NHSBT ODT Research Process Handbook

Contents

Purpose of Document

The purpose of this document is to outline the procedure for setting up research studies and implementing novel therapies/technologies that involve NHSBT's organ donation, retrieval and/or transplantation processes. It is provided to guide prospective applicants wishing to:

- Obtain access to organ donors and/or organs, tissues and cells from donors for research purposes
- Set up qualitative studies with members of the wider Organ and Tissue Donation and Transplantation (OTDT) team such as Specialist Nurses or National Organ Retrieval Service (NORS) team members
- Set up service evaluations appraising the OTDT process
- Test and/or implement novel therapies/technologies (such as novel transplants)

This document contains details of the various approvals, documents, and stakeholder engagement required to gain approval from NHSBT, via the Research, Innovation and Novel Technologies Advisory Group (RINTAG), and where appropriate the OTDT Senior Management Team (SMT).

The term **"relevant material"** is used throughout this document to refer to organs, tissues and cells. Please refer to the Human Tissue Authority (HTA) website for more information about what is and isn't "relevant material".

The ODT Research Approval process has been established to provide assurance to NHSBT that donated "relevant material" is only supplied to research studies that have gained all the appropriate approvals, and that NHSBT's operational considerations are met. It aims to facilitate and implement research projects without adversely impacting upon organ donation, retrieval and transplantation.

Executive Summary

This document outlines the NHSBT approval process for research studies involving organ donation, retrieval and/or transplantation. In summary:

- Researchers are encouraged to engage early with the Research Team, by emailing ODTResearch@nhsbt.nhs.uk
- The Research Team will provide advice on governance and the operational considerations of a study.
- The Research Project Manager facilitates applications to the Research, Innovation and Novel Technologies Advisory Group (RINTAG), for their review.
- RINTAG will score and rank studies requiring access to organs via the National Allocation Scheme, according to a prioritisation matrix.
- The approval timeframe varies between study categories. We are committed to keeping timescales to a minimum. In some cases, final approval will be required from the OTDT Senior Management Team (SMT).
- Before a study can commence, the study's Chief Investigator and Sponsor will be required to sign an agreement with NHSBT, which outlines their responsibilities.
- Researchers with active studies are expected to complete progress reports. These are used for improvement and monitoring purposes, and to re-rank studies that receive organs through the National Allocation Scheme.
- If a research study's circumstances change (e.g. the number of organs/tissues required, planned duration or intended use), the researcher should complete a resubmission form which will be submitted to RINTAG for their approval.

The Research Team

The Research Team is made up of a Research Project Manager (RPM) and a Specialist Nurse for Research (SNR), both managed by the Innovation and Research Lead Specialist. The team is also supported by the Head of Transplant Development.

The RPM's responsibilities are to guide researchers through the RINTAG approval process, advise on external approvals and monitor studies once live.

The SNR's responsibilities are to advise on the operational aspects of making a study work, including training Specialist Nurses, writing Standard Operating Procedures (SOPs) and gaining operational approval for studies.

The Innovation and Research Lead focuses on the strategic delivery and promotion of all organ donation and transplantation research activity.

Together the team works with colleagues in NHSBT's Quality Assurance, R&D, Hub Operations and Information Services departments to set up studies, making sure they are operationally feasible and abide by regulations.

Navigating research approvals can be daunting, but the Team will do their best to guide researchers through them.

The term 'research' is used extensively throughout this document, but the Team support any study that is covered under 'scheduled' or 'other' purposes[1], as well as service evaluations.

Categorisation

Most of the studies that the Research Team are approached about fall into one of the following categories:

Category No.	Category Title	Description
1	**Data Study**	Studies with a pure statistical focus, not requiring access to "relevant material"[2] e.g. undertaking analysis of existing data on transplantation. RINTAG application form not required. **Please apply to Statistics & Clinical Studies directly. You can find more information here.**
2	**Qualitative Study**	Studies with a descriptive or behavioural focus, not requiring access to "relevant material" e.g. examining attitudes to organ donation.

[1] Purposes requiring consent/authorisation, as outlined in the Human Tissue Act 2004 and Human Tissue (Scotland) Act 2006.
[2] As defined by the Human Tissue Authority (HTA).

3	**Biological Sample Study**	Studies looking to access blood, urine, bronchioalveolar lavage (BAL) and small tissue samples from deceased organ donors. Facilitated via the Quality in Organ Donation (QUOD) biobank. Samples are collected at four different time points covering the donor management period, all the way through to the point of organ retrieval. RINTAG application form not required. **Please apply to QUOD directly. You can find more information about QUOD here.**
4	**Study Accessing "Relevant Material" Through Generic Consent / Authorisation**	Studies requesting access to "relevant material" (e.g. hearts, lungs, pancreases, kidneys and livers) by generic research consent/authorisation[3]. These organs are offered by Hub Operations to approved studies through the National Allocation Scheme. RINTAG prioritises and ranks approved research studies. There are specific circumstances by which this "relevant material" becomes available. Please see the Section on Category 4 studies for more information.
5	**Study Accessing "Relevant Material" Through Study-Specific Consent / Authorisation**	These are usually studies proposing to remove "relevant material" that is not routinely transplanted (e.g. nerves, bladders), purely for research purposes. This removal requires study-specific consent/authorisation from donor families. This "relevant material" is *not* offered through the National Allocation Scheme. Studies in England, Wales and NI require HTA licences to remove this material, in accordance with the Human Tissue Act 2004. Licenses are not required in Scotland. Research applications wishing to access "relevant material" via the specific consent/authorisation route will only be considered if material cannot be accessed through the National Allocation Scheme.
6	**Donor Intervention Study**	Studies looking to undertake interventions in DCD donors prior to death, and/or interventions in DBD donors e.g. drug administration to facilitate organ preservation.
7	**Other Studies**	Studies which *may* require access to "relevant material" and/or donors and are expected to have an impact on the donation, retrieval, and/or transplantation processes. This includes novel therapies and technologies such as novel transplants and service evaluations.

On occasion, studies may fall into more than one category (particularly category 4, 5 and 7). In these circumstances, parallel approvals will be sought. The applicant is expected to work with the Research Team to categorise their study accordingly.

[3] Due to differing legislation, families **consent** for organ donation in England, Northern Ireland and Wales but they **authorise** it in Scotland.

For researchers looking to access donated tissues, where the proposal is not reliant upon viable cells within 48 hours, the request may be considered by NHSBT's Tissue and Eye Services (TES).

Research undertaken in transplanting units that does not impact upon ODT services (e.g. studies on recipients) generally falls outside the remit of NHSBT ODT and RINTAG. Please discuss these studies with the Research Team to confirm whether any approvals are required. Local approvals are however likely to apply. Prospective researchers are advised to contact their local R&D Office for further guidance.

Early Engagement

Researchers should contact the NHSBT Research Team to discuss their proposal as early as possible. Usual practice is to hold a teleconference with the researcher and the Research Team. The purpose of this first telecon is to discuss and categorise the proposal and advise on approvals and operational considerations. Agreed actions, next steps and categorisation will be sent by email to the researcher shortly after the telecon.

If the proposal stays within the Research Team's remit, researchers are then required to submit a completed application form (available from the ODT Clinical Website) and a study protocol.

Writing a protocol

Applicants are advised to follow study protocol guidelines provided by their institution. However, the following details are required for the purpose of NHSBT assessment (where applicable):

- Specific inclusion and exclusion criteria
- Standard Operating Procedure (SOP) describing the surgical procedure involved in removing "relevant material", if this is not covered by existing SOPs
- Confirmation of compliance with all appropriate legislative and regulatory frameworks within the UK, such as HTA licences (including agreement from Designated Individuals)
- Process for appropriate storage and disposal of human "relevant material"
- Details of the transport arrangements including mode of transport and the transport company
- Proposed plans for training of Specialist Nurse teams to take consent/authorisation for research
- Media management section describing an agreed communications strategy with NHSBT

Should your institution not provide any templates or protocol guidelines, the Health Research Authority (HRA) website provides basic recommendations here.

Immortalised Cell Lines

The subject of creation of immortalised cell lines from deceased organ donors' tissue was discussed at several RINTAG and Clinical Audit, Risk and Effectiveness (CARE) meetings.

In May 2019, RINTAG agreed that due to:

- the risk of the donor family not fully understanding what an immortalised cell line is, and the implications of it, on the night of donation (when they are in an acute stage of grief)

vs.

- the small number of studies wishing to create them
- the possibility of those studies accessing immortalised cell lines commercially or from living donors

immortalised cell line creation would not be supported by ODT.

Any study wishing to create immortalised cell lines from the tissue they receive from ODT will be advised that they must not.

Approval Routes and Documentation

External Approvals

Most of the projects that the Research Team work with require ethical approval from a Research Ethics Committee (REC) and further approval from a national research approval body.

The approval body depends on which devolved nation the study is being led from:

Nation	Research Authority
England	Health Research Authority (HRA)
Scotland	NHS Research Scotland (NRS)
Wales	Health and Care Research Wales (HCRW)
Northern Ireland	Health and Social Care Northern Ireland (HSCNI)

The Integrated Research Application Service (IRAS) is an online portal which is used to apply for research approvals such as REC and HRA. The Research Team must also see a copy of the IRAS form before it's submitted, alongside the NHSBT application form and study's protocol.

Additional approvals may be needed depending on what the project proposes to do. For example, studies involving radioactive substances must get approval from the Administration of Radioactive Substances Advisory Committee (ARSAC). These additional approvals are flagged in IRAS if they are necessary.

Letters of Support

If a project is aligned to NHSBT's strategies, the Research Team may provide letters of support for funding applications. This will be discussed on a case-by-case basis, so please contact the team for more information. Proposals may be circulated to RINTAG before a letter of support is issued, so please contact the team in plenty of time.

Clinical Trial Management

Clinical Trials Units (CTUs) can help researchers to set up clinical trials and navigate research approvals. More information about NHSBT's CTU can be found here.

Please note that working with a CTU does not negate the need for RINTAG approval.

NHSBT Approvals

The Research, Innovation and Novel Technologies Advisory Group (RINTAG) grants approval to research studies, novel therapies, service evaluations, qualitative studies and research tissue banks involving organ donation, retrieval and/or transplantation. More information about RINTAG can be found on this page.

In some cases, RINTAG will refer a project to the OTDT Senior Management Team (SMT) for final approval.

Depending on the complexity of a study, approvals from other ODT Advisory Groups may be sought. Each routinely-transplanted solid organ has its own advisory group and there are also advisory groups representing donation (the National Organ Donation Committee [NODC]) and retrieval (the Retrieval Advisory Group [RAG] – formerly known as NRG).

Studies involving the transfer of data may require a full Data Protection Impact Assessment and sign off from NHSBT's Information Governance team.

The Research Team will advise if any additional NHSBT approvals are necessary.
Ideally, researchers apply to REC, their nation's approval body and RINTAG in parallel. However, if RINTAG have comments or requirements about a study's proposed process, this may result in

needing to make changes to the study's documentation. It is much easier to make those changes before IRAS submission.

Operational Considerations

Category 2:

Qualitative studies in ODT are assessed by RINTAG so that requests for interviews and surveys can be directed to the most appropriate group. If the request involves NHSBT employees (such as Specialist Nurses) this ensures that any one regional team is not overloaded.

Depending on the group of participants, and whether their care is being changed or not, qualitative studies may also need ethical and national research authority approval. The HRA has helpful tools on its website to determine whether these projects are classed as research and whether ethical approval is required.

Category 4:

The organs that Category 4 studies gain access to become available under specific circumstances:

The organ is retrieved from the donor with the intention to transplant it. However, upon assessment by the surgeon on the 'back bench' or at the recipient centre, the organ is found to be unsuitable for transplantation.

If the donor's family have given appropriate consent/authorisation, the organ can be offered to RINTAG-approved studies instead of being disposed of or returned to the donor's body.

Purpose of removal: transplantation
Offer time: after removal

At the time of discussing scheduled/other purposes with the family, the Specialist Nurse does not know which study the donor's organs will be placed into. Category 4 studies are also known as 'generic studies' because the family has given their generic consent/authorisation to research without knowing exactly which study the donor's organs will go into.

The National Research Organ Allocation Scheme

Hub Operations (formerly known as the Duty Office) operates a 24-hours-a-day, 365-days-a-year service, and among its many roles, carries out research organ offering.

Organs that have become available for research are simultaneously offered to all appropriate research studies using an offer message.

The offer message can be sent by text or email to researchers and includes the following information:

- Organ Type
- ODT Number *(6-digit number used to identify a deceased organ donor)*
- Donor Hospital
- Donor Age
- Donor Blood Group
- Organ's Current Location *(as this may be different to the donor hospital)*
- Perfusion Time
- Primary Reason Declined for Transplant
- Restrictions on consent or authorisation *(e.g. animal, genetic, commercial, research, audit, education – **see section below**)*
- Offer Expiry Time *(45 minutes after the message has been sent)*

Hub Operations can relay information about a research kidney's anatomy over the phone as they do this for transplant centres. Further information about a research organ can be found out by logging in to NHSBT's Electronic Offering System (EOS Mobile).

The highest-ranked study that responds within the 45-minute deadline will receive the organ. Should the highest-ranked study not respond within this timeframe, the organ will be offered to the next highest-ranked respondent.

If no ranked studies respond and the organ has already been removed, Hub Operations offer it to research tissue/biobanks.

Studies are given a provisional rank when they are assessed by RINTAG, and the rank is confirmed when they go live. All studies receiving organs in this way are re-ranked following return of progress reports.

Research organs allocated through this scheme are perfused and packed as they would be for transplantation, meaning that they are also packed with samples to support transplantation, such as blood and spleen samples. These samples (as well as any other 'surplus tissue') must not be used for research, as they would never be transplanted into a recipient, and the generic consent does not cover their use in research.

Approximately 75% of the research offers made are made outside of core hours. RINTAG expects researchers to be available to receive research organ offers 24/7. This maximises research organ utilisation rates and fulfils donor family wishes.

Anonymity

As research organs offered through the National Scheme are packed and perfused as they are for transplantation, and some research organs are transplanted by researchers, there is a need for traceability and identification of organs throughout the organ donation process.

As standard, a blood group print-out (NB. the format and associated PID will vary among hospitals) and the HTA A form (completed by the retrieving surgeon) accompany the organ in transit. In the case of an organ being allocated to a research study, these forms will arrive with the organ, and therefore the researcher will see any donor data on them. It is the researcher's responsibility to shred any paperwork and anonymise the tissue appropriately, keeping only the 6-digit ODT number for traceability. Researchers should check their Sponsor's requirements for this.

Similarly, if researchers use EOS Mobile to determine suitability of an offered organ for their research, personal data about the donor is viewable there.

It is therefore important to note when completing an IRAS form that the organs received for research through the National Allocation Scheme are not anonymised.

Consent/Authorisation Restrictions

The HTA Code of Practice on Research recommends that if studies are known, or likely to involve:

- the commercial sector/cost recovery (tissue banks)
- genetic testing
- the use of human tissue in animals

then references to this should be provided in the information used to support the consent/authorisation process.

Donor families are given a research information leaflet by their Specialist Nurse which explains what animal research, genetic (including DNA and RNA) testing and research involving the commercial sector are.

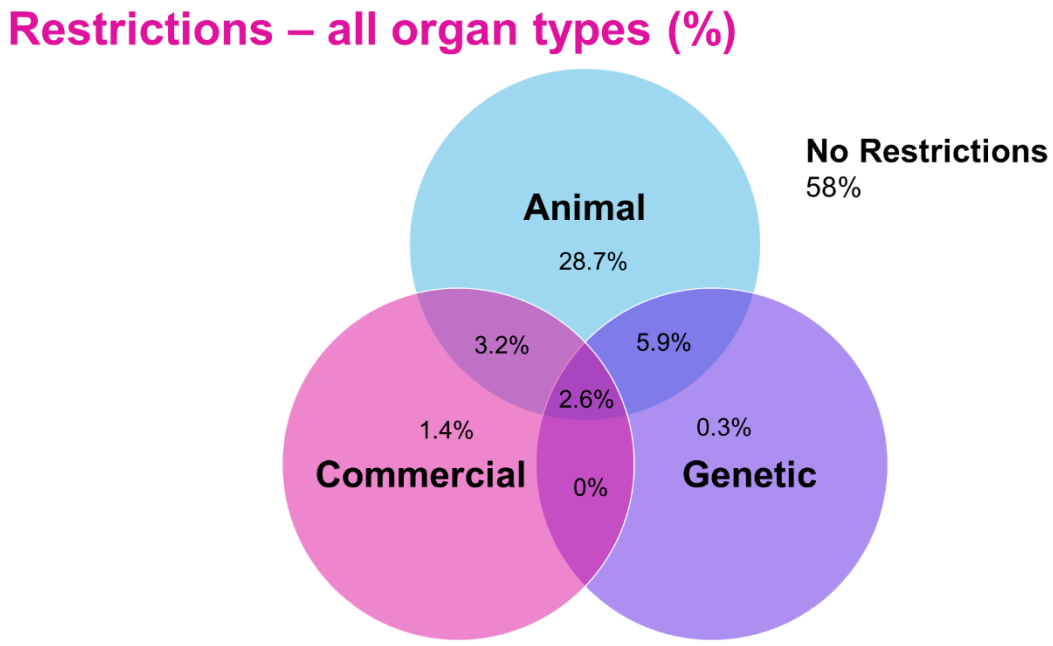
The family can restrict these types of studies. Families can also request additional restrictions that they feel strongly about but this happens very rarely. The Specialist Nurse passes the restrictions onto Hub Operations, and the Hub communicates them to researchers in the offer message. The restrictions are also written down on the consent/authorisation for organ donation form.

Researchers must not use an organ with restrictions in that type of research and it is expected that researchers will not respond to an offer that rules them out. The restrictions that apply to each study are kept track of in the ODT Research Registry, which Hub Operations have access to when allocating organs.

Due to differing legislation in Scotland, in addition to the above restrictions, Scottish donor families can also place restrictions on research, audit and education/training. For example, a Scottish donor family could say 'yes' to use of their loved one's organs in education and training, but 'no' to use in research or audit.

As the research organ allocation scheme is national, all studies receiving organs this way are asked to declare if they involve education and audit as they may receive an offer of an organ from Scotland.

During the 2019/2020 financial year, 58% of 781 organs offered for research had no restrictions on their use at all. The most common restriction placed is on animal research, with a total of 40.4% of offers during the year containing an animal restriction (NB. some of these also had genetic/commercial restrictions placed).



HTA B forms

If a research organ is transplanted, an electronic HTA B form must be completed for traceability.

Islet and Hepatocyte Labs

Islet and hepatocyte labs often have research programmes running alongside their clinical isolation work. Once the isolation process has begun, but it becomes apparent that the cells can't be transplanted, they can be kept for research by the lab in a RINTAG-approved study if there is appropriate consent/authorisation. Researchers in the islet/hepatocyte lab need to call Hub Operations to check this consent/authorisation is in place.

If the isolation process has not begun but the cells can't be used for transplantation, the transplant coordinator must contact Hub Operations to advise this. If there is research consent/authorisation in place the organ will be offered through the National Allocation Scheme.

Split Organs

Sometimes part of a liver is left over after splitting. If there is appropriate consent/authorisation then the remaining liver tissue can be used for research, but should be offered to all ranked studies as per the National Allocation Scheme.

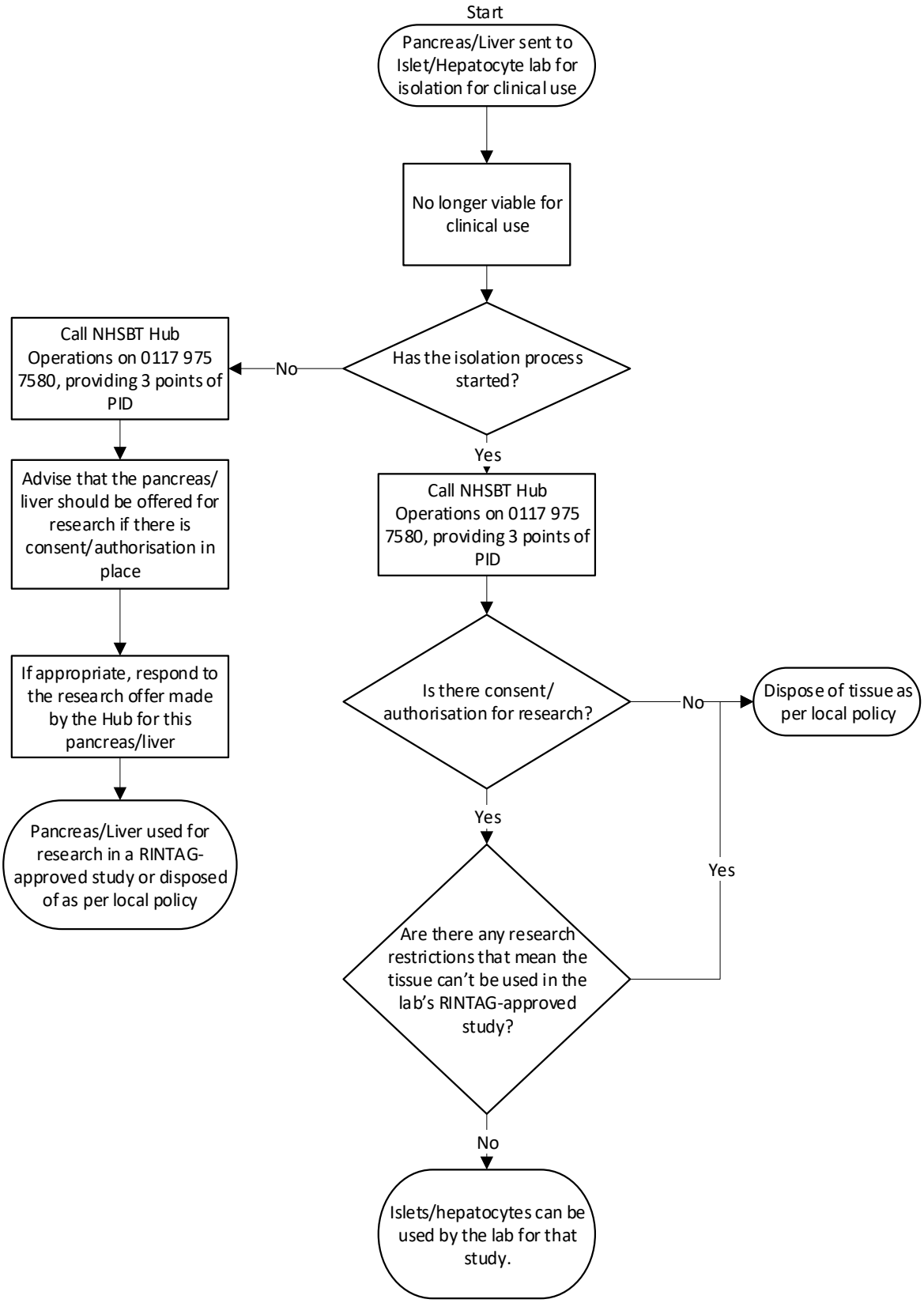


Figure 1: Process for islet and hepatocyte labs to keep tissue for their own research (or other Scheduled/Other Purposes)

Categories 5, 6 and 7:

Studies that require specific consent/authorisation are not subject to the national allocation of organs by Hub Operations. These studies often need to remove tissues that are not available through the National Allocation Scheme (e.g. nerves) or they carry out and evaluate interventions made to the organ donor. Donor families are given study-specific information by their Specialist Nurse so that they can make an informed decision about participating.

If "relevant material" needs to be removed from a donor then this must take place at a HTA-licenced site, with written approval from the site's Designated Individual (DI). A list of DIs can be found on the HTA's website. Licences are not required for removal of this material in Scotland.

It is the responsibility of the researcher to demonstrate to NHSBT that all legislative aspects have been considered and evidenced. ODT's Quality Assurance team will be consulted.

RINTAG will assess these studies according to their suitability, the overall estimated impact on donation, retrieval and transplantation processes, and any reputational risk. If required, a regional operational review will be undertaken prior to RINTAG approval, to ensure that a given Organ Donation Services Team (ODST) is in a position to support the research study.

As proposals within Categories 5, 6 (and 7 where relevant) are likely to require wider input and consultation from a number of internal and external stakeholders, NHSBT ODT reserves the right to adjust the approval requirements and timeframes, on a case-by-case basis. Researchers are strongly advised to contact the Research Team at an early stage.

A full description of the different operational teams' responsibilities in organ donation and transplantation is available in Appendix 4.

Novel Therapeutic Interventions

Novel therapeutic interventions will be assessed on a case by case basis for their impact on organ donation, retrieval and transplantation. As such, approvals from several advisory groups may be required.

As these projects are often ground-breaking, they tend to attract media attention, so a well thought through communications strategy is essential. The Research Team will discuss this further with prospective researchers and direct them to NHSBT's Press Office.

Consideration should be given to formal project management support for large-scale projects. Assessment from NHSBT's Business Transformation Services regarding NHSBT's capacity to support is advisable.

Change Control, Risk Assessment and Standard Operating Procedure (SOP) Creation

These studies require the creation of a change control and risk assessment, resulting in actions for researchers and the Research Team to complete. Dates will be assigned for completion of these actions and regular catchups held to assess progress.

If the study requires a deviation from normal practice for the Specialist Nurses, the Specialist Nurse – Research (SNR) will draft Standard Operating Procedures for them to follow in order to facilitate the study. The SOP will be reviewed by all stakeholders and a controlled document generated once a go-live date is agreed.

Every study is different, and their individual requirements will differ.

Designated Individual (DI) Approval

The HTA licenses several activities in England, Northern Ireland and Wales relating to the removal and storage of "relevant material". The activity of concern for these types of ODT research study is removal of relevant material from the deceased.

DIs are the people under whose supervision an HTA-licenced activity is authorised to be carried out. Therefore, a pre-requisite for a study that will remove relevant material from an organ donor is a letter of approval from the DI at that site.

The Research Team have template approval letters and researchers can use these to write to the appropriate DIs once REC, RINTAG and Research Authority approvals have been gained.

Operational Prioritisation and Specialist Nurse Training

Even though these types of project may only happen in a small number of hospitals within an ODST, due to cross-cover, all of the Specialist Nurses in the team will be trained (and consideration will also be given to training neighbouring ODSTs).

To manage the introduction of training and change within the ODT workforce, regular strategic meetings take place to prioritise and schedule changes. These changes include training for research projects. Once all approvals are in place, a research study will be discussed at the next scheduling call and given a date for training to commence.

The standard training period for the Specialist Nurse and Hub Operations teams is 8 weeks.

The Research Team will assess studies individually to determine their training requirements and these will be discussed with researchers. Researcher input is always gratefully received.

RINTAG

RINTAG brings together representatives from donation, transplantation, research, development, operations, regulation, commissioning, governance, retrieval and finance.

The aims of RINTAG are to provide NHSBT and other stakeholders with an overview of current innovation, and to support the implementation of appropriately approved and funded research, innovation, novel technologies, service development and horizon scanning.

RINTAG works with commissioners and other key stakeholders to ensure the introduction of novel approaches to improve the outcomes of patients undergoing solid organ transplantation is in line with NHSBT's strategy for organ and tissue donation and transplantation.

The Research Project Manager is responsible for liaising with researchers to ensure that all relevant paperwork is provided prior to submission to RINTAG.

Following confirmation that NHSBT can operationally facilitate a research study, the proposal (usually the study's protocol and a copy of the ODT Research application form) will be sent to RINTAG's Executive Group for assessment.

Proposals are reviewed by email every two months and upcoming deadlines can be found on the ODT Clinical Website.

Particularly complex studies may be asked to present to RINTAG in person; face-to-face RINTAG meetings take place twice a year.

Approvals

The Group will be given two weeks to decide whether they:

- approve;
- approve in principle (for early stage applications or to request additional information) or;
- reject an application

The Research Project Manager undertakes the role of the RINTAG Secretariat. The RINTAG Secretariat aims to contact the researcher with RINTAG's decision within 14 days. If approval has not been given, a letter including the reasons and advice on re-application, (or OTDT SMT appeal if appropriate), will be issued.

The SMT is responsible for reviewing appeals relating to RINTAG decisions.

Go Live

RINTAG approval is not a green light for a study to commence. Only the Sponsor of a study can issue this, and they will do so on receipt of HRA, REC approval and all necessary Capability and Capacity (C&C) statements. The Research Team will liaise directly with the Sponsor to confirm and agree the go-live date, particularly for study categories 5-7 when Specialist Nurses are required to discuss specific research consent or authorisation.

Sponsorship

Any research requiring the collaboration of the NHS requires a research Sponsor. Local Hospital Trusts/Boards and academic institutions can act as study Sponsors.

A Sponsor is defined by the UK Policy Framework for Health and Social Care Research as:

> "The individual organisation or partnership that takes on overall responsibility for proportionate, effective arrangements being in place to set up, run and report a research project."

Essentially, a Sponsor must have good oversight of a research project as they take legal responsibility for that project.

This includes ensuring that all approvals have been obtained before commencement of the research and that it will be conducted in accordance with the ICH Good Clinical Practice (GCP) Guidelines and other applicable standards and legislation.

The Sponsor is usually the Data Controller in light of the General Data Protection Regulation (GDPR).

NHSBT Sponsorship

NHSBT will consider acting as Sponsor where the CI holds a substantive employment contract with NHSBT, or where the requirements for Sponsorship as laid out by the HRA are met, and the proposal:

- Does not pose significant legal, financial or reputational risks;
- Is well-designed, peer reviewed and statistically sound;
- Is aligned with R&D strategy across the organisation, and;
- Is supported by the relevant operational personnel - NHSBT R&D must be assured that there is operational capacity for the research.

To request that NHSBT acts as Sponsor, the protocol, completed NHSBT R&D application form (**FRM5209**) and risk assessment (**FRM5208**) any other available documentation should be emailed to the R&D office (at research.office@nhsbt.nhs.uk) with 'Sponsorship request' in the subject line. This should be done before submitting to an NHS Research Ethics Committee.

	Function	Responsible Department / Directorate	Distinction
NHSBT Sponsorship	Ultimate responsibility for the conduct and delivery of a given study.	R&D Office, Clinical Directorate	Assumes legal liability and financial oversight
RINTAG Approval	Reviews research/novel therapy proposals and acts as the advisory group for the OTDT SMT	OTDT Directorate	Responsible for study ranking and/or operational assessment.

Study Ranking

Studies which fall within Category 4 (and 7, if applicable) will be subject to the National Allocation Scheme and will be processed through a prioritisation matrix. This is to ensure that the organs are allocated to studies which are estimated to have the highest benefit for transplantation and patient outcomes. These studies will be scored according to the classification, criteria and categories detailed in the Allocation Policy (**POL263** - available from the ODT Clinical Website).

After establishing the score, each new study will be ranked against all existing studies on the ODT Research Registry. The ranking exercise will be undertaken by the Research Team and agreed by RINTAG's Executive group. Once the new ranking has been approved by RINTAG, all active studies will be notified of the revision and any implications this may have to their study.

Agreements with NHSBT

Before the project starts, the CI and a representative of the Sponsoring organisation (often a member of the R&D or Research Governance office) will be required to sign an agreement with NHSBT, confirming that they understand their responsibilities. This ensures compliance with all regulations.

The respective stakeholder responsibilities, including that of the CI/study team, are described in more detail in Appendix 4.

Appeals

Researchers who do not receive approval from RINTAG, including cases which cannot be resolved through discussion within this forum, may appeal against this decision to the OTDT Senior Management Team (SMT).

The applicant is advised to discuss their next steps and/ or intent to appeal, with the RPM, before submitting a written appeal. The appeal must be made in writing and will be formally considered at the next appropriate OTDT SMT meeting. These meetings occur on a monthly basis.

Once a Study Is Live

EOS Mobile access

Researchers can request access to NHSBT's Electronic Offering System (EOS Mobile) in order to find out more information about the organs that are offered for research. EOS Mobile is primarily used by transplant centres to assess the suitability of organs for their recipients, so there are donor data on the system, which need to be taken into account when completing an IRAS form (see the section on Anonymity for more details).

Only email addresses ending in nhs.uk, nhs.net and ac.uk are allowed access to EOS Mobile. Please email the NHSBT Service Desk at service.desk@nhsbt.nhs.uk to request access.

Hub Operations will forward any additional information they receive to all accepting centres (including research studies).

Progress Reports

Researchers are expected to complete progress reports when requested – the Research Team will send these out to researchers by email. The reports are used to assess performance, provide data for improvement and monitoring purposes, re-ranking, as well as confirm that the information held about a study on the Registry is correct.

Resubmissions

Studies that are active on the ODT Research Registry that wish to extend their study beyond the original approval need to resubmit to RINTAG. This includes changes to procedures/protocols as well as requests for more time or more "relevant material".

A study is considered to be completed when the study duration lapses or the number of requested organs has been reached - whichever occurs first. RINTAG will adopt a pragmatic approach by allowing up to 5 abdominal organs, 2 cardiothoracic organs or an additional 2 months without requiring re-submission.

The Resubmission Application Form is available on the ODT Clinical Website.

Changes to Contact Details

If the contacts for a study need to be changed (e.g. phone numbers, email addresses, change of CI) please email the Research Team who will make the required changes to the Registry and inform Hub Operations if necessary.

Pausing a Study

If a study needs to be paused (e.g. because the ethical approval has lapsed and is being renewed, or due to a period of absence) please let the Research Team know. If a study involves Specialist Nurses taking study-specific consent/authorisation then the Research Team will ask the relevant ODSTs to stop consenting or authorising for that study and create a Process Deviation if necessary.

Finishing a Study

The RPM will contact studies that are due to end within a couple of months to check if they are on track to finish or will be resubmitting to RINTAG. Studies will be marked as completed on the Registry and contact details removed from Hub Operations' research pager list if appropriate. Unless required for clinical use, EOS Mobile access will be revoked as part of the study closure process.

An End-of-Study report must be completed by the researcher and sent back to the Research Team. The contents of the report will be published on the ODT Clinical Website.

Useful Websites

Details of all approved research studies are included on the ODT Research Registry and published on the ODT Clinical Website, found here. Further resources are available here:

RINTAG
ODT Research
ODT Advisory Groups
NHSBT R&D
NHSBT CTU
NHSBT Tissue Services
Health Research Authority (HRA)
UK Policy Framework for Health and Social Care Research
NHS Research Scotland
Human Tissue Authority
Research Ethics Service and Research Ethics Committees (RECs)
QUOD

Contact Details

If you have any questions about the content of this handbook, please email the Research Team at ODTResearch@nhsbt.nhs.uk

Appendix 1 – Acronyms and Definitions

Acronym	Definition
AGs	Advisory Groups
C&C	Capacity and Capability
CAG	Confidentiality Advisory Group
CE	Chief Executive
CI	The Chief Investigator is responsible for the conduct of the proposed research
CLOD	Clinical Lead for Organ Donation
CTU	Clinical Trials Unit
DI	Designated Individual
HCRW	Health and Care Research Wales
HRA	Health Research Authority
HSCNI	Health and Social Care Northern Ireland
HTA	Human Tissue Authority
ICH GCP	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP)
IRAS	Integrated Research Application System
MOU	Memorandum of Understanding
NHS	National Health Service
NHSBT	NHS Blood and Transplant
NODC	National Organ Donation Committee
NORS	National Organ Retrieval Service
NRS	NHS Research Scotland
ODST	Organ Donation Services Team. One of 12 teams across the U.K. responsible for facilitating donation – made up of Specialist Nurses, Team Managers, an Office Manager and Administrators.
ODT	Organ Donation and Transplantation
ODT Research Registry	A registry including all NHSBT ODT approved active research studies
Research Team	The Research Project Manager and the Specialist Nurse for Research
OTDT SMT	Organ Donation and Transplantation Senior Management Team
PI	The Principle Investigator is responsible for a research site. In the case of a single-site study, the CI and the PI will normally be the same person.
QA	Quality Assurance
QUOD	QUality in Organ Donation
R&D	Research and Development
RAG	Retrieval Advisory Group (formerly NRG)
REC	Research Ethics Committee
Relevant material	“Relevant material” from deceased donors refers to the definition set out by the HTA and encompasses solid organs, associated tissues, blood, urine and/or biopsy samples
Researcher or Investigator	The person/persons involved in conducting the study
RINTAG	Research, Innovation and Novel Technologies Advisory Group
RM	Regional Manager
RPM	ODT’s Research Project Manager
SMT	Senior Management Team
SN	Specialist Nurse
SNR	ODT’s Specialist Nurse for Research
SoA	Statement of Activities
SoE	Schedule of Events
SOP	Standard Operating Procedure
TM	Team Manager

Appendix 2 - Worked Examples

Category No.	Category title	Description	Working examples
1	**Data Study**	Studies with a pure statistical focus, not requiring access to relevant material e.g. undertaking analysis of existing data on transplantation	**Name:** *Cancer risks from medical radiation exposures - impact of organ transplantation on associated cancer risks* **Aim:** *Researching the cancer risks from computed tomography (CT) scans and cardiac catheterizations in children and young people (under 22 years). The team have established respective cohorts of individuals who have had these procedures, estimated their radiation doses and matched members with the NHSCR to determine who has developed cancer. The research team would like to know who, from a list of NHSBT cohort members, has received a transplant, the organ involved and the date of transplant. Initially, propose restricting only to our smaller cardiac cohort as the CT cohort is very large.* **Approvals**: *REC, CAG[4] and HRA approvals. Shared with RINTAG for awareness. Application managed by the NHSBT Statistics and Clinical Studies.*
2	**Qualitative Study**	Studies with a descriptive or behavioural focus, not requiring access to relevant material e.g. examining attitudes toward organ donation, including the participation of donor families or Specialist Nurses	**Name**: *Mind the Gap: Exploring the differences in UK consent rates from the perspectives of the Specialist Nurses in Organ Donation (SNODs)* **Aim**: *To explore what the experts working in the field view as the key factors that contribute to the different consent rates between the DBD and DCD in the UK* **Approvals**: University ethics*, RINTAG for approval.*
3	**Biological Sample Study**	Studies looking to access blood, urine, bronchioalveolar lavage (BAL) and tissue samples from deceased organ donors. Facilitated via the national biobank resource Quality in Organ Donation (QUOD). Samples are	**Name:** *Investigation of transcriptional signatures predictive of suboptimal short- and long-term outcomes in deceased circulatory death kidney transplants* **Aim:** *To measure the expression of genetic information in kidney biopsies using a method that can read-out hundreds of thousands of genes. To*

[4] Confidentiality Advisory Group

		collected at four different time points covering the donor management period, all the way through to the point of organ retrieval	*subsequently select a small number of markers from this big group that best associate with bad or good outcomes.* **Approvals:** *QUOD Steering Committee. Other approvals as required[5]. Application managed by the QUOD team.*
4	**Study Accessing "Relevant Material" Through Generic Consent / Authorisation**	Studies requesting access to "relevant material" (e.g. hearts, lungs, pancreases, kidneys and livers) by generic research consent/authorisation[6]. These organs are offered by Hub Operations to approved studies through a national allocation scheme. RINTAG prioritises and ranks approved research studies. There are specific circumstances by which this "relevant material" becomes available. Please see the Section on Category 4 studies for more information.	**Name**: *Exploring the structural and functional effects of normothermic machine perfusion and de-fatting agents on human steatotic livers.* **Aim**: *To investigate the effects of normothermic machine perfusion (NMP), with and without de-fatting agents, in the preservation of steatotic human livers through structural and functional liver assessment.* **Approvals**: *REC, HRA, RINTAG. Application managed by the Research Team.*
5	**Study Accessing "Relevant Material" Through Specific Consent / Authorisation**	These are usually studies proposing to remove "relevant material" that is not routinely transplanted (e.g. nerves, bladders), purely for research purposes. This removal requires study-specific consent/authorisation from donor families. Studies in England, Wales and NI require HTA licences to remove this material, in accordance with the	**Name**: *Collection and characterization of human olfactory ensheathing cells* **Aim**: *To obtain both olfactory bulbs from adult, brain stem dead patients who undergo organ donation after brain stem death confirmation (DBD)* **Approvals**: *REC, HRA, HTA, RINTAG and OTDT SMT. Application managed by the Research Team.*

[5] The QUOD biobank holds generic ethical approval for research projects concerning improving quality in organ donation. Additional local approvals may apply.

[6] Due to differing legislation, families **consent** for organ donation in England, Northern Ireland and Wales but they **authorise** it in Scotland.

		Human Tissue Act 2004. Licenses are not required in Scotland. Research applications wishing to access "relevant material" via the specific consent/authorisation route will only be considered if material cannot be accessed through the ODT National Allocation Scheme.	
6	**Donor Intervention Study**	Studies looking to undertake interventions in DCD donors prior to death[7], and/ or interventions to DBD donors i.e. drug administration to facilitate organ preservation.	**Name**: *An evaluation of the physiological changes of circulatory-determined death with respect to organ donation and transplantation* **Aim:** *This research specifically seeks to address:* *1. The physiological processes that occur during the dying process after withdrawal of life supporting therapy (WLST).* *2. Whether key markers can be identified that predict time to death following WLST in the potential organ donor.* *3. Whether the function of transplanted organs can be predicted from premortem changes identified in the donor.* *4. Whether an intervention in the donor can be identified that improves the function of a transplanted organ.* **Approvals**: *REC, MCA, HRA, HTA, RINTAG and NHSBT operational written confirmation. Application managed by the Research Team.*
7	**Other Studies/Novel Technologies and Therapies**	Proposals which *may* require access to relevant material and/or donors and are expected to have an impact on the donation, retrieval, and/ or transplantation processes. This includes novel technologies and therapies such as novel transplants.	**Name**: *The PITHIA trial: Pre-Implantation Trial of Histopathology In renal Allografts* **Aim**: *to evaluate pre-implantation kidney biopsies as a tool to help increase the number and quality of kidneys transplanted* **Approvals**: *REC, HRA, HTA, RINTAG, Retrieval and Kidney Advisory Groups, NHSBT R&D as Sponsor. Application managed by the Research Team and NHSBT Clinical Trials Unit.*

[7] Studies looking to remove tissues from DCD donors before asystole should be aware of the implications of the Mental Capacity Act 2005 and/or the Mental Capacity Act (Northern Ireland) 2016

Appendix 3 – Legal Requirements for Removal of Organs and Tissues from Organ Donors

Removal of tissue/organs for research purposes

Consent and removal of human tissue and organs for the primary purpose of research are regulated in the UK under the Human Tissue Act (2004) and the Human Tissue (Scotland) Act (2006).

Outside of Scotland, removal of tissue from deceased donors for the primary purpose of research must be carried out on Human Tissue Authority licensed premises.

Removal of tissue and organs from deceased donors for the purpose of transplantation is governed by a different legislation (Quality and Safety of Organs Intended for Transplantation Regulations). If organs or tissue are then deemed unsuitable for transplantation, they may be used in a RINTAG approved study – as long as the appropriate consent or authorisation is in place.

The RINTAG approval process will confirm that appropriate consent and licensing requirements are in place for any study. NORS teams must not remove any material from organ donors for the primary purpose of research unless the research study has been approved by RINTAG and retrieval agreements and regulatory requirements are in place.

It is the responsibility of the researcher to ensure their study fulfils the requirements of the Human Tissue Act (2004) in England, Wales and Northern Ireland and the Human Tissue (Scotland) Act (2006). Researchers are therefore encouraged to take the time to familiarise themselves with the HTA guidance available on the HTA website and all local guidance.

The HTA has issued good practice guidance in its Codes of Practice, which includes Code E: Code of Practice for Research. Answers to Frequently Asked Questions are also available. The HTA also licences a number of activities under the Human Tissue Act (2004), one of which is the storage of tissue for “scheduled purposes”, which includes research. The Research Project Manager can provide further advice on licensing issues.

Local Guidance

Local NHS Trusts/ Boards and Universities may have local policies on the handling of human tissue for research. Applicants must ensure that research involving human tissue, whether undertaken by University or NHS Trust/ Board employees, is subject to common governance procedures in line with local policies and current legislation.

Consenting/authorising to use human tissue in Scheduled/Other Purposes or Novel Therapies

The legislative framework for donation in England, Scotland and Northern Ireland is that of an 'opt-in' system of consent. The Human Transplantation (Wales) Act 2013 introduced ‘deemed consent’ in Wales.

The HTA Code of Practice on consent provides detailed guidance on all aspects of consent for the use of human tissue for a scheduled purpose. It is routine in discussions with families of organ donors to be asked to provide consent/authorisation in cases where organs are retrieved for transplantation and subsequently not transplanted and for removal of organs for research where appropriate. The equivalent Explanatory Notes are available for those following the Human Tissue (Scotland) Act 2006.

Appendix 4 – Responsibilities

This section outlines the various stakeholders involved in the application process and their respective responsibilities. It provides a description of the different operational teams involved in organ donation and transplantation.

Title	Responsibility
AG Chairs	Members of RINTAG. Responsible for providing expert input into research applications.
Chair of RINTAG	Responsible for liaising with the Research Project Manager (RPM) to ensure all relevant research studies, service evaluations, novel technologies and other projects are reviewed appropriately by RINTAG, as described in this document.
Chief Investigator / Research Team	Responsible for liaising with the RPM regarding the relevant aspects outlined in this document; for ensuring all the regulatory and governance issues are addressed and evidenced appropriately; for adhering to any operational considerations deemed suitable by NHSBT. Provide periodic feedback/ updates on the research and at completion of the study to NHSBT and the ODSTs involved, where relevant.
Clinical Lead for Organ Donation (CLODs)	Function: Within the hospital Trust/ Board. Lead on promoting, supporting and advising clinical staff and Specialist Nurses in Organ Donation Regional/ hospital: Each region has an overall clinical lead for organ donation to advice/ support and disseminates new information/ protocols as advised by NHSBT. Impact on research: CLODs are to be informed of new research which will require any additional resources/ input at local hospitals. Complex studies may be discussed further at National Organ Donation Committee (NODC) for feedback for the research team.
National Organ Retrieval Service (NORS).	Function: Comprises abdominal and cardiothoracic teams who attend organ donations to perform organ retrieval. Regional/ hospital: Adheres to the agreed national NORS standards to provide a high standard of operative care and safety. Impact on research: NORS teams will retrieve organs for transplantation which may subsequently be offered for research if deemed untransplantable. NORS teams should retrieve organs/ tissues solely for the purposes of research provided that: i. They are already attending the donor. ii. They have been given reassurance that the local study is on the NHSBT Registry of 'live' research programmes and the necessary consent is in place regarding the retrieval of the organ. iii. When mobilised, NORS teams will be notified about all organs required - including for research purposes. iv. That local licences and approvals are in place, where required. v. The team is competent to retrieve the required organ/ tissue. vi. The organs or tissues fall within the normal NORS remit (e.g. NORS teams would not be required to retrieve pituitary glands) The decision to remove "relevant material" for research purposes is therefore made at a national level. "Relevant material" for research should be retrieved after all organs accepted for clinical transplantation have been retrieved safely. For more complex studies, where research retrieval outside the normal NORS teams' remit and competency is proposed, further agreement and

	consultation is required as to who will perform the retrieval. The Research Team will be available to facilitate such discussions.
NHSBT R&D Office	Providing support and advice to the RPM and SNR. Maintaining oversight of activity. Separately, responsible for NHSBT Sponsorship.
ODT Associate Medical Director	Responsible for bringing any relevant proposals to the attention of ODT CARE.
ODT Research Project Manager (RPM)	Coordinates and facilitates the ODT research approval process, liaising with prospective applicants and other relevant stakeholders throughout the entire process. First point of contact for all applications. Works closely in collaboration with the SNR and the Quality Assurance Manager.
OTDT SMT	Final decision regarding the approval of relevant studies. Has the right to veto any recommendations made by RINTAG. Responsible for reviewing appeals relating to RINTAG decisions.
Quality Assurance Manager	Function: Ensures Quality and safety for NHSBT and external stakeholders. Regional/ hospital: Maintains safety within organ donation and transplantation Impact on research: Oversees the implementation of studies/novel therapies and technologies which require additional ODT input. QA will provide advice on Regulatory requirements and working within processes and frameworks and ensure studies are carried out in accordance with QA process – which will reduce risks. Supports the RPM and SNR with HTA licensing requirements and consent/authorisation processes, providing expert advice prior to RINTAG submission.
Research, Innovation and Novel Technologies Advisory Group (RINTAG)	Overall responsibility to ensure studies meet the strategic needs of NHSBT; to assess the impact studies may have on organ donation, retrieval and transplantation; the potential operational impact, and relevance of the study in meeting organisational objectives; and considers the reputational risk to the organisation. Provides advice to the OTDT SMT.
RINTAG Executive Members	Responsible for reviewing all relevant study proposals and provide expert advice regarding the suitability of the request.
Specialist Nurse for Research (SNR)	Coordinates and facilitates operational considerations for ODT studies, working closely with the ODT Research Project Manager, liaising with the applicant and other relevant stakeholders through the implementation phase. Provides Specialist Nurses with study-specific training on obtaining consent/authorisation.
Specialist Nurse (SN)	Function: Primary role is to coordinate and support the organ donation process. To obtain valid consent/authorisation from the appropriate person under the relevant legislation (Human Tissue Act 2004, Human Tissue (Scotland) Act 2006 or Human Transplantation (Wales) Act 2013. Works to agreed SOPs to ensure study requirements are met. Records the consent/authorisation and any restrictions as detailed in the NHSBT Consent/ Authorisation procedures. Regional/ hospital: 12 ODSTs across the UK. Embedded within hospitals and also cover all other hospitals whilst on call.

	Impact on Scheduled/Other Purposes: Ensuring any organ retrieved for transplant purposes and subsequently deemed unsuitable, after being offered to all the appropriate transplant centres, has been considered for use in Scheduled/Other Purposes. Provides updates to the NORS team during the handover in theatres, about any local research studies that have gained research consent for which the team has been asked to remove. If required, facilitates ODT-approved attendance of research teams to the organ donation process.

Appendix 5 – Transportation of Organs for Scheduled/Other Purposes

- Transport of organs for Scheduled/Other Purposes is not a licensable activity under the Human Tissue Act (2004). These organs will not need to travel under an HTA licence.
- Licensable activities for Scheduled/Other Purposes under this legislation are; removal and storage.
- There are however expected standards around transport of human material for Scheduled/Other Purposes such as suitable transport arrangements, traceability and records of transport and delivery that researchers are required to adhere to.
- It is the responsibility of the researcher to ensure appropriate transportation arrangements are in place, and to assume any transportation costs acquired.
- Researchers are allowed to transport organs in their own vehicles as long as they follow all health & safety, traceability, packaging, recording and labelling of research organs as would be taking place by a courier.
- Large organ boxes are the property of the NORS teams, commissioned by NHSBT. Small organ boxes are the property of NHSBT.
- On receipt of an organ, organ boxes will need to be emptied of its contents and wiped inside and out with an antibacterial wipe. The box will need to be air dried before closing. Stains must be removed immediately with a mild detergent and warm water followed by a solution of warm water and 5.25% sodium hypochlorite. No abrasive cleaners of any kind are to be used.
- It is important NHSBT is notified when an organ (kidney or pancreas) is received, so the box can be collected as soon as possible. An email is to be sent to odtcommissioning@nhsbt.nhs.uk with the collection address, contact telephone number and preferred day/date for collection.
- All other organ boxes must be sent back to the NORS team that they belong to. The address will be listed on the box. This must be returned as soon as possible by first class post.