NHS
Blood and Transplant

NHSBT ORGAN DONATION AND TRANSPLANTATION: OBTAINING SUPPORT FOR RESEARCH STUDIES

Guidelines to Prospective Applicants

PURPOSE OF DOCUMENT

The purpose of this document is to outline the NHSBT Organ Donation and Transplantation (ODT) procedure for obtaining support for research studies. It is provided for prospective applicants wishing to obtain access to organ donors and/ or "relevant material"[1] from donors for research purposes.

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

The process has been established to provide assurance to NHSBT that donated relevant material are 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.

[1] "Relevant material" from deceased donors refers to the definition set out by the HTA and encompasses solid organs, associated tissues and/ or biopsy samples, as outlined here.

1. EXECUTIVE SUMMARY

This document outlines the NHSBT ODT approval process to obtain support for research studies. In summary:

- Researchers are encouraged to engage early with the NHSBT ODT Research Project Manager.
- The ODT Research Project Team[2] will provide advice on governance and operational considerations of a study.
- Studies will be categorised according to their nature to guide the subsequent approval route. The categorisation will inform which documents and operational considerations are required.
- The Research Project Manager will facilitate submission to the Research, Innovation and Novel Technologies Advisory Group (RINTAG), for review.
- RINTAG will score and rank studies requiring access to organs via the national research allocation scheme, according to a prioritisation matrix.
- The approval timeframe varies between study categories. NHSBT ODT is committed to keeping timescales to a minimum. In some cases, final approval will be required from the ODT Senior Management Team (SMT).
- Before a study can commence, the CI will be required to sign a Memorandum of Understanding, which outlines their responsibilities and compliance with regulations.
- Researchers with active studies are expected to provide regular progress reports to ODT. This will be requested by the Research Project Manager for improvement and monitoring purposes.

[2] See Appendix 1 for acronyms and definitions

2. CATEGORISATION

The category of the proposed study (Table 1) will determine the approvals required and the level of NHSBT operational coordination necessary for a given study to be undertaken.

Table 1: Study categorisation and description[3]

Category No.	Category title	Reference	Description
1	Data study	DS	Studies with a pure statistical focus, not requiring access to "relevant material" e.g. undertaking analysis of existing data on transplantation
2	Qualitative study	QS	Studies with a descriptive or behavioural focus, not requiring access to "relevant material" e.g. examining attitudes toward organ donation
3	Biological sample study	BS	Studies looking to access blood, urine and tissue samples from deceased organ donors. Facilitated via the national biobank resource Quality in Organ Donation (QUOD). Samples are collected at four different time points covering the donor management period, all the way through to the point of organ retrieval
4	Study on organs deemed untransplantable following removal from the donor	UR	Studies requesting access to solid organs by generic research consent/ authorisation[4] i.e. organs that are removed from the donor for the purpose of transplantation but are subsequently deemed unsuitable for transplantation. Organs are offered via the NHSBT Hub Operations to approved studies. RINTAG prioritises and ranks approved research studies.
5	Study on organs removed specifically for research	RR	Studies proposing to retrieve relevant material from donors, purely for research purposes and as such will require specific consent/ authorisation from donor families, in addition to normal consent/ authorisation to remove other organs for transplantation. Studies in England, Wales and NI require HTA licensing considerations, according to the Human Tissue Act 2004. Licenses are not required in Scotland[5].
6	Donor intervention study	DI	Studies looking to undertake interventions in DCD donors prior to death[6], and/ or interventions to DBD donors e.g. drug administration to facilitate organ preservation.
7	Other studies	O	Studies which *may* require access to "relevant material" and/ or donors and is expected to have an impact on the donation, retrieval, and/ or transplantation processes.

On occasion, studies may fall into more than one category (particularly category 4 and 5). In these circumstances, parallel approvals will be sought (Figure 2). The applicant is expected to work with the ODT Research Project Team to categorise their study accordingly.

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 Tissue Services.

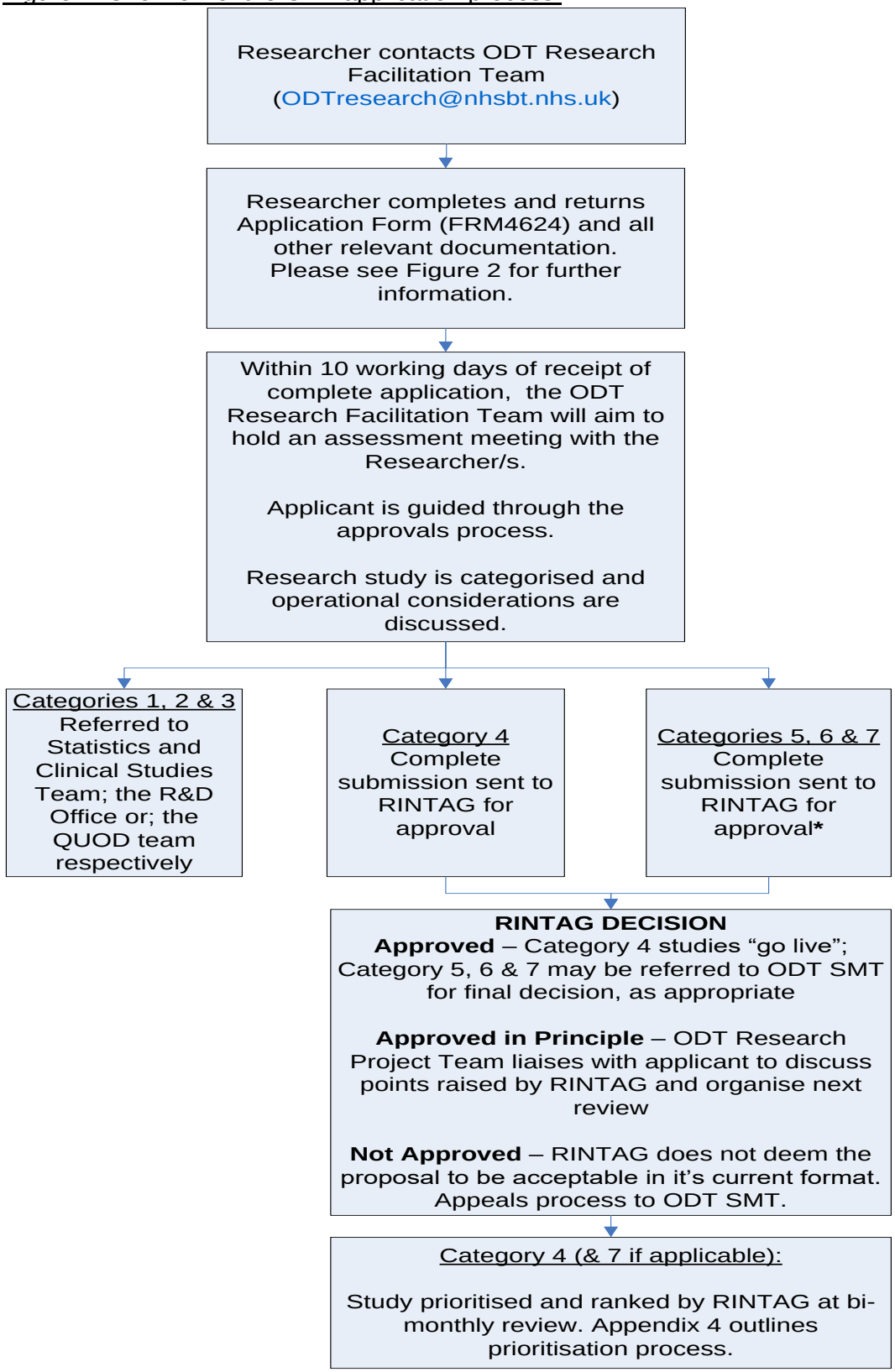
Research undertaken in transplanting units that does not impact upon ODT services (i.e. does not require donor family consent, or similar) falls outside the remit of NHSBT ODT and RINTAG. In cases when such studies are brought to the attention of ODT, it will be sent to RINTAG for information where appropriate. Local approvals are however likely to apply. Prospective researchers are advised to contact their local R&D Office for further guidance.

[3] Working examples for each category is found in Appendix 2.
[4] The Human Tissue Act 2004 (England, Wales and Northern Ireland) specifically uses the term *'consent'*, whilst The Human Tissue Act 2006 (Scotland) uses the term *'authorisation'*.
[5] Please find more details about the legislative requirements in Appendix 3.
[6] Studies looking to remove tissues from DCD donors pre asystole falls under the Mental Capacity Act 2005 and/ or the Mental Capacity Act (Northern Ireland) 2016

3. APPLICATION PROCESS OVERVIEW

The flowchart below (Figure 1) provides an overview of the complete ODT application process. Further guidance is given in subsequent sections of this document.

Figure 1. Overview of the ODT application process:



* Please note that studies in Categories 5, 6 & 7 require NHSBT to assess the deliverability of a study. This requires communication and coordination of a multidisciplinary team. Assessment can therefore take additional time and early engagement from the applicant is vital.

4. EARLY ENGAGEMENT

Researchers are recommended to contact the NHSBT ODT Research Project Manager (RPM) to discuss their proposal as early as possible. The RPM will provide advice about the steps required to gain approval.

Subject to advice from the RPM, researchers are then required to submit a completed application form (FRM4624) and a study 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[7]:

1. Specific inclusion and exclusion criteria.
2. Standard Operating Procedure (SOP) describing the surgical procedure involved in removing "relevant material", if this is not covered by existing SOPs, where applicable (Figure 2).
3. Confirmation of compliance with all appropriate legislative and regulatory frameworks within the UK[8], such as HTA licences (including agreement from Designated Individuals) where applicable (Appendix 3).
4. Process for appropriate storage and disposal of human "relevant material", where applicable.
5. Details of the transport arrangements including mode of transport and the transport company, where applicable[9].
6. Process for training of SNODs and NORS teams, where applicable.
7. Media Management section describing an agreed communications strategy with NHSBT, where applicable.

Should your institution not provide any preferred templates or protocol guidelines, the HRA website provides basic recommendations, here.

On receipt of the application and the study protocol, a reference number will be allocated to the proposal. Within 10 working days of receipt of a complete application, the RPM will aim to hold a telecon to discuss the documents with the applicant and the Specialist Nurse for Research (SNR), including any other key NHSBT personnel as appropriate.

The purpose of this telecon is to review and categorise the study proposal. Agreed actions, next steps and categorisation will be sent by email to the researcher, shortly after the telecon.

The subsequent steps of the process are dependent on the categorisation of the study (Table 1).

[7] NHSBT ODT reserves the right to amend this list on a case-by-case basis depending proposal complexity

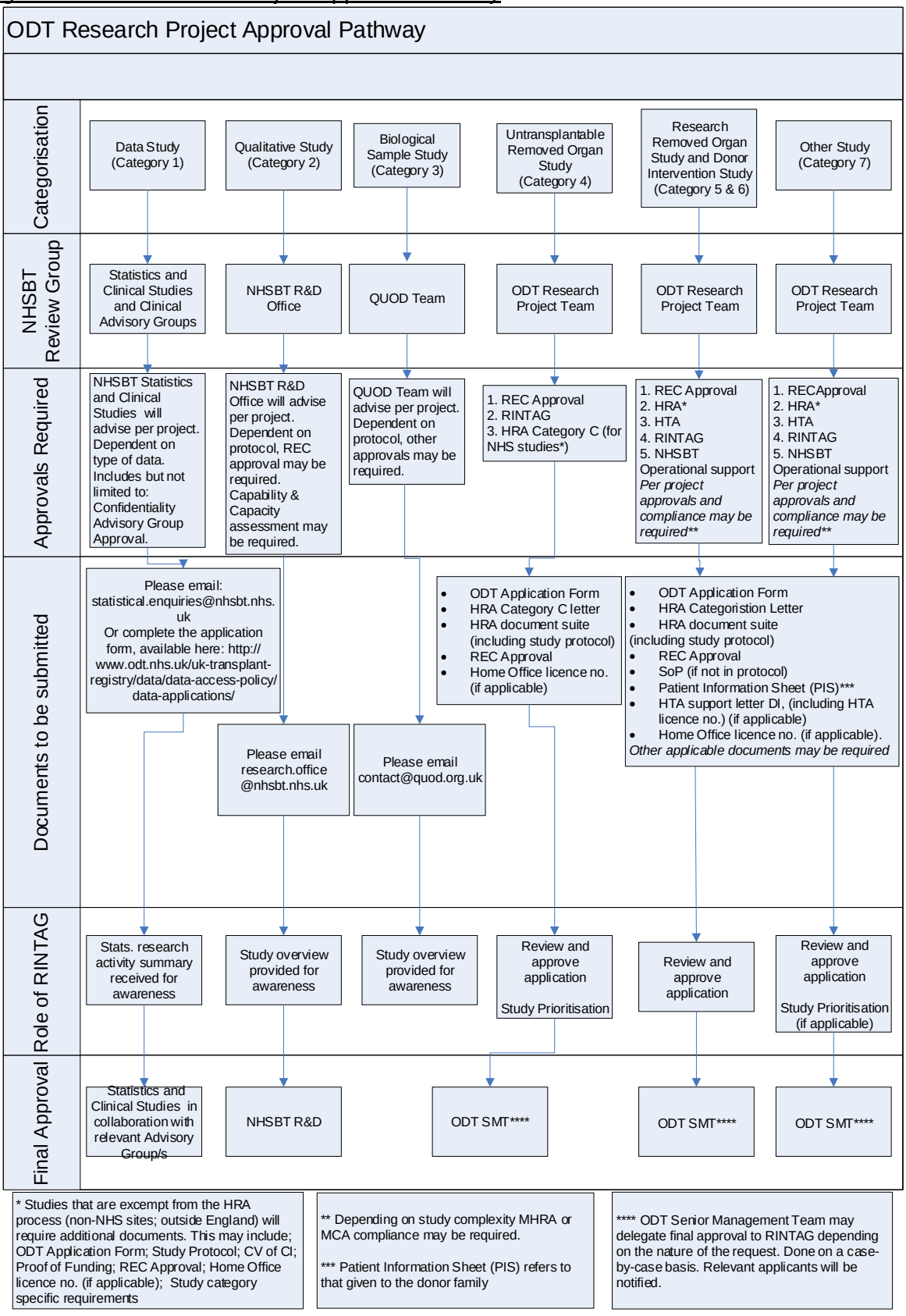
[8] Including the UK Policy Framework for Health and Social Care Research, found here: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

[9] Details of transportation requirements are available from the RPM upon request

5. APPROVAL ROUTES AND DOCUMENTATION

Figure 2 below provides an overview of the approval routes and documentation required for each study category.

Figure 2. ODT Research Project Approval Pathway:



6. OPERATIONAL CONSIDERATION

6.1 Category 4 – Study on organs deemed untransplantable following removal from the donor (UR) and; Category 7 Other (O) when applicable

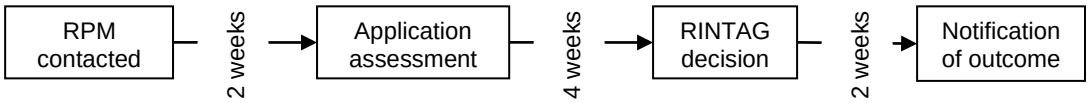
Organs in category 4 have been removed from the donor with the intention of transplantation but found to be unsuitable for transplantation after assessment. Studies in this category will not require SNODs to obtain additional research-specific consent/ authorisation from donor families. An established process[10] exists through the NHSBT Hub Operations to support these studies.

In short, solid organs that have been subsequently declined for transplantation by all centres will simultaneously be offered to all research studies in a given organ group via a fast-track system. Studies are ranked and prioritised by RINTAG on a bi-monthly basis (Appendix 4). The highest ranked study in a given organ group responding within a 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.

RINTAG is increasingly expecting researchers to be available to receive research organ offers 24/7. This will maximise research organ utilisation rates and donor family wishes.

6.1.1. The HTA Code of Practice on Research recommends that if studies are known, or likely to involve a) the commercial sector/ cost recovery (tissue banks); b) genetic testing, or; c) use of animal studies, then a reference to this should be provided in the information used to support the consent process. This is captured in the information leaflet given to donor families by the SNODs. It is also built in to the research allocation scheme to ensure donor family wishes are guaranteed[11].

RINTAG aims to reach a decision for proposals which fall within Category 4 within 8 weeks of receipt of a completed application.



6.2. Category 5, 6 and 7 – Study on organs removed specifically for research (RR); Donor Intervention studies and; Other (O)

Studies which require research-specific consent/ authorisation and HTA licence requirements to remove “relevant material” from donors (see Appendix 3), will not be subject to the allocation of organs via the NHSBT Hub Operations. These organs/ “relevant material” will be sourced at the local, HTA approved, site. It is the responsibility of the researcher to ensure all legislative aspects have been considered, and evidenced, according to Figure 2.

RINTAG will assess these studies according to their suitability, the overall estimated impact on donation, retrieval and transplantation processes, and any reputational risk. Where SNOD involvement to obtain specific consent/ authorisation and additional NHSBT resource are required, the studies will undergo an operational impact and risk assessment. A regional operational review will be undertaken prior to RINTAG approval, to ensure that a given region is not saturated by research studies requiring the same organs.

[10] The full policy document outlining this process is available from the RPM upon request. An overview is provided in Appendix 4.
[11] Please find further details in Appendix 4.

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 ODT Research Project Team at an early stage to discuss the application procedure, timings, consultation and the most suitable approach for REC approval[12].

A full description of the different operational teams' responsibilities in organ donation and transplantation is available in Appendix 5.

7. RINTAG

RINTAG brings together representatives of transplantation, research, development, operations, regulation, commissioning, governance, retrieval and finance. The aim of RINTAG is to provide NHSBT and other stakeholders with an overview of current innovations, and to support the implementation of appropriately approved and funded research, innovations, 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 the UK Strategy 'Taking Organ Transplantation to 2020' and the 'Transplantation Plan for Scotland 2013-2020'

The ODT Research Project Manager is responsible for liaising with researchers to ensure that all relevant paperwork is provided prior to submission to RINTAG. Documents submitted to the HRA will need to be forwarded onto the ODT RPM in all cases, along with the HRA Initial Assessment Letter or HRA Approval letter. Details of the required documents can be found in Figure 2.

On receipt of all necessary documents, and following confirmation that NHSBT can operationally facilitate a research study (Category 5, 6 and 7 where appropriate), the proposal will be sent to RINTAG's Executive Group for assessment. RINTAG[13] meets every 6 months. If a given application is completed more than 3 weeks prior to the planned RINTAG meeting date, it will be assessed by the group via bi-monthly offline reviews.

7.1 Approvals

The Group will be given two weeks to inform the RPM, with either decide to:

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

The RINTAG Secretariat aims to contact the researcher with confirmation of RINTAG's decision within 5 working days of the decision. If approval has not been given, a letter including the reasons and advice on re-application, (or ODT SMT appeal if appropriate), will be issued.

ODT SMT has ultimate responsibility for the approval of relevant research studies (Appendix 5). The SMT is responsible for reviewing appeals relating to RINTAG decisions and has the right to veto any recommendations made by RINTAG. This may be particularly relevant for study Categories 5, 6 and 7. Section 11 outlines the formal appeals process.

[12] Including the requirement to use NHSBT's standardised consent forms and stickers. The PIS will need to incorporate HTA Code details (section 6.1.1). Failure to engage early may require REC amendment and/ or delay the approval process.
[13] For information about RINTAG and its upcoming meetings, including details about its aims and functions, please visit the website, here.

7.2 Re-submissions

Studies that are active on the ODT Research Registry wishing to extend the study beyond the original approval[14] a re-submission to RINTAG is required.

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

The Re-submission Application Form is available upon request form the RPM.

7.3 Live date

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 Approval and all necessary capability and capacity (c&c) statements. The ODT Research Project Team will liaise directly with the Sponsor to confirm and agree the live date, in particular for study categories 5-7 when SNODs are required to obtain specific research consent.

Important distinctions between NHSBT Sponsorship and RINTAG approval are highlighted in Table 2 below.

Table 2. NHSBT Sponsorship versus RINTAG approval:

	Function	Directorate	Distinction
NHSBT Sponsorship	Ultimate responsibility for the conduct and delivery of a given study.	NHSTB R&D Office	Assumes legal liability and financial oversight.
RINTAG approval	Reviews research proposals and acts as the gatekeeper for research access of organs/ tissues.	NHSBT ODT (SMT)	Responsible for the prioritisation ranking and/ or NHSBT operational assessment.

[14] RINTAG approvals are valid for a period of 6 months. Re-submission is required if the study is not live prior to the expiry date.

8. SPONSORSHIP

Any research requiring the collaboration of the NHS requires a research Sponsor[15]. Local Trusts and Academic Institutions may act as study Sponsors. A Sponsor is 'the person who takes responsibility for the initiation, management and financing (or arranging the financing) of that trial[16].

This includes ensuring that all authorisations 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.

8.1 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 the NHSBT R&D Strategic Plan 2015-2020. The Strategic Plan outlines the priorities that the NHSBT has committed to addressing and supporting, and;
- Is supported from the relevant operational personnel - NHSBT R&D must be assured that there is operational capacity[17] for the research.

To make a request for NHSBT to act as Sponsor, the protocol, completed NHSBT R&D application form (FRM5208) and risk assessment (FRM5209) 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[18].

9. PRIORITISATION MATRIX

Studies which fall within Category 4 (and 7, if applicable) will be subject to the national research organ allocation scheme and will be processed through a prioritisation matrix. This is to ensure that available 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 Appendix 4.

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 ODT Research Project Team, and agreed by RINTAG's Executive group on a bi-monthly basis, to accommodate new studies and align the ranking with RINTAG reviews. 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. The ranking of studies, together with a lay summary, will be made available on the ODT Research Registry through the ODT website, here.

[15] A Sponsor in this context does not relate to the responsibility to obtaining funding, although the Sponsor may also undertake the role of Funder.
[16] Medicines for Human Use (Clinical Trials) Regulations 2004, Part 1, 3 (1)

[17] Irrespective of sponsorship, NHSBT will assess operational impact and will issue a statement confirming NHSBT support where appropriate. This is relevant for studies requiring specific research consent (Categories 5, 6 and 7 where relevant).
[18] Ideally, the R&D Office should be informed about a proposed application as early as possible in the design of the research. Further details can be found in INF1348, available upon request.

10. MEMORANDUM OF UNDERSTANDING (MOU)

Before the project starts, the CI will be required to confirm in writing, via a MoU, that they understand their responsibilities and ensure compliance with all regulations.

The respective stakeholder responsibilities, including that of the CI/ research team, are described in more detail in Appendix 5.

11. 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 ODT 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 ODT SMT meeting. These meetings occur on a monthly basis.

12. PROGRESS REPORTING

Researchers are expected to provide six-monthly progress updates and annual reports. These will be used to assess performance and provide data for improvement and monitoring purposes.

Researchers are required to notify the RPM, and Hub Operations, with new contact details, including when a given study require a period of suspension due to annual leave or similar circumstances.

13. USEFUL WEBSITES

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

RINTAG
ODT Research
NHSBTs AGs
NHSBT R&D
NHSBT CTU
NHSBT Tissue Services
HRA
Research Governance Framework
NHS Research Scotland
Human Tissue Authority
Department of Health - Tissue
National Research Ethics Service
QUOD

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
HRA	Health Research Authority
HT Act	Human Tissue Act 2004
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 Heath Service
NHSBT	NHS Blood and Transplant
NIGB	National Information Governance Board for Health and Social Care
NODC	National Organ Donation Committee
NORS	National Organ Retrieval Service
NRG	National Retrieval Group
ODT	Organ Donation and Transplantation
ODT Research Project Team	The Research Project Manager and the Specialist Nurse for Research
ODT Research Registry	A registry including all NHSBT ODT approved active research studies
ODT SMT	Organ Donation and Transplantation Senior Management Team
ORGAN	When referring to the term organ in this document it encompasses all "relevant material" as per the HTA definition (including organs, tissues, bloods, urine samples etc)
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
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 and/or biopsy samples, as outlined here.
Researcher or Investigator	The person/persons involved in conducting the study
RINTAG	Research, Innovation and Novel Technologies Advisory Group
RINTAG Secretariat	The Clinical & Support Services team member and the ODT Research Project Manager
RM	Regional Manager
RPM	NHSBT ODTs Research Project Manager
SMT	Senior Management Team
SNOD	Specialist Nurse in Organ Donation
SNR	NHSBT ODTs Specialist Nurse for Research
SoA	Statement of Activities
SoE	Schedule of Events
SOP	Standard Operating Procedure
TM	Team Manager

APPENDIX 2 - Working examples
NHSBT ODT Research Study Categories

Category No.	Category title	Ref.	Description	Working examples
1	**Data study**	DS	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[19] and NIGB[20] approvals. Shared with RINTAG for awareness. Application managed by the NHSBT Statistics and Clinical Studies.*
2	**Qualitative study**	QS	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 SNODs	**Name**: *Mind the Gap: Exploring the differences in UK consent rates from the perspectives of the Specialist Nurses Organ Donation* **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 awareness. Application managed by the NHSBT R&D Office.*
3	Biological sample study	BS	Studies looking to access blood, urine and tissue samples from deceased organ donors. Facilitated via the national biobank resource Quality in Organ Donation (QUOD). Samples are collected at four different time points covering the donor management period, all the way through to the point of organ retrieval	**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 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[21]Application managed by the QUOD team.*

[19] Confidentiality Advisory Group
[20] National Information Governance Board for Health and Social Care

4	**Study on organs deemed untransplantable following removal from the donor**	UR	Requesting access to solid organs by generic research consent/ authorisation[22] i.e. organs that are removed from the donor for the purpose of transplantation but are subsequently deemed unsuitable for transplantation. Organs are offered via the NHSBT Hub Operations to approved studies. RINTAG prioritises and ranks approved research studies.	**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**[23]: *REC, RINTAG. Application managed by the ODT Research Facilitation Team.*
5	**Study on organs removed specifically for research**	RR	Studies proposing to retrieve relevant material from donors, purely for research purposes i.e. require specific consent/ authorisation from donor families, in addition to normal consent/ authorisation. Studies in England, Wales and NI require HTA licensing considerations, according to the Human Tissue Act 2004.	**Name**: *Improving Transplantation outcomes by investigation of novel methods of organ procurement, preservation and reconditioning. Further Evaluation of Ex Vivo Lung Perfusion to Improve Transplantation Outcomes* **Aim**: *The strategic aim is 'to develop and evaluate novel approaches and technologies that increase the availability of suitable donor organs for transplantation, while improving graft survival'. To establish a robust experimental system for the evaluation of donor organs.* *We propose to utilise the substantial number of UK unused donor lungs to evaluate the currently accepted physiological EVLP assessment criteria alongside novel physiological, biological, ultrastructural, radiological and microbiological assessment tools performed during EVLP. Our aims are firstly to find improved indices and biomarkers of donor lung viability and future graft function that will allow increase the conversion rate to transplant for extended criteria donor lungs.* **Approvals**: *REC, HRA, RINTAG, NHSBT operational written confirmation. Application managed by the ODT Research Facilitation Team.*

[21] The QUOD biobank holds generic ethical approval for research projects concerning improving quality in organ donation. Additional local approvals may apply.
[22] The Human Tissue Act 2004 (England, Wales and Northern Ireland) specifically uses the term *'consent'*, whilst The Human Tissue Act 2006 (Scotland) uses the term *'authorisation'*.
[23] This is an example of a study taking place at a University, non-NHS site, in England and is exempt from HRA assessment

6	**Donor intervention study**	DI	Studies looking to undertake interventions in DCD donors prior to death[24], 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 ODT Research Facilitation Team.*
7	**Other studies**	O	Proposals which *may* require access to relevant material and/ or donors and is expected to have an impact on the donation, retrieval, and/ or transplantation processes.	**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 ODT SMT. NHSBT operational written confirmation TBC. Application managed by the ODT Research Facilitation Team.*

[24] Studies looking to remove tissues from DCD donors pre asystole falls under 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 tissues 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[25].

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, including the recently released Code of Practice for Research. Answers to Frequently Asked Questions are available. The HTA also licences a number of activities under the HT Act, 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 research

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 for the families of organ donors to be asked to provide consent/ authorisation for the use of non-transplantable tissue to be used in research. Please consult with the Research Project Manager over issues around generic consent or if specific research consent is required. The equivalent Explanatory Notes are available for those following the Human Tissue (Scotland) Act 2006.

HRA approval will need to be sought. Please find further details, here. In order to ensure that the correct consent and legislative requirements are adhered to, all research studies that involved removal and use of organs and tissues from organ donors must be approved by RINTAG.

[25] For more information, see Appendix 5

APPENDIX 4 – PRIORITISATION MATRIX
Matrix

Studies will be scored and ranked according to the following classification, criteria and criteria.

Banding classification:

I. If successful will the research organ be transplanted?

Scoring criteria:

1. Feasibility – number of research organs required per year
2. Time-scale from start of study to increase number of organs available for transplantation
3. Peer-reviewed study

Binary categories:

1. Does the study involve multiple transplant units and/or educational institutions working together?
2. Is the study aligned to Taking Transplantation to 2020?
3. Does the study aim to evaluate novel technology/ies in organ transplantation?

Scoring approach

Studies with the intention to transplant offered research organs are given the highest priority. Thereafter, ranking will be made in line with the following assessment criteria;

- Highest score and highest number of binary categories (i.e. highest score in the prioritisation criterion and highest number of 'Yes' in the binary categories)
- In the event of an equal score the number of binary categories will determine the priority.
- In the event of an equal score and equal number of binary categories, priority will be given to the study with the highest scored categories. For example, Study 'X' and Study 'Y' have equal number of binary categories and both have a score of 18. Study X has 4 'A's and 1 'C'. Study Y has 3 'A's and 2 'B's. Therefore, Study X is ranked above Study Y.
- In the event that two scores are identical, the studies will be given equal ranking. In the event that both studies accept an offered organ, organs will be allocated on a geographical basis.

Re-scoring and re-ranking of all studies will be made on a 6-monthly basis to accommodate for changes (such as criteria no. 2: Time-scale). Researchers are required to provide regular progress reports to aid in monitoring and evaluation.

Ranking approach

The ranking will be undertaken per organ group. The ODT Research Project Team will undertake the ranking exercise. The outcome will then be forwarded on to RINTAG executive members[26] for approval.

The ranking exercise will be undertaken bi-monthly, to accommodate new studies. Once the ranking has been approved by RINTAG, all active studies will be notified of the revision and any implications this may have to their study.

[26] This group consists of clinical experts as well as NHSBT staff members. Please see RINTAG's ToR for more details

Offering procedure
The Hub Operations will send a joint SMS message to all relevant researchers, providing them with the details of available organ (e.g. location, organ condition). Researchers will be required to respond within 45 minutes if they wish to accept the organ. The organ will be allocated to the highest ranking study that responded to the offer within the 45-minute deadline.

In the event of acceptances from two studies with exactly the same rank, research organs will be offered on a geographical basis. Any research organs that have not been accepted by NHSBT ODT approved studies would be offered to NHSBT ODT approved tissue banks.

HTA Code of Practice
In accordance with the Human Tissue Authority's Code of Practice on Research, donor families should be provided with information to support the consent process and given the option to withhold consent for research that involves one or more of the following:
1) the commercial sector including cost recovery (tissue banks) and/ or;
2) genetic testing/ DNA analysis and/ or;
3) animal studies

This has been built in to the current allocation pilot scheme as follows:

- The Hub Operations will make offers to all studies in a given organ group, informing of any restrictions placed on the offer
- The additional filter will occur once the 45 min deadline has passed
- In cases when a family has opted-out from any of the above categories, offering responses from such studies will be omitted
- The organ will be offered to the next highest ranked study

For Research Tissue Banks and Islet Labs etc, the Hub Operations will relay information about any restrictions during the offering procedure. In cases when a family has opted-out from the above categories, the relevant Research Tissue Banks and Islet Labs etc will be expected to ensure internal processes are in place to guarantee donor family wishes in accordance with the HTA code.

APPENDIX 5 – 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 SNOD teams involved, where relevant[27].
Clinical lead for organ donation (CLODs)	Function: Within the hospital Trust/ Board. Lead on promoting, supporting and advising clinical staff and SNODs 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[28]. NORS teams should retrieve organs/ tissues solely for the purposes of research[29] 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 organ/ tissue falls within the normal NORS remit (e.g. NORS teams would not be required to pituitary glands) The decision to retrieve for research purposes is thereby made at a national level. Organs placed for research should be retrieved after all organs accepted for clinical transplantation have been retrieved safely.

[27] A detailed account of responsibilities are outlined in the Letter of Agreement, available upon request
[28] Applicable to study category 4
[29] Applicable to study category 5, 6 (and 7,where relevant)

	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 ODT Research Project Team will be available to facilitate such discussions.
NHSBT R&D Office	Responsible for issuing written confirmation of NHSBT operational support for study categories 5, 6 (and 7, where relevant). Providing support and advice to the RPM and SNRSD. Maintaining oversight of activity. Separately, responsible for NHSBT Sponsorship.
ODT Associate Medical Director	Responsible for providing the final approval sign-off from ODT for all supported research studies and to bring 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.
ODT SMT	Final decision regarding the approval of relevant research 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 research studies which require additional SNOD/ NORS input. QA will provide advice on Regulatory requirements and working within processes and frameworks and ensure research is carried out in accordance with QA process – which will reduce risks. Supports the RPM and SNR with HTA licensing requirement and consent processes expertise prior to RINTAG submission.
Research, Innovation and Novel Technologies Advisory Group (RINTAG)	Overall responsibility to ensure the research meets the strategic needs of NHSBT; the impact research 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.
RINTAG Executive Members	Responsible for reviewing all relevant research proposals, and provide expert advice regarding the suitability of the request.
Specialist Nurse for Research (SNR)	Coordinates and facilitates operational considerations for ODT research projects, working closely with the ODT Research Project Manager, liaising with the applicant and other relevant stakeholders through the implementation phase. Provides SNODs with study-specific training on obtaining research Consent/ Authorisation.
Specialist Nurse in Organ Donation (SNODs)	Function: Obtaining valid consent/ authorisation from the appropriate person under the relevant legislation (Human Tissue Act 2004 or Human Tissue (Scotland) Act 2006, whilst working within the NHSBT procedures for Consent/Authorisation. Recording the Consent/ Authorisation as detailed in the NHSBT Consent/ Authorisation procedures. Informing the researcher that Consent/ Authorisation has been given. Regional/ hospital: 12 regions of SNOD teams across the UK. Embedded within hospitals and also cover all other hospitals whilst on call. Impact on research: Ensuring any organ retrieved for transplant purposes and subsequently deemed unsuitable, after being offered to all the appropriate transplant centres, has being considered for research. Provides update to the NORS team during the handover in theatres, about any local research studies that has gained specific research consent for which the team has been asked to retrieve.

APPENDIX 6 – TRANSPORTATION OF ORGANS FOR RESEARCH

- Transport of organs for research is not a licensable activity under the HT Act 2004. These organs will not need to travel under an HTA licence.

- Licensable activities for research under this legislation are; removal and storage[30].

- There is however expected standards around transport of human material for detailing relevant transport arrangements, traceability and records of transport and delivery[31] 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 under a courier research organ transport.

- Organ boxes are the property of the NORS teams, commissioned by 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.

[30] Please see Appendix 3 for more information
[31] Please refer to the HTA framework, found here.