NHS BLOOD AND TRANSPLANT

MINUTES OF THE RESEARCH, INNOVATION AND NOVEL TECHNOLOGIES ADVISORY GROUP HELD AT 10.30 A.M. ON FRIDAY 11 MAY 2018 The Wedgewood Room, The Principal York Hotel, Station Road, York YO24 1AA

PRESENT:

Mr Gabriel Oniscu	GO	**Chair**
Ms Oluwayomi Adebaju	OA	National Research Manager, NHSBT (telephone)
Mrs Liz Armstrong	LA	Lead Nurse, Service Development
Mrs Hazel Bentall	HB	Lay Member
Mr John Casey	JC	Chair, Pancreas Advisory Group
Mr Anthony Clarkson	AC	Assistant Director for Organ Donation & Nursing, ODT
Prof John Dark	JD	National Clinical Lead – Governance, ODT
Prof Andrew Fisher	AF	NIHR BTRU
Prof John Forsythe	JF	Associate Medical Director, ODT, NHSBT (telephone)
Prof Peter Friend	PF	Chair, Multi-Visceral & Composite Tissue Advisory Group
Ms Victoria Gauden	VG	National Quality Manager, ODT, NHSBT
Mr Dan Harvey	DH	National Medical Education Lead for Organ Donation
Prof John O'Grady	JOG	Chair, Liver Advisory Group
Ms Sally Johnson	SJ	Director of Organ Donation & Transplantation
Mrs Maria McGee	MMG	ODT Research Project Manager
Mrs Jennifer Mehew	JM	Statistical & Clinical Studies, NHSBT
Mrs Elizabeth Murphy	EM	Lay Member
Ms Karen Quinn	KQ	Assistant Director for Commissioning, ODT
Mr David Roberts	DR	Observer
Ms Maggie Stevens	MS	Specialist Nurse Research & Service Delivery
Prof Chris Watson	CWa	Chair, Kidney Advisory Group
Mrs Claire Williment	CWi	Head of Transplant Development, ODT

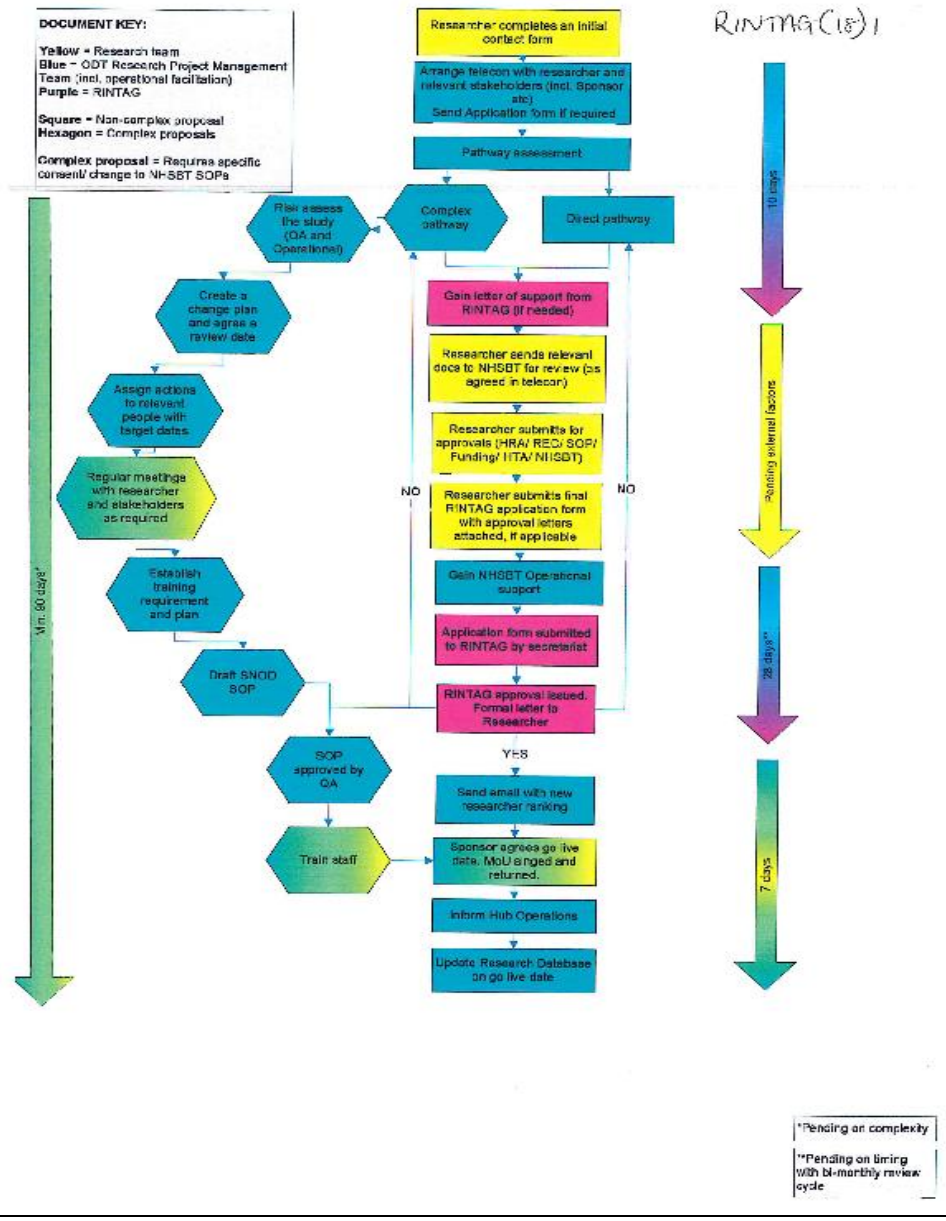
APOLOGIES

Dr Rebecca Cardigan	RC	Head of Components Development, NHSBT
Dr Jayan Parameshwar	JP	Chair, Cardiothoracic Advisory Group
Prof Rutger Ploeg	RP	Chair, National Retrieval Group, Director of QUOD
Mr Michael Stokes	MS	Hub Operations Manager, ODT, NHSBT
Dr Nick Watkins	NW	Assistant Director – Research & Development, NHSBT

IN ATTENDANCE

Miss Heather Crocombe	HC	Clinical & Support Services, NHSBT

		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 today's agenda** AF stated that he, JD and JC are involved in one of the studies being discussed and therefore there is a conflict of interest. At that point AF JD and JC will briefly leave the meeting.	
3	**Minutes of the Research, Innovation and Novel Technologies Advisory Group Meeting held on Monday 9 October 2017 RINTAG(M)(17)(2)**	
3.1	**Accuracy of Minutes** Minutes of the previous meeting were reviewed and were deemed to be an	

		ACTION
	accurate reflection of what was discussed at the previous meeting	
3.2	**Action Points from the Meeting RINTAG(AP)(17)2** All actions completed – nothing to add.	
4	**LEAN Event**	
	Actions following event (A3, flowchart, KPI's) A LEAN Event was held in November 2017. The purpose of the event was to look at how best to streamline the research application process. MMG advised that the event, held over two days, was very productive, and there were representatives there from the research community, Quality Assurance and other key stakeholders in the research application process. MMG shared a video which has been created to raise awareness of the remit of RINTAG (copy available on request). MMG presented a flowchart showing the new application process which has been developed. 	

		ACTION
	Actions following the event included: • New research application process, presented to and approved by RINTAG • Communicate the new research application process to external stakeholders (researchers and transplant surgeons, sponsors) • Development and trial of electronic forms (Cognito) • Confirm Information Governance risk regarding the use of Cognito • Discussion with PDS team regarding roll out of specific research training • Communication of the purpose of RINTAG and ODT Research via a mission statement • Create FAQs for RECs • Prepare organs for research cost recovery paper • Control the new research application process on QPulse and update the ODT website • Create an animation video for research community and put this on the website, circulate to RMs and SNODs for information • Training on new controlled docs as appropriate (MPD1029) • Development of ODT Research KPIs • forms All actions have been duly completed and the new process went live on 20 February 2017. Progress following implementation will be monitored monthly, and will be reported on, on a quarterly basis. *Also see point 5 below.*	
	Review of Research Matrix RINTAG(18)3 MMG said that concerns have been raised by several researchers that the "highest ranking studies" could disadvantage others. Various researchers are concerned that they are not receiving sufficient organs because they are ranked low in the organ allocation scheme. The criterion adding to this concern is: *Timescale from start of study to increase number of organs available for transplantation*. The researchers felt that the end date set by researchers is subjectively judged or can be manipulated. MMG asked: *Should that criterion remain? Should it be removed? If it is removed, what will it be replaced with?* CW stated that as well as research ranking, geography will be a factor as researchers will have to consider geography and the availability of staff out of hours. Currently there is a scoring system	

Time-scale from start of study to increase number of organs available for transplantation	Mark	Score	Definition
Within 18 months	A	4	It is estimated that the project will increase the number of organs available for transplant within an 18 month period from the start of the study. This includes either directly (e.g. through novel forms of organ preservation making previously unsuitable organs safe for transplantation) or directly (e.g. through reducing the risk of patients developing organ failure or extending graft survival rates).
19 - 36 months	B	3	It is estimated that the project will increase the number of organs available for transplant between 19 and 36 months from the start of the study
> 37 months	C	2	It is estimated that the project will increase the number of organs available for transplant after 37 months or more from the start of the study
Not applicable	D	1	The study is not intended to increase the number of organs available for transplantation either directly or indirectly.

		ACTION
	RINTAG is asked to agree: 1. If the scoring criteria should be changed? 2. If so, how should the scoring criteria change? 3. If the scoring criteria should be removed? 4. If so, should it be replaced with some other parameter? There is a potential risk that if milestones within individual studies are not met, funding could potentially be removed from research studies. Following discussion and review of relevant Statistics and Clinical Study papers, it was agreed that the current allocation scoring system would remain unchanged.	
5	**Research Activity – Statistics & Clinical Studies Update RINTAG(18)4**	
	Consent ***Research Consent Rates from Actual Donors*** JM presented a paper which summarised how research consent/authorisation rates for organs from actual donors have changed over the last ten years in the UK. Overall UK research consent/authorisation rates for solid organ donors have increased from 80% in 2008 to 93% in 2017. Families give generic consent/authorisation for research use of any organs that are retrieved for the purposes of transplantation and subsequently found to be unsuitable for use. England & Wales have had the highest consent rates over the past 4 years ranging from 91% to 95%. Northern Ireland has seen an overall increase in research consent rate since 2008, although it remains lower than the rest of the UK at 83% in 2017. The rate for Scotland rose from 81% to 90% between 2015 and 2017. DH made the point that we should aim to embed research studies as a normal and usual part of the consent process. Families are usually keen to help in any way they can, and this would include research. MS said that conversations for research donation are now included as part of SNOD cohort training and yearly update training. **Two Month Review – Research Allocation Scheme** (*also see point 4 above)* This paper presented the results of a second two-month review to determine the effectiveness of the research organ allocation scheme. Prior to the new research allocation scheme, research organs were offered to studies on a geographical basis: now studies are ranked in order of priority. Please see attached paper for data. RINTAG(18)4 RINTAG(18)4 Allocati GO asked if we should use QUOD as the infrastructure which says that any organ which is not used for transplantation or research can then be "banked" with QUOD for availability for studies who require tissue and partial organs? Attendees agreed that this would be a good plan, however problems can arise	

		ACTION
	because some studies don't have out of hours capacity within their agreed remit. MS and MMG agreed that they need to advise researchers that overtime and out of hours capacity needs to be built into their standard practice. It was noted that any changes to the offering scheme need to be taken back to Hub. The 2-month review data was collected at the same time period in 2017. In both 2-month review periods, acceptance of organs for research was highest midweek and within core working hours. JD highlighted that the figures within this paper confirm the small numbers of cardiothoracic organs available for research via the generic route. The acceptance rate for cardiothoracic organs offered for research is 100%. JF highlighted a very clear message coming from this data, in that very often the research studies only accept organs for transplant within core hours Monday to Friday. If a study might potentially have transplantation as an end result, those studies need to be able to accept organs 24/7. JF suggested that if a team continually turns down organs they may in future drop down the priority list. **Conclusion:** • Whilst 91 (128) of organs with consent for research were offered, 43 (31%) were not used • 111 organs were offered through the research organ allocation scheme, 72% of which were used • Utilisation of offered research organs appears to be higher between 9am and 9pm, and mid-week • The average number of responses per offer was 1, which gave studies a good chance in receiving an organ if the study was active. This meant that studies that were lower in the ranking were still able to receive an organ. **Availability of Organs for Research** In the last year there has been a large decrease in the number of organs that were accepted for research and a higher discard rate. The paper details numbers of organs accepted and declined for research broken down by organ type. The decrease in the numbers of organs offered and accepted for research is in the main liver and kidneys. *Questions raised included?* *Do we have data on offering sequence?* *Do we know why organs were turned down?* *Was cost exorbitant in shipping organs?* *Differential consent for different organs?* We need to understand what happened to the number of organs which weren't placed. VG made the point that some studies are shown as transplantable studies, so they would normally be the ones to receive the organs "top of the list". The onus should be on the researchers to be upfront and honest about what they want to do. GO proposal: *Should a study be obliged to transplant at least one study per year, and if they fail to do so, be placed down the list?* CW and Mike Nicholson together with look at the potential to make improvements as mentioned above	**CW/MN**

		ACTION
6	**HTA Form – Perfusion Data Collection** JM presented an exciting development, that HTA forms are being made electronic. JM talked the meeting through and HTA(A) and (B) forms and also the new electronic prototype form which John Asher has formulated. JM asked attendees to check that these new forms contain at the very least all the fields which RINTAG woould like to see included in the electroinic forms. SJ asked: Should we, as well as the box which records ”time of arrival of organ at theatre” also have a box which records ”time of organ arrival at hospital”? JF questioned that this would not add value to the forms, and was hesitant of adding too many boxes/questions CW advised that the new HTA electroinc forms would need to be completed in their entirety including a signature prior to submitting. It will not be possible to press Submit on the forms until every mandatory field had been completed. JM to send the link to both forms to attendees for comments and feedback.	**JM**
7	**Novel Transplants – Uterine Transplant and Olfactory Bulbs**	
7.1	**Uterine Transplants** <u>Deceased</u> Isabel Quiroga on call/operating and unable to join meeting GO advised that the deceased donation team have indicated that they would like to pursue a live donation programme in addition to \ deceased programme. GO advised that hospitals involved no longer wish to do a “dry run” of a deceased uterus donation. JF questioned this, because the deceased donor dissection was supposed to be a safety net and to verify that the technique had been properly agreed. Both hospitals’ representatives had been to Masterclass and have seen the relevant dissection KQ advised that she is still awaiting to receive reassurance that there will be no further costs with the introduction of a deceased donation programme. **Action: GO to go back to the Units involved and say that the matter has been discussed at RINTAG, that he understands units want to have a change of direction, and that we need more details before we can allow that to happen** <u>Live</u> **Nick Karydis RINTAG18(5)b** GO introduced NK. NK is a consultant transplant surgeon at Guy’s. NK, together with a group of clinicians from Guy’s and St Thomas’, are planning to develop a living donor uterine transplant (LTUx) programme, which would provide the unique treatment to women with absolute uterine factor infertility (AUFI) at a local and national level. NK’s aim is to inform RINTAG about the recent developments in this direction, to ask permission from RINTAG and explore opportunities for further support from RINTAG. It is possible that training will be carried out on cadavers.	**GO**

		ACTION
	 RINTAG(18)5(b) Living donor uterine NK explained the benefits of live uterine transplantation as opposed to deceased in particular completion of donor characterisation. The procedure for living donation of a uterus has now been reduced to 4-5 hours from the 10 hours it took initially This live uterine programme is very much still at the early stages of discussion. Funding has not been secured for a live uterine programme. NK and his colleagues plan to discuss the intended programme with NHS England. A local charity has expressed interest in investing in the programme and the intention is to also approach local commissioners. Mentoring has been secured with Dr J Fronek (Associate Professor, Head of Transplant Surgery Unit, IKEM Prague). Dr Fronek's Unit is one of two major centres for UTx in Europe. Professor M Olausson (Gothenburg) and Professor Mats Brannstrom (Gothenburg) have also offered their support to the programme. NK will be travelling to Prague more regularly to follow the progress of the team there. SJ: Raised that waiting lists for unusual transplants are held locally rather than nationally. A lot of women will see this as their only chance to have their own baby so recipients need to be selected very carefully and their expectations need to be managed. Any recipient of a uterus from a living donor will receive massive media attention and intrusion, and must be aware of this and able to cope with it. CW asked NK to keep in touch with herself, MS and MMcG, and NHSBT Comms Team with updates and developments *Summary of RINTAG view:* • *Interest noted and look forward to further developments* • *Encouraged by development* • *Should communicate and collaborate with UTx team at Imperial/ Oxford* • *Continue to support innovation in transplantation* • *Strongly advise a single patient selection across all groups*	**NK/MS/MMMG/NK/NHSBT Comms**
7.2	**Olfactory Bulbs** • One successful Olfactory bulb retrieval to date • Visible cells retrieved CW thanked MS, MMG and others who contributed to the success of this programme and first retrieval and recognised the huge amount of work that has been put into this programme. SJ asked CW to prepare and send her a Celebrating Success email.	**CW**
7.3	**Face Transplant** MS and MMG attended conference. Early exploratory meeting with key stakeholders, funding identified as being a potential challenge	**CW**

		ACTION
8	**INOAR – *Increasing Number of Organs for Research*** Update on progress RINTAG(18)6 INOAR May 11th RINTAG - F INOAR's focus is to increase the number of organs available for research and to ensure that as many organs as possible are used for research. The second aim is to ensure that a donor's/family's wish to donate for research purposes where transplant is not an option are honoured wherever possible. The extension of the Liverpool Research HTA Licence (12069) to permit the removal of whole organs for research will enable organs to be retrieved from the 41 QUOD hospitals for the purposes of research. Activity will be limited under the new Licence procedure to remove only organs/tissues that NORS Teams are currently trained and competent to remove. Development will simplify the consent process and the aim is that specific consent for organs to be removed for research will no longer be required. GO confirmed that RINTAG will continue to give support to this project. JD is presenting an update to SMT May 2018. An allocation priority has been proposed, taking into account transplant and clinical tissue banking requirements and the existing RINTAG research allocation framework (please see attached paper for details). Changes to the consent process will be required and software development required to support INOAR. Required changes to the system may not be implemented until the end of 2018.	**AC/JD**
9	**Studies for approval and Information** *Conflict of interests on this study - relevant parties left the room* One study up for resubmission: *Active up and running study in Newcastle is looking to extend into several sites. RINTAG asked to approve further extension into northern region, Yorkshire region, north west region (20+ sites). No objections. Request approved.* <u>Application to EU/International Multi Centre Grants</u> Horizon 20:20 Project has approached GO. GO could see a lot of positives in the project : however the timeline for the programme was very short. DH advised Horizon 20:20 will come back to RINTAG if and when they get funding.	
10	**Operational Issues** Working with research team at Imperial on how introduce thank you letters from researchers to donor families.	
11	**Lunch**	

		ACTION
12	**NRP Service Evaluation Update** NRP now been performed in Harefield. Consensus was that this could have been performed more proficiently. Perfusion is being increasingly used in a variety of transplant settings. Questions will be raised as to the accreditation and training of perfusionists. Requirement to demonstrate that a clear training process is in place. Perfusionist role to be defined that is fit for purpose for the future. This needs to encompass cold and warm perfusion. Mobile perfusion units are all run by qualified perfusionists, static units not always. We need to be able to show adequate training of all related staff to use perfusion equipment. JD will report back at next RINTAG what has been done in Newcastle. GO is going to ask (*Please insert name)*.to come and present at next RINTAG to explain what has been done in Edinburgh as a baseline for developing a process for this JD will feed back any perfusion related governance issues	**JD** **GO** **JD**
13	**QUOD Report** JD spoke to the QUOD Report in Rutger Ploeg's absence. Successful MRC application. QUOD is fully supported by NHSBT and there is now a commitment to generate income for NHSBT at a rate of 10%. QUOD MRC grant is around £900,000 over three years.	
14	**Cell-Lines Position RINTAG(18)(a) & (b)** VG presented two papers on Cell Lines. <u>Consent for the creation of cell lines</u> The first paper presented background on the current consenting and regulatory requirements relevant to the creation of cell lines from donated material. Best practice dictates that specific consent should be obtained when material will be used to create cell lines. RINTAG was asked to: • Discuss the level of consent required from donor families before donated material is used to create cell lines; and • Provide recommendations to NHSBT on this issue. VG advised that cell lines divide in culture, can then no longer be classed as cells and therefore fall outside the HTA guidelines. Cell lines have the potential to be stored for years prior to processing and consent for this is not considered currently. Cells can be extracted, frozen down, and it can be months later when the decision is made to immortalise them.	

		ACTION
	The supplementary paper **RINTAG(18)8(b)** sets out three options to manage consent for cell lines in ODT: 1. Specific consent 2. Generic consent – with information provided in the research information leaflet 3. ODT do not support research studies that intend to generate cell lines DH - We need a tiered or staged approach. Take the consent we need at the time of donation then if further consent is needed, it can be obtained. Discussion around who would be placed to do this, SNODs or researchers. AF: Trying to access this arrangement from deceased donors adds a whole other complexity to the issue. EM: After losing a loved one in the middle of the night, patients families are not going to take the information in and it is almost dishonest to try to obtain consent for cell lines at that time. JF: The key here is cells being kept for a long period of time in a laboratory and/or truly immortal cells. There is a huge difference and this must be made very clear. SJ is unconvinced that we need to use deceased donors for cell retrieval and is it not easily accessible elsewhere? AF said that it is cheaper, and you can then collect many cells which can be commercially viable. Best people to obtain cell research consent are research nurses rather than SNODS *Summary Recommendation from RINTAG* *We need to make a brochure available setting out what research we do and what it involves. We should not go for specialist cell line consent during the middle of the night. First approach should be by SNODS with experts brought in at a later stage if needed.*	
15	**DCD Hearts** **RINTAG(18)9** JM presented a summary of the data we have on DCD Hearts up until the end of February 2018. See paper for details Mechanical support should be broken down between DP and NRP. CJW would also like time to death to be a key thing to compare. **DCD Heart Activity** The UK carries out 80% of DCD Hearts worldwide. **DCD Working Heart Group** DCD Hearts Working Group is meeting up in June 2018. Representatives from each of the Cardio Transplant Centres, NHS England, operational teams represented by Marian Ryan. This will be an opportunity for heart community to advise RINTAG on any developments.	

		ACTION
16	**Horizon Scanning** AF brought the **Proposal for a Joint Project between NHS Blood & Transplant (RINTAG) and the NIHR Innovation Observatory to generate a pipeline analysis in organ transplantation** to the meeting.  RINTAG(18)10 Innovation Observat AF and MMG met up with Mike Trenell from the Innovation Observatory. Recommended a full pipeline review. IO may be able to waive costs, therefore this review could potentially be at no cost to NHSBT. SJ hopes that this will provide NHSBT as a whole with an in-depth overview of what is on the horizon, what we need to prepare for, what we need to think about doing over the next 5 or 10 years and is incredibly useful. SMT Strategic proposals: *Continue with "Miss no Opportunity" theme* *Make the best of new legislative opportunity* *Continue to become more effective and efficient as a service*	
18	**Any Other Business** None	
	Date of next meeting: Tues 2 October 2018, First Floor, BJA Library, The Royal College of Anaesthetists, 35 Red Lion Square, London WC1R 4SG	

Organ Donation & Transplantation Directorate
May 2018