THE USE OF HUMAN TISSUE SAMPLES: WHEN AND WHERE TO APPLY FOR ETHICS REVIEW

Staff and students of the University of Oxford regularly undertake work that requires the use of tissue samples from healthy human volunteers.

Collection of human tissue samples (including, but not restricted to, blood, urine, saliva and faeces) presents potential risks to the health and safety of both the donor and the person taking or using the sample, and to regulatory requirements. The risks are the same, regardless of whether samples are collected from patients or healthy volunteers. The same risk assessment and safety procedures should, therefore, be followed, and consideration must be given to the health and safety of all involved, and to important ethical issues and regulatory requirements that may arise.

When planning work with tissue samples from human volunteers, it is important to consider both of the following:

- the requirement for ethics review/approval to collect, use and/or store human material
- the need to meet Human Tissue Authority (HTA) regulations for the storage of human material

Is ethics review required?

Ethics review and approval should be obtained for the taking and/or use of human tissue samples, except in the following cases:

- where, as part of their training or employment, students/staff are being taught how to take blood (phlebotomy training), and the blood will not subsequently be stored or used for another purpose;
- where samples will be used for evaluation or assessment of established diagnostic devices or in-vitro diagnostic kits then destroyed (performance assessment);
- where material is used in a programme for systematic monitoring/evaluation of a project, service or facility to ensure that standards of quality are being met (Quality assurance);
- where the tissue sample is being used in research laboratories as a reagent – e.g. as a source of feeder cells for maintenance of cell lines or clones, or substrate for growth of virus stocks (i.e. no knowledge is being derived from the tissue itself);
- where blood is to be taken as part of a practical class and will not subsequently be stored or used for another purpose;
- where the tissue is an established in-house or commercially available cell line

In such cases, consent should still be obtained from the donor, but if the sample is being taken for any of the above purposes, this use will not require formal review and approval by either a University or NHS Research Ethics Committee (REC).

In some cases, tissue is taken from colleagues. If such tissue is taken for any of the above non-research purposes, staff and students should follow the guidance provided on the University Occupational Health website.

For research involving the taking of urine, saliva, stool and/or venous blood samples from healthy adult volunteers, University researchers should adhere to CUREC Approved Procedure 24 (AP24) when seeking ethics review/approval and conducting the research.

Human Tissue Authority Guidelines on 'Relevant Material'

The HTA requires 'relevant material' for research to be held under the governance of either NHS ethics approval or an HTA licence.

It is therefore important to first establish whether the human tissue samples would be considered 'relevant material' under the Human Tissue Act 2004. The Human Tissue Act 2004 is an act of the UK Parliament applying to England, Northern Ireland and Wales, which consolidated previous legislation and created the Human Tissue Authority to "regulate the removal, storage, use and disposal of human bodies, organs and tissue."

The definition of relevant material in the Act is:
Section 53: Relevant material:

1. *In this Act, "relevant material" means material, other than gametes, which consists of or includes human cells.*
2. *In this Act, references to relevant material from a human body do not include embryos outside the human body, or hair and nail from the body of a living person.*

Please contact the University's Human Tissue Governance group for advice regarding the use and storage of human tissue samples for research: hta_help@admin.ox.ac.uk

Examples of relevant material (taken from the HTA website)

The fundamental concept of relevant material is that if a sample is known to contain even a single cell that has come from a human body, then the sample should be classified as relevant material.

1. Specifically identified relevant material
This includes material such as bodies, organs and tissues, consisting largely or entirely of cells, and clearly identifiable.

2. Processed material
Where a processed material is generally agreed – as a result of the process – to leave it always either cellular or acellular, then the presumption should be that all examples should be regarded as such. The HTA would rely on an assurance that the process in question had been carried out. Under this category, plasma or serum, for example, will not be regarded as relevant material provided the process is demonstrated to render them acellular. Note that if the process used to separate plasma is intended to generate platelet-poor or platelet-rich plasma (as opposed to platelet-free), then there may still be cells within the plasma, making it relevant material.

3.

Bodily waste products (including excretions and secretions)
The HTA considers bodily waste should normally be regarded as relevant material. The Act's wording is clear and reflects the possibility that even a single cell can be subject to an activity such as research. There will be cases where a person believes that material, intended for a scheduled purpose, is actually acellular. In such cases, the HTA can be approached for advice.

4. Cell deposits and tissue sections on microscope slides
In general, cell deposits or tissue sections on microscope slides are considered to constitute relevant material. This is because such deposits or sections are likely to contain whole cells, or are intended to be representative of whole cells.

For more detail on whether specific materials fall within the definition of 'relevant material' under the Human Tissue Act, please refer to the Human Tissue Authority website.

Where to apply for ethics review

Which committee must review research proposed depends on a combination of whether the tissue samples are considered 'relevant material', and the subsequent processing/storage of the samples. The chart below provides a guide.

Where NHS Research Ethics Committee review is required, documents first must be submitted to the Sponsorship group of the Research Governance, Ethics and Assurance (RGEA) team, who will confirm whether the University can act as Sponsor of the research.

There are some types of study that can be reviewed by the MS IDREC or the Oxford Tropical REC (OxTREC). Importantly, ethics review/approval from one of these Committees is essential for the use of tissue samples in research where they are not categorised as 'relevant material'.

Applications should be made on the CUREC form for research using only previously collected biological samples.

The following information, coupled with the flow chart on the next page, should help you decide which review route to follow. However, as this is not always a clear-cut decision, please contact either the MS IDREC or OxTREC Secretariat or RGEA for advice as necessary.

Title: The use of human tissue samples: When and where to apply for ethics review

Sample type	Example	Ethics Review Process stages	Storage of HTA relevant material
Any samples from patients (where research is conducted in the UK)	Biopsy from someone with cancer	Departmental Review (if required) University as Sponsor (via RGEA) NHS Research Ethics Committee (REC - via IRAS)	Provided research has NHS REC approval, samples can be stored for the duration of the study. Note that samples need to be destroyed at end of study unless the consent stated that samples can be used for future research, in which case samples need to be either: - registered into a new NHS REC approved project; or - adopted under an HTA licence for storage then, when the samples are to be used in new research, apply for CUREC ethics approval
Any samples from patients (where research is conducted in the UK or the EU with Local Ethics Approval)		Will depend on the circumstances under which the tissue is being used. Contact RGEA for advice.	Storage under HTA licence, for storage in the UK if brought here. Samples must be registered on one of the University's HTA licences before shipping to the UK.
Any samples from patients (where research is conducted outside the UK and the EU)	Faeces from someone infected with typhoid	OxTREC ethics review Local Ethics Committee in Country where research is being conducted	Storage under HTA licence, for storage in the UK if brought here. Samples must be registered on one of the University's HTA licences before shipping to the UK.
Cellular samples from healthy volunteers used in research and destroyed on day taken (i.e. not stored at all)	Blood taken to conduct a whole blood count for research data purposes	Department Review (if required) MS IDREC or OxTREC (refer to flow chart below)	No – samples are not stored in this case.

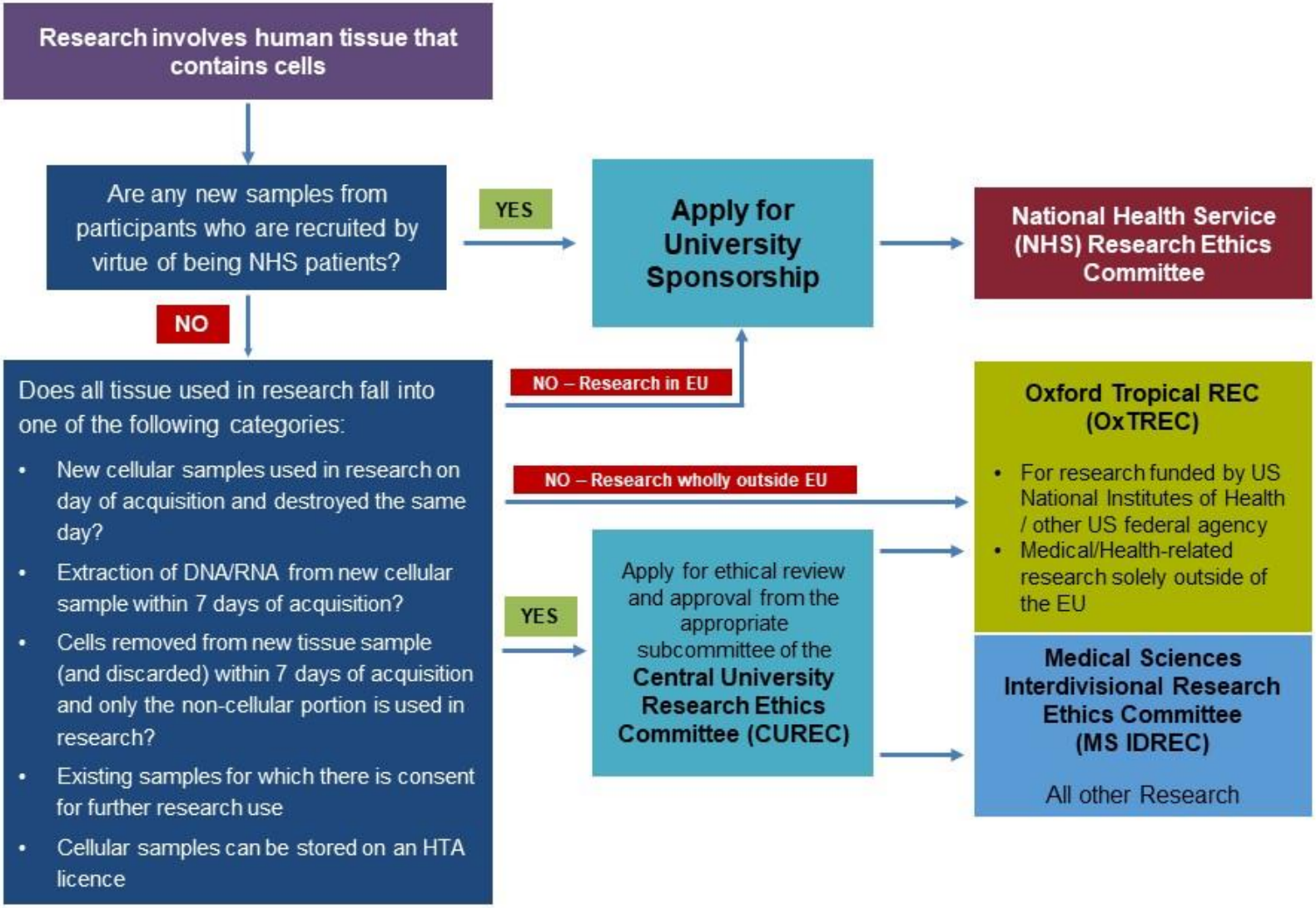
Sample type	Example	Ethics Review Process stages	Storage of HTA relevant material
Cellular samples from healthy volunteers taken and DNA/RNA extracted as soon as possible (within a maximum of 7 days) to render acellular. Only DNA/RNA used/stored for research.	Blood drawn into Tempus tubes for RNA extraction	Department Review (if required) MS IDREC or OxTREC (refer to flow chart below)	No – Samples are processed to be HTA non-relevant material within 7 days, therefore storage under an HTA licence is not necessary.
Cellular samples from healthy volunteers taken and rendered acellular as soon as possible (within a maximum of 7 days) with only acellular material being used/stored for research.	Blood collected and processed to obtain acellular plasma	Department Review (if required) MS IDREC or OxTREC (refer to flow chart below)	No – Samples are processed to be HTA non-relevant material within 7 days, therefore storage under an HTA licence is not necessary.
Cellular samples from healthy volunteers taken and/or being stored in order to perform research on the cells, where the site does not have access to an HTA licence (storage for longer than 24 hours)	Cells viably cryopreserved from fresh blood samples, Buffy coats, or leucocyte cones	Department Review (if required) University as Sponsor (via RGEA) NHS REC (via IRAS)	Samples cannot be stored without an HTA licence; hence NHS REC approval is required to allow storage in this case.

Sample type	Example	Ethics Review Process stages	Storage of HTA relevant material
Cellular samples from healthy volunteers being stored in order to perform research on the cells, where the samples are registered on an HTA licence (storage for longer than 24 hours)	Cells viably cryopreserved from fresh blood samples, Buffy coats, or leucocyte cones	Department Review (if required) MS IDREC	Yes – samples must be stored on HTA-licensed premises and be registered on one of the University HTA licences before they are acquired.
Previously collected cellular samples (excluding cell lines) purchased from a commercial company or NHS Blood & Transplant (NHSBT)	Buffy Coats or leucocyte cones	Department Review (if required) MS IDREC (if samples can be registered on an HTA licence) NHS REC (via IRAS) where HTA licencing is not possible	Yes – samples must be stored on HTA-licensed premises and be registered on one of the University HTA licences before they are received by the researcher. If licencing is not possible, then NHS REC approval required instead.
Samples obtained under the ethics approval of a research tissue bank (RTB).	Colorectal tumours fresh frozen are sought from a tissue bank for a specific project	Relevant tissue bank will comment on feasibility of project (whether they have suitable samples) RTB Access Committee procedure As long as the research tissue bank has approval to release samples under the generic ethics approval of the biobank, there is no need for the researcher to apply for additional REC review or hold the samples on HTA licenced premises	Official Research Tissue Banks have RTB NHS REC approval. This usually allows them to extend their RTB REC approval to projects making use of the samples from the RTB. Provided the samples are obtained under the ethics approval of the research tissue bank (check your project approval letter from the supplying RTB), there is no need for separate HTA licensing.

Sample type	**Example**	**Ethics Review Process stages**	**Storage of HTA relevant material**
Existing tissue samples collected under ethics approval in a foreign country, imported to Oxford and stored on an HTA licence	Samples collected under foreign ethics approval (a study that has completed), and samples to be sent to Oxford for use in a new study	Department Review (if required) OxTREC if the foreign ethics approval covering tissue collection was received from a country outside of the UK/EU, or if the study is funded by a USA federal funding agency (e.g. NIH) MS IDREC – all other studies	Yes – samples must be stored on HTA-licensed premises and be registered on one of the University HTA licences before they are exported to the researcher in the UK.
Existing tissue samples collected under ethics approval in a foreign country, imported to Oxford for analysis and stored on an HTA licence	Sample collection has foreign ethics approval (for an ongoing study), where a member of the University is acting as a formal collaborator on the study, but will not have any contact with participants (e.g. sample analysis only)	Foreign ethics approval is sufficient	Yes – samples must be stored on HTA-licensed premises and be registered on one of the University HTA licences before they are exported to the researcher in the UK.

Sample type	**Example**	**Ethics Review Process stages**	**Storage of HTA relevant material**
Tissue samples collected under ethics approval in a foreign country, with Oxford collaborators. Samples imported to Oxford and stored on an HTA licence	Sample collection has foreign ethics approval (for an ongoing study), where a member of the University will have contact with human participants and work on the samples	Ethics approval in the country/countries where samples are collected Department Review (if required) OxTREC if the foreign ethics approval covering tissue collection was received from a country outside of the UK/EU, or if the study is funded by a USA federal funding agency (e.g. NIH) MS IDREC – all other studies	Yes – samples must be stored on HTA-licensed premises and be registered on one of the University HTA licences before they are exported to the researcher.

Where to apply for ethics review



Further Information

Medical Research Council (MRC) ethics series - Human Tissue and Biological Samples for Use in Research: Operational and Ethical Guidelines

CUREC Approved Procedure 24 for studies taking urine, saliva, stool and/or venous blood samples from adult participants

University Occupational Health website

University of Oxford Human Tissue Governance website

Human Tissue Authority Code of Practice for Research

Governance Arrangements for (NHS) Research Ethics Committees