NHS Blood and Transplant

Research and Development Committee Meeting

10am Tuesday 15th November 2016
Royal College of Nursing, 20 Cavendish Square, London

Committee Members
Paresh Vyas (Chair of RDC, Non-Executive Director)
Louise Fullwood (Non-Executive Director)
Jeremy Monroe (Non-Executive Director)
Harvey Klein (NIH, USA: External expert)
Rob Bradburn (Finance Director)
Gail Miflin (Medical & Research 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)
Claire Williment (Head of Transplant Development, Deputising for Sally Johnson)

Observers
Emanuele Di Angelantonio (PI observer)
Dave Collett (Associate Director, Statistics & Clinical Studies)
Sarah McAllister (National Research Manager, Minutes)
Rutger Ploeg (PI observer)
Chris Sims (Planning and Management Accountant, Group Services)
Simon Stanworth (PI observer)
Nick Watkins (Assistant Director, Research & Development)

In Attendance
Nicola Farrar (Research Governance Manager)

Apologies
Sally Johnson (Director of Organ Donation and Transplantation)
Peter Lidstone (Director of Manufacturing & Logistics)
Mike Stredder (Director of Blood Donation)

1. Introductions, Apologies and Conflicts of Interest

Apologies were noted as above. No conflicts of interest were declared.

2. Minutes of meeting held 16th May 2016

The minutes of the last meeting were approved and agreed as a correct record.

3. Update on Actions from May 2016 meeting

NW informed the Committee that the majority of the actions were complete or on the Agenda, with the following exception:

- Action item 4c - recruitment to a new tenure track position at Bristol: this was discussed in Item 4a.

4. 2015 – 2020 R&D Strategy

a. Update on objectives

NW spoke to this item. Committee were assured that satisfactory progress is being made against agreed objectives and strategic goals. The Committee were asked to review and approve the detailed scope of four proposals that were within the agreed strategy and available budget:

- Committee discussed the request to allocate £100k towards funding pilot studies in Big Data/Machine Learning. Committee endorsed this as an important area of research, noting that £100k was a small investment. Committee felt that external companies would be keen to be involved with NHSBT; therefore this funding should be aimed at supporting the NHSBT element of each proposal, with the external partners providing their own resource. There was agreement that without internal expertise in this area, the proposals should be tightly structured around outcome and knowledge transfer and that NHSBT should seek external legal advice where appropriate. Committee's external experts were content with the topics included in the Big Data call which include: Genomics, Matching, Links to hospital databases, Donor behaviour and Quality control of products;
- The renewal of QUOD, Nick Matheson's Work package and Rutger Ploeg's workpackage were discussed later on in the meeting;
- NW noted that the recruitment process had not started for the 2nd Tenure Track position in Bristol. Committee requested that this issue is brought back to the Summer 2017 meeting for review;
- One objective in the strategy was ranked as amber: to increase the proportion of female group leaders and Principal Investigators. SM described the actions that had been taken to scope Athena SWAN activity by collaborators. It is clear that major funders will be seeking for assurance that equality and diversity is taken into serious consideration by those awarded funding. Furthermore, there may be scope for NHSBT to seek accreditation from the ECU for Athena SWAN. Committee encouraged progressing this piece of work and the proposed actions. HK noted that a similar issue exists at NIH when recruiting to senior positions. GM explained that whilst turnover of NHSBT PIs is low, it is important to ensure that support is provided for development of junior female scientists;
- One objective in the strategy was ranked as red, see Appendix 2 below.

Outcome: The recommendation to approve £100k from within the 2016/17 R&D Budget to support "big data/machine learning" demonstration projects was accepted and the external call is to progress as planned.

Action: NW to provide an update on recruiting the Tenure Track position at Bristol to the summer 2017 meeting.

Action: SM to develop the Athena SWAN plans and feedback progress to the summer 2017 Committee.

b. Finance Presentation - 2015/2016

CS spoke to this item. The following was discussed by Committee:

- The reduction in RCF funding continues to increase pressure on the blood price levy, with an unpredicted additional £0.1M reduction in RCF bringing the 2016/17 adverse variance to £0.34M.
- CS stated that there was confidence to reduce the variance to £0.18M by the end of the financial year.
- The adverse variance of £0.34M excludes new funding applications previously from reserves.
- PV commented on the vulnerability associated with reliance of NHSBT on RCF as a core finance strategy. RB noted that loss of RCF would result in increased pressure on blood prices, and R&D would need to compete with other parts of NHSBT for the support. PV suggested that a review of how RCF is used within R&D is undertaken, with the aim of transitioning core work funded by RCF to a different source.
- CS noted the addition of "Applications for funding" to the summary of investment by strategic R&D theme slide. The Executive Team expressed that they would like a reduction of the £750k allocation for year 2017/18, 2018/19 and 2019/20 to £400k per annum;
- PV welcomed the inclusion of external funding in the finance presentation. As this metric is a measure of success, PV requested that additional information is included in future papers;
- PV queried the support that NHSBT provides to scientists making new applications. NW noted that this was a topic at a recent PI Day and that the PIs were against having an internal review process as they felt that they get support from the universities they are embedded in. PV stated that unless NHSBT really engages with funders, they will not understand each funding call fully.

Outcome: The Committee accepted the report and the Executive Team's request to reduce the annual planned spend on new applications to £400k per annum.

Action: CS to work with the R&D Office to include data on external funding gathered through the Annual Returns in the finance paper in the summer 2017 meeting.

Action: NW to assess core R&D activity currently supported by RCF, with a view to making the transition to an alternative funding source.

Action: NW to discuss with Principal Investigators and the R&D Office how relationships with external funders can be enhanced.

c. ABO report update

NW presented the Alliance of Blood Operators (ABO) 2015-2016 R&D Performance Metrics Report. This is the second ABO R&D performance report and this year a new member, Etablissement Francais du Sang (EFS), bringing the number of participants to nine. NW highlighted that NHSBT has the highest average H-Index, external

funding levels and number of completed PhDs, compared to the other organisations in the report. Committee expressed their thanks to the PIs for participating in the Annual Returns process which provides the data for this report, and also noted that they were impressed with the ranking that NHSBT has amongst the participating member organisations. NW noted that the ABO Chief Executives have requested that this report is now completed every 2 years. NHSBT will continue to request Annual Returns from PIs, and include information on international collaborators – a metric not reported on this year.

Outcome: Committee accepted the report, passing on congratulations and thanks to NHSBT PI's for their hard work and for completing their Annual Returns.

Action: SM to continue with the Annual Return process and include international collaboration as a reported metric.

Action: Considering the productivity of EFS in patent activity, studentships and number of papers accomplished per annum, GM is to make contact with EFS to discuss their ways of working and identify best practice that could be adopted by NHSBT.

5. Items for Approval

Following from Item 4a, detailed applications to Committee for Approval of Scope were presented.

a. Theme 2: WP15-02 - Viral regulation of T-cell metabolism: opportunities for selective immunomodulation (For approval of scope)

NW spoke to this item, providing a summary of the work that Dr Nick Matheson intends to cover as part of this workpackage which includes the use of proteomics to identify proteins key in viral infection and use these as a therapeutic target.

HK noted that it is important to maintain expertise of infectious disease within NHSBT. Committee were supportive of this workpackage, noting that it is first-rate basic science and a well written proposal. A discussion took place about ways of ensuring translational links with the business of NHSBT. It was noted that as Dr Matheson has a clinical background, long-term links with patients and donors is within scope.

Committee felt it is important to ensure that Dr Matheson receives effective mentorship and is encouraged to meet with international peers to enhance his development.

Outcome: Committee fully supported the proposal.

b. Theme 5: WP15-16 - QUOD renewal, including projects using BioBank (For approval of scope)

As the applicant PI, RP presented this item and answered questions from the Committee. RP left the room whilst Committee discussed the application and made a decision. RP described the successes achieved by QUOD, complementing the input from NHSBT ODT operations as key to delivering the BioBank. The proposal is to continue the established infrastructure of QUOD.

RP noted that the intention is to develop the business delivery side of the BioBank to recoup costs of up to 20% by 2020.

JW asked whether living donor samples are included in the biobank, noting that it is essential to maintain this cohort as a control group and also to correlate the

bioresource with patient outcomes. RP stated that there are a number of interested centres and that NHSBT are keen to increase the number of living donations in the future. The possibility of European collaboration was discussed and it was clear that some work had been carried out to engage with potential partners.

HW noted that the Executive Team would like a more ambitious target of recouped costs and reach a 50% replacement of infrastructure costs, in three years' time. RP described the pricing work that is underway – that funding members receive a discounted price and pharma groups will be charged more. Committee commented that NHSBT has experience with marketing and proposed that NHSBT developed this further, a suggestion welcomed by RP.

With RP out of the room, Committee continued to discuss the application. GM noted the challenging discussion had with the Executive Team and that support costs of QUOD could impact on other projects in ODT in the future. The external experts noted that the QUOD Biobank is an excellent resource, critical to the field of transplantation, a unique project that will require support for its infrastructure for some time as the appeal to pharma is limited. Indeed, Committee felt it important to begin work now so as to ensure that QUOD is financially supported in the long-term. Once the impact of QUOD on patient/donor outcomes is clear, that this is used to stimulate discussions with the Department of Health (DH).

Outcome: Committee supported this proposal, noting RP's scientific leadership. Committee would like for NHSBT to make a contribution to marketing QUOD.

Action: GM and NW to explore avenues to discuss the future infrastructure support for QUOD with DH.

Action: NW to make links between QUOD and NHSBT marketing teams.

c. Theme 5: WP15-07 - Organ Conditioning Unit: repair injury and recover organs for transplantation (For approval of scope)

RP described this workpackage proposal, noting that the funding is to support two postdoctoral positions. Their work will focus on a) experimental and translational research in organ donation and transplantation: identification of mechanistic pathways of organ injury/repair; and b) validation and diagnostic chip/kit development, applied clinical research in organ donation and transplantation.

RP stepped out of the room. Committee expressed some concern over the referee comments of the proposal. NW explained that the proposal had not originally been written for external review. GM stated that the process of external review will be managed differently in the future. In response to HW's question about being confident that RP's responses to referee reviews were sufficient, Committee stated that it was in that the technical questions were answered. PV noted that the nature of biomarker research means that milestones are vague – answering the hypothesis is not easily determinable as it is unclear what biomarkers will be identified.

Outcome: Committee is assured that RP's responses to referee comments are appropriate. Committee recognised that this is an ambitious project and that the outcome is unclear at this time. However, given RP's track record and the potential output of this work, Committee supported the application.

Action: RP and JW are to discuss the talk about using positive controls, offline.

Action: SM to communicate comments from Committee for Items 5a, 5b & 5c back to award holders.

6. Progress Reports

a. Theme 1: 11-01-GEN: INTERVAL (Progress Report)

EdA spoke to this item and gave a confidential presentation to Committee showing the results of the INTERVAL trial (Phase I). GM noted that there is a process to now be followed to take the findings of this study into policy and ways of working.

Outcome: R&D Committee congratulated the whole team on delivering a successful, high impact study. Committee passed on particular recognition of the role of the donor centres. Committee also felt it important to ensure that the Executive Team is aware that £20M external funding has been leveraged as a result of the £2.9M investment and that there is now a valuable cohort.

Action: EdA to continue to update Committee on the outcome of Phase II and III, and additional spin-off studies, related to INTERVAL.

b. Theme 3: 12-01-CSU TREATT (Report to Committee)

SS spoke to this item, noting that 105 patients had been randomised to date. HK stated that it is a tough but important trial and JW noted that it was important to reach 600 participants.

Outcome: Committee endorsed the trial and will review progress at the summer 2017 meeting.

c. Theme 4: Update on clinical trial of manufactured red blood cells

GM spoke to this item and highlighted sections of the report to Committee. Overall, Committee felt the project is progressing and noted the papers published and leveraged funding.

The GMP facilities were discussed, HK highlighting that access to high quality facilities is important. RB and HW updated Committee on the CBC extension and that NHSBT has ATMP licensed facilities at four centres.

Committee noted the 9-month delay for the clinical trial and queried what impact this had on the underlying scientific projects in the NIHR BTRU and the impact on the financial profile of the project

NW stated that the budget is monitored on a month-by-month basis but that we are expecting expenditure this year to match the available transformation funds. This will be dependent upon the number of GMP runs that take place in 2016/17. Committee recognised the importance of securing holotransferrin, EvdS in particular is facing a similar problem with the Sanquin supply. She said that the manufacturing team at Sanquin were working on other priorities but she was trying to rectify the situation. As a member of the NIHR BTRU SAB, EvdS will keep the study team appraised of this.

Action: Study team to provide an update at the summer 2017 meeting.

Post meeting note: Prof Anstee has responded to the query about the impact on the 9 month delay, stating that is will have no major impact on parallel research projects. Several members of the Filton group (Taylor, Cogan, Spring, Bruce) are very actively involved in facilitating the tech transfer to SCI and could have spent more time on other things if the transfer had gone more smoothly. However, delays in the recruitment of staff to work on the storage properties of cultured cells mean this project (lead: Bruce) could not have started earlier. The other staff named above will be involved in the workup for the proposed trial of cord derived reticulocytes and although the start of this work has been delayed much of the trouble shooting they have been doing should make the tech transfer of cord retic manufacture more straightforward. The major parallel research projects (retic maturation; use of scaffolds to improve yield, production of immortalised cell lines) with one exception (Cogan/ immortalised cell lines) involve different members of the NIHR BTRU and so have not been materially affected by the delays to the adult clinical trial.

d. Theme 5: Report on Living Kidney Donation update

EdA provided a verbal update on this report, noting that limited progress had been made. DC stated that the Clinical Research Fellow identified to assist this study was unable to participate due to other commitments. He also stated he importance of identifying the next steps for this work. GM noted that it is unfunded, however important to know the impact of donating a kidney.

After discussion, Committee stated that this work is important however no clear champion of the study has been identified. It is the right study and the right cohort; however it needs to be led by a committed individual.

Action: GM to work with colleagues in ODT to identify a lead for this work.

7. Workplan for future meetings

SM provided an overview of the reporting that will be brought to Committee over the next two years. SM noted an amendment to ABO reporting is now every two years, so the next report will be presented in November 2018.

The quinquennial review of the R&D Programme was added to the workplan. NW described the five-yearly review of R&D activity, looking to review the programme progress and future strategy. HK noted his participation in the last review, that it involved external experts visiting each site and that it took a year to complete. HK suggested inviting additional external experts to comment on specialised aspect of the R&D programme.

Committee agreed that this review was an important task to inform the 2020-2025 R&D Strategy. RB highlighted the necessity of alignment of R&D activity with NHSBT business areas and suggested that they are invited to present to the quinquennial review members and Committee to help inform future direction of work.

Outcome: Committee agreed that a quinquennial review should take place to seek external validation of current and future work, to ensure that future plans are fit-for-purpose and to seek assurance that R&D remains relevant to NHSBT patient and donor outcomes.

Action: NW to develop a detailed plan of the quinquennial review and present it to the Summer 2017 R&D Committee.

8. Next Meeting Dates:

13th June 2017 – Room 3bc, West End Donor Centre, London

7th November 2017 – MRC, Kemble Street, London