**NHS BLOOD AND TRANSPLANT**
**ORGAN DONATION AND TRANSPLANTATION DIRECTORATE**

**RESEARCH, INNOVATION AND NOVEL TECHNOLOGIES ADVISORY GROUP**

**TUESDAY 8 NOVEMBER 2016 10:30 – 14:30**

**MAIN MEETING ROOM, CORAM, 41 BRUNSWICK SQUARE, LONDON WC1N 1AZ**

# Minutes

**1 10:30 Welcome and apologies** G Oniscu

The Chair welcomed the attendees to the 3rd RINTAG meeting and announced the following apologies:

Paul Murphy - Chair, National Organ Donation Committee
Derek Manas - British Transplantation Society
Sally Johnson – Director of Organ Donation & Transplantation
Anthony Clarkson - Assistant Director for Organ Donation and Nursing, ODT
John O'Grady - Chair, Liver Advisory Group
John Casey - Chair, Pancreas Advisory Group
Peter Friend - Chair, Bowel Advisory Group
Steven Tsui - Chair, Cardiothoracic Advisory Group
Rachel Johnson - NHSBT Statistics and Clinical Studies, with Dave Collett in attendance

The Chair welcomed Amanda Small (who was attending the meeting on behalf of AC) and Elisabeth Murphy and Hazel Bentall who are new Lay members at RINTAG**.** Kathy Hopkinson was introduced as the new NHSBT Statistics and Clinical Studies replacing Rachel Johnson.

A warm welcome was also extended to Fiona Marley who represented NHS England as a one-off attendee.

**2 10:35 Declarations of interest in relation to the agenda** – RINTAG(16)1 All

*Please note that it is the policy of NHSBT to publish all papers on the website unless the papers include patient identifiable information, preliminary or unconfirmed data, confidential and commercial information or will preclude publication in a peer-reviewed professional journal. Authors of such papers should indicate whether their paper falls into these categories.*

The Chair reminded members of their obligation to declare any conflict of interest in relation to the agenda.

RP announced an additional CoI in association to the COPE study. AF announced an additional CoI with regards to the BTRU study which was up for Decision under agenda item 9, whereby AF would be asked to leave the room.

**3 10:40 Minutes of the Research, Innovation and Novel Technologies Advisory Group Meeting** RINTAG(M)(16)1

**3.1 Accuracy of Minutes** G Oniscu Attached

The Chair asked the Group to comment on the minutes. The minutes were ratified with the following amendments:

- RP noted that there was no mention of QUOD updates. It was agreed that QUOD should be a standing agenda item at RINTAG meetings going forwards, for information.

***1. ACTION: Heather Crocombe (RINTAG Secretariat support) to ensure QUOD is included as a standing item on the RINTAG agenda in the future***

- Page 6: "*Aimed*" instead of "*Promised* to do x2 EVLP procedures"
- Page 8: "Progress report *from* researchers"

**3.2 Action Points from the Meeting** RINTAG (AP)(16)1 — G Oniscu — Attached

The chair noted that the following four actions were outstanding from the previous meeting:

8. To explore in further detail the analysis of impact of DCD hearts on the retrieval of other organs - Steven Tsui and the DCD hearts steering group

Update: Work is underway to investigate the incidents. A report will be completed shortly.

***2. ACTION: GO to ensure the DCD hearts report is produced***

16. The issues of microbiology and virology testing for machine perfusion to be properly addressed. This is to be explored in the next few months once replies are received from all AGs – *Gabriel Oniscu, Maria McGee, Claire Williment*

Update: This action point has now been submitted to AG Chairs. A final view is yet to be agreed.

***3. ACTION: GO to ensure a final view on microbiology and virology testing for machine perfusion is agreed amongst AG Chairs***

17. RINTAG to write a letter to all centres that HEV testing should be undertaken for any blood products that are to be used in normothermic perfusion systems of organs, in line with current SaBTO recommendations for transfusion of blood in transplant recipients – *Gabriel Oniscu, Claire Williment*

Update: The HEV testing advice is nearly finalised. Recommendations are not yet in the public domain. The guidance will be issued once advice from SaBTO is received.

18. Derek Manas to liaise with Fiona Marley at NHS England with regards to the Face transplantation programme – *Derek Manas*

Update: In DM's absence, FM advised that this action point is still outstanding and is awaiting to hear from DM

***4. ACTION: DM to liaise with FM reg the Face Transplantation programme***

**4 10:55 Revised RINTAG ToR and Remit** — Oral report

For approval: — M McGee

- Terms of Reference RINTAG (16)2 — Attached
- RINTAG Remit Flowchart RINTAG (16)3 — Attached

**Terms of Reference:**

MM provided a brief update on the revised RINTAG ToR. The main revisions are as following:

- Updated membership list, including Lay members and Executive group
- More clearly defined frequency and format of meetings, including email consultation with RINTAG's Executive Group taking place every quarter for the purpose of reviewing new proposals and assessing the allocation ranking exercise.
- Inclusion of RINTAGs operational responsibility of studies requiring specific research consent, now assuming the capacity and capability (c&c) assessment as per HRAs requirements.

The following amendments were requested by members:

- 1.1.10 "Assumes the role of *NHSBT's Research Strategy Group*"
- Novel *technologies* instead of Novel *therapies*, throughout the document
- Clarify the relationship between RINTAG and BTRU
- Clearly define the potential integration of QUOD and RINTAG application procedures

***5. ACTION: MM to amend RINTAG ToR to reflect the above requests and ensure it is uploaded onto the website***

The Group discussed aspects of the application process and how QUOD and RINTAG can integrate their procedures to avoid duplication of applicants' efforts, while ensuring there is no breach to the consent processes nor any risks associated with sampling time points, if deviating from QUOD protocol and governance.

This may require restricting the number of biopsies taken per research study. It was noted that certain samples may be easier to facilitate within the QUOD infrastructure than others. This would need to include reassurances that any samples provided to QUOD as part of a study would not be allocated to other projects. The need for a clear pathway was reiterated and will require further discussions.

It was mentioned that the NHSBT ODT Exec. team is challenging the future funding for QUOD, while aiming to extend funding for QUOD another 3 years.

**RINTAG REMIT:**

MM gave a brief update on the RINTAG REMIT and described the main revisions as following:

- The addition of collaborating with the CTU regarding clinical trials
- The addition of developing business cases for innovative proposals

The Chair opened up for comments and the following were noted:

- It needs to be more clearly defined where RINTAG responsibility ends and the Transplant Centre responsibility begins.

It was agreed that RINTAG should be made aware of studies undertaken in transplant centres, to support RINTAG's role in oversight of research in the field of organ donation, retrieval and

researchers to report back to RINTAG should an organ, which has undergone some form of intervention, be discarded (i.e. from a clinical trial looking to transplant an organ into a recipient, but subsequently deemed unsuitable). In such rare cases this would need to be re-offered for transplantation. Other Units may have concerns regarding the suitability of such organ for transplantation or alternatively for research.

***6. ACTION: RINTAG Secretariat to ensure the REMIT of RINTAG clearly outlines the boundaries of RINTAG and Transplant Units responsibilities.***

- The legal responsibilities for transportation of organs were discussed. It was noted that transporting of organs for research is not a licensable activity under the HTAct. Licensable activities for research are removal and storage. These organs do not need to travel under an HTA licence.

***7. ACTION: MM and VG to ensure the MoU (MTA) is amended to reflect researchers transportation responsibilities***

**5 11:05 Demand and Availability of Organs for Research** RINTAG(16)4 & RINTAG(16)5 — M McGee/ C Hopkinson — Attached Attached

- Demand
- Offered
- Placed

Demand Data Summary - RINTAG(16)6 — M McGee — Attached

CH provided a statistics update on the Consent and Research Activity.

**Consent and Activity:**

- This data was based upon a 6 months data period
- 95% of patients in Eng, W and NI, had consented for research
- In Scotland the authorisation rate stood at 90%
- 68% of discarded organs were recorded as being used for research
- Kidneys were most highly consented for
- NHSBT is working to capture data on research organs that have subsequently been transplanted

MM provided an update on the Demand data for research organs

**Demand:**

- There are currently 26 studies active, with a current annual demand at 470 organs.
- Staff unavailability was the number one self-reported reason for declining a research organ.
- The outstanding data is due to the nature of self-reported statistics.

The Group was asked to reach a decision about how best RINTAG would like this data to be presented in the future.
Comments included:

- It would be advantageous if the data on lungs reflected data on pair of lungs, to minimise misleading the reader
- The consent form FRM281/4 was no the most up to date version. There was a concern that the paperwork on EOS forms was not consistent with the current version and did not reflect QUOD

- While giving a general picture, the information on research activity lacks robustness
- The capacity per centre to receive research organs was misleading. It is important that these are reported accurately, for the purpose of fair scoring of studies as per the new allocation policy
- It is vital that all researchers and transplant units are engaged and report back to NHSBT if anything seems to appear outside the system, in order that data reporting can be refined

The Group decided that the data should be provided in the future with the knowledge that more robust data will be available with time. However, the two data-sets needs to be combined to demonstrate the demand for and availability of organs for research.

***8. ACTION: MM to ensure the data-set is combined into one paper to demonstrate demand and availability and capture how many organs offered for research was transplanted.***

***9. ACTION: MM to link in with QUOD representatives to share learning reg. data reporting to better match supply and demand***

**6 11:30 Introduction of Next Working Group** C Williment Oral report Attached

**Sub-Group ToR** RINTAG(16)7
Claire W gave an update on the next working group, which will be tasked at looking at ways to increase the number of organs available for research.

The group will be co-chaired by JD and EM and highlighted that the remit will be to review the various UK legislation and ethical frameworks, together with UK policies, guidance and clinical practice to:

- Identify current barriers to the availability of organs for research purposes
- Suggest appropriate steps to overcome these barriers
- Make recommendations for a new approach that will increase the consent rates and the number of organs available for research in the UK (which may include changes to UK legislation and national guidance and changes to UK clinical practice

It is anticipated that the first meeting will take place by the end of the calendar year, pending co-chairs and member's availability.

Comments from RINTAG members included:

- Membership should be revised to include HTA and legal expertise.
- Advice from HTA via Lorna Williamson was recommended
- Group should have access to legal advice within NHSBT should this be needed.
- It would be a good idea to survey all studies currently registered with NHSBT ODT to request their views on any hurdles
- It was recognised that the ability to remove some of these barriers may fall outside of NHSBT's ability to implement.

nations is recommended
- Recommendations are expected to be issued in June 2017

***10. ACTION: Claire W to ensure a survey is included in the remit of the next working group***

| | | | | |
|---|---|---|---|---|
| **7** | **11:45** | **Working Group Report Update – Allocation of Organs for Research** | N Watkins | Oral report |
| | | **7.1. Ranking of current studies/Matrix for discussion** RINTAG(16)8 | | Attached |
| | | **7.2. SOP4442 Allocation of Research Organs ODT duty office** RINTAG(16)9 | | Attached |

**Allocation of Organs for Research:**

NW provided an update on the new Allocation of Organs for Research Policy. In view of time, it was noted that the presentation would be followed by one comment each from members around the table.

NW highlighted the fact that these were the final recommendations from the working group, with the following summary:
- The aim of the policy work was to create a fair and transparent scheme
- It consists of a ranked list of studies which would receive simultaneous offerings
- The organ would be placed with the highest ranked study out of those who responded
- A degree of self-selection and geography will remain, enabling a more efficient offering process for the Duty Office
- The Secretariat will play a role in ensuring relevant approvals are in place and assess the scores
- The ranking exercise will take place quarterly. Each new study will rank at the bottom of the list until the quarterly ranking exercise takes place
- The matrix contains banding, binary and scoring categories
- Should two studies score the same, rotational offering will be explored
- The Secretariat will monitor the impact of the 6-months pilot very closely
- The ranking is to be published on the website

Members were encouraged to look beyond their own interests and comments included the following themes:
- While some considered the system to be “as fair as possible”, some members found it to be a complex system
- There are still concerns that one project at the top will block all other studies from receiving organs
- A call for monitoring transport costs was made
- The pilot needs to be monitored to assess whether any studies are severely disadvantaged.
- Robust monitoring is also required on a case by case basis when an organ is being retrieved in one centre and then sent on to another as this may not the best use of the resources
- It is important to ensure the scheme is sufficiently objective and may require re-wording around the 2020 strategy
- The suggestion of introducing x3 regions with x3 allocation pools were discussed. This could be considered as the next

- The need for intelligent allocation of organs was also raised, to accommodate inclusion/ exclusion criteria to increase utilisation and encourage collaboration
- Members also highlighted the importance of strategic oversight to enable some level of flexibility with the ranking
- There is a potential issue with the texting method not being sufficient to alert research teams and "no caller"ID from the Duty Office phone line.

***11. ACTION: Mick S to arrange a phone line without "No caller" id, to ease the new offering process***

It was agreed that the pilot should be monitored weekly on an informal basis between the Secretariat and the Duty Office, but would also include a formal user survey after 3 months. Measures to monitor the impact will need to include the number of organs available for research. This may require 4-5 markers, against which the success of the pilot is to be judged.

The Group decided that this should go to SMT for approval of the pilot, and to be launched pending its approval.

The error of numbering in the SoP4442 was identified and it was noted under point 7 that the ODT number and donor hospital are vital information for researchers.

***12. ACTION: MM to work with the Duty Office and ensure the SoP is updated according to feedback***

**12:15 Lunch**

**8 12:45 Research Approval Process**

| | | |
|---|---|---|
| **8.1 Study Decision Tree** RINTAG(16)10 | M McGee/ | Attached |
| **8.2 INF1204 Research Approval Process (flowchart at the back of the MPD1029/4)** RINTAG(16)11 | C Williment | Attached |
| **8.3 POL263 Research Organ Allocation** RINTAG(16)12 | C Williment | Attached |
| **8.4 Research Applicant's Checklist** RINTAG(16)13 | M McGee | Attached |

**Research Approval Process:**

MM and Claire W gave an update on the proposed Research Approval Process.

MM provided an introduction to the documents envisioned to be included in the Application pack to researchers, and available on the website:

8.1. Study Decision Tree
8.2 ODT Research Approvals
8.4 Applicants checklist (revised without the rational per item)
8.5 Application form
8.6 External flowchart

MM reiterated that the reasons behind the suggested changes are to ensure NHSBT provides effective oversight and management of research organ allocation and ensure due diligent processes, including governance framework and regulatory requirements are followed.

Claire W acknowledged that some studies had been caught in the middle of the transition period, and extended an apology to CW in particular, for any inconvenience caused to his study as a result

It was reiterated that the development of the website is underway, and will contain all relevant information for researchers pending the approval of the above mentioned documents.

A discussion regarding the documents was subsequently held. Several members found the document to be confusing, overly bureaucratic and duplication of work. This needs to be addressed and the following comments for improvements were suggested by members:

**Decision tree**

- To more clearly distinguish between transplantation and general health care
- To more clearly define the categories, by including *donor* to the wording/ adding another category to capture donor observational or non-invasive studies
- To clarify or amend the terminology *specific* and *generic* proposals
- Spell out what the approvals are for and when and why required
- Provide reasoning behind why RINTAG should be approached in the first place
- Provide advice on early engagement with the Secretariat

**Application checklist**

- The HRA approval assumes that the HRA has checked the CV, which makes this requirement redundant in cases where HRA approval has been granted
- In cases where other national bodies issues approvals, then there should be no need to duplicate the process.
- The primary focus for NHSBT is to collect data where necessary and then act as a "helper" to researchers
- The fundamental difference with the introduction of the HRA is that NHSBT will need to ensure that capacity and capability is covered
- The clinical trial toolkit can be used as a guide to develop the documentation further

Given the extent of the comments, the Chair stopped the discussions and proposed that a small short-term working group is set up to address these issues and to ensure the process is effectively streamlined.

***13. ACTION: Working group to develop and streamline the application process, based on the documents provided***

NW was chosen to head up the working group, given his clinical expertise and no conflict of interest. Members of the working group were identified as following: Sarah McAllister, CW, VG, Claire W, MS, AS and MM.

***14. ACTION: MM to ensure up to date contact information is uploaded on the website while the application process is being finalised by the working group***

**9 13:00 Study Update**

| | | |
|---|---|---|
| **9.1 Studies For Approval and Information Only/Studies approved since last Meeting** RINTAG(16)14 | M McGee | Attached |
| **9.2 Islet proposal** | J Casey | Oral report |

**9.3 Uterine Transplant Update** RINTAG(16)15

| | |
|---|---|
| I Quiroga | Attached |
| B Jones | Attached |
| R Smith | Oral report |
| G Flint | Attached |
| M Papadopoulos | Attached |
| G Oniscu | Oral report |
| G Oniscu/ D Collett | Oral report |
| J Dark | Oral report |
| J Forsyth | Oral report |

**Uterine Transplant Update:**

Due to the timing of external presenters, the Uterine Transplant Update (9.3) was discussed next.

MS gave a brief update before the group was invited to present, mentioning that they have addressed the concerns raised at the NRG, NODC, NHS England and at the most recent RINTAG meeting.

FM confirmed she had met with the Group, and reiterated that the final decision rested with the PSSAG and Ministers regarding whether, if successful, the service should be commissioned by NHS England.

The proposal had been amended, to reflect a joint application with the Oxford transplant team. The following points were covered by the presenting team Isabel Quiroga, Benjamin Jones and Mr Richard Smith:

1. Clarification on whether the donor family have any potential claims on the baby (requested by NODC).
2. Confirmation regarding the steps that would be taken to prevent invasion of the privacy of the donor and their family and respect the sensitivities of the donor family and/ or nursing staff. There should be discussion with ICU nursing and donor family representatives regarding this issue. (requested by NODC)
3. Liaise with Commissioners to gain their support for the programme prior to any launch (requested by RINTAG).
4. Liaise with other representatives of other solid organ transplant programmes and retrieval teams to agree the approach for intra-operative access of vessels (requested by RINTAG and NRG).
5. Confirmation regarding which hospitals will participate in the programme to identify and refer donors (requested by NODC).
6. Confirmation regarding the donor consent process and training requirements for SN-ODs(requested by NODC)
7. Confirmation of the process for referring potential recipients and where the transplant procedure will be undertaken. In particular, confirmation that all recipients will be NHS patients and that the transplant will take place within an NHS institution (requested by RINTAG).
8. Both groups advised that you liaise with the Regional CLODs and Regional Managers to review your programme protocols and undergo external stakeholder engagement to explore these points in more detail.
9. Confirmation regarding Oxford retrieval teams' involvement in retrieval process

In summary:
Transplants would be undertaken in Oxford, who has begun the R&D process. The retrieval would not have an adverse impact on solid organ retrieval and would not have any delay on the current retrieval. Retrieval from ten DBD donors would be undertaken in the first instance. It was noted that the transplants in other countries had been from living donors but the team stated that this process was lengthy and places the donor at unacceptable levels of risk. The team has received REC approval. HTA license is still outstanding, as needed NHSBT approval.

Comments during the subsequent discussion arose as following:

- The project calls for a small number of patients, with high level of costs and expertise required.
- The reasoning behind live vs. cadaveric donors were discussed
- Next steps, including HTA requirements and meetings with the commissioning team, were briefly discussed
- There would be an expectation from the research team that, if pilot is successful, this would move straight in to a commissioned service. This expectation would need to be carefully managed.

The research team left the meeting and the Group agreed to issue an approval for 10 cases within RINTAG's advisory capacity to SMT, under the following conditions:

1. There is written support from the Executive team of Oxford NHS Trust that they are supporting this pilot.
2. The team will provide reassurance that no costs of the pilot will be imposed to NHSBT beyond the routine commissioning of NORS terms.
3. The team continues to liaise with Maggie Stevens and Maria McGee within NHSBT to finalise the operational approach, governance procedures and the protocols.
4. The protocol is strengthened to state that informed consent is given from the families regarding the additional tests and procedures for the donor.
5. There is clarification in the protocol of the intent that the programme in its pilot form and beyond (should it be funded) will only be offered for patients eligible for NHS treatment.
6. The donor hospital sites and transplantation facilities where this pilot will be carried out are clearly identified.
7. Supporting documentation clarifies why cadaveric donation was more appropriate over the living donor approach.
8. There is continued liaison with the National Clinical Lead for Organ Donation, the NRG, NODC, ICU and SN-OD teams within donating hospitals for any outstanding aspects of the pilot.
9. NHSBT's media department is engaged to develop and agree a strategic communications plan. Maria McGee will help facilitate this discussion.

It was made clear that the proposal is subject to final approval by the ODT SMT.

It was noted that there is a great deal of work to be done from an operational point of view.

9.4 **Olfactory bulbs presentations x2:**

The Chair invited the two neurosurgeons/ researchers, Graham Flint (from Birmingham) and Marios Papadopoulos (from St Georges), to give a presentation of their respective Olfactory bulbs proposals.

GF is proposing a trans nasal route of access, while the MP is proposing to undertake a craniotomy. The researchers advised that there was benefit to trialling both approaches in the first instance, to assess which is the most effective approach. The following aspects

- What question the proposal is aiming to answer;
- How it will do so;
- Why this is being investigated;
- How many procedures the proposal is aiming to undertake;
- Who the team will need to engage with to achieve this;
- Where the team are in the application process;
- What issues the team anticipates

It was highlighted that the two research groups should work together.

The subsequent discussion included the following points:

- Defined as stem cell culture, or transplantation? The two require different approvals processes.
- Would the immunosuppressant impact on nerve growth. The researchers clarified that the study would seek to answer this query.
- Animal models. It was identified that it is difficult to extrapolate relevant data from animal models.
- The need to consider GMP requirements.
- Ischemic time and its effect on the projects.
- Media involvement and its potential risks.

When the teams had left the room, the Group agreed that RINTAG should not restrict, but facilitate research, unless there are very good reasons for not doing so (such as for pre-solid organ retrieval olfactory bulb recovery in this case). RINTAG members found it reasonable to lend support for three procedures each post-organ retrieval, provided the teams go through all relevant approvals.

It was also agreed that:

- The teams will need to be open and clear when seeking family consent. NHSBT should be able to review donor family consent.
- RINTAG need to review next steps prior to further approvals
- There is a potential clash with the Uterine retrieval project. It was agreed that donors at St George's could not be approached for both research studies.
- Studies should not proceed if there is any indication that a family may remove consent for solid organ donation due to the olfactory bulb removal.

The RINTAG approval was granted with the following conditions outlined to both research teams:

- That the teams seek to work collaboratively to maximize the outcome and findings of your research.
- Investigate all governance requirements as this will need to be evidenced prior to any work being undertaken. These include the provision of copies of REC approval, GMP conditions, along with an HTA support letter from the Designated Individual at the relevant site, to evidence the support to remove relevant material for specific research purposes.
- To link with NHSBT's media team to develop and agree a strategic communications plan.
- Formally present preliminary findings and any issues experienced, at the next appropriate RINTAG meeting before seeking approval for any further procedures

- Contact the RINTAG Secretariat after each completed or attempted procedure, to allow for review of any potential adverse or unwanted events. It is suggested that these are facilitated via teleconferences including any stakeholders as recommended by RINTAG.
- It is particularly important that careful attention is given to the training of SNODS for study specific consent.
- RINTAG reserves the right to withdraw its support for this pilot at any stage, should the committee deem it necessary to do so, for example if there are any significant issues or incidents during the first three cases. It is also important to note that RINTAG approval does not guarantee any future approvals once the pilot has been completed and the proposals are subject to final review and approval by the ODT SMT.

**Agenda item 9.1 Studies For Approval and Information Only/Studies approved since last Meeting RINTAG(16)14**

MM introduced the five studies which required decision from the Executive group. It was noted that all of the studies had gained operational support.

For approval:
1. Newcastle, Cambridge - *Further Evaluation of Ex Vivo Lung Perfusion to Improve Transplantation Outcomes*

JD and CW left the room due to conflict of interest.
This is the first out of three that the Secretariat has been approached about.

REC and HRA was evidenced prior to the meeting. The study seeks to gain access to 40 lungs over 5 years, via specific and generic consent required. The study is looking to use EVLP to investigate transplantation outcomes in three trusts in the Newcastle area. The outstanding details include training of SNODs, signed MoU and approval for local capacity and capability. There are two other lung studies currently active on the Research Registry.

The Group approved the study.

2. King's Collage Hospital - *Improving cell viability and function*
3. King's Collage Hospital - *Improving Cell Engraftment*
4. King's Collage Hospital - *Improving isolation and cryopreservation of Hepatocytes*

These three sub-study proposals are from the Hepatocyte programme at King's. There is an animal component to the first sub-study. The studies require generic consent only and seek to gain access to 60 livers, per sub-study, spanning until 2020. The outstanding details include signed MoU and approval for local capacity and capability. There are currently 7 other liver studies active on the research registry.

The Group did not approve the study in its current form but recommend that the team revises the protocol to reflect that they are willing to recycle the livers they are allocated to other studies and that a total of 60 livers are used to isolate hepatocytes for all three sub-studies.

cells from organs declined locally, as NHSBT is about to introduce the new research organ allocation system.

5. University of Edinburgh - *Development of a therapeutic 3D implantable liver organoid -scaffolding materials for liver tissue engineering*

GO left the room due to conflict of interest.
This is an add-on study to John Halletts' ongoing project in Edinburgh. It is a study requiring generic consent only and will use the same livers as Mr Halletts team. There is an animal component to this research. The outstanding details include signed MoU, proof of funding and Home Office licence number. There are currently 7 other liver studies active on the research registry.

The Group approved the study.

For information:
1. Portsmouth - *Mind the Gap: Exploring the differences in UK consent rates from the perspectives of the Specialist Nurses Organ Donation*

This is a study that is being approved via the NHSBT R&D Office.

Live since last RINTAG:
1. Oxford and Birmingham - *Viability testing and transplantation of marginal livers (VITTAL)*

This is a large clinical trial requesting access to 55 livers over 5 years, and is looking to transplant 22 livers into recipients. It gained support from the AMD at NHSBT.

*2*. Oxford - *Exploring the structural and functional effects of normothermic machine perfusion and de-fatting agents on human steatotic livers.*

This was approved at the last RINTAG meeting and is an NMP study looking to access 25 livers over a limited time period.

For update:
1. Guy's Hospital London - *Transplanting the untransplantable - extending antibody incompatible transplantation using a normothermic perfusion model with cytoprotective agents*

This is a genomics and proteomics study. Reassurance has been gained by the Sponsor and the HRA that this study does not require REC. It was approved by ODT CARE and is about to go live imminently. It is looking to gain access to 20 kidneys via generic consent. There are currently 9 other kidney studies active on the Research Register.

***15. ACTION: MM and MS to proceed with governance and operational aspects reg. all above studies that gained approval***

**Agenda item 9.2 Islet proposal**

GO gave a verbal update about an islet proposal in JC's place.

It was noted that there is a need for further discussion regarding this research category as there are new rigorous regulations for GMP via the MHRA. There is a cross over with this area and how

***16. ACTION: GO to discuss with an MHRA representative and return a report to RINTAG with a proposal for how to manage islet research proposals***

**9.5 Data recording for organ recovery with Novel Technologies**

GO gave an update on the data recording for organ recovery with novel technologies and noted that there are some changes to these forms that will be presented to the NRG.

**9.6 Requirement for clear documentation and data records for DCD and NRP procedures.**

DC gave an update about the requirement for clear documentation and data records for DCD and NRP procedures.

There is a need to identify what additional data could be provided at the retrieval stage for the benefit of surgeons at the receiving end. It was suggested that a supplementary form is agreed and introduced, to capture as much data as possible. The form could be completed and then attached to DRT, which surgeons could then access via EOS This will be beneficial as the surgeon will be able to access details about pathology (microbiology, histopathology etc). The current system does not enable surgeons to access attachments.

***17. ACTION: MS/ AS to explore if it is possible to upload scans and thus capture this additional information into the NTxD and DonorPath/EOS systems***

**9.7 EVLP/NRP**

EVLP:
JD gave an update about the EVLP & NRP service evaluations. It was noted that one more EVLP has been performed since the last meeting.

9 procedures have been undertaken and 4 have proceeded to transplantation.

NRP:
GO announced that there has been issues with the manufacturing company for NRP equipment. This has delayed the delivery of the project.

25 procedures have been undertaken and 16 have proceeded to transplantation.

Preliminary data for NRP suggests that there is a 0% ischemic cholangiopathy compared to 24% in non-NRP cases. NRP is progressing on the international stage and in France NRP is mandatory for all DCD retrievals where a liver is recovered. It was clarified that the service evaluation is measured against utilisation and function.

It was highlighted that at the moment, the teams only use NRP within their zone. It was agreed by the Group that NHSBT and RINTAG is lending its support to allow the already NORS competent teams to attend DCD donors with NRP anywhere in the country, when the team is called out.

**9.8 DCD Hearts**

JF gave a verbal update about the DCD Hearts programme. He informed that the business case went to the NHSBT Board and gained approval, after which it was put forth to the x4 Departments of Health in the UK and a decision is to be made regarding funding. In the meantime, the heart programme is continuing in Harefield and Papworth under local funding provisions. Approval has been given to Manchester to introduce the service, but to date no DCD heart retrievals had been undertaken.

**10 13:45** Governance issues

10.1 **Incident Reports** – Biopsies, Lesions and Reporting back to SNODS RINTAG(16)16 — J Dark — Attached

G Oniscu — Attached

JD gave an update about three Incident Reports; Biopsies; Lesions and; Reporting back to SNODS.

INC 1639 - A pancreas from a DCD donor subjected to NRP was eventually turned down, after fast-tracking – on the basis of a prolonged CIT. PAG has published a clear framework for regarding the CIT as too long for successful outcome and the fact that NRP times should note be counted towards CIT.

INC 1832 - A biopsy was taken from a liver which was turned down for transplant because of poor initial perfusion, but was included in a research perfusion study. The lesion turned out to be benign, but because no transplant was involved, there was no route for feeding the biopsy result back to the SNOD and hence to the recipient centres.

It is suggested that a route to inform the original SNOD/ transplant team via the Duty Office of any unexpected and clinically relevant findings during research on organs turned down for transplant is needed. The Group suggested that there should be a mechanism for this, a similar route as the one the used for reporting fungus culture. This should be highlighted in the approval process.

It is of particular importance to highlight this to researchers who may not be familiar with the Duty Office and NHSBTs transplantation processes.

***18. ACTION: The approvals process working group to consider the introduction of a mechanism for how to report back about any organ related issues via the Duty Office***

INC 2002 - Outdated perfusion fluid was being kept for research use, kept in the same fridge as the in date fluid, and then was used, inadvertently, for a retrieval. RINTAG would be a good route to re-emphasise the need to label non-clinical, or expired products "For Research Only" and to store them separately from clinical service solutions or equipment.

***19. ACTION: JD and JF to liaise about including labelling of perfusion fluids for research in the next cautionary tales***

10.2 **CARE Update – Blood Products** RINTAG(16)17

The Chair announced that he would like to give an update about a proposal for blood utilisation for ex-situ perfusion and preservation

technologies at the time of retrieval. It was highlighted that this request originated at the NRG.

GO is discussing with Olive McGowan, VG and Donaldson regarding the HTA requirement to ensure complete traceability for bloods throughout the process. There is a need for a local feedback mechanism following issues when bloods are used on perfusion machines that leaves the donor hospital. It was suggested that a form could accompany the respective organs, and that it should be recorded in the donor notes. This is particularly relevant for donor blood and medication at the retrieval stage.

This is a work in progress, for information only at this stage. There is a need for an agreement and protocols regarding who has access to donor blood. This will be discussed at NRG.
It is to be discussed at the NRG, 9th November.

***20. ACTION: GO to raise the issue of blood utilisation for ex situ perfusion and preservation technologies at NRG and to seek advice from Sarah Morley on the blood team.***

**11 14:15** G Oniscu Oral report

**RINTAG-BTS meeting** Attached

11.1 Preliminary agenda RINTAG(16)18

It was noted that the date of this meeting, 19 January 2017, clashes with a European lung transplant event. No other comments were raised.

**12 14:20** All

**Any Other Business** G Oniscu

M McGee

RINTAG/BTS Stakeholder Day: 19 January 2017 G Oniscu

**13.1 Dates of next Meetings: 15 May 2017 & 9 Oct 2017** Derek Manas

No comments were raised.

**13.2 QUOD**

RP gave a verbal update about QUOD. It was highlighted that while NHSBT has indicated that it will provide support up to March 2020, a new business proposal has been developed to help support QUOD costs and manage expenditure. There is a need to recover a percentage of the funding through sample provision. The NHSBT CE had set a target of QUOD providing 50% of the funding, to increase recuperation of costs even more. It will require a low threshold to support QUOD becoming self-supporting, whilst not being prohibitive for researchers. The threshold for this was discussed by the Consortium and a cost per bio bank item (slide or RNA) for £5.37/ sample is proposed. This is being submitted to ODT SMT. A marketing strategy is to be launched.

It was reported that there is an increased sensitivity amongst NHSBT and clinical colleagues due to renal and liver issues in relation to QUOD samples. This was met by significant concerns at the CT AG. There is work underway to develop an information sheet to patients on the waiting list, to raise awareness about the issue.

**AOB**

The Group agreed that RINTAG meetings in the future should run between 10.30am and 4pm.

**13** **14:30** Close

Organ Donation and Transplantation Directorate November 2016

**For information only:** UK Renal Research Strategy (attach link)
Publications since 2016

Publications since 2016.pdf

## RINTAG MEMBERSHIP

| **Name** | **Role** |
|---|---|
| Gabriel Oniscu* | Chair |
| John Forsythe* | Associate Medical Director, ODT |
| Chris Watson* | Chair, Kidney Advisory Group |
| Sally Johnson | Director of Organ Donation & Transplantation |
| Andrew Fisher | NIHR BTRU |
| Elizabeth Murphy | Lay Member |
| John O'Grady | Chair, Liver Advisory Group |
| John Casey* | Chair, Pancreas Advisory Group |
| Peter Friend* | Chair, Bowel Advisory Group |
| Steven Tsui* | Chair, Cardiothoracic Advisory Group |
| Paul Murphy* | Chair, National Organ Donation Committee |
| Rutger Ploeg* | Chair of National Retrieval Group; Director of QUOD |
| Nick Watkins* | Assistant Director – Research & Development, NHSBT |
| John Dark | National Clinical Lead – Governance |
| Dave Collett/ Rachel Johnson | NHSBT Statistics and Clinical Studies |
| Karen Quinn* | Assistant Director for Commissioning, ODT |
| Dave Metcalf | NHSBT Finance |
| Anthony Clarkson* | Assistant Director for Organ Donation and Nursing, ODT |
| Derek Manas | British Transplantation Society |
| Victoria Gauden | National Quality Manager |
| Hazel Bentall | Lay Member |
| **In attendance** | |
| Claire Williment | Head of Transplant Development, ODT |
| Maria McGee | ODT Research Manager |
| Maggie Stevens | Specialist Nurse Research and Service Delivery |
| Heather Crocombe | Clinical & Support Services, ODT |