Research and Development Committee Meeting Minutes

10.00 a.m. Tuesday 12th June 2018
Board Room, West End Donor Centre,
26 Margaret St, London W1W 8NB

Committee Members

Louise Fullwood (Non-Executive Director)
Harvey Klein (NIH, USA: External expert)
Gail Miflin (Medical & Research Director)
Jeremy Monroe (Non-Executive Director)
Ellen van der Schoot (Sanquin, The Netherlands: External Expert)
Huw Williams (Director of Diagnostic and Therapeutic Services)
Jonas Wadstrom (University of Stockholm, Sweden: External Expert)
Paresh Vyas (Chair of RDC, Non-Executive Director)
Greg Methven (Director of Blood Manufacturing & Logistics)

Observers

Emanuele Di Angelantonio (PI observer)
Chris Sims (Planning and Management Accountant, Group Services)
Nick Watkins (Assistant Director, Research & Development)
Yomi Adegbaju (National Research Manager, Minutes)
Paul Iliffe (Business Support Accountant - Additional Observer)
Ana Mora (Clinical Operations Manager)
Dave Roberts (PI observer, deputising for Mike Stredder)
Helen Thomas (Principal Statistician deputising for Rachel Johnson)
Rutger Ploeg (PI observer, deputising for Sally Johnson)

Apologies

Mike Stredder (Director of Blood Donation)
Simon Stanworth (PI observer)
Sally Johnson (Director of Organ Donation and Transplantation)
Rachel Johnson (Associate Director Statistics and Clinical Studies)
Rob Bradburn (Finance Director)

1. Introductions, Apologies and Conflicts of Interest

PV opened the meeting, apologies and deputies were noted as above. No conflicts of interest were declared.

2. Minutes of meeting held 7th November 2017

The minutes were approved subject to a minor amendment to the minute for *item 4biii: NIHR BTRU renewal.*

Action: Amend minutes of 7th November 2017 meeting accordingly. Post-meeting note: Minutes have been revised and sent to Board for information.

3. Update on Actions from 7th November 2017 meeting

NW reported that 3 of the 4 actions are closed with 1 ongoing (HLA epitope):

- HLA epitope: An operational plan to make use of the findings of the study is development with HLA-epitope matched platelets being issued on a named patient basis if required. Additional analyses on secondary outcomes linked to level of increment and epitope is ongoing. The paper describing the epitope matching approach has been to Transfusion Medicine.

4. 2017/18 R&D Annual Report and Strategy update

NW gave a general update on R&D Annual reports, item 4 is taken as read. In discussions the following was noted:

- The Patient Blood Management Strategy Group are currently reviewing and prioritising a list of clinical questions that may inform the PBM strategy
- There should be clarity on 'How PBM research can contribute to NHSBT's strategy and efficient use of blood'
- Areas under consideration for the next strategy include Improved stock management and Artificial Intelligence, however, Committee felt that improving hospital inventory link and patient blood management are 2 separate questions/issues
- Potential clinical questions for the PBM Strategy could include:
    - Do sickle/thalassemia patients really need fresh red cells?
    - Alloimmunisation – why and whom?
    - What are best red cell triggers/strategy in haem patients? (who use 23% red cells)?
    - What is role of prophylactic platelets in chronic BMF syndromes +/- TXA?
    - How clinically beneficial are granulocytes?
    - Appropriate use of FFP
- Although these questions will have an operational impact, they should be clinically driven.

There was a discussion around the genotyping platform, which can be used to determine a donors' full blood type (HLA, HPA and red cell antigens) as well as

genetic variants which are linked to donor health and resilience for around £30 currently. This genotyping platform will be used to type 6,000 donors in the COMPARE study initially. Over the next 3 years all 250,000 donors recruited to the NIHR BioResource through the STRIDES study will be typed on this platform providing NHSBT with information on donor blood groups at an unprecedented level. This typing will enable the identification of donors with rare blood groups. It was noted that:

- A paper on the potential operational impact of this approach to donor typing will be brought to the ET in the Autumn. There are still a few factors to work through i.e. involving appropriate regulators, developing IT systems.
- The platform could potentially be used to find rare donor types in organ donation
- The platform is owned by Thermofisher and NHSBT are negotiating a future royalty payment.
- NHSBT's contracts team are involved in ongoing negotiations.
- The platform represents a scientific breakthrough as the technology in current use is still 19th century technology. An upfront investment in this technology will have huge and beneficial outcomes when implemented.
- The development supports the importance of our partnerships with COMPARE and STRIDES studies
- That an overarching strategy for NHSBT is required that should focus on transfusion and transplantation
- That bone marrow and blood donor sequencing falls within NHSBTs' remit whereas the sequencing of the larger patient population is a discussion to be had by NHS England
- An important question to consider in this piece of work is to distinguish between type and immune responses i.e. patients in which an alloresponse cannot be identified.

Outcome: Committee accepted the report and asked for their congratulations to be passed on to the individual award holders

Action: Committee requested a paper for the November 2018 RDC to update on discussions and forward plan of the Genotyping platform work, including a summary of the science behind this work

It was noted that one of the 8 strategic objectives relating to establishing a Behavioural Research Programme was at risk. This was of particular importance because of the need to recruit and engage with minor ethnic donors (organs, stem cells and blood). Committee recognised that:

- Progress over the past 20 years had been limited
- Funding from NIH for activities in this area was limited
- It remains a very important area of research but not much work is being done Internationally at the moment. This may be due to the difficulty in publishing.

There seems to be conflict between the reviewers (clinical/non-clinical). Early engagement with the reviewers may be the solution.

- In the Netherlands the progress of research in this area is not great as it is seen as a marketing issue and not research.
- Developments in donor characterisation (e.g. molecular typing method) may solve the issue by early identification of the most valuable donors
- NHSBT is a little behind in this area of work and that reflects the state of the issue
- A proposal to the Trust Fund from Prof Eamonn Ferguson aims to investigate the issue of trust in BAME population
- Current marketing activities may start to focus on geographic regions with a higher ethnic population
- There are 2 major issues to explore in order to change current practise: 'Money and People'. This should play a big role in the R&D strategy

Committee asked for further information on the level of external funding obtained in 2017/18 which was lower than in previous years. It was noted that:

- There is some uncertainty in future funding due to Brexit
- Committee shouldn't be unduly concerned about the apparent 'low' funding this year as there were good grants awarded
- The funding climate is buoyant and there is no increased risk to research capacity.
- The success rate for grant applications in the Netherlands is about 1 in 10
- It is important to be aware of how much money we have tied into Horizon 2020 projects because of the potential risk of a hard Brexit.

Action: YA and NW to provide data on Horizon 2020 funding held by NHSBT PIs.

a. PlaNeT-2 – trial results and next steps

AM presented results on the primary outcome of the study which remain confidential until publication of the manuscript. The Committee noted that this was a complex study and that the results had the potential to impact upon clinical practice. Committee congratulated the team on the successful completion of this landmark study.

Action: NW to write to Dr Stanworth passing on Committee's congratulations.

b. STRIDES – update on roll-out

EA gave an update on the STRIDEs study, a randomised controlled trial of interventions to reduce faint rates, the feasibility phase of which is scheduled to start in October. It was noted that:

- Following discussions with NHS Supplies, the tablets can be brought for ~10p a tablet

- "Taste tests" are still required to determine acceptability
- It was not possible to obtain sponsorship for the study
- Funding for the purchase of the tablets was available from the R&D budget due to the vacant junior group leader position

Outcome: Committee confirmed their support to fund the isotonic tablets from the existing R&D budget

c. RESTORE and manufactured red cells – update

NW presented an update on the programme of work on manufactured red cells. It was noted that:

- Dr Ash Toye has replaced Prof David Anstee as the Director of the NIHR BTRU
- Scale-up of the manufacturing process remains an issue but recent discoveries in the labs in Bristol had led to an increase in yield
- The current focus was on preparing the documents required to gain the necessary approvals.
- The activities in advanced therapies was in support of the Advanced Cell Therapy Strategy which will be presented to NHSBT's Board in July

Outcome: Committee expressed their continued support for this challenging project and requested a further update at November 2018 meeting.

d. NIHR BTRU Progress

NW presented the progress of the other 3 NIHR BTRUs. In reviewing the reports the Committee noted that:

- The reports do not show the linkage between the BTRU and NHSBT, there is no obvious path that directs back to NHSBT research goals
- Overall management and reporting for the NIHR BTRUs is carried out by NIHR
- Each NIHR BTRU has a nominated lead that sits on the management committee
- Recommissioning of the NIHR BTRUs is very important and should play a role in the R&D strategy
- There needs to be an assessment of the impact of the Stem cell NIHR BTRU work and its alignment with NHSBTs' goals.
- Future priorities for the NIHR BTRUs will be a part of the ongoing QQR work.
- Given the role of NHSBT and the challenges around donor recruitment and consent for organ donation, funding of behavioural research is likely to be a future priority

e. Artificial Intelligence and Machine Learning Project Update

NW presented this paper which updated on the progress of the AI/ML pilot projects. During the discussions it was noted that:

- The next steps are to work closely with the new Data scientist to develop the data science strategy, explore the right questions to ask and what support is needed
- The projects have cost approximately £25,000 each to deliver
- Delivery of the projects had been completed in conjunction with appropriate internal stakeholders (e.g. ICT and M&L)
- The platform used in the Hospital Integration project was limited in its utility and a significant amount of work would be required to implement an automated solution

Data completeness and hospital engagement were key to a successful outcome

5. Financial Report

CS gave a presentation on the finance, with Committee noting that:

- There is a need to develop a longer team financial plan beyond 2020/2021
- The QQR process requires a robust financial plan with clear information on how funding is allocated across the programme
- Research capability funding is likely to continue to fall which will lead to a bigger gap.
- There is a continued need to invest in the right people and projects for greatest impact
- Discussions to identify future challenges across the organisation are ongoing and these will enable an identification of key collaborators/partners

Outcome: Committee agreed that the forecast underspend could be used to support the delivery of the R&D Strategy

6. Quinquennial Review – update

NW provided an update on current QQR activities. During the discussions it was noted that:

- Site visits were carried out at the last QQR, 75% of the reporting focused on reviewing the last 5 years and 25% focused on future. Principal investigators as well as junior staff were interviewed, some of the areas reviewed included staffing, resources, space allocation, central core verses disparate facilities. This time around 80-90% of this can be done without the need to visit each site and it is also more cost effective.
- The current QQR seems very PI focused, the PIs should create short overviews of his or her staff for the report and include the output for the whole group
- It would be helpful for the panel to understand (1) what is organisational priority and (2) what is the impact of the individual team member

- It would help to get a sense of co-located PIs and researchers to determine what staff NHSBT supports.
- A formal assessment of the junior staff should also be carried out to gauge their understanding of the current strategy
- The draft report template appears to convey the PIs viewpoint only, it is important to understand how the PIs function within their environment and what the research team think about their workplace. How do they plan to deliver NHSBT's priority and who will deliver them? Are the individuals in the team working in a functional environment, do they publish, what is the impact of the work, is there training and development available? If the PI were to leave NHSBT will the team fall apart?
- It would be useful to identify the cross cutting projects or teams. Increasing contact with other teams could improve individual projects and cross fertilisation of research ideas.
- Teams should be asked if there are any skills or equipment that they are missing and how has this affected their work.
- There is a need to capture a better overview of the individual teams, key priorities and questions. A multidisciplinary approach should be taken in this QQR.

Specific points raised relating to the prioritisation process were:

- The need to keep in mind the changes in Public Health England and how this may affect some strategy group priorities especially microbiology
- The components strategy group should work more closely with donors and where their priorities lie
- RINTAG acts as the ODT strategy group, however, its main priorities are to facilitate and support access to organs for research. Unlike other strategy groups, RINTAG is very externally facing with members who are not involved in NHSBT operations or R&D
- Directors, PIs, patients and the public should all be involved and represented. This will mean that the final priorities can be received with full confidence that all relevant parties were involved.
- Identified priority areas will be submitted to RDC in Nov 2018
- The horizon scanning must identify new blood products because the demand for blood is decreasing and it should also focus on what can be done with cells
- The NIHR BTRUs need to align with NHSBT priorities
- External experts will be invited to review submissions and reports are required
- External experts could provide input in to the Advanced Cellular Therapies horizon scan to identify areas on which NHSBT should focus
- The National Blood Transfusion Committee will be asked to provide their thoughts on the identified priorities

Outcome:

QQR update at Nov 2018 RDC should include a clear timeline and address the issues raised in discussions

There is an urgent need to prioritise engagement with PIs and Strategy groups in horizon scanning process

7. Women in Science – update

YA gave an update on the development of the Women in science work, this is a serious issue and the lack of female PIs cannot continue. Working group analysed NHSBT R&D staff but needs to explore lack of PIs in the organisation. Committee noted that:

- There is a need to diagnose the problem before identifying the treatment
- The appointment of PIs needs to be a clear and transparent process
- There are areas of NHSBT, for example DTS, where there are a significant number of senior female staff

There is a need to explore developing a career pathway within NHSBT R&D that encourage more women to apply for PIs posts. This could include internal coaching programmes

Outcome: Committee supported this piece of work and noted that the recommendations would be important to the delivery of the current and future strategies.

Actions: The following actions were agreed for YA and the working group:

- **Circulate terms of reference to the RDC including membership;**
- **Compare NHSBT to other organisations (NHS trusts and academia)**
- **Use R&D website to champion Women in Science work;**
- **Collate data from last 5-10 years (NHSBT PI job adverts, applicants, shortlisted candidates, interview panel, successful candidate);**
- **Recommendations for Nov 2018 RDC to consider**

8. Annual Reports for discussion:

a. Report on PI Activity

Committee accepted the report on PI activity, noting the significant outputs across the R&D Programme and the need to complete the work on defining an NHSBT PI.

Outcome: Feedback to RDC in November 2018 meeting

b. Intellectual property report

Committee accepted the report and noted the issues surrounding distribution of the BEL-A cell lines and the need for appropriate agreements to permit this.

c. Report on Clinical Fellows

Committee accepted the report and noted that their work is of great value to NHSBT.

d. Clinical Trials Unit (HT)

HT presented an overview of the clinical trials unit (CTU). During discussions it was noted that:

- The CTUs role in studies in organ donation is increasing but they are not the only unit specialising in studies in this area
- The CTU collaborate with external parties on a regular basis if if they have the funding and the research aligns with NHSBT strategy
- The INTERVAL and Compare studies were conducted through the University of Cambridge because the expertise needed for the studies was available at the university.
- The NHSBT R&D Office act as the sponsor for studies run by the CTU in the majority of cases
- It was helpful for the Committee members to be aware of the work of the CTU and act as ambassadors for the Unit

The CTU head of operations has a good system of moving staff onto new studies when current studies are complete or close to complete.

Outcome: Committee congratulated the CTU team for their successes and asked for an annual report for the June 2019 meeting. This report should include a section on income and expenditure.

e. Components Development Laboratory (CDL)

NW presented an overview of activities in CDL over the past year. Committee noted that:

- CDL projects feed directly into Manufacturing and Logistics
- A year and half ago the priorities were not clear but that has now improved.
- There has been an increase in external funding
- CDL are unique in the UK and collaborate with similar International laboratories
- CDL is a good unit that is solving practical problems

Outcome: Committee accepted the report and asked to receive annual updates

9. Workplan for future RDC meetings

The Committee requested that annual updates from CTU and CDL were included on the workplan

Outcome: To include annual CTU, CDL and WIS reporting

10. Review of Terms of Reference

The revised terms of reference which included the addition of the Director of Manufacturing & Logistics were approved

11. AOB

a. Organisation of the meeting:

- The committee asked NW and YA to significantly reduce the volume of papers for the meeting as well as providing clearer guidance on the key papers.

Action: NW/YA to review reporting requirements for work packages

b. WP15-11:

- It was noted that the Workpackage held by Prof David Roberts comes to an end on 30th September 2018. Committee agreed to consider the future funding for this work at their next meeting and extend until 30th November 2018.

Action: DR to provide a business case with recommendations regarding future funding for the next Committee meeting

PV closed the meeting by reiterating that there must be clear input from external parties in setting NHSBT R&D priorities, praising the work being done by CTU and CDL and commenting that R&D activities are in great shape and great value to NHSBT.

Date of next meeting: 27th November 2018 – WEDC, London