QUality in Organ Donation (QUOD)

"Success in transplantation starts in the Donor"

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Foreword by Prof. Rutger Ploeg and Dr Zeeshan Akhtar

We are pleased to introduce this access policy for samples and accompanying data from the Quality in Organ Donation (QUOD) programme, which is the result of a joint initiative between NHS Blood and Transplant and Academic Transplant Centres across the United Kingdom. To date ten founding centres have contributed to the establishment of the QUOD programme, namely Birmingham, Cambridge, Cardiff, Edinburgh, Leeds, Manchester, Newcastle, Oxford, Royal Free London and King's College London. The global objectives of this project are:

- To increase the number and quality of organs procured from DBD and DCD donors for transplantation by optimising donor management and resuscitating and preserving high-risk organs.
- To make previously unusable organs transplantable and increase the "donor pool".
- To identify pathways of injury and apply targeted interventions to repair donor organ injury.
- To translate validated experimental methods and technologies into clinical use and best practice protocols.
- To identify bio-markers and functional parameters that predict outcome following transplantation.
- To streamline collaboration and dissemination between scientific and clinical experts in academic institutions across the United Kingdom.

Greater harmonisation between academic institutions will enable the linking of resources to open up new avenues of research, and to avoid unnecessary duplication. The goal of this document is to enable the responsible sharing of data and samples for the benefit of all: patients, the public and researchers. This document provides information concerning access to the QUOD bio-bank and associated clinical data. This bio-resource has been established through collection of biological samples by QUOD centres, sponsored by NHS Blood and Transplant and is hosted by the University of Oxford.

In producing this document, we have worked closely with Dr Karen Melham (Researcher in Ethics, University of Oxford) Mrs Gemma Marsden (Oxford Radcliffe Biobank Manager), Professor Chris Watson, Ms Lorna Marson and members of the QUOD Steering Committee and National Management Team.

Professor Rutger Ploeg
QUOD Co-ordinating Principal Investigator

Dr Zeeshan Akhtar
QUOD Scientific Secretary

Introduction

1. Access Policy Background

1.1. There is growing awareness that without the sharing of data and biological samples, medical research will become increasingly wasteful of resources. Funds will be spent on unnecessary duplication of research or the collection of new data when existing data could serve the purpose just as well[1,2]. The public expects that money collected through taxes or charitable giving will be used wisely[3,4], and this has created an imperative for more effective sharing of data and samples.

1.2. At the same time it is recognised that there must be safeguards around the movement of samples and data, to protect the interests of the individual donors or data subjects. These are provided by a regulatory and ethical framework which, among other things, sets the boundaries for access. Within these boundaries it is incumbent on institutions to minimise the barriers to research that has the greater public good as its ultimate aim.

1.3. In this context, the National Cancer Research Institute (NCRI), together with onCore UK and the National Cancer Intelligence Network (NCIN), held a consultation on 'Access to Samples and Data for Cancer Research' from August to October 2008. The consultation received responses from research funders, regulatory bodies and bio-banks, as well as individual researchers, healthcare professionals and patient representatives. These responses have been summarised in a document available from the NCRI[5], and they have been used as a basis for the development of this access policy for QUOD.

2. Aim

2.1. The aim of this document is to provide an overview of the access policy for samples and data relating to the QUOD programme.

2.2. This policy aims to reflect established principles of good practice for sharing of samples and data for research.

3. Terminology

3.1. In what follows, 'Collection' denotes any dataset, including summary datasets, or set of human samples with associated data, that may be made available for researchers or investigators.

3.2. The 'Requestor' is an individual or group seeking access to data and/or samples. Once access has been granted, a requestor becomes a 'Recipient'.

3.2.1. 'Originators' i.e. the Principal Investigators who have contributed to the establishment of the QUOD initiative;

[1] OECD, Principles and Guidelines for Access to Research Data from Public Funding, 2007.
[2] National Institutes of Health, Final NIH Statement on Sharing Research Data, 2003.
[3] HM Treasury, *Managing Public Money*, 2008.
[4] The Charity Commission, Charities and Public Benefit. 2008.
[5] NCRI, Summary of responses to consultation on 'Access to Samples and Data for Cancer Research', 2009.

3.3. ‘Recipients’ are those researchers who receive material or data from the QUOD collection. Recipients include:

3.3.1. Those whose research fits with the primary objectives of QUOD;

3.3.2. Investigators with secondary research questions for which the Steering Committee (SC) agrees to provide samples and data.

3.4. The QUOD SC has formal responsibility for the collection at the time a request for access is received. This committee is accountable for maintaining the integrity and security of the collection and for providing access under the terms of this policy.
The QUOD Steering Committee comprises:

- Principal Investigators from founding QUOD centres (x 10)
- Co-ordinating Principal Investigator
- Intensivist
- NHSBT R&D representative
- NHSBT ODT representative
- Statistical support
- Lay member
- Invited expert advisors including: Laboratory, Bio-banking and Statistical experts, representation from CTAG, KAG, LAG, PAG, Ethics experts and NHSBT Designated Individual.

3.5. The National Management Team (NMT) is responsible for the day-to-day running of the bio-resource and reports to the Co-ordinating Principal Investigator. The team comprises:

- Scientific Secretary
- National Operational Co-ordinator
- National Data Manager
- Translational Research Co-ordinator
- ODT Research Manager
- Assistant Director Research and Development (when required)
- ODT National Quality Manager (when required)

3.6. There is no consistent term in use for individuals who provide samples or to whom data may apply. ‘Donor’ is frequently used in respect of samples and ‘Data subject’ in respect of data. Since in the UK the regulations and principles governing data are different from those applying to tissue samples, both of these terms are used in this document.

3.7. The term ‘Transfer’ generally refers to the transfer of personal data or samples in compliance with data protection requirements.

3.8. ‘Research Ethics Committees’ (RECs) oversee clinical research in the four countries of the UK. REC approval is a requirement for research involving NHS patients, their identifiable data or their tissues

(full details of the requirements are available from the National Research Ethics Service (NRES): www.nres.nhs.uk.)

4. Scope and Applicability

4.1. The QUOD access policy concerns data and/or samples that have already been collected and are being held in the QUOD Biobank. Samples may include tissue, blood and urine. As the project expands it is expected other samples types including bronchoalveolar lavage and bile will be available. These samples comprise 'relevant materials' under the Human Tissue Act (2004) and come within its regulatory purview.

4.2. QUOD has been established with funding awarded by NHSBT R&D and hosted by the University of Oxford.

4.3. The data or samples to be accessed may have been collected expressly for research, or may have included research as an acceptable possible use.

4.4. Samples and data may be used for clinical purposes i.e. for aiding in the patient care of a transplant recipient.

4.5. Samples and data can be used for quality assurance and auditing purposes.

5. Overview of the collection and the access process

5.1. The collection consists of biological samples including tissue, blood and urine collected from deceased donors and associated clinical data for use in research projects concerning improving the quality of organs for donation. Further information, including details of the sample availability are available from the QUOD office (contact@quod.org.uk) and is available on the QUOD website (www.quod.org).

5.2. Access to the collection involves four stages, with a two stage application process, which must be completed before samples or data are provided:

1. PART A: Determining the suitability of the collection and the eligibility of the proposed study for access. The requestor completes a preliminary application form. This is reviewed by the NMT. The SC will oversee the NMT where applications are not progressed.

2. PART B: If suitability is confirmed, a full application is invited. This is reviewed by the SC.

3. Application is considered by the SC for approval.

4. Requestor agrees to the conditions of access and/or signs the material transfer agreement (MTA).

6. Eligibility for access

Ethics approvals held by the collection

6.1. The QUOD programme holds ethical approval [REC ref: 13/NW/0017] to provide data/samples to researchers who are undertaking research in the area of improving organ quality for the purposes of transplantation. The QUOD SC has the overall responsibility for approving projects that are both

ethically and scientifically appropriate. Researchers in secondary research areas are expected to have appropriate approval from a REC prior to access being granted.

Eligibility for access to the collection

6.2. Requestors should be employees of a recognised academic institution or NHS organisation; or of a commercial research organisation with experience in research.

6.3. Researchers should be able to demonstrate, through peer-reviewed scientific publications, their ability to carry out the proposed study.

Limitations on the availability of the collection

6.4. The collection is made available as a community resource and detailed information on this is provided in the project description. Users of the collection are required to acknowledge QUOD in all publications arising from their work where relevant materials or data have been used (see 9.16 below).

Limitations on use of the collection

6.5. The terms of Research Ethics approval for QUOD make possible use of the collection's samples/data for projects concerning improving the quality of organs for the purposes of transplantation. The ethical approval does not cover secondary research. Access requests for secondary research questions are subject to review by the QUOD SC and will only be made available to projects with their own REC approval.

Prioritisation of access to the collection

6.6. Where demand for material exceeds its availability, access will be prioritised based on:

- Scientific merit (as judged by Steering Committee with possible external Scientific Expert review)
- Priority to research in connection with donor organ quality for the purposes of transplantation.

7. Application for access

Information to be supplied by requestors

7.1. Researchers who wish to access the collection should complete the form (PART A: Preliminary application for access to the QUOD Bioresource) available on the QUOD website [www.quod.org.uk] and submit this to the QUOD office (contact@quod.org.uk). Information required includes a brief outline of the study proposed, and the number and types of samples requested. The NMT will assess the suitability and respond. Following NMT assessment, a further detailed application form (PART B: Full application for access to the QUOD bioresource) will need to be completed for review by the Steering Committee.

Timing for requests for access

7.2. Applicants are asked to submit a preliminary application (PART A) outlining the aims of the study and the quantity and nature of requests from the bank. This will be reviewed to establish whether material/data would be available for the applicant. Applications considered suitable and for which QUOD has capacity will then be invited to submit a full application (PART B). Forms for applications are available on the QUOD website [www.quod.org.uk].

7.3. We aim to acknowledge all applications as soon as possible after receipt.

7.4. Applications where the project sits within the scope of the QUOD programme will be reviewed biannually (please see website for next SC review date).

7.5. Applications requesting small numbers of samples for pilot studies (<10) will be fast tracked and will be reviewed by e-mail outside of the biannual SC meetings.

Consideration of requests before funding and ethics approvals are in place

7.6. Applications to the collection can be made before funding is obtained. In these cases a letter stating the intent to grant access subject to the funding conditions being met will be issued to the requestor.

7.7. Secondary projects are required to have received REC approval prior to samples being released. However, the SC will consider applications before REC approval is obtained and a letter of intent to grant access subject to REC approval will be issued for projects awarded access to the QUOD resource.

7.8. Any letter of intent will be valid for a period of 6 months from the date issued but does not guarantee access to the particular samples. If the requested samples are not available when research ethics and funding are approved, QUOD will attempt to provide similar samples although this will not always be possible and cannot be guaranteed.

8. Processing applications

8.1. A preliminary application (PART A) form is completed to determine the suitability of the collection and eligibility of the study for access.

8.2. The process for dealing with preliminary (PART A) and full applications (PART B) is shown in Figure 1.

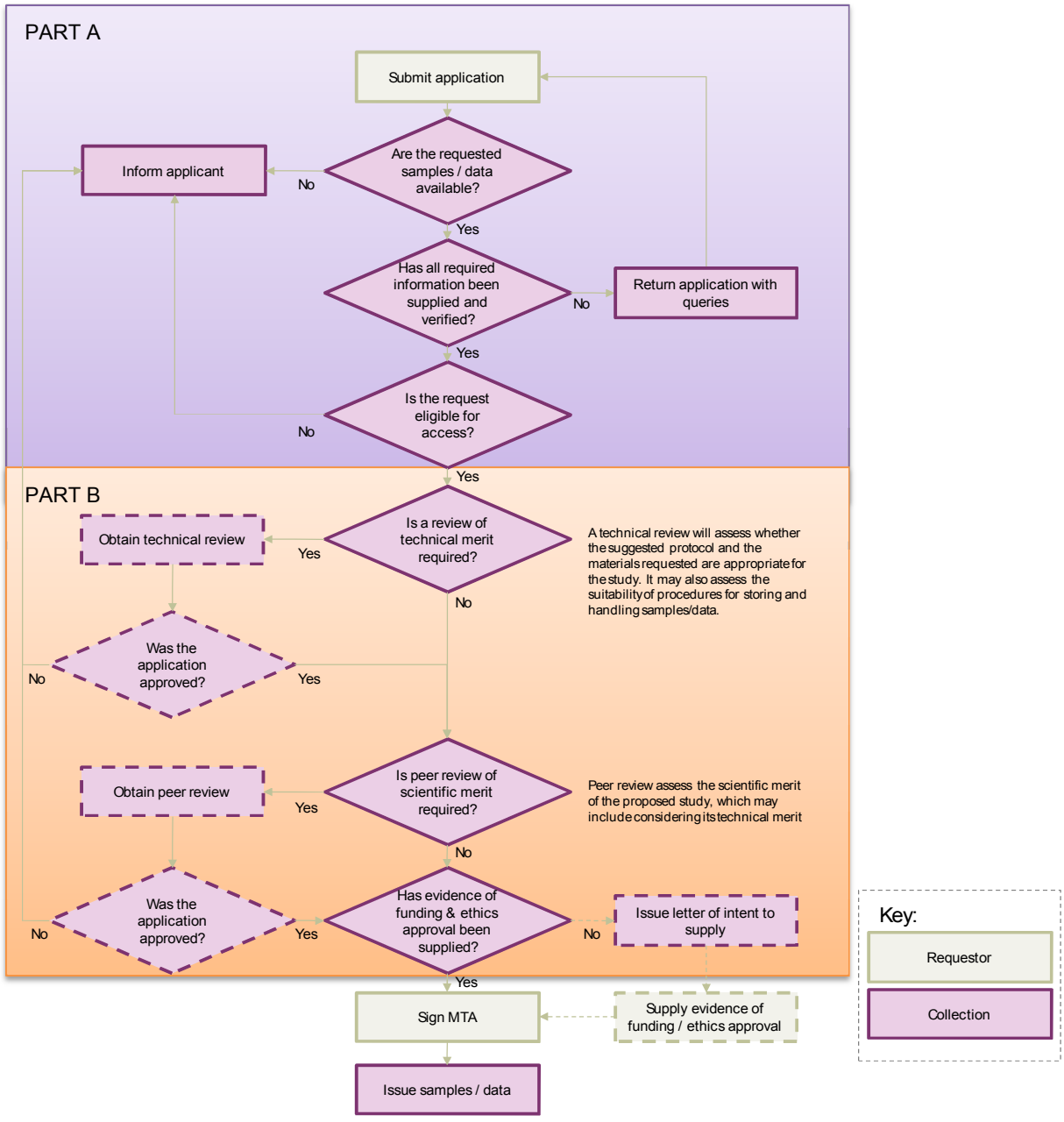

Figure 1. Depiction of full application handling including administrative aspects co-ordinated by the National Management Team (PART A) and by the Steering Committee (PART B)

Technical review

8.3. For some very limited or complex studies i.e. those involving large quantities of samples/multiple sample types, it may be appropriate for Steering Committee to arrange for the proposed study methodology to be reviewed to ensure best use of the collection. Recipients' standard operating procedures for handling and storing data or samples may also be included in such a review. A technical review will be performed by a QUOD SC member, or when required by an independent expert or a panel of experts.

8.4. If the original protocol is not considered appropriate but is of promising quality, guidance will be provided to requestors that will allow them to submit an improved protocol.

Screening for scientific merit

8.5. Due to the rare and depletable nature of the collection, all applications for the data and samples will be reviewed and prioritised on the basis of scientific and technical merit by the SC.

8.6. If requestors would like to exclude particular individuals from acting as reviewers (for example, where a conflict of interest exists) they must inform the QUOD team of this with the appropriate justification.

8.7. Requests from academic researchers and industry/commercial organisations will be subject to the same scientific review process.

8.8. The SC will obtain external peer review of proposed projects when required. Applicants will be informed of this.

8.9. The final decision for the selection of reviewers rests with the SC.

Handling of competing applications

8.10. Since material is limited, requestors who propose similar studies may be notified of this, with a suggestion that they collaborate. If the requestors are not willing to collaborate then both applications will be considered as usual. However, it is very unlikely that access to the collection will be granted for two similar studies.

Requests made without funding or ethics approvals in place

8.11. Once the conditions for access specified in any 'letter of intent' are met, evidence of this (for example from letters from funding bodies/REC) should be submitted to the National Data Manager.

8.12. If gaining funding or the required approvals will require significant changes to the study, the National Data Manager should be informed as soon as possible together with the details of the changes. Depending on the nature of these changes, the SC may decide that a new application may be required.

Appeals

8.13. If access to the collection is refused, an appeal may be made to the Coordinating Principal Investigator. This should be made in writing within 30 days of the decision and will be considered by an established independent appeal board. Any decision by the appeal board is final.

9. Conditions of access

9.1. Before access to the collection is granted, requestors must agree to the conditions of access set out in the MTA.

Fees

9.2. The recipient will be required to cover the costs of retrieving, processing and dispatching the samples and data. Details of these costs are available from the National Operational Coordinator[6].

Transparency

9.3. Study titles will be published on the collection website, together with lay summaries and the names of the institutions where the work is taking place. Contact details for the Principal Investigator of each study will be provided by the National Operational Coordinator upon request.

9.4. Requestors who do not wish details of their study to be openly available should state this in their application to the collection and give a reason.

Usage Limitation

9.5. Data or samples supplied from the collection must only be used for the purposes proposed in the requestor's application and according to terms stipulated in the data or materials transfer agreement.

Onward transfer

9.6. Data or samples supplied from the collection may only be transferred to collaborators named at the time of the original application or in subsequent applications and specified in the data or MTA or later amendments.

9.7. Applications for onward data transfer will require the agreement of the SC (application form available at www.quod.org.uk).

Data identifiability

9.8. Recipients must agree not to link the anonymised data or samples provided with any other data set.

9.9. If recipients believe that they have inadvertently identified any individual from the data or samples provided, they must inform the National Operational Coordinator and provide details of the circumstances under which this occurred.

9.10. No attempt to contact the family of donors or transplant recipients should be made by the requestor/recipient.

Publication

9.11. Recipients are expected to submit their results to a peer reviewed publication within 12 months of completing their study.

9.12. Publications should also be deposited in the UK PubMed Central database within 12 months of publication.

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[6] OECD, Principles and Guidelines for Access to Research Data from Public Funding, 2007.

9.13. Recipients should aim to publish the results of all studies, including negative results. If it is not possible to publish negative findings, the manuscript should be submitted to the National Operational Coordinator for inclusion in the collection.

9.14. Recipients should provide a copy of any publications based on data or samples from the collection to the National Operational Coordinator.

9.15. To maintain a record of publications based on the collection, the National Operational Coordinator will ask recipients to provide copies of papers upon publication.

9.16. Any publication or presentation using data or samples from the collection should include an acknowledgement using the text below:

"This research has been conducted under the remit of the UK QUOD Consortium supported by NHS Blood and Transplant"

Maintenance and enrichment of the collection

9.17. On completion of their study, recipients should provide their data or materials to the National Data Manager for possible inclusion in the collection. Data or materials should be provided within 6 months unless a delay is required to protect IP.

9.18. Submission of results to the collection does not affect the requirement for recipients to maintain their own research records.

9.19. Derived data or materials submitted to the collection may be made available to other registered users of the collection. Contributing groups will be acknowledged in this process.

Withdrawal of consent

9.20. Samples/data which have already been issued are considered "in use" and therefore the withdrawal of consent would not affect the use of these samples.

Start and end of study

9.21. The start date for the project will be the date of issue of samples.

9.22. Once the study agreed with the SC is complete, any remaining samples must be destroyed by the recipient in keeping with institutional Standard Operating Procedures and/or HTA requirements. The recipient will notify the National Operational Coordinator in writing in an end of study report submitted within 6 months of completion of the project.

9.23. Once the study agreed with the SC is complete, the recipient must ensure that any original data files submitted to the recipient are deleted. The recipient should notify the Custodian that the study is complete and that the data has been destroyed in an end of study report.

Monitoring of compliance

9.24. Recipients must complete a declaration to the SC using the form available from the collection website every year until all samples have been used or destroyed (www.quod.org.uk). This form includes a declaration that the recipient has complied with the terms of the data or materials transfer agreement.

9.25. The Custodian also reserves the right to audit the recipient's use of samples if this is considered necessary.

10. Intellectual property

10.1. QUOD seeks to encourage use of the bio-resource. To this end, the QUOD bio-resource 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.

10.2. QUOD 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 intellectual property rights (IPR) in the data in the resource (notably database rights and copyright). Researchers are granted limited licences (but not any ownership rights) to use the data and samples to conduct the approved project for a particular period of time. These rights are not assignable or transferable, and nor is there any ability to sublicense.

10.3. 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 QUOD. These datasets will, therefore, be available for use by other researchers who are granted access to use the resource. QUOD will have no claim over inventions and associated IPRs.

11. Governance processes

Steering Committee

11.1. This is the committee with overall responsibility for the collection and comprises:

- Voting members:
  - Principal Investigators from founding QUOD centres (x 10)
  - Co-ordinating Principal Investigator
  - Intensivist
  - NHSBT R&D representative
  - NHSBT ODT representative
  - Lay member

- Non-voting members:
  - Expert advisors including Laboratory, Bio-banking and Statistical experts, representation from CTAG, KAG, LAG, PAG, Ethics experts and NHSBT Designated Individual.

Scientific Reviewers

- When appropriate, the SC will ask scientific reviewers to comment and advise on proposed studies. They may be involved in reviewing and prioritising applications on the basis of scientific merit.

Technical Reviewers

- Technical reviewers will provide advice on the suitability of proposed methodologies, such as sample handling or security of a data enclave. The panel may help review applications for their technical merit.
- The technical review panel may be the same body as the scientific reviewers, a subset of this or have a separate membership.

Ethics Expert

- The ethics expert advises the SC on ethics matters including the establishment of the governance structure and the access policies. Where appropriate the ethics expert may be approached to comment on specific proposed studies by requestors.

Appendix A. Useful Resources

Human Tissue Authority

Provides information on licensing and other requirements for the use of human tissue under the Human Tissue Act 2004.

www.hta.gov.uk

Integrated Research Application System

Aims to provide a single application system for gaining permissions and approvals for health research in the UK. Includes applications to Research Ethics Committees, NHS R&D Offices and the NIGB.

www.myresearchproject.org.uk

Information Commissioner's Office

Provides information and guidance on the implementation of the Data Protection Act 1998.

www.ico.gov.uk

MRC Data and Tissues Toolkit

Legislative and good practice requirements relating to the use of personal information and human tissue samples in healthcare research in the UK. Focuses on the planning and approvals stage of setting up a research project.

www.dt-toolkit.ac.uk

National Research Ethics Service

Information on applying to RECs for ethical review of research.

www.nres.nhs.uk

National Information Governance Board for Health and Social Care

Information on the NIGB and on the Ethics and Confidentiality Committee that reviews applications under Section 251 of the NHS Act 2006.

www.nigb.nhs.uk

Wellcome Trust

Information on the Wellcome Trust, including reports on biomedical ethics.

www.wellcome.ac.uk

Appendix B. Glossary and Abbreviations

Collection	Any dataset, including summary datasets, or set of human samples with associated data
Data Subject	An individual who is the subject of personal data that forms part of a collection
Donor	An individual who provides samples that form part of a collection
GMC	General Medical Council
HTA	Human Tissue Authority
IP	Intellectual Property
IRAS	Integrated Research Application System
MRC	Medical Research Council
MTA	Data and Material Transfer Agreement
NRES	National Research Ethics Service
Originator	Person or leader of the team who collected the data and/or samples comprising a collection
REC	Research Ethics Committee (encompasses such committees operating in respect of clinical research conducted in the four countries of the UK)
Recipient	An individual in receipt of data and/or samples from a collection
Requestor	An individual seeking access to data and/or samples from a collection

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