NHS BLOOD AND TRANSPLANT
ORGAN DONATION AND TRANSPLANTATION DIRECTORATE

RESEARCH, INNOVATION AND NOVEL TECHNOLOGIES ADVISORY GROUP MEETING

Wednesday 9 October 2019, The Montague on the Gardens, London WC1B 5BJ

MINUTES

Attending

Mr Gabriel Oniscu	GO	Chair
Mrs Liz Armstrong	LA	Head of Transplant Development
Dr Richard Baker	RB	Clinical Governance Lead
Mrs Sarah Belgium	SB	Clinical Support Services, NHSBT (Observer)
Ms Hazell Bentall	HB	Lay Member
Ms Deborah Clarke	DC	Clinical Support Services, NHSBT (Observer)
Prof Andrew Fisher	AF	NIHR BTRU Representative
Prof John Forsythe	JF	Associate Medical Director, ODT, NHSBT
Prof Peter Friend	PF	Chair, Multi-Visceral & Composite Tissue Advisory Group
Ms Victoria Gauden	VG	National Quality Manager, ODT, NHSBT
Dr Dan Harvey	DH	National Innovation & Research Clinical Lead, Organ Donation
Ms Lisa Mumford	LM	Head of ODT Studies, NHSBT
Prof Rutger Ploeg	RP	Director of QUOD
Ms Maggie Stevens	MS	Specialist Nurse, Research & Service Delivery
Ms Samaher Sweity	SS	Clinical Trial Manager, NHSBT
Ms Hannah Tolley	HT	ODT Research Project Manager
Prof Chris Watson	CJW	Chair, Kidney Advisory Group
Mrs Fiona Wellington	FW	Assistant Director, Organ Donation & Nursing
Ms Michelle Willicombe	MW	BTS Representative

Apologies

Mr Marius Berman	MB	National Clinical Lead, Retrieval
Mr John Casey	JC	Chair Pancreas Advisory Group
Mr Ian Currie	IC	Chair, National Retrieval Group
Mr Ben Hume	BH	Assistant Director, Transplantation Support Services
Prof Elizabeth Murphy	EM	Lay Member
Dr Jayan Parameshwar	JP	Chair, Cardiothoracic Advisory Group
Ms Karen Quinn	KQ	Assistant Director, UK Commissioning, NHSBT
Mr Michael Stokes	MS	Head of Hub Operations
Dr Douglas Thorburn	DT	Chair, Liver Advisory Group
Dr Nick Watkins	NW	Assistant Director, Research & Development, NHSBT

In attendance:

Miss Heather Crocombe	HC	Clinical Support Services, NHSBT

	Agenda Item	Action
1.	**Welcome and Apologies** GO welcomed everyone to the meeting and gave details of apologies as shown above.	
2.	**Declarations of Interest in relation to the Agenda**	

	There were no declarations of interest in relation to the Agenda	
3.	**Minutes of the Research, Innovation and Novel Technologies Advisory Group Meeting held on Tuesday 7 May 2019** **3.1 Accuracy of the Minutes RINTAG(M)19(1)** The Minutes of the meeting were deemed to be a true and accurate representation of the meeting, except: Page 2, point 3. Delete the words "during today's meeting" Page 4, point 5. Remove "if appropriate" from paragraph 3 **3.2 Action Points from the Meeting RINTAG(AP)19(1)** 1. **Allocation Review Data collection** HT (on behalf of the ODT Research Team) has collated the allocation data for today's meeting using research offer messages instead of the Statistics department. 2. **Research Kidneys Declined** HT has had conversations with researchers and the results of those conversations will be referred to further on in these Minutes. 3. **Annual Review of National Research Organ Allocation Scheme and Ranking System** HT has collated information regarding acceptance criteria. Further work on definitions is required before studies can be rescored. 4. **Cell Line Consent Process** Look into ways to address the challenges regarding ICL creation and future-proof our approach. Ongoing. 5. **Uterine Transplant Update** See point 6. 6. **Status of the Business Plan** Update to follow.	**HC** **HC** **HT** **HT** **HT** **DH** **DH** **KQ**
4.	**Research Activity Consent RINTAG(19)19** This paper summarises how research consent/authorisation rates have changed over the last ten years in the UK. These rates were analysed for actual organ donors (where at least one organ was retrieved for the purposes of transplantation) in the UK from 1 January 2010 to 31 July 2019. When considering organ specific consent/authorisation rates, donors with contraindications for specific organs were excluded. See paper for detail, but key points: • The overall UK consent/authorisation rate for research was 83% in 2010 and has so far risen to 91% in 2019 (up to the end of July) • England and Wales have had the highest consent rates for research over the last few years, ranging from 91% to 95%. • In the last 7 months, Wales has dropped to 86% and Scotland has had the highest authorisation rate for research in the last 10 years at 96% *A question was raised about what happens if an organ intended to be removed for transplant is then found to be unsuitable for transplant, but suitable for research, can the organ then be removed solely for the purpose*	

	of research with specific consent? This is currently not possible within the present consent process. LM advised that the consent form has recently been updated which will result in additional data being available for the next RINTAG meeting to inform about the number of donors who consent specifically for removal of organs for research. **Availability of Organs for Research RINTAG(19)20** This paper investigates the pathway of organs that have been retrieved and not transplanted, to assess the availability of organs for research. It also identifies the number of organs received by research studies within the last 7 months (1 January 2019 to 31 July 2019) See paper for details, but key points: • Overall, the total number of organs retrieved and not transplanted has steadily increased. In addition, the proportion of these organs that have consent/authorisation for research has increased to 94% so far in 2019. • In 2015, the number of organs used for research was at its highest, 531, and since then has started to decline to 400 in 2018. Thus far, figures for 2019 show a similar trend. • The proportion of discarded organs where research consent/authorisation was ascertained is substantially higher than in previous years: 13% in 2015 to 47% from January to July 2019. Mostly abdominal organs had a higher discard rate. • Apart from pancreas, utilised research organs were distributed across many studies. This suggests that mostly studies that were ranked lower through the allocation scheme were still able to obtain research organs. The main reason for non-utilisation of organs is that most are being offered out-of-hours. Research teams are not funded 24/7 so there are regular occurrences of them being turned down. Teams need to work together more closely to ensure 24/7 cover. Centre systems need upgrading somehow to become more responsive to offers. It is disappointing, given the effort being put into INOAR, that organs are still being discarded. Newcastle Study team is working closely with other lung studies to try to ensure that there is 24/7 cover to guarantee that no organs are wasted. *Qu. Is there a tendency for the highest ranked studies to be offered more organs?* Offers are made by group pager to all studies at once, so no study receives any more offers than any other. A Study's priority ranking could potentially be lowered if there is a repeated refusal to accept organs. It was agreed that express permission be given to HT and GO to reduce a study's ranking. There needs to be a way to penalise studies that do not engage and regularly turn down organs within their specified criteria. Research teams also need to do a thorough	

	assessment of staff availability and resource before their applications are even submitted. AP: It was agreed that more information about study acceptance criteria is required to determine if a study is not responding to an offer just because it doesn't meet their criteria or for another reason. HT noted that acceptance criteria were part of the most recent progress report. The task before the next RINTAG meeting will be to work out how to compare these criteria to each research offer to determine how many offers met the criteria of each study. At the next RINTAG meeting, HT will produce data showing reasons for decline, numbers offered etc. That way it will become more apparent which centres are repeat offenders. **Allocation RINTAG(19)21** The data in this paper have come only from the ODT Research Team. There may be some organs which were allocated directly to studies without an offer message being sent out, and therefore these would not be included. Please see paper for details of **Organs Offered between 1 April and 30 September 2019, Number of organs Accepted by each Study between 1 April and 30 September 2019** (results are shown by Organ). **Research Team KPIs RINTAG(19)22** HT noted that these data are collected each month and submitted to the ODT Performance Improvement Team to produce the scorecard. The Research team will discuss which metrics can be added to the scorecard to measure INOAR's implementation. **Analysis of kidney acceptance for research studies RINTAG(19)23** At the May 2019 RINTAG meeting, the ODT Research Team presented an analysis into the reasons for decline of research kidneys. Several potential influential factors were analysed, however only univariately. RINTAG(19)23 presents a more detailed multivariable analysis carried out by the Statistics department. Variables considered: • Date/time of research offer (categorised into core hours (Mon – Fri 8am – 6pm), outside core hours on weekdays (6pm – 8am) and weekends (including Bank Holidays) • Cold ischaemic time at offer (CIT) • Research restrictions – categorised into animal, commercial, DNA, QUOD or a combination of these • Donor age • Reason for organ not being transplanted • Kidney offered – unspecified, left or right kidney Please see Table 1 for details. However, key points: • Results show that offers made during core hours are most likely to be accepted, odds of an offer being accepted outside of core hours on a weekday are 64% less than in core hours and 83% less on a weekend than in core hours, when adjusting for CIT	**HT**

	• Odds of acceptance of a kidney for research reduce by 4% with every hour's increase in CIT AP: HT to email heads of Studies (those on record as receiving offers) to ask if they would like to have a conversation to discuss reasons for non-acceptance. **Recruitment** Clare Denison has been appointed into the Research Team and will start on 4 November 2019. Two research studies which had been supported by RINTAG recently won awards at the BTS and ESOT Congresses. The researchers expressed specific gratitude to RINTAG for introducing the allocation scheme to support the studies which had enabled them to receive the required organs.	**HT**
5.	**New Study Ranking and Studies for Approval and Information RINTAG(19)24** Re-ranking happens every six months. The category 'timescale to increase organs available for transplant' has been replaced with 'clinical study related to transplantation/basic science study related to transplantation/unrelated to transplantation'. All active studies have been rescored accordingly. Action point: GO noted that Study 56 has an MRC Grant so has been externally peer reviewed. HT to amend ranking accordingly. **Study 94: Assessment of Current Organ and Tissue Donation Referral and Authorisation Processes within NHS Scotland, and NHS staff members' views and awareness on donation and the change to opt-out authorisation, in preparation for the 2020 Implementation of "The Human Tissue (Authorisation) Scotland Act"** Applicant is Lilian Kennedy affiliated with the Scottish Government. Aim is to carry out a baseline review of attitudes to organ donation amongst healthcare professionals in Scotland before "opt out" legislation is implemented, by interviewing SNODs in the Scottish Team as well as CLODs and other specialist healthcare professionals. Recently approved by NHS Lothian Quality Improvement Team Transplant Board. RINTAG gave approval. **Study 95: Learning from Deaths – A National Picture related to Training and Good Practice Examples** Applicant is Stephanie Millichope affiliated with Health Education England. Aim is to identify specific training and other factors enabling good practice and continued learning for staff working directly with patients and their families prior to and around the time of death, as well as gaining an insight from staff about what helps and what gets in the way at the time of a death, by means of interviews/focus groups with SNODs in the South Eastern team. RINTAG raised no objection to this study, however Cliona Berman (RM for South East) has highlighted that if interviews are held with	**HT**

	longstanding staff, they may not have received the same bereavement training as new SNODs going through the cohort training system. **Study 96: Development of a Human Precision Cut Slice (PCS) Model to study Renal Inflammation and Fibrosis** Applicant is Lee Borthwick affiliated with Newcastle University. Aim is to test the use of a Precision Cut Slice (PCS) system on 8mm X 0.25mm discs of living human tissue that contain all cell types found in the tissue in the correct orientation – as a model for investigating kidney fibrosis. Request for 72 kidneys, via the National Allocation Scheme. Provisional ranking of 7. RINTAG approved this. **George Greenhall** George Greenhall's cancer linkage study was part of the last email circulation. There are other sub-studies covering diabetes, endocarditis and proteinuria. GG is working closely with Statistics and Clinical Studies on this – Rachel Johnson is his supervisor. Papers brought to RINTAG for information rather than approval. **Study 61: Collection of Peripheral Nerves for Control Cells for Brain Tumour Treatment Research** Aim is to develop new treatments for low grade brain tumours. Study had issues with ethical approval but now resolved. Would like to extend to January 2020. RINTAG gave approval.	
6.	**Innovation** **DCD Heart Activity RINTAG(19)25** This report contains information on DCD heart activity from 1 February 2015 – 30 June 2019. For any queries on the paper please contact cardiothoracicstatistics@nhsbt.nhs.uk Please see papers for detail on **Outstanding DCD Heart forms for the period 1 February 2015 – 30 June 2019, DCD heart transplant activity from 1 January 2015 – 30 June 2019, by quarter and centre, Heart Activity by period and centre** for the same dates, **DCD heart patient outcomes at 30 days post-transplant by centre, for transplants performed** for the same period, and **DCD heart offers recorded on the UKTR as being made to participating centre between 1 August 2017 – 30 June 2019 and results, by financial year.** **Uterine Transplant Update RINTAG(19)27** DH advised that this project now has a go-live date for end November 2019, that training is underway, that CLODS have given their approval and coroners in London have given approval. The living donor project needs to be kept strictly separate from this project – there is a possibility of significant confusion. DH is not involved in the living donor project. If a transplant from a deceased donor takes place and there is subsequently a live birth, it will be very easy for a deceased donor family to identify their relative as the donor. There would need to be specific confirmation from donor families as to confidentiality – a leak of information would be quite possible.	

	Imperial will be leading the Communications Release Plan, but all hospitals are participating. There will be no communications/press releases unless by Imperial. Each hospital does however have a communications lead. It would be worth speaking to Simon Kay (SK) as he was involved in hand transplant and he can give guidance on how to deal with the press etc. SK managed to keep a press embargo for a week. Previous transplants have hit the headlines, but it is unclear whether there was a financial transaction between the press and the recipient. Anyone who needs to see a copy of the updated SOP/Protocol, contact DH. There is a practical issue around retrieval team availability. DH is trying to retain a full standby team. It is very likely that the first uterus retrieved will not result in either a transplant or live birth. **NRP** **Current Status in the UK** Oxford and Birmingham live, Royal Free soon to be live, Cambridge and Edinburgh ongoing activity at variable levels. There is now interest from other hospitals. **Status of the Business Plan** This has now been approved by Welsh and Scottish governments, it looks hopeful that the Irish Government will approve it, the UK government has not committed yet. KQ has made a commitment to support this development in the UK. Debbie Macklam has been appointed to progress. Every centre that is live has been asked to come up with numbers so that a near-exact cost of consumables can be predicted. At present, hospitals need to make a commitment upfront to make initial payments, and costs are reimbursed after sets are utilised. Despite the economic viability of this proposal, a final decision is still awaited from DH England. In the meantime, NHSBT has committed to support the development of NRP until national funding is required**.** **Non-transplant related research retrievals** Several research groups working together from Cancer Research UK have contacted the ODT Research team to see if they could receive samples from GI tracts. Their request includes whole stomachs. At this early stage they are unsure if they could find a surgeon to do the removal for them and have queried if the NORS teams could help. IC noted by email that there is already pressure on NORS teams before retrieving organs for research. The point was made that bowel must not be removed ahead of any other organs as there is the slight risk of contamination. It was raised that QUOD and INOAR are already possible routes for obtaining research organs.	

	Discussion points: • Should this be peer reviewed? We will have to grade projects purely on quality. Are we happy that our current method of grading projects is the correct one? • We need to know the scientific rationale behind the request for the whole stomach. Without that we cannot know if the request is justified • Neither the peer review nor Ethics have considered the impact on donor families or logistics • The rule of thumb should be that if there is any threat to organ retrieval for transplant, research retrieval can't proceed. There is potential to slow down the cardiothoracic team if what is removed for research is anything more than a biopsy • If a research team requires a stomach, they must come and collect it AP: A working group (PF, DH, IC) will meet to discuss this and come up with a proposal before next RINTAG **TA-NRP Review** This has been concluded by Alex Manara and the results will be published soon.	**PF,DH,IC**
7.	**INOAR – *Increasing the Number of Organs Available for Research* – RINTAG(19)30 (plus Appendices 1-4)** <u>Update and Next Steps for the Project</u> • A workshop took place on 3 October 2019 where Ian Bateman (Director of Quality at NHSBT and DI for NHSBT's HTA Licence) was in attendance, to gain assurance that the end to end process is robust and compliant with legislation • The INOAR project has encountered ICT delays meaning that the initial go-live date of 23rd October 2019 is no longer achievable. The ICT changes have a new scheduled release date of the 4th November, and after they have been delivered, a new go-live date will be set. • After go-live, a period of monitoring and evaluation will continue, to ensure continuous improvement GO wished to minute his thanks to LA, VG and Kam Rai (Project Manager) for all the work they have put into the INOAR Project, which has been substantial. GO and JF are both very grateful to the team who have managed to get this to the final stages. The delay to go live will not be long and will have had little effect. *Discussion Points:* • **Research heart perfusion**: LA noted that a NORS team would never be asked to do anything they are unfamiliar with ie. if an abdominal team were retrieving a heart for research, that heart would not be perfused. Active heart studies have been consulted	

	and have indicated that they think unperfused hearts will be usable. • **NORS team expectations:** NORS teams need to know that this is part of their job, and not to be done as a 'favour'. LA said that this will need to be taken up with Comms. • There will be occasions when cardiothoracic teams may wish to leave once they have retrieved the target organ or if the organ is clinical unsuitable. The wording on the INOAR SOP states that retrieval of organs for research should be treated as routine retrievals and cardiothoracic teams should treat them as such and undertake those retrievals prior to departure. **DCD Lung Removal** Regarding DCD lungs, LA had a conversation with MB and the conclusion was that lungs need to continue to be removed as they are currently. Given all the issues that currently surround DCD lung removal (e.g. reperfusion, anaesthetist availability), a question was raised if we should decide to use lungs from DBD donors in future. To make things simple it was agreed that lungs will not be reinflated in principle (unless adequately trained personnel is present, and this does not interfere with other clinical commitments). Participating centres have confirmed that they will take unperfused deflated lungs. Research centres will be notified that the lungs will not be reinflated or perfused. They can then decide whether to accept.	
8.	**Interpreting Research Restrictions RINTAG(19)31** The Human Tissue Authority's Code of Practice for Research has been in place for over two years. ODT Research's restrictions system records objections from the donor family to particular types of research (namely animal research, DNA analysis and the commercial sector) and passes these on to active studies. <u>Asks of RINTAG</u> • Should the definitions in the Research Information leaflet be more specific? • Should studies doing restricted research be allowed to accept organs with restrictions and allocate them to their unrestricted projects? • Should there be a hard line that organs with restrictions cannot be accepted by a study even remotely associated with those types of research? <u>Discussion Points</u> • Defining restrictions is difficult and the donor families' understanding of restrictions when they are in a time of huge emotional distress is almost impossible. Particularly in regards animal or DNA research, a lot of families will find these prospects unpalatable and would not be happy with the idea of their relative's organ(s) going to a study that is even remotely associated with that type of research, even if the organ is used in a project that doesn't involve them	

	• If different work packages of a particular study contain eg. animal research, these should be listed as separate studies to provide clarity and should be submitted as a separate study to RINTAG. • DNA analysis is not defined explicitly by the HTA. • Animal research is easier to define as studies must have a licence from the Home Office to do it. If a study has a licence, then it does animal research and should not accept any organs with this restriction. • Approx. 30% of research offers have at least one restriction on them. Animal research is the most common restriction. • Research should be carried out with donor families to determine what they understand by DNA analysis and Commercial research • RP suggested using the definition from QUOD's ethics for DNA analysis/commercially funded research • Table "Definitions" for the next RINTAG Meeting. Carry on as is until a new Definitions List is provided at the next RINTAG meeting.	**HC + HT to table the list of definitions.**
9.	**QUOD Report RINTAG(19)32** See paper for details on **QUOD Bioresource Key Figures, QUOD Donors in total and per region, QUOD Samples in Total and per Type, QUOD Biopsy and Incident Metrics, Consent for QUOD Research and Actual Quod Donors, QUOD samples issued to applications** <u>Key Points (for period May 2015 – August 2019)</u> • Biobank items issued to applications: 13,330 • Total number of research project applications: 55 • New applications (currently at preliminary stage): 14, including 2 being reviewed • Applications approved by the Steering Committee: 41 • Among the approved applications, 16 were completed by QUOD and 25 are in progress.	
10.	**The New NHSBT Strategy and Implications for Research and Innovation** Several RINTAG attendees have been involved in the development of the new Strategy. The themes are: • Service sustainability and responsiveness • Living and Deceased Donation • Recipient Living Donor and Transplant Outcomes • Research & Innovation • Organ Quality • Diversity & Inclusion A few more development sessions are planned, which will then be followed by writing and consultation processes.	
11.	**NIHR Funding Call for Transplantation** Several applications to go into various funding streams. The NHSBT R&D Office have organised a Patient and Public Involvement and Engagement (PPIE) meeting to discuss potential studies with recipients, donor families and members of the public, which is taking place on 11 October 2019.	

12.	**Clinical Governance Update RINTAG(19)33** RINTAG was asked to note the findings within this report and in particular consider clear guidance to the researchers to avoid misinterpretation of the restrictions. The Information Governance Team within NHSBT are working with the research team to agree the process AP: RB will investigate and come back to next RINTAG with any issues we need to address about this and if there are any other issues about RINTAG supported studies or innovations (DCD hearts, NRP).	**RB**
13.	**Any Other Business** AF was approached to do an article on therapeutics used during normothermic perfusion. A question was asked about the need for consent for images of organs whilst on the bench or on the machine perfusion. GO confirmed that no particular consent for those images is required (GMC has specific regulations about this which the researchers should consult). ***Heart Perfusion Studies*** Two hearts have been retrieved by Papworth thus far for the machine perfusion study. It was noted that there is a paediatric version of their machine available, which was discussed at paediatric NODC. Newcastle have removed a heart locally and used it in the cold storage part of their study – use of their perfusion machine has necessitated an amendment with the HRA which has only recently been approved. Updates on these two studies to be added to Agenda for next meeting.	**HC**
	Date of next meeting: 29 April 2020, The Principal Hotel, York	