UK Biobank Coordinating Centre, which will conduct a set of standard checks and seek advice on particular applications as required (Section C12.5 & Annex I). Recommendations on each application will be made by the UK Biobank Principal Investigator (or their designate) and will be subject to confirmation by UK Biobank’s Access Sub-Committee (see Sections C12.3 & C12.4). Applications that raise particular concerns (e.g. involve potentially contentious uses of the Resource) will typically be referred to the Access Sub-Committee or to UK Biobank’s Board.
C2 **Registration Form**

C2.1 Each researcher wishing to use the Resource first needs to register, setting out:

C2.1.1 Their name, address, email and direct telephone number (appending an electronic version of their curriculum vitae);

C2.1.2 A list of their peer-reviewed publications (with hyperlinks to the papers whenever possible), and details of any complaints, within the previous 3 years; and

C2.1.3 The research department, address, telephone and web site for their Institution.

C2.2 UK Biobank Coordinating Centre staff will take the steps needed (Annex I) to confirm the identity and the bona fides of the researcher. When this has been done satisfactorily, the researcher will be issued with a unique identifying number (indicating that they are an approved researcher) which should be used for any subsequent applications.

C3 **Preliminary Application Form**

C3.1 The applicant Principal Investigator (PI) of a research project, who must be an approved researcher, is required to complete a Preliminary Application Form with the following information:

C3.1.1 Lay summary (200 words or less) of the research project, including an explanation of how it meets UK Biobank’s purpose (i.e. it is both health-related research and in the public interest: see Section A2);

C3.1.2 Required data and/or quantity and type of samples, and any need for re-contact, with a brief justification;

C3.1.3 Whether funding is available or will need to be sought;

C3.1.4 Any ethical or potentially contentious issues related to the proposed use; and

C3.1.5 Any questions about the Resource (e.g. available data and/or samples).

C4 **Response to Preliminary Application Form**

C4.1 UK Biobank Coordinating Centre staff will check the Preliminary Application Form (Annex I) and seek any further information that is required (which may relate to the scientific basis, feasibility, or some other characteristic of the proposed research project).

C4.2 A summary of the status of each Preliminary Application (highlighting any potential issues) will be available to the Access Sub-Committee so that it can consider any Application at any time during the review process (as well as to the EGC for its oversight role).

C4.3 When the review has been completed, UK Biobank will communicate one of the following responses to the applicant PI:

C4.3.1 An invitation to complete a Main Application and an approximate indication of the likely costs for the access to data and/or samples. If re-contact of participants is proposed (or for any other reason at UK Biobank’s discretion), the applicant PI will be asked to obtain REC approval before submitting the Main Application. UK Biobank would also endeavour to answer any of the applicant PI’s questions; or

C4.3.2 An indication that UK Biobank is minded to decline the Application (with summary reasons given), which will typically be determined by the Access Sub-Committee. The applicant PI can then elect to (i) clarify or amend the application; (ii) withdraw the application; or (iii) request that the decision be reconsidered.
C5 **Main Application Form**

C5.1 If the applicant PI has received an invitation to complete a Main Application, they will then need to complete a Main Application Form and provide the following information:

C5.1.1 Lay summary (updated, if necessary, from the Preliminary Application);

C5.1.2 Names of all collaborators (who also need to be approved researchers);

C5.1.3 Scientific rationale of project (background and any pilot data; experimental details and design; power calculations; expected value of results; relevant references);

C5.1.4 Required data and/or quantity and type of samples, and any need for re-contact, with a brief justification (updated, if necessary, from the Preliminary Application);

C5.1.5 Protocols for storage of the data and/or samples (data security; physical security of the samples; ability to handle withdrawals);

C5.1.6 Feasibility issues (e.g. research capabilities; collaborators);

C5.1.7 Proposed timetable (start; duration; availability of results; submission of publication);

C5.1.8 Details of funding (or applications for funding);

C5.1.9 Details of any peer review (actual or proposed); and

C5.1.10 Applicants may (but are not required) to submit letters of support from third parties.

C5.2 The applicant PI also needs to ensure that each collaborator associated with the research project has registered with UK Biobank.

C6 **Response to Main Application Form**

C6.1 UK Biobank Coordinating Centre staff will check the Main Application Form (Annex I) and seek any further information that is required (which may relate to the scientific basis, feasibility, or some other characteristic of the proposed research project).

C6.2 A summary of the status of each Main Application (highlighting any potential issues) will be available to the Access Sub-Committee so that it can consider any Application at any time during the review process (as well as to the EGC for its oversight role).

C6.3 When the review has been completed, UK Biobank will communicate one of the following responses to the applicant PI:

C6.3.1 Approval subject to entering into an MTA (Annex II) and paying the access charges (which will be itemised in the response);

C6.3.2 Approval conditional on certain outstanding matters (e.g. award of funding; obtaining separate REC approval) being met within a set period of time;

C6.3.3 An indication that UK Biobank is minded to decline the application (with summary reasons given), which will typically be determined by the Access Sub-Committee. The applicant PI can then elect to (i) clarify or amend the application; (ii) withdraw the application; or (iii) request that the decision be reconsidered.

C7 **Reconsideration of Applications**

C7.1 If an applicant PI is advised that UK Biobank is minded to decline either a Preliminary or Main Application then they may request that the application be reconsidered by UK Biobank.
C7.2 The process for having an Application reconsidered is as follows:

C7.2.1 Within 3 months of the relevant decision, the applicant PI should submit a written request, giving their reasons why they consider that the decision should be revised;

C7.2.2 Within 4-6 weeks of receipt of such a request, the Access Sub-Committee or the Board (as appropriate) will aim to consider it along with the original application (and any other information that it considers pertinent) and UK Biobank will then respond to the applicant PI;

C7.2.3 If considered necessary, the Access Sub-Committee or the Board may seek additional advice (e.g. from scientific or other experts, or the EGC), in which case the applicant PI will be advised by UK Biobank of any revision to the timetable for review.

C7.3 If, following reconsideration, the application is declined then the applicant will not be able to submit the same proposal again within a 12 month period (unless the Access Sub-Committee has indicated specifically that it may be submitted subject to specific changes being made).

C8 Material Transfer Agreement

C8.1 If the Research Project is approved then UK Biobank will send its standard MTA (Annex II), to the applicant PI (along with a Request for Payment of the Access Charges) for review and completion by their institution (Annex II).

C8.2 Apart from inclusion of the specific details of the approved research project (e.g. details of the researchers; the required data and/or samples; the completion date for the project), the content of UK Biobank’s MTA, and the conditions contained within it, are non-negotiable.

C8.3 The MTA will be considered to have been executed when UK Biobank has received both:

C8.3.1 The MTA signed by the applicant PI and their institution; and

C8.3.2 The Access Charges in cleared funds.

C8.4 After the MTA has been executed and the required data (including any sample assays) have been supplied to the applicant PI, the lay summary of the research project will be put on the UK Biobank website (with any confidential information removed) in order that participants and the wider public can see what the Resource is being used to study.

C8.5 If a researcher breaches the provisions of the MTA then this could lead to immediate revocation of the licence to use the Resource. It could also lead to other actions, such as informing the researcher’s institution and/or funders, as well as other regulatory bodies, and prohibiting further access to the Resource from the researcher’s institution.

C9 Provision of data

C9.1 Data from the UK Biobank Resource will be provided in the following formats:

C9.1.1 Certain data sets will be made available by issuing hyperlinks and passwords to the applicant PI so that the relevant data can be accessed and downloaded. UK Biobank will require that transfer of datasets outside of the applicant’s institution be restricted whenever reasonably possible and that prior agreement be obtained from UK Biobank for such data transfers; or

C9.1.2 In respect of data sets of very large size where downloading is not a practical solution, in situ access will be made available to the applicant PI and their collaborators on UK Biobank’s servers.

C9.2 Data generated from sample assays conducted by, or on behalf of, UK Biobank will be provided in the same manner, in a timeframe agreed between UK Biobank and the applicant PI.
C10 Provision of samples

C10.1 In those circumstances when assays are not to be conducted by UK Biobank, samples will be provided to the applicant PI in the following manner:

C10.1.1 UK Biobank will notify the applicant PI when the samples will be retrieved from the archive and ready for delivery, and of the cost of delivery by an approved third party;

C10.1.2 The applicant PI will then notify UK Biobank of convenient dates and location for delivery of the samples;

C10.1.3 UK Biobank will arrange for delivery to be made through an approved third party and the applicant’s institution will be liable for payment of the third party; and

C10.1.4 Within one working day of receipt, the applicant PI must confirm to UK Biobank that the samples have been received.

C11 Publication of findings and return of results

C11.1 The applicant PI is required to use their best endeavours to publish the findings of any research deriving from the Resource in an academic journal or on an open source publication site within 6 months after the date when it was agreed that the research would be completed.

C11.2 Approval of such reports is not required from UK Biobank, but the applicant PI must provide all of them to UK Biobank at least 2 weeks before their expected date of first public presentation or publication in any format (e.g. meeting abstract, on-line report, paper journal). The applicant PI is also required to advise UK Biobank in advance if any report is reasonably likely to provoke controversy or otherwise attract significant public attention.

C11.3 All publications should include the acknowledgement “This research has been conducted using the UK Biobank Resource” which is to be linked, when possible, to reference search tools (such as Pubmed and MEDLINE).

C11.4 Within 6 months of publication or 12 months of when the research project was to be completed, the Applicant PI is required to provide the results of the research, and the raw data behind them, for inclusion in the Resource in such detail and format as UK Biobank reasonably requires.

C11.5 UK Biobank will give reasonable consideration to written requests (containing an appropriate explanation) for an extension of these time limits.

C12 Roles of parties involved in the access review

C12.1 The roles of, and interactions between, the different parties involved in the application review and oversight process are depicted in the schematic at the beginning of section C.

C12.2 The UK Biobank Board has overall responsibility for the access procedures and all access decisions. The Board includes individuals with expertise in the use of genetic-epidemiological research resources. It delegates oversight of the review process to its Access Sub-Committee.

C12.3 The Access Sub-Committee of the UK Biobank Board is responsible for making the key access decisions, notably those regarding the use of depletable samples or potentially contentious research. It is constituted as follows:

C12.3.1 it is chaired by a “non-scientist” member (with a legal and/or ethics background) of the UK Biobank Board and includes three further Board members with appropriate scientific expertise;

C12.3.2 at a minimum, it meets quarterly immediately before UK Biobank Board meetings;
C12.3.3 as appropriate, and on the advice of the UK Biobank Principal Investigator (UKBPI) and at the discretion of the Chair of the Access Sub-Committee, relevant experts can be invited to attend specific meetings of the Sub-Committee to give advice on particular applications.

C12.3.4 considers the report provided to it by the UKBPI on the status of each application (which will highlight any material issues) at its quarterly meetings;

C12.3.5 has continuous access to an overview of the review process for all applications and can review the detail of any individual application;

C12.3.6 is able to feedback comments at any time to the UKBPI about any applications that it wishes to review in more detail before any data and/or samples are released; and

C12.3.7 refers all applications on which it does not reach a unanimous decision to the UK Biobank Board, along with any others on which it requires further guidance.

C12.4 The UK Biobank Principal Investigator is responsible for providing scientific leadership to UK Biobank and ensuring that the resource is used to optimum effect by setting clear criteria and priorities for its use. The UKBPI is advised by a Steering Committee which contains individuals with appropriate scientific expertise. In particular, the UKBPI (or their designate):

C12.4.1 is responsible for developing and managing the access process, and for proposing modifications to the access process to the UK Biobank Board as experience with access to the resource increases;

C12.4.2 seeks advice on applications from the Steering Committee and, as required, from other relevant experts (including the Ethox Centre; see below);

C12.4.3 reports to the Access Sub-Committee and the Board (the UKBPI is not a member of the Access Sub-Committee or the Board) on the status of each Preliminary and Main Application, and any other issues that may arise with the access processes; and

C12.4.4 makes a recommendation on each application (subject to final review by the Access Sub-Committee) or, as required, seeks guidance from the Board, the Access Sub-Committee and/or the Ethics & Governance Council (EGC).

C12.5 The UK Biobank Co-ordinating Centre (UKBCC) undertakes the administrative work related to access applications and conducts checks against the established criteria. In particular, the UKBCC:

C12.5.1 establishes the identity of potential researchers;

C12.5.2 reviews each Preliminary Application Form against the standard checklist (Annex I);

C12.5.3 reviews each Main Application Form against the checklist; and

C12.5.4 provides a report on the status of each Preliminary and Main Application for review by the UKBPI (or their designate) with, as required, advice from the Steering Committee, the Board, the Access Sub-Committee and/or the EGC.

At any time during this review process, the UKBCC can seek:

C12.5.5 scientific advice from the UKBPI (or their designate), the Steering Committee or other experts; and

C12.5.6 ethics advice through its consultancy agreement with the Ethox Centre.

C12.6 The UK Biobank Steering Committee provides advice to the UKBPI on the development of the UK Biobank Resource. It is constituted as follows:
C12.6.1 is chaired by the UKBPI and includes about 6 members with appropriate scientific expertise that covers a wide range of health-related research and represent particular areas of ongoing development (e.g. follow-up and adjudication of health outcomes; enhancements of participant phenotyping);

C12.6.2 it typically meets quarterly and, as requested by the UKBPI, can provide advice on particular applications or on more general issues related to uses of the Resource;

C12.6.3 as appropriate, and at the discretion of the UKBPI, relevant experts can be invited to attend specific meetings of the Steering Committee to provide advice.

C12.7 The Ethox Centre (Ethox) is a multidisciplinary bioethics research centre based in the University of Oxford’s Department of Public Health. It has an arrangement with UK Biobank to provide ethics advice on request, and by regular discussion of applications under review, related to:

C12.7.1 specific issues raised by particular applications;

C12.7.2 general considerations involved in certain types of research; and

C12.7.3 more general ethics advice related to the work of UK Biobank.

C12.8 The independent Ethics & Governance Council (EGC) continues its advisory and oversight role (www.egcukbiobank.org.uk). In particular, with respect to the access process, the EGC:

C12.8.1 is not responsible for review of applications, but will monitor and report publicly on the conformity of UK Biobank with the EGF and these access procedures;

C12.8.2 will have continuous access to an overview of the review process for all applications, and can request further information about particular applications from UK Biobank (subject to the requirement that all such information will be kept confidential);

C12.8.3 will be asked by UK Biobank for advice on any applications that involve the re-contact of participants; and

C12.8.4 may provide comments at any time to the UKBPI, the Access Sub-Committee and/or the Board about the working of the access procedures or about particular applications.
Annex I: Summary Checklist for Access Application Review

Registration Form

- check identity of Applicant/Institution
- confirm application completed

Preliminary Application Form

- receipt of preliminary application fee
- assess summary description of research project (including any concerns or planned re-contact)
- check availability of requested data and/or sample access
- estimate cost for requested data and/or sample assays
- confirm application completed

Main Application Form

- check registration of applicant PI and collaborating researchers
- confirm in accordance with:
  - participant consent
  - access criteria (i.e. research is health-related and in the public interest)
- assess risk of re-identification
- check feasibility, timeframe and cost
- check adequate security protocols
- funding status (obtained or pending)
- if sample assays sought, check:
  - scientific review obtained
  - number of samples required
  - volume of samples required for assay
  - sample assays required
  - location for conduct of assays
  - overlapping studies
- if re-contact sought, check:
  - EGC advice sought
  - REC consent obtained
- confirm application completed

Review process (chiefly for Main Application)

- seek input from Ethox
- seek input from Steering Committee
- seek/consider any input from EGC
• seek/consider any input from Access Sub-Committee

Recommendation by UKBPI
• provisional acceptance
• minded to decline

Approval by Access Sub-Committee
• confirm (or not) decision of UKBPI
• if issues remain, refer to Board

Execution of approved application
• execute MTA
• receipt of funds to cover access

Release of data and/or samples (typically)
• monthly release of data
• quarterly release of sample assays
Annex II: Material Transfer Agreement for data and/or samples

Dear Sir / Madam

UK Biobank is pleased to approve your Application [reference number] to use the UK Biobank Resource. Execution of this Material Transfer Agreement (MTA) and payment of the Access Charges are the final steps before access is granted. UK Biobank’s approval of this Application is valid for 90 days, after which the Applicant Principal Investigator (PI) will need to re-apply for access. The content of UK Biobank’s standard MTA, and the conditions contained within it, are non-negotiable.

Parties

This is an agreement between UK Biobank Limited on the one hand and the Applicant Institution and the Applicant PI on the other hand. The obligations to UK Biobank from the Applicant Institution and the Applicant PI are joint and several, except for the obligation to pay the Access Charges to UK Biobank which is the sole responsibility of the Applicant Institution.

The Applicant Institution and the Applicant PI will be responsible for the conduct of any and all of the related Applicant Researchers involved in this Research Project.

Structure of agreement

The MTA will become effective on receipt by UK Biobank of both:

(i) A copy of this MTA Agreement executed by an authorised signatory of the Applicant Institution and the Applicant PI; and

(ii) Cleared funds covering the Access Charges from the Applicant Institution.

UK Biobank will then promptly send a dated confirmatory email.

Provision of samples and/or data

Annex A summarises the data and/or samples that UK Biobank will make available to the Applicant in accordance with their approved Application [reference number]. The timeframe and methodology by which the data and/or samples will be dispatched is also set out in Annex A.

Payment

The Access Charges which are payable are set out in Annex B. This also serves as an invoice on which VAT will be included (as appropriate). The derivation of these Access Charges is also set out in Annex B.

This payment should be submitted in cleared funds to [UK Biobank a/c details].

Standard terms and schedules

This Agreement incorporates the attached terms and conditions (including any documents and/or materials that are referred to in them), the Annexes and where applicable the contents of the Preliminary and Main Application Forms [reference number].

Yours faithfully

Accepted and agreed

For and on behalf of UK Biobank

For and on behalf of Applicant Institution

For and on behalf of the Applicant Principal Investigator

ACCESS_030 v1.0 November 2011
Terms and Conditions

1 Supply of Materials by UK Biobank

1.1 UK Biobank agrees to supply the Materials set out in Annex A to the Applicant, in the timeframe and manner set out in that Annex, subject to the provisions of this MTA.

1.2 UK Biobank confirms that for the purposes of this MTA:

1.2.1 It is entitled to supply the Materials to the Applicant;

1.2.2 Consent in relation to the Data Protection Act 1998 and (where applicable) the Human Tissue Act 2004 has been obtained from the relevant UK Biobank participants; and

1.2.3 Unless specified in Annex A, the use of the Materials falls within UK Biobank’s generic Research Tissue Bank (RTB) approval from the NHS North West REC.

1.3 The Applicant acknowledges that the Materials are provided on an “as is” basis without any warranty of satisfactory quality or fitness for a particular purpose or use or any other warranty, express or implied.

2 Usage of Materials by the Applicant

2.1 The Applicant agrees that the Materials may only be used for the Permitted Purpose, namely:

2.1.1 solely to conduct the Approved Research Project in the manner and timeframe set out in Annex A (namely the Permitted Purpose); and

2.1.2 solely by the Applicant PI and the related Applicant Researchers (and, in particular, are not to be shared with any other person without UK Biobank’s explicit written approval).

2.2 The Applicant will ensure that the Applicant Researchers are made aware of, and will be bound by, the terms of this MTA. Any act or omission of any Applicant Researcher will be deemed to be an act of the Applicant for which the Applicant is fully responsible.

2.3 This MTA confers on the Applicant only those rights that are expressly granted to the Applicant. For the avoidance of doubt, nothing in this MTA will prevent UK Biobank from supplying the same Materials (or other data and/or samples in the UK Biobank Resource) to another third party.

3 Grant of rights to the Applicant

Provision of samples

3.1 UK Biobank is the owner of the property in the Samples in the Resource.

3.2 UK Biobank hereby grants the Applicant a limited, revocable, worldwide, royalty-free, non-exclusive licence (but not any ownership rights) to use the Samples for the Permitted Purpose only.

Provision of data

3.3 UK Biobank is the owner of the Intellectual Property Rights in the Data currently in the Resource.

3.4 UK Biobank hereby grants the Applicant a limited, revocable, worldwide, royalty-free, non-exclusive licence (but not any ownership rights) to use the Data for the Permitted Purpose only.

Generation of data during the Approved Research Project

3.5 The following provisions shall apply:-
3.5.1 UK Biobank shall be the owner of the Intellectual Property Rights in any and all Assay Data generated during the Approved Research Project;

3.5.2 UK Biobank hereby grants the Applicant a limited, revocable, worldwide, royalty-free, non-exclusive licence (but not any ownership rights) to use the Assay Data for the Permitted Purpose only; and

3.5.3 Subject to the license-back provisions below, the Intellectual Property Rights in the Results Data deriving from use of the Resource for the Permitted Purpose will belong to the Applicant.

3.6 The Applicant hereby grants a perpetual, irrevocable, worldwide, fully paid-up, royalty-free, fully sub-licensable licence to UK Biobank to use, reproduce, distribute, publish, store and otherwise disseminate the Results Data.

Rights to inventions/developments made by the Applicant

3.7 Subject to the exception in Clause 3.8, UK Biobank confirms that it will have no rights or licence to the Intellectual Property Rights in relation to any inventions or findings developed by the Applicant as a result of using the Materials ("Applicant-Generated Inventions").

3.8 The exception would apply where Applicant-Generated Inventions are, or are in the process of being, used unreasonably to restrict health-related research and/or access to healthcare anywhere in the world ("Unreasonable Restriction"). If, at its reasonable discretion, UK Biobank considers that an Unreasonable Restriction exists or is likely to exist then it shall promptly notify the Applicant and automatically, on receipt of such notification, the Applicant shall be deemed to grant a perpetual, irrevocable, worldwide, fully paid-up, royalty-free, fully sub-licensable licence to UK Biobank to use such Applicant-Generated Invention in order to remove or mitigate the Unreasonable Restriction.

Limitation on rights granted

3.9 UK Biobank expressly excludes (directly or indirectly) (i) any right of the Applicant to sub-licence any of the rights granted to the Applicant hereunder and/or (ii) any right of the Applicant to re-publish any of the Materials except for the sole purpose of including a commensurate amount of Data in the Applicant's publication of its Results.

3.10 For the avoidance of doubt, the rights granted under this MTA are for the Permitted Purpose only and any other purposes or usages shall require the Applicant to make a further Application.

4 Confirmations from the Applicant

General

4.1 The Applicant hereby confirms to UK Biobank that all work using the Materials will be carried out in compliance with all applicable laws, regulations, guidelines and approvals, including without limitation the Human Tissue Act 2004, the Data Protection Act 1998 and any approvals required from a Research Ethics Committee (or the applicable equivalent in the jurisdiction where the Approved Research Project is to be conducted).

Security

4.2 The Applicant will retain the Materials in a secure location as regards Samples or a secure network system as regards Data at such standard as would be reasonably expected for the storage of valuable and proprietary samples and/or sensitive/confidential data.

Withdrawal

4.3 The Applicant confirms that it will deal promptly and appropriately (within the parameters set out in the withdrawal protocol [www.ukbiobank.ac.uk/principles-of-access/]) with any withdrawals by Participants which UK Biobank notify to the Applicant.
Identification of participants

4.4 The Applicant shall not attempt:

4.4.1 to identify any Participant from the Materials provided by UK Biobank; or

4.4.2 to contact any Participant, save only as may be permitted under an Approved Research Project involving re-contact by the Applicant.

4.5 In the event that an Applicant inadvertently identifies any Participant then they will notify UK Biobank immediately setting out (in reasonable detail) the circumstances by which it happened.

4.6 Other than for the purposes of clause 4.5, the Applicant will not:

4.6.1 share the identification of that Participant with any other person; or

4.6.2 attempt to contact the Participant themselves.

Provide periodic updates to UK Biobank

4.7 The Applicant will provide UK Biobank with:

4.7.1 a report on the progress of the Research Project in a form as required by UK Biobank on an annual basis (from the date on which the MTA was executed); and

4.7.2 a copy of any patents whose claims cover, or are intended to cover, an Applicant Generated Invention within two months of their publication.

5 Additional provisions for different types of Material or Research Project

Samples

5.1 The Applicant acknowledges that the Samples provided may contain viruses, latent viral genomes or other infectious agents. The Applicant undertakes to treat such Samples as if they are not free from contamination and to ensure that all Samples are handled by appropriately trained personnel under laboratory conditions that incorporate adequate biohazard containment. From the time of receipt, the Applicant is fully responsible for the safe and appropriate handling of the Samples.

5.2 The Applicant confirms that the Samples will be kept on the premises of the Applicant at the address specified in the Application and not transferred (in whole or part) to any other location without the prior written approval of UK Biobank.

5.3 The Applicant confirms that the Approved Research Project has been subject to independent scientific review by a recognised body in the manner described in the Application.

5.4 On the Completion of the Research Project, the Applicant will destroy the Samples and confirm to UK Biobank (in writing) that this has taken place.

Assays

5.5 In the event that the Applicant has requested that certain assays be conducted on selected Samples (and UK Biobank agrees to conduct such assays on behalf of the Applicant):

5.5.1 UK Biobank agrees to conduct such assays, or have them conducted by an appropriately qualified third party, with reasonable skill and care;

5.5.2 UK Biobank shall provide the Applicant with the data from the assays (“UK Biobank Assay Data”);
5.5.3 The UK Biobank Assay Data shall be treated in the same manner as other Assay Data (as set out in clauses 3.5.1 and 3.5.2) and subject to clause 5.5.4 below, the UK Biobank Assay Data will be deemed to be incorporated within the Data supplied to the Applicant and inter alia subject to the provisions of this MTA;

5.5.4 the Applicant will have a period of 3 months in which to use this Assay Data before UK Biobank makes them available to other Applicants.

6 Return and publication of Results

Publication of summary on UK Biobank’s website

6.1 After the Applicant has received the Data (including any sample assays) agreed for the Research Project, UK Biobank will be entitled to publish on its website:

6.1.1 The summary of the Research Project contained in the Application (with the exception of any material that has been agreed by the parties would be kept confidential);

6.1.2 Summary details of the Applicant (unless it has been agreed by the parties that this information would be kept confidential).

Publication of Results

6.2 The Applicant shall use its best endeavours to publish the Results within 6 months after the Completion Date for the Research Project:

6.2.1 in an academic journal; or

6.2.2 on an open source publication site.

6.3 By the earlier of 6 months after the publication of the Results, or 12 months after the Completion Date, the Applicant will provide to UK Biobank a copy of:

6.3.1 the Results themselves in such form and format as UK Biobank will reasonably require;

6.3.2 the Results Data in such form and format as UK Biobank will reasonably require.

6.4 UK Biobank will consider reasonably any written requests (containing an appropriate explanation) for an extension of the time limits set out in this clause.

Notification to UK Biobank

6.5 The Applicant is not required to obtain UK Biobank’s approval to any report of its Results.

6.6 The Applicant shall provide a copy of any report of its Results that derive from use of the Resource to UK Biobank at least 2 weeks before their expected date of first public presentation or publication in any format (e.g. paper journal, on-line report, meeting abstract).

6.7 In addition, the Applicant is required to notify UK Biobank (in writing) if any report of its Results is reasonably likely to provoke controversy or otherwise attract significant public attention. In such circumstances, UK Biobank reserves the right to make such recommendations, reservations or suggestions on the report as it sees fit (and which it may make public) for consideration by the Applicant.

Credit to UK Biobank

6.8 UK Biobank requires that any publication of Results includes the following credit:

“This research has been conducted using the UK Biobank Resource.”
6.9 This acknowledgement to UK Biobank should, when possible, be linked to reference search tools (such as Pubmed and MEDLINE).

7 Charges

7.1 The Applicant agrees to pay the Access Charges set out in the invoice (Annex B) to UK Biobank in the manner set out in that invoice. Where VAT is applicable, the Access Charges will include it.

7.2 This MTA is conditional on the Access Charges being paid and so, for the avoidance of doubt, no Materials will be provided to the Applicant until or unless the Access Charges are received in full.

8 Audit

8.1 On reasonable notice to the Applicant, and in order to confirm or investigate compliance with the provisions of this MTA, UK Biobank may itself or via appropriate third parties:

8.1.1 choose to inspect the premises and other relevant facilities of the Applicant, in order to review the security, storage or other arrangements for the Materials;

8.1.2 request such additional information about the Approved Research Project and/or its progress as UK Biobank may, from time to time, reasonably require.

8.2 UK Biobank will bear the costs of such audits unless a material default within the procedures and processes of the Applicant is discovered, in which case the Applicant will be obliged to re-imburse the reasonable costs of UK Biobank and any relevant third parties.

9 Confidentiality

9.1 Subject to the exceptions in Clause 9.2, UK Biobank will keep confidential any information disclosed to it in writing by the Applicant that is marked confidential (“Applicant’s Confidential Information”) and will not disclose such information to any person.

9.2 UK Biobank may disclose Applicant’s Confidential Information where allowed by this MTA or when:

9.2.1 it is required to be disclosed by law, by any governmental or other regulatory authority, by a court or other authority of competent jurisdiction; or

9.2.2 it can be shown by UK Biobank (to the Applicant’s reasonable satisfaction) to have been known by UK Biobank before disclosure to it by the Applicant; or

9.2.3 it was lawfully disclosed to UK Biobank by a third party who did not impose any restrictions on its disclosure;

9.2.4 the information was in (or enters into) the public domain other than by reason of a breach of this clause by UK Biobank; or

9.2.5 UK Biobank and the Applicant agree, acting reasonably, that such information is trivial or obvious, or they agree in writing that such disclosure may be permitted.

10 Indemnity

10.1 The Applicant will indemnify UK Biobank against all losses (whether direct or indirect, reasonably foreseeable or specifically contemplated by the parties), damages, costs, expenses (including but not limited to reasonable legal costs and expenses) that it incurs directly as a result of: (i) any material breach of clauses 2, 4, 5 or 6 by the Applicant; or (ii) any negligence or wilful default of the Applicant, provided that UK Biobank agrees to use its reasonable endeavours to mitigate any loss.
11 Term

11.1 The term of this MTA shall commence on the Effective Date and shall end on the later of: (i) twelve (12) months after the Completion Date; or (ii) the date on which UK Biobank receives a copy of the Results Data in accordance with the provisions of clause 6.3.

11.2 This term may be extended by UK Biobank, in its reasonable discretion, on application to UK Biobank by the Applicant setting out (in reasonable detail) the reasons for any delay or extension, (for example where the Applicant seeks to publish further or supplemental Results).

12 Termination

12.1 UK Biobank will be entitled to terminate this MTA forthwith by written notice to the Applicant if:

12.1.1 The Applicant commits any breach of a material provision of this MTA and, in the case of a breach capable of remedy, fails to remedy the same within 10 days after receipt of a written notice giving particulars of the breach and requiring it to be remedied;

12.1.2 The Applicant PI ceases to be employed (or otherwise engaged by) the Applicant Institution; or

12.1.3 The Applicant Institution ceases, is likely to cease, or threatens to cease carrying on business.

12.2 For the purposes of clause 12, a breach will be considered capable of remedy if the Applicant can comply with the provision in question in all respects other than as to the time of performance, provided that time of performance is not of the essence.

12.3 The rights to terminate this MTA given by this clause will be without prejudice to any other right or remedy of either party in respect of the breach concerned, if any, or any other breach.

13 Consequences of termination

13.1 Upon expiry of the MTA pursuant to clause 11 above or termination of this Agreement by UK Biobank pursuant to clause 12:

13.1.1 The grant of rights to the Applicant will be automatically terminated;

13.1.2 The Applicant shall destroy the Data or otherwise render it inaccessible; and

13.1.3 The Applicant shall, at the option of UK Biobank, destroy or return forthwith any unused Samples.

13.2 Without prejudice to the foregoing and to any other rights that UK Biobank may have in relation to termination as a consequence of a material breach, UK Biobank may take the following steps in respect of a breach under clause 12.1:

13.2.1 It may prohibit the Applicant PI and other researchers from the Applicant’s Institution from accessing any further materials from within the UK Biobank Resource; and/or

13.2.2 It may inform relevant personnel within the Applicant PI’s Institution, funders of the Applicant and/or governing or other relevant regulatory bodies.

13.3 Notwithstanding termination of this MTA for any reason, the provisions of clauses 1, 2, 3, 4, 5, 8, 9, 10, 12, 13, 14, 15, 17 and 18 shall continue in force in accordance with their respective terms.
14 Notices

14.1 Notices required under this MTA will be in writing and will be delivered by email to the addresses set out below or (in the event of a failure to deliver an email) by post to UK Biobank or the Applicant and will be deemed to be given, in the case of delivery by email, upon receipt at the recipient’s email server (unless an automatic response indicating an undeliverable message is received) and, in the case of delivery by post, on the date of delivery (or, if not a business day, on the first business day thereafter).

14.2 Notices to UK Biobank will be sent to the Research Access Administration Manager with a copy to access@ukbiobank.ac.uk and marked for the attention of [ ]. Notices to the Applicant will be sent to the Applicant with a copy to the Applicant Institution.

15 Assignment and sub-contracting

15.1 Neither party will be entitled to assign this MTA or any of its rights or obligations hereunder without first having received the written approval of the other party, which approval not to be unreasonably withheld or delayed.

15.2 The Applicant will not sub-contract the performance of any of its obligations under the MTA or any part thereof without having first obtained the prior written consent of UK Biobank, such consent not be unreasonably withheld.

15.3 In the event that consent is granted under clause 15.2, the Applicant shall be responsible for the acts, defaults and omissions of its sub-contractors as if they were the Applicant’s own, and any consent given will not relieve the Applicant of any of its obligations under this MTA.

16 Force majeure

16.1 If any party is prevented from, hindered or delayed in performing any of its obligations under this MTA by reason of a Force Majeure Event, such party will promptly notify the other of the date of its commencement and the effects of the Force Majeure Event on its ability to perform its obligations under this MTA. If mutually agreed by the parties, then the obligations of the party so affected will thereupon be suspended for so long as the Force Majeure Event may continue.

16.2 The party affected by a Force Majeure Event will not be liable for any failure to perform such of its obligations as are prevented by the Force Majeure Event provided that such party will use every reasonable effort to minimise the effects thereof and will resume performance as soon as possible after the removal of such Force Majeure Event. If the period of non-performance exceeds 28 days from the start of the Force Majeure Event then the non-affected party will have the option, by written notice to the other party, to terminate this MTA.

16.3 For the purpose of this clause, Force Majeure Event means any event beyond the reasonable control of a party including, without limitation, acts of God, war, terrorism, riot, civil commotion, malicious damage, compliance with any law or governmental order, rule, regulation or direction, accident, fire, flood or storm. For the avoidance of doubt, strike, industrial action, failure of technology systems, third party insolvency and failure of UK Biobank or any other third party will not be considered to be Force Majeure Events.

16.4 The provisions of this clause 16 will not affect any other right which either party may have to terminate this MTA.

17 Dispute resolution

17.1 Any party may give the other party written notice of any dispute arising out of or in connection with this MTA (“Notice of Dispute”) not resolved in the normal course of business. Within five (5) business days following delivery of such notice, a UK Biobank representative and an Applicant representative will discuss by telephone or meet at a mutually acceptable time and place, and thereafter as often as they reasonably deem necessary, to attempt to resolve such Dispute.
17.2 If any Dispute raised pursuant to clause 17.1 is not resolved by the respective representatives of the parties within ten (10) business days of the date on which delivery of the Notice of Dispute is deemed to be given then the Dispute will be referred to the UK Biobank Principal Investigator and an appropriate senior member of the Applicant Institution. These senior representatives of the parties will convene as soon as reasonably practicable (in person or by phone) after such referral to discuss the Dispute in an attempt to resolve it.

17.3 If any Dispute remains unresolved ten (10) business days following such referral, either party may initiate non-binding mediation of the Dispute to the London Court of International Arbitration ("LCIA") for mediation in accordance with the LCIA Mediation Procedure. All negotiations related to this referral shall be confidential and treated as compromise and settlement negotiations. The place of such mediation will be London and the language of the mediation shall be English.

17.4 Nothing in this clause 17 will serve to prevent either party from seeking interim relief in the High Court of England and Wales or from terminating this MTA.

18 General

18.1 This MTA governs the relationship between the parties to the exclusion of any other terms and conditions and, together with any other document referred to in this Agreement, constitutes the whole agreement between the parties in relation to the subject matter hereof.

18.2 If there is any conflict between the provisions of this MTA and any of the annexes and related documents (including, but without limitation, the provisions of the Access Procedures) then the provisions of this MTA will apply.

18.3 A waiver, delay or forbearance by either party, whether express or implied, in enforcing or exercising any of its rights or remedies hereunder will not constitute a waiver of such right or remedy.

18.4 No provision of this MTA is intended to be enforceable by any person who is not a party to this Agreement and nor are any rights granted to any third party under statute or otherwise.

18.5 Nothing in this MTA will create a partnership, joint venture or relationship of agency between the parties.

18.6 All variations to this MTA must be agreed, set out in writing and signed on behalf of the parties before they take effect.

18.7 This MTA will be governed by and construed in accordance with English law and, subject to clause 17 above, the parties irrevocably agree that the English courts will have exclusive jurisdiction over any suit, action, proceedings or dispute arising out of, or in connection with, this Agreement.
Definitions used in the Material Transfer Agreement (MTA)

Access Charges: the charges payable by the Applicant (which may include VAT) to access the Materials.

Applicant: the Applicant Institution and the Applicant Principal Investigator.

Applicant-Generated Invention: an invention developed by the Applicant as a result of carrying out the Approved Research Project.

Applicant Institution: the institution making the Application for access in respect of the Research Project and by which the Applicant PI is employed or otherwise contractually attached.

Applicant Principal Investigator (PI): the Principal Investigator of the Research Project.

Applicant Researcher: a researcher who is working with the Applicant PI on the Research Project.

Application: the application by the Applicant to UK Biobank for access to the Materials for use in relation to the Research Project.

Approved Research Project: the Research Project approved by UK Biobank (specifically including any conditions or stipulations made by UK Biobank).

Assay Data: any data generated pursuant to analyses of the Samples or other Materials (including but without limitation any data variables derived from the analysis of combination(s) of any Data or Assay Data), irrespective of whether such Assay Data is generated (a) by or on behalf of UK Biobank (in which case it is UK Biobank Assay Data) (b) by the Applicant or (c) other third party.

Completion Date: the date contained within Annex A on which the Applicant represents that the findings of the Approved Research Project will be published (or as such date may, from time to time, be altered by agreement with UK Biobank).

Consent: the consent provided by each Participant.

Data: the data being supplied to the Applicant by UK Biobank for the Approved Research Project.

Effective Date: the date on which a confirmatory email is sent by UK Biobank to the Applicant confirming receipt of a copy of this MTA executed by the parties and cleared funds covering the Access Charges.

Findings: the findings made by the Applicant pursuant to the Approved Research Project.

Intellectual Property Rights (IPRs): all present and future intellectual property rights including but not limited to patents, trade and service marks, design rights, copyright, database rights, trade secrets and know-how, in all cases whether registered or not or registerable, and including all registrations and applications for registrations of any of these and rights to apply for the same as well as any renewals, extensions, continuations, combinations or divisions thereof, and all rights and forms of protection of a similar nature or having equivalent or similar effect to any of these anywhere in the world.

Materials: the Data and/or Samples supplied by UK Biobank to the Applicant under this Agreement.

Participants: the individuals who consented to participate in UK Biobank.

Permitted Purpose: to conduct the Approved Research Project in the manner and timeframe set out in Annex A, subject to the provisions of this MTA.

Resource: the collection of Data and Samples within UK Biobank which are accessible by Applicants.

Results: the findings generated by the Applicant pursuant to the Approved Research Project.
**Results Data**: the data generated and derived by the Applicant, other than any Assay Data, which underlie the Results.

**Samples**: the samples held by UK Biobank that are being used for the Approved Research Project.

**Term**: the period starting on the Effective Date and ending at the time and on the basis set out in this Agreement and as may be extended or terminated in accordance with the terms of this Agreement.
Annex III: Conflict of Interest Policy

1 Introduction and Background

1.1 This policy aims to ensure that UK Biobank’s decision-making processes for access to the UK Biobank Resource are conducted in accordance with the highest standards of integrity. The key principle guiding access is the promotion of high quality health research for the public benefit.

2 Application of Policy

2.1 This policy applies to UK Biobank’s:

- Board of Directors, including its Access Sub-Committee;
- Principal Investigator and UK Biobank staff; and
- Any advisors involved in the access review process.

2.2 Each person covered by this policy (Individual) has an ongoing responsibility to comply with the terms of this policy. In complying with these terms, an interpretation should be taken which ensures adherence to both the spirit and the letter of this policy.

3 Guiding principles

3.1 Decisions concerning applications for access to the Resource should be guided by UK Biobank’s Ethics & Governance Framework and its Access Criteria, and made free from external influences (such as related academic interests or positions of responsibility held outside of UK Biobank).

3.2 Individuals must be alert to the risk of a conflict of interest arising, and appreciate that this is an ongoing responsibility. They must not make any academic or financial gain as a result of involvement in UK Biobank’s decision-making processes.

3.3 A conflict of interest in this context specifically includes academic, financial or other conflicts which (directly or indirectly) might interfere with, limit or compromise the ability of the Individual to review applications to use the Resource in an objective manner.

4 Managing Conflicts

4.1 If an Individual identifies an actual or potential conflict of interest with any Application under review, they should disclose the nature and extent of this conflict to UK Biobank’s Board Secretary immediately. An actual or potential conflict of interest will include any situation which could reasonably be perceived to result in such conflict.

4.2 Individuals should declare all direct and indirect academic interests relating to an Application, including (but without limitation) being involved in the preparation of the Application, being involved in a “competing” research activity, and/or being funded by the same institution as the Applicant.

4.3 If an Individual has a commercial interest in the Applicant Institution and/or funding organisation for the Applicant Institution, this should be disclosed to UK Biobank’s Board Secretary. A commercial interest is deemed to exist where that interest is deemed to be worth more than £25,000.

4.4 Disclosures of conflicts of interest may either be specific to a particular Application or may be general with respect to an Applicant Researcher, Applicant Institution and/or funding organisation. A general disclosure will exempt an Individual from making repeat disclosures in respect of future Applications involving that Individual, Institution and/or funding organisation.

4.5 Any Participant, Applicant, Researcher or other person who considers that a conflict of interest exists should disclose their concern to UK Biobank’s Board Secretary.
5 Conflict Action Points

5.1 At the beginning of each meeting of the Access Sub-Committee or the Board, the Board Secretary will request that members declare any potential conflicts of interest related to the Applications that are under consideration.

5.2 In the event that a disclosure is made, it will be for UK Biobank’s Board Secretary to determine whether it is a material conflict of interest:

5.2.1 in conjunction with the Chair of the Access Sub-Committee if the conflict relates to a member of the Access Sub-Committee or a member of UK Biobank Staff (including the UK Biobank Principal Investigator) or an advisor to UK Biobank;

5.2.2 in conjunction with the Chair of the Board of UK Biobank if the conflict relates to the Chair of the Access Sub-Committee or a member of UK Biobank’s Board; or

5.2.3 in conjunction with the Deputy Chair of the Board of UK Biobank if the conflict relates to the Chair of the Board of UK Biobank.

5.3 In the event of a material conflict of interest, the Individual must not take part in any decisions relating to that Application. In particular, the Individual must not:

5.3.1 be involved in the review of the Preliminary or Main Application, or any Reconsiderations;

5.3.2 be involved in decisions about the Preliminary or Main Application, or any Reconsiderations;

5.3.3 receive any further papers or information concerning the Application; and

5.3.4 attend those parts of any meetings in which the Application is discussed.

6 Conduct

6.1 This policy will be subject to periodic review. Individuals should be familiar with the most recent version of the policy.

6.2 If Individuals have any queries or concerns regarding the application of this policy, they should consult with UK Biobank’s Board Secretary.

6.3 Breaches of this policy will be treated seriously and disciplinary action taken in appropriate cases.
Annex IV: Data Protection Policy for the personal data of Applicants

1 Policy statement

1.1 UK Biobank is committed to the fair and lawful processing of personal data, in accordance with the Data Protection Act.

1.2 This data protection policy explains how UK Biobank uses personal information collected about Applicant Principal Investigators and Researchers (collectively Applicants) seeking access to the UK Biobank Resource.

1.3 This data protection policy has no application to the personal data of participants, which are dealt with under entirely separate criteria.

2 What information will UK Biobank collect about Applicants?

2.1 All Applicants intending to request access to data and/or samples will be required to provide their personal details before UK Biobank is able to process their Preliminary Applications.

2.2 Applicants will be required to update their personal details before UK Biobank is able to process their Main Applications.

2.3 UK Biobank will retain a record of all correspondence/contact with Applicants.

3 How will UK Biobank use information about Applicants?

3.1 During the course of UK Biobank’s activities, it will collect, store, and process personal information about Applicants. Information that the Applicants supply will be treated in accordance with the principles of the Data Protection Act.

3.2 Information collected will be used to verify the identities of individuals requesting access to the Resource, and will be retained so that UK Biobank has a record for all Applications.

3.3 In reviewing Applications, UK Biobank may need to disclose Applicants’ personal data to its Access Sub-Committee, Ethics & Governance Council, International Scientific Advisory Board and/or others (as it deems reasonably necessary).

3.4 UK Biobank seeks to keep the wider public informed of research findings deriving from access to the Resource. For this reason, unless agreed otherwise, details of approved Research Projects identifying the Principal Investigator will be made available on UK Biobank’s website. Periodic updates of research that has been conducted, and publications that derive from use of the Resource, will be linked to UK Biobank’s website.

3.5 UK Biobank may contact Registered Researchers by e-mail and/or by post, with updates on the Resource. For example, it may inform them when the resource is likely to be sufficiently mature to establish case-control collections for various conditions; when linkage to health outcomes data has been introduced; and when research yields material extra data that are added to the Resource.

3.6 From time to time, UK Biobank may seek views from Applicants concerning the access procedures that are in place. Responses to such enquiries will be voluntary and any feedback used solely for evaluation purposes.

4 Data protection principles

4.1 In processing Applicants’ personal information, UK Biobank is guided by the following principles (as contained in the UK’s 1998 Data Protection Act):

4.1.1 Information will be processed fairly and lawfully;
4.1.2 Information will be processed for the purposes outlined in this policy;

4.1.3 Information collected will be relevant and not excessive for these purposes;

4.1.4 Information stored will be kept up to date;

4.1.5 Information stored will not be kept for longer than is necessary;

4.1.6 Information will be processed in accordance with Applicants’ rights;

4.1.7 Appropriate organisational and technical measures will be in place to help ensure that information is kept secure; and

4.1.8 Information will not be transferred to people or organisations situated abroad without adequate protection.

5 Applicants’ rights

5.1 Applicants have the right to ask for a copy of information that UK Biobank holds about them and to have any inaccuracies in information about them corrected (and UK Biobank may charge a small fee). Any such requests should be made to UK Biobank in writing at: UK Biobank Coordinating Centre, 1 & 2 Spectrum Way, Adswood, Stockport, Cheshire SK3 0SA.

5.2 If Applicants have questions about their rights under the Data Protection Act, or require any further information, they should e-mail dataprotection@ukbiobank.ac.uk or write to the Data Protection Officer, UK Biobank Limited, Units 1&2 Spectrum Way, Adswood, Stockport, Cheshire SK3 0SA.