NHS BLOOD AND TRANSPLANT
ORGAN DONATION AND TRANSPLANTATION DIRECTORATE
RESEARCH, INNOVATION AND NOVEL TECHNOLOGIES ADVISORY GROUP MEETING
Via Microsoft Teams, Tuesday 27 October 2020, 10:30 – 15:30
MINUTES

Attendees:

Gabriel Oniscu	GO	Chair, RINTAG
Liz Armstrong	LA	Head of Transplant Development
Richard Baker	RB	Joint Clinical Governance Lead
Hazel Bentall	HB	Lay Member
Marius Berman	MB	Associate National Clinical Lead, Organ Retrieval
John Casey	JC	Chair, Pancreas Advisory Group
Akila Chandrasekar	AC	Consultant Haematologist, NHSBT
Sarah Cross	SC	QUOD Representative
Ian Currie	IC	Chair, Retrieval Advisory Group
John Dark	JD	University of Newcastle
Clare Denison	CD	Innovation and Research Lead Specialist
Andrew Fisher	AF	NIHR BTRU Representative
John Forsythe	JF	Medical Director – OTDT, NHSBT
Peter Friend	PF	Chair, Multi-Visceral & Composite Tissue Advisory Group
Victoria Gauden	VG	National Quality Manager, OTDT, NHSBT
Dan Harvey	DH	National Innovation & Research Clinical Lead, OTDT
Debbie Macklam	DM	Senior Commissioning Manager, NHSBT
Jenny Mehew	JM	Principal Statistician, NHSBT
Elizabeth Murphy	EM	Lay Member
Jayan Parameshwar	JP	Chair, Cardiothoracic Advisory Group
Rutger Ploeg	RP	Director of QUOD
Susan Richards	SR	Operations, NHSBT (for John Richardson)
Paul Rooney	PR	Research & Development Manager, NHSBT
Maggie Stevens	MSt	Specialist Nurse, Research & Service Delivery
Michael Stokes	MS	Head of Hub Operations
Doug Thorburn	DT	Chair, Liver Advisory Group
Hannah Tolley	HT	Research Project Manager, NHSBT
Nick Watkins	NW	Assistant Director, Research & Development
Chris Watson	CW	Chair, Kidney Advisory Group
Michelle Willicombe	MW	BTS Representative
Heather Crocombe	HC	(Minutes), Clinical Support Services, NHSBT

No.	Agenda Item	Action
1.	**Welcome and Apologies** GO welcomed everyone to the meeting. Apologies were received from Ben Hume, Karen Quinn and John Richardson **Introduction to new Chair** JF advised that the new RINTAG Chair will be Gavin Pettigrew. All the applicants for the role were outstanding and the choice of Chair was one of the more difficult ones that JF has been involved in. JF wanted to thank GO for his outstanding RINTAG leadership, and for his involvement in the Clinical Teams Meetings, which have been key to the way in which we have managed the pandemic in the last few months. RINTAG has become	

	a very important group, and this is thanks to GO. JF expressed RINTAG's gratitude for this.	
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 29 April 2020 – RINTAG(20)(M)1**	
3.1	**Accuracy of the Minutes** The Minutes of the meeting held on 29 April 2020 were deemed to be a true and accurate reflection of the content of that meeting. Minutes approved.	
3.2	**Action Points from the Research, Innovation and Novel Technologies Advisory Group Meeting held on 29 April - RINTAG(20)(AP)1** **AP6 - Non-Transplant Related research retrievals** *Action: DH to set up a working group to discuss this, and report back at the next RINTAG Meeting* *Background*: One of the questions asked at the last RINTAG Meeting was whether we would support research retrievals as a two-pronged affair, (i) to increase the competency and experience of the Teams, and (ii) to facilitate the use of organs for INOAR. DH advised that this Working Group has been pushed down the priority list due to recent events. Some progress has been made in organising the group, but the first meeting has not yet taken place. There is a plan to get this resolved as soon as possible. DH will report back at the next RINTAG meeting, or earlier by separate email.	**DH/JC/IC/PF**
	AP4.2 *Background:* Islets will be discarded if there is no consent for research. If an organ has been accepted for clinical use, it undergoes isolation and the resulting preps go under the Regulations for each lab and MHRA. If the prep is insufficient for clinical use, the labs can distribute organs to the network of studies which they support. RINTAG needs a list of projects that are supported in this way and how many preps are allocated to each study, to understand the full picture of organ utilisation for research and minimise the loss of potential islets for research use. ***Action: JC to take this issue to the Islet Consortium and Islet Steering Group, and report back.*** *Add to next agenda to be addressed*	**JC** **HC**
	AP8.2 *Background:* A paper was tabled at the last meeting from R&D, suggesting that QUOD could be used in a wider way to facilitate research and organ allocation. It was considered at the last meeting that this was premature. ***Action: GO to prepare a paper highlighting how QUOD can be used to facilitate research. (Agenda item 8.2 today)*** Given that INOAR is not yet up and running and that the Hub is going through a period of change, now is not the time for QUOD to take over allocation responsibilities. GO will brief GP offline about future plans. *Points raised:* • RP, in close collaboration with HT, CD and others, is looking at first steps to see how we could pilot a more general allocation system on a national	**GO/GP**

	level, with a 24/7 individual on call who could select organs based on RINTAG priority (to shorten the transport time)	
	AP13.2 Shipment of Organox devices between Centres *Background:* There have been instances where organs were perfused but didn't meet transplantation criteria. However, in those situations there were other interested parties, but problems were faced with the transportation and transfer of organs. The question was how we were going to engineer those transfers so that we maximised utilisation of organs. ***Action: CW and others to look at challenges faced, coordinate a response and incorporate this into work already completed on blood utilisation. Issue to be tabled at LAG and RINTAG*** **RINTAG(20)21** CW got together a group of representatives from each transplant centre to go through various options to remedy this issue. It was decided that for a trial period of 6 months, the receiving centre would travel to the donor centre, collect the liver on Organox but take their machine as a "swap". Organox were happy to facilitate this. It was agreed that various things must accompany the machine: vessels from donor, sample of donor blood, spleen, HTA(A) form and retrieval form, and a printout of the biochemical parameters that had been recorded on the machine. A liver has not yet been moved during that 6-month trial period. The process was agreed at LAG, but COVID came soon after, so this has not yet been put into place properly. It may be worth putting this in front of LAG again.	**CW**
4.	**Research Activity**	
4.1	**Consent** **Research Consent/Authorisation Rates** **RINTAG(20)22** Please see paper for full details. Key points: • This paper summarises how generic research consent/authorisation rates have changed over the last ten years in the UK. Families can give generic consent/authorisation for research use of any organs that are found to be unsuitable for transplantation. Families are only asked this question if consent/authorisation for transplantation has already been obtained. • Research consent/authorisation 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 2011 to 31 July 2020 <u>Conclusions</u> The overall UK consent/authorisation rate for research was 83% in 2011 and has risen to 90% January – July this year. Consent/authorisation rates in 2020 so far have varied by nation from Scotland at 79% to Northern Ireland at 92% DH advised that he is in the process of setting up a service evaluation to look in detail at both staff and family responses to being asked about research consent, both specific and generic, relating to deemed consent. This evaluation will help to establish why families say Yes/No in certain situations. This will be a qualitative approach.	
4.2	**Availability of Organs for Research** **RINTAG(20)23** This paper combines the data provided for Availability of Organs for Research paper generally prepared by Statistics and Clinical Studies, together with data from the Research Team, which when combined has provided richer data. Please see paper for full details. Key points: • 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 such organs that were offered to and received by research studies within the first 7 months of 2020 Conclusion • Overall, the total number of organs retrieved and not transplanted has steadily increased over time. In addition, the proportion of these organs that have consent/authorisation for research has increased to 95% for 2019. However, the impact of Coronavirus has meant that the number of organs retrieved and not transplanted in 2020 to date has been lower than usual • Currently in 2020, 156 organs have been used for research to date, which again is lower than usual due to Coronavirus • The proportion of discarded organs where generic research consent/authorisation was ascertained is substantially higher than in previous years, 13% in 2015 compared to 46% for the period January to July 2020 • During the period January 2020 to 31 July 2020, 254 retrieved but untransplanted organs were offered to researchers through the National Allocation Scheme (NAS). 133 of the 254 organs offered for research were accepted by studies on the ODT Research Registry. In addition to these 133 organs used for research, an additional 23 were used but were not offered through the NAS • Utilised research organs were distributed across many studies GO thanked JM for putting this very useful data together. *Points Raised* • When INOAR kicks in, we will have even more organs that will go to waste • It had previously been mooted that QUOD become the national biobank for discarded organs – however neither QUOD nor any other biobank in the country will have capacity to store the likely number of discarded organs retrieved for research. The solution would be to create a new much larger biobank • It is beholden upon the cardiothoracic community to make the most of organs retrieved for the purposes of research	
4.3	**Impact of COVID-19 on Research Activity** **RINTAG(20)24** The purpose of this paper is to provide an update on the impact of Coronavirus on research activity. The COVID pandemic began to have an impact on ODT Research in early March 2020. Revised donor selection criteria affected the number of organs available for transplantation, and consequently research. Almost all studies shut down whilst universities were closed during the initial wave in the spring, and researchers instructed to focus on COVID-19 related research. We have seen recovery as restrictions were relaxed over the summer, with the number of research offers returning to pre-COVID levels, matching the recovery of donation and transplantation. At present, all studies receiving organs through generic consent/authorisation and the NAS have reopened. Only a small number of service evaluations or specific consent/authorisation studies are yet to reopen. These are reviewed weekly at the Transplant Development & Research recovery programme board, and are: • Study 58: ENLIGHTEN lung project • Study 75: the PITHIA clinical trial • Study 76: Ex-Situ Normothermic Machine Perfusion	

	• Study 80: Uterine Transplantation	
5.	**Study Re-Ranking RINTAG(20)25** HP presented the most recent study re-ranking spreadsheet. GO raised an issue regarding an Edinburgh Study (ranked 56) which is listed as not being peer reviewed/externally reviewed –is an MRC funded study, so it is externally reviewed. HT will amend this. No other comments on the re-ranking document	**HT**
	New Studies and Resubmissions **Cover Letter RINTAG(20)25(a)** • Study 107 *(Delivery of Adipose-Derived Regenerative Cell (ARDC) Therapy during Ex-Vivo Normothermic Perfusion of Kidneys)* No comments, study approved • Study 108 *(AboutFace – The Affective and Cultural History of Face Transplants)* No comments, study approved • Study 109 *(Statins for Improving Organ Outcome in Transplantation (SIGNET)* JD to present – see below • Study 21 *(Development of Pre-Transplant Normothermic Perfusion Reconditioning for Human Livers donated after Circulatory Death)* CW advised that the University of Cambridge might need a longer end date than stated in the paper (31.12.2020), possibly a further three or six months, CW will advise the Chair. • *Studies 20, 52 and 66 (Improving Transplant Outcomes by Novel Organ Preservation Protocols)* No comments, studies approved • Study 63 *(Transplanting the Untransplantable – Extending Antibody Incompatible Transplantation Using a Normothermic Perfusion Model with Cytoprotective Agents)* No comments, study approved • Study 2 *(Study of Renal Ischaemia Reperfusion Injury and Its Amelioration)* No comments, study approved **Study 107 RINTAG(20)25(b)** See above. Approved. **Study 108 RINTAG(20)25(c)** See above. Approved. **Study 109 RINTAG(20)25(d)** See below. Approved. **SIGNET (Information confidential to RINTAG Group)** Members viewed a presentation by J Dark (being shown at all Advisory Groups), outlining the findings from a study published by Karl Lemstrom from Helsinki in 2019. This led to the design of the SIGNET Study which received approval in October. The Helsinki Study involved 84 recipients, of whom half received organs from donors given Simvastatin and analysed the outcomes on the heart and the effect on all other organs. It was noted that there was no harm to lung recipients, and Simvastatin may have helped improve outcome, with a halving of PGD rate. The SIGNET Study is envisaged to start in April 2021 using 2600 adult DBD donors, for a period of 4 years, to be randomised after consent for donation and research	**CW/GO/GP**

to receive Simvastatin 80mg as a single dose. All potential recipients will receive information about the study, with a description of the potential benefits - there is unlikely to be any risk to recipients and the intervention will occur before the potential recipients have been identified so no consent, additional data or samples will be required from the recipients. This will be the largest donation intervention study in the world.

The following were confirmed:

- Simvastatin 80mg given as a single dose is a safe drug to use with no measurable amount transferred to the recipient. The delay between consent and retrieval is usually around 24 hours, so by the time the organ has been flushed and on ice, essentially no drug will be present
- As this Study will last for 4 years, J Dark confirmed that he would be happy for donors to take part in parallel studies (eg. PITHIA study), and there will be no problem with co-recruitment
- Some details still need regulatory approval, once we have this, we can talk to SNODs and CLODs on the front line

JD is looking for RINTAG approval to this study – after discussion, RINTAG was happy to give approval.

GO congratulated J Dark for getting this study to the "green light" stage.

It is hoped that NIHR will see that organ donation and transplantation is a fertile area for future investments

DH thanked HT, MS and the research team for their help in ensuring that the study fits with the operational requirements of NHSBT.

Qu. Is this study powered on cardiac utilisation?
No, it is powered on a combined end point of death, mechanical support and haemofiltration following cardiac transplant.

Wearable Tech Protocol **RINTAG(20)25(e) and (f)**

This relates to wearable, hands free technology for live streaming and communication between organ retrieval and remote transplant teams in the United Kingdom. The retrieval surgeon wears a glass-mounted camera, a microphone and headphones. Software will allow connection via 3G, 4G or Wi-Fi between retrieving and transplanting surgeons, using a designated single-use telecom secure link.

Papworth charity funds have already been provided (£3260) for hardware, software, training and ongoing support.

The study has been given approval by Information Governance and Information Security. To avoid any governance issues, images will not be recorded but can be shared (under GMC Article 51) so long as they do not contain any identifiable information.

MS/MB

MS would like to catch up with MB when he is back from leave, to agree a system for cascading information out to SNODs and identify any areas of risk in theatres, including theatre staff giving consent to being filmed.

	We need to thank Barry Richardson for the huge amount of work he has done to expedite the Data Protection Impact Assessment for this study. There were no objections, and RINTAG is happy to support this study.	
6.	**Innovation**	
6.1	**DCD Heart Activity** **RINTAG(20)26** This report contains information on DCD heart activity from 1 February 2015 – 30 June 2020. Please see paper for full details. Key points: *(i) Outstanding DCD heart forms for the period 1 February 2015 – 30 June 2020, as at 8 September 2020* *(ii) DCD heart transplant activity, by quarter and centre* *(iii) DCD heart activity by period and centre* *(iv) DCD heart patient outcomes at 30 days post-transplant by centre* *(v) DCD heart offers recorded on the UKTR as being made to participating centres between 1 April 2018 – 30 June 2020, and results* *Qu: would attendees still like to see this DCD Heart Activity paper on future Agendas for information?* Agreed that yes, please make available for information at future meetings.	
6.2	**NRP** **RINTAG(20)27** This paper provides an update following the service evaluation undertaken by Edinburgh and Addenbrookes and regarding the current position of A-NRP in relation to funding and future development in the UK Please see paper for full details. Key points: • There is a lack of substantive funding, and A-NRP is being supported on an ad hoc basis by Scotland Wales and N. Ireland health departments • A Steering Group for A-NRP has been set up (chaired by Chris Watson). The initial meeting is on 2 November. • The draft purpose and scope of the A-NRP Steering Group is to: • Review, refresh and enhance the 2018 business case, to support continued funding discussions • Provide management and oversight for the safe and effective delivery of A-NRP services in line with available funding commitment • To monitor the financial governance of funds allocated to support A-NRP *Conclusion* The service evaluation for A-NRP has concluded, and there is now a decision point regarding the future funding and commissioning of A-NRP. Without identified recurrent funding from 2021/22 it will be difficult to continue to deliver the benefits of A-NRP in a sustained manner, and the ability to widen the use of the technology will be impacted.	
7.	**INOAR**	
7.1	**Increasing the Number of Organs available for Research** • INOAR was due to go live just before the last RINTAG meeting in April – Coronavirus then hit, so go-live was paused. • For the sake of clarity, the delay has only been due to COVID • CD has been working with the OTDT recovery team to get this back on track • Proposed go live now due Wednesday 13 January	

	GO wished to give huge thanks to LA and her team who have made this happen.	
7.2	**Updates to the Research Organ Allocation Policy (POL263) for INOAR** **RINTAG(20)28** Please see paper for full details on changes (highlighted in grey on that paper) RP thanked HT for drafting this paper, which is very helpful *Discussion Points:* *Clause 4.1 In accordance with the Human Tissue Authority's Code of Practice on Research, donor families should be provided with information to support the consent/authorisation process and given the option to withhold consent/authorisation for one of more of the following:* • *Human tissue in animals* • *Genetic testing* • *Commercial sector (including fees for cost recovery)* The commercial sector says that commercial companies can support healthcare research in several ways, one of which is to buy samples for research and take them away A research tissue bank is not-for-profit and non-commercial but has been made to sound such in the paper. It comes down to the family's choice to restrict, and what they understand that restriction to be, honouring those restrictions and the family's wishes It would be helpful to know how much benefit comes back to the NHS from commercial use It would be a good idea to set up a Working Group to finalise Definitions in this paper. Definitions have been previously agreed, but we need to revisit. (Liz/Clare/PF/AF/HB/JC/DH/VG/RP/RB) plus someone from the Operations Team – SR will recommend a Specialist nurse or Specialist requestor. This needs to be wrapped up before January 2021.	**LA/CD/PF/AF/HB/ JC/DH/VG/RP/RB**
8.	**QUOD Update**	
8.1	**QUOD Report RINTAG(20)29** After a brief pause between March and the end of July 2020 QUOD has restarted. RP wished to thank the Research Team and the QUOD Team for their hard work to proactively prepare for QUOD to restart. Thanks to Liz/Clare/Hannah and all the QUOD team for all their hard work Sandrine Rendel has now left QUOD and has been replaced by Sarah Cross, a senior research scientist. Tomas Surik (Data Manager) has moved on, and has been replaced by Sheba Ziyenge who has a neuroscience background	

	Please see paper for details. QUOD bioresource key figures: • Donors: 5,045 • Samples: 91,601 in total, including: • Blood: 47,598 samples • Urine: 11,068 samples • Kidney: 12,749 samples (6,457 biopsies) • Liver: 6,728 samples (3,381 biopsies) • Ureter: 7,340 samples (3,709 biopsies) • Spleen: 3,767 samples (3,767 biopsies) • BAL: 137 samples • Heart: 2,214 samples (1,113 biopsies) • Biobank items issued to applications: 22,964 • Total number of research project applications: 63 • New applications (currently at preliminary stage): 12 • Applications approved by the Steering Committee: 51 • Among the approved applications, 36 were completed by QUOD and 15 are in progress • NHSBT has confirmed that they will continue to support QUOD until 2025 • There have been two biopsy incidents, one has been defined as a serious adverse event, and the other as a serious adverse reaction. A biopsy was taken from the wrong part of the kidney and there was recipient impact.	
8.2	**How QUOD can be used to facilitate research RINTAG(20)30** QUOD now has 24/7 availability of technicians in Oxford and Newcastle, who are available to call for any project which requires a whole organ for research. QUOD also attempts to share whole organs with other projects, eg. three centres can use one heart	
9.	**Challenges for researchers at local level where research restrictions are in place** GO advised that one of his collaborators in Edinburgh who have restrictions on their research study, were approached by both university lawyers and the R&D office. It was felt that specific consent should have been obtained because samples are required for genetic research/DNA testing. GO has done his best to explain that we have discussed this with HTA and others and are compliant but is still awaiting a response from the legal people. *Qu. How do we make this completely clear at grass roots level? How do we resolve this?* GO suggested some sort of communiqué out to R&D Departments in universities and in the NHS, stating that RINTAG needs to ensure that all legal processes have been looked at and that studies are compliant with current regulations and law. HT and MS are the initial points of contact for new researchers and when having initial conversations with these researchers, try wherever possible to have a representative from their sponsor (usually the local R&D) on these calls.	
10.	**Heart Perfusion Studies**	
10.1	**John Dark (HOP Study Update)** • The HOP Study has been running for 21 months (since RINTAG approval) and 17 months since local approval • In those 17 months, only 5 perfusions have been carried out	

	• The delays to INOAR have been a serious headache/disastrous for this study – 11 organs have been missed out on in August	
10.2	**Simon Messer (ES-NMP Study Update)** MS advised that the ES-NMP study has not yet restarted, so far as the Research Team is aware. Steven Large – potential new study HT had a preliminary conversation with Steven Large yesterday. He is looking to work with *AstroZeneca to trial a Micro R&A treatment* on hearts whilst they are being perfused. Research Team will review all the information provided. If they can use INOAR to obtain all the samples they require, this will make it much easier. The point was made that the retrieval service is a national retrieval service, so if one particular retrieval team needs to be on call to go out for certain hearts, this is going to cause a real problem and will have implications for several teams	
11.	**NHSBT Clinical Trials Unit – working with OTDT RINTAG(20)31** *The NHSBT Clinical Trials Unit's (CTU) mission is to work with investigators to design and manage clinical trials in therapeutic areas within NHSBT's remit, which include trials in organ donation and transplantation. The aim is to provide evidence for treatments and techniques that will increase the number of transplantable organs and/or improve patient outcomes.* AD presented a proposal paper to RINTAG for consideration. If agreed, the proposal will be implemented, with any suggested amendments. We need to be mindful how we give everyone a fair share of this. It could be seen as a way of promoting the CTU. CTU need to be seen to facilitate research and should not come across as being restrictive. *Qu. What is your capacity at dealing with simultaneous studies?* Recently been working on 4 applications at once, have capacity to support simultaneous studies at the same time. After further discussion, RINTAG was happy to support this proposal.	
12.	**Clinical Governance Update RINTAG(20)32** No update or comments for Clinical Governance at today's meeting.	
13.	**NHSBT IT Update RINTAG(20)33** This paper has been circulated to update attendees on where we are. No comments raised.	
14.	**Sharing Donor PID (SNBTS Concerns)** Sharing of Donor PID: this has now moved forward significantly in the last few weeks. Concerns surrounding wording were previously raised by SNBTS, but these have now been resolved, and the English and Scottish Research Information leaflets have been combined into one leaflet.	
15.	**Cost Recovery of Organs/Tissues used in Research** This is a project that CD and PR have been working on with their wider team and the business recovery programme. CD and PR presented various options to the	

	wider Business Developments Team, and the BDT have opted for a tiered approach, where studies will be split into specific categories. CD asked for volunteers to work on the implementation of this with him, and it was agreed that the same members who had agreed to work on Definitions in point 7.2 would also help CD with this work.	**LA/CD/PF/AF/HB/ JC/DH/VG/RP/RB**
16.	**Any Other Business** ODT Priority Areas and Challenges **RINTAG(20)34** **Members held a confidential conversation, not for minuting.** **Thank You** Today will be the last RINTAG Meeting for both HB and NW, and they were both thanked for the time and dedication they had given in order to enable RINTAG to become the very important group it is today. PF wished to thank GO on behalf of the RINTAG membership for his leadership, vision and good nature during his term as Chair.	
	Date of next meeting: Proposed date is Tuesday 25 May 2021 – to be confirmed by new RINTAG Chair	