

Introduction

Over half a million people have provided information and samples as part of their participation in the medical research initiative, UK Biobank. Following a public consultation, UK Biobank has recently published a detailed governance document setting out the procedures to be followed where researchers apply to gain access to this valuable resource¹. Marking the publication of these procedures this paper aims to (1) re-state the nature of the UK Biobank Ethics and Governance Council's (EGC) monitoring and advisory role in relation to the access phase and (2) indicate the issues that the EGC regards as important to keep under review as UK Biobank gains experience of the access process in operation.

(1) The nature of the EGC's monitoring and advisory role

The EGC is an independent committee that is charged to advise on revisions to UK Biobank's Ethics and Governance Framework (EGF) and to keep under review applications for access to the resource with regards to the interests of both participants and the public. The Council exists as an extra safeguard to the trust that participants have placed in the project by providing a unique and on-going ethical and operational review of UK Biobank. The principal focus of the EGC's work over the last year has been to advise UK Biobank on the development of its access procedures.

Monitoring

The EGC is an arm's-length body which monitors the access process; however the EGC is not part of the decision-making for each individual access application

According to the newly published procedures, the EGC has an 'oversight' responsibility in relation to the access process. What does this mean? It is important to understand that this does not mean that, as a general rule, the EGC will be directly involved in reviewing applications and making the decision whether or not to grant access. Rather, the EGC's oversight role is that of an arm's-length body, overseeing the access process

as a whole. In this way, the EGC's oversight function in relation to access is in line with its general responsibility to ensure that UK Biobank always acts in a manner that is consistent with the participants' consent and the EGF. In short, while it is the responsibility of UK Biobank to handle applications with integrity, accountability and transparency, it is for the EGC (as well as UK Biobank itself) to monitor and report publicly on access governance.

It goes without saying that, if the EGC is to discharge its oversight responsibilities, it must have sufficient information about the operation of the access process. The access procedures provide for the EGC to have 'real-time' access to the lay summary (abstract) section of applications, with the possibility of requesting sight of the full application. The EGC, having discussed with UK Biobank what level of information it considers necessary, requested that it should have access to the methodology section of applications. UK Biobank now intends that application abstracts be structured in such a way as to provide sufficient information about the study (including their

¹ www.ukbiobank.ac.uk/using-the-resource

methodology) in order to facilitate their checking, review and EGC-oversight. If, once the access process starts, the EGC finds that the level of information available to it is insufficient for it to be able to fulfil its remit as set out in the EGF (for example, if experience shows that ‘on request’ access to the full applications does not suffice), then it will call for the arrangements to be reviewed.

The monitoring role might also include:

- *Monitoring the level of re-contact* and assuring itself that UK Biobank has mechanisms in place to ensure participants are not overburdened.
- *Monitoring the effectiveness and appropriateness of engagement with the public and participants concerning potential and actual uses of the resource.*
- *Monitoring how the access application review process works in practice*, e.g., balancing the needs of the research community with safeguards for participants, fairness and consistency of the decisions to release samples and data, timing of review, transparency, handling of any disputes, handling of conflicts.
- *Monitoring the outcomes of approved research* in order to evaluate whether or not there are any particular issues of public interest.
- *Monitoring the public accountability aspects of UK Biobank’s access policy*, e.g., the EGC assuring itself that research outcomes are disseminated and available to be utilised for public good and that the obligation for researchers to return results to UK Biobank is being effectively discharged.

Advising

The EGC will be both reactive and proactive when discharging its advisory role; responding to appropriate requests from UK Biobank (e.g., applications that involve re-contact with participants) or proactively advising on specific applications

Generally, the EGC is not part of the normal reviewing process for access applications, with the exception of applications that involve re-contact with participants. There is, however, provision for the EGC’s advice to be sought by UK Biobank during the ‘real-time’ application review process and the EGC itself might request further information about a particular application (e.g., if the application appears to be problematic but this cannot be ascertained fully from the lay summary). In such circumstances the EGC would request access to the full main application.

The Council expects that the majority of issues will be addressed and resolved through UK Biobank’s access review process. It is important to note that the EGC is not the ethics committee of UK Biobank, but rather is there to monitor and ensure that UK Biobank has maintained ethical safeguards and standards. As part of its monitoring and oversight role it is anticipated that novel or complex issues will be brought to the attention of the EGC for advice and consideration. The following non-exhaustive list gives an indication of the kinds of issues that might be referred to and/or proactively considered by the EGC: an application raises significant ethical issue or one which risks the reputation of UK Biobank; there is any doubt about the research being for the public benefit or whether it is ‘health-related’ and granting access to an application creates a precedent for future use.

(2) Access issues to be kept under review

The access procedures were discussed with UK Biobank over an extended period, during which time the EGC consistently argued that it was imperative that the process should command the confidence of participants and the public. The published procedures, and the accompanying report on its public consultation, represent the culmination of a great deal of work by UK Biobank but the work does not stop there. As it is impossible to foresee all eventualities, it will be important to review the procedures once UK Biobank has gained experience of the access process in operation.

The timing and nature of the review will need to take account of the fact that there will be a sequential release of data. In the immediate-term researchers will be able to apply for access to the rich collection of baseline data and samples (e.g., for use in cross-sectional studies). In time more information will become available during the long-term follow-up of participants' health through linkages to health-related records. Accordingly, the types and complexities of access applications are likely to increase over time.

There are a number of issues that the EGC has highlighted throughout the development of these procedures and which it will press to be on the agenda for such a review:

A resource for the public good

UK Biobank is founded on a model of trust and broad consent and with the primary objective to build a resource to be managed in the public interest. It is clear that there is a strong public interest in scientifically sound health-related research, but other public interests may be at stake with any given application, such as (lack of) public support for the uses to which the resource will be put or public concern about the ways in which research results are commercialised. Therefore it is crucial that UK Biobank has the mechanisms to distinguish instances when the public good is in tension with the scientific good; for while there is often overlap between these goods this is not always the case.

The review should assess whether the access mechanism is able to identify and respond appropriately to the range of public interests at stake.

Ethics review of applications

The majority of research applications will fall under UK Biobank's generic Research Tissue Bank approval and so will not need to have individual research ethics committee (REC) approval. Nonetheless, the Council is of the opinion that all applications should receive appropriate ethics scrutiny – encompassing the matters that are subject to REC approval but also taking account of UK Biobank's purpose, the interests of participants, and public good criteria. Thus UK Biobank will need to ensure that review equivalent to REC approval is completed and the additional criteria specific to UK Biobank met; some of the ethics review might be done independently (for instance by institutional committees) and some internally by UK Biobank in conjunction with the Ethox Centre².

² The Ethox Centre is a multidisciplinary bioethics research centre 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. (See Section C12.7 of the Access Procedures Version 1.0 November 2011.)

UK Biobank's mechanism of ethics review, including the process of escalation and advice from the Ethox Centre, should be addressed in the review along with how effectively the check-list of access criteria facilitates both an objective assessment of an application and the subjective prioritisation of competing applications and the needs of UK Biobank as it aims to ensure the best use of the resource for the public good.

Scientific review of applications

Throughout the development of the procedures the Council has strongly advocated for all applications to receive an appropriate level of scientific review. UK Biobank has always intended to require independent scientific review of applications involving access to depletable samples. Recently, after further discussion, it has made a provision that can require scientific review when there are concerns about the scientific value of any proposal (i.e., including data only requests).

In due course an assessment should be made to determine whether the access process has been effective in filtering out research that has insufficient scientific merit.

Applications involving re-contact with participants

Re-contact with participants must meet the highest ethics and scientific standards in order to justify any burden or potential risk to participants. The protection of privacy is central to the interests of participants which are at stake in the use of UK Biobank. The likely impact of an access request on privacy must be considered for all applications but most especially for studies where re-contact is requested.

Applications involving re-contact will require REC approval and generally independent scientific review will also be required. Advice of the EGC will be sought on every re-contact application.

While the detailed mechanism for handling re-contacts has yet to be described, the review could usefully assess the demand for and process by which such requests and re-contacts are handled.

Charging policy

One of the most-debated questions during the drafting of the access procedures has been the charging policy. The Council has advocated a two-tier variable fee structure for academic vs commercial applicants. However, UK Biobank has decided to open with a policy of charging all researchers on the same cost-recovery basis in order to encourage wide use of the resource for all types of health-related research that is in the public interest.

It has already been agreed that the opening charging policy will be reviewed to ensure that it represents an equitable, balanced and pragmatic approach, reflecting UK Biobank's status as a resource for the public good.

Respective roles and responsibilities of the parties involved

The access process draws on a number of parties to identify and address issues that might give rise to ethical or public interest concerns. The Council has consistently argued that the Access Sub-Committee (AC) should be the hub in this process.

The review could usefully assess the operation of the access process in terms of the respective roles and responsibilities of the decision-makers (e.g., the access management team, the Principal Investigator, the AC and the Board) to ensure that processes of escalation, provisional acceptance and approval are working optimally.

It is also for review whether the level and frequency of information available to the EGC is sufficient for it to fulfil its remit most effectively.