Research and Development Committee Meeting

10.00 a.m. Tuesday 13th June 2017
Room 3BC, West End Donor Centre,
26 Margaret St, London W1W 8NB

Committee Members

Louise Fullwood (Non-Executive Director)
Sally Johnson (Director of Organ Donation and Transplantation)
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)
Mike Stredder (Director of Blood Donation)
Huw Williams (Director of Diagnostic and Therapeutic Services)
Jonas Wadstrom (University of Stockholm, Sweden: External Expert)
Paresh Vyas (Chair of RDC, Non-Executive Director)

Observers

Emanuele Di Angelantonio (PI observer)
Dave Collett (Associate Director, Statistics & Clinical Studies)
Helen Thomas (Principal Statistician)
Rutger Ploeg (PI observer)
Chris Sims (Planning and Management Accountant, Group Services)
Simon Stanworth (PI observer)
Nick Watkins (Assistant Director, Research & Development)
Elizabeth Muir (Research Contracts Manager, Minutes)

Apologies

Rob Bradburn (Finance Director)
Greg Methven (Director of Blood Manufacturing & Logistics)

1. Introductions, Apologies and Conflicts of Interest

PV opened the meeting and conveyed apologies from Rob Bradburn and Greg Methven.

GM said a few words to DC in advance of his retirement on 30 June, thanking him for his hugely appreciated and important work in his post.

Conflicts of interest were declared. SS stated he was chief investigator for TREATT. PV is Chair of IMPACT Scientific Advisory Committee.

2. Minutes of meeting held 15th November 2017

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

3. Update on Actions from 15th November 2017 meeting

NW reported that all actions are closed or on the Agenda.

The Athena Swan work is being delivered through our University partners, and will be part of the review for the next RDC.

An extension to QUOD has been shortlisted for second round MRC funding call. RP stated that MRC came with capital investment for the infrastructure. It is receiving a lot of interest from other departments and infrastructure investment will be important. They are holding interviews on 4 August. The outcome is expected September/start October.

4. Update on delivery of R&D Strategy

a. Overview of progress and recommendations

NW reviewed the progress of the R&D programme generally and provided recommendations for committee to consider.

SS updated the progress of PlaNeT-2, which has 18 more babies to be recruited from a total of 660. The babies will be followed for 2 years.

EDA stated that his large external award from the MRC (£8M) is related to the global challenge to develop a large training platform for research in Bangladesh.

LF asked about the dip in EU funding. The consensus view was that there is much uncertainty regarding the future of EU funding and it was not clear what the impact on our PIs ability to attract external grants.

Outcome: Committee accepted the recommendations for the project grants and workpackages, with specific comments noted below.

Action: NW to communicate recommendations from Committee to award holders.

b. Clinical trial of manufactured red cells (WP15-04)

NW spoke regarding Dave Anstee's work package report regarding the scientific progress in the immortalised cell line BELA-2 and its importance in understanding red cell maturation. CRISPR is has been used to genetically engineer the cell line to produce different blood group expression profiles. Discussions are ongoing with QUOTIENT about an evaluation of these cell lines in a diagnostic setting. The clinical trial is challenging to deliver and time lines have slipped. Transferring research protocol into GMP protocol has proven difficult but has been accomplished; further challenges include the quantity of cells produced under GMP. Donor and volunteer recruitment for the clinical trial has commenced.

LF asked if there was sufficient capacity to support GMP production. GM stated that clean room capacity may be a problem and that we are looking at options to provide access to R&D space. Staff levels are appropriate. HW noted that remedial work on air handling units was required following the last MHRA inspection.

EvdS stated that collaboration and an exchange of knowledge is happening between Sanquin and NHSBT scientists and that high production levels have been achieved in the Netherlands.

GM noted that timelines and dates are difficult. The team are trying to have everything ready in the clinical trial but we don't know if we are confident in providing the cells.

Outcome: Committee agreed that good progress was being made despite the challenges the project brings. Committee also encouraged collaboration with other organisations, particularly Sanquin.

c. INTERVAL (11-01-GEN)

NW presented the final report which demonstrates how effectively the project has been delivered, the value it has added value and how NHSBT can support clinical trials in set in its operational environment. EDA commented that the paper has been accepted for publication in the Lancet.

PV congratulated EDA on the study and noted that one of its great successes is the enrolment of donors into the NIHR BioResource.

JM asked about what impact INTERVAL had on the number of appointments at each donor centre and risk to supply. MS noted that the return of donors to their local sessions had been underestimated and that a drop off was observed. It was also noted that the motivation of donors and the impact of different reminder strategies was being assessed in phase two of INTERVAL.

The impact of the findings from INTERVAL on donation policy will be determined once the results of COMPARE are known. Recruitment to COMPARE finished in March and a preliminary report will be available in late June

Outcome: Committee accepted the final report and congratulated the team on the successful delivery of the clinical trial.

d. Translational Data Science pilot studies

NW gave an overview of the Big Data studies. He provided an update on the IBM donor behaviour study for which data has been released following relevant approvals being obtained. This study will report back to the RDC in November.

LF noted that the end date of this study is November and confirmed the study should be circulated by email. She asked to have an agreement to extend this if it is useful, without waiting for the next RDC, because there will have to be re-consent due to GDPR.

GM responded that we will take this away, but GDPR will not be an impact right now. However, it will be when we take it forward with non-anonymised data.

NW commented that the Genomics project is further behind. It shares a similar data set with INTERVAL and the team are meeting with Altius next week.

For the Matching Allocation project with ATOS, we are using the transplant registry to improve likely waiting time predication.

PV stated that all reports are to come back to RDC and that they should inform future research proposal.

NW confirmed that additional resource is being made available to support these projects and that a number of delays have occurred as new processes have been developed for approval of data release.

Action: NW to circulate study findings to RDC once available

Action: GM to review impact of GDPR on NHSBT's use of data it holds

e. Quinquennial review – proposed format

NW presented this paper which outlined plans for the review of the R&D Programme and the development of the future R&D Strategy. The three phases proposed would provide an operational context for future priorities for investment in R&D. The priority setting should be operationally led and ideally the outcome should be for R&D Strategies to be embedded within future operational strategies. The proposal will see the current programme split into four themes and include site visits to enable discussions with academic partners and junior members of each research group. The next step is stakeholder mapping, and there will be a more detailed plan provided in next six months. During the discussions the following points were noted:

- HK stated that it must be clear throughout where funding for specific activities is coming from given the multiple funding streams;
- JW agreed this is a complex way of funding and needs close collaboration. The review should focus on NHSBT's requirements with the organisation determining what research is required, what control NHSBT has and the relevance to operational targets/objectives;
- PV stated that there was external money, BTRU money, and external grant income from PIs. PIs are funded partly by university positions or fully funded by NHSBT;
- GM said there is a good relationship between the NIHR and NHSBT;
- RP stated there used to be ring-fenced funding, and a change is going to be reviewed in the Quinquennial review. He asked if there should be a focus on translational research or esoteric research.
- PV stated that the report should review these questions, timelines will be discussed with NIHR in Autumn 2017 for renewal of NIHR BTRU funding. Research should inform policy and this should go to the NIHR in the future. We should talk about the process now. He believes NHSBT doesn't spend much on research but should have a laser focus on patient health, and use research to grow the business in order to then increase the funding;
- LF would like a streamlined report which is aligned with horizon scanning. We should reuse existing materials to streamline process and queried the purpose of the site visits. NW stated site visits give a feel of the environment of the study, and provides relationships with departments. HK said that comments on the facilities were important.

Outcome: Committee accepted the proposals for the Quinquennial Review

Action: NW/GM to develop and implement detailed plans for the QQR working with operational colleagues

f. Finance Presentation

CS presented the Finance report. The forecast reported at the November 2016 meeting for 2016/17 was for an adverse variance of £180k against an original of £335K adverse. The year-end position for 2016/17 was actually £224k adverse which included unplanned redundancy costs of £115k. The starting position for 2017/18 was break even, however an adverse variance of £229K is now forecast because of a reduction in research and capability funding. There is an allocation of £400K in transformation funds for R&D projects, subject to approval by the Transformation Programme Board.

PV thanked CS for the valuable report which shows all the research funded by NHSBT.

JW stated that we must be thoughtful about health economics. We should consider what are

we saving the public and use that as an argument to increase R&D funding in-house.

PV thanked him for the point, and stated that RCF may disappear completely. PIs should understand on what decisions regarding transformational funding are based on. This should be disseminated to the PIs so they can have focused applications for funding for that research.

Action: NW to consider projects with PIs which could be eligible for transformation funding

5. Items requiring decision:

a. **Call for clinical trial in acquired coagulopathy - A pilot randomised trial of diagnostic strategies for acquired coagulopathy in critical care and Core Outcome Set development (For approval of funding)**

GM presented this paper. SS noted that this was an application for prophylactic use of plasma. This is a proposal for a pilot study to see how the different test strategies perform. This is also a feasibility study in this new area to understand the core outcomes. SS left the room at this point due to a conflict of interest as the lead applicant.

During the discussion the following were noted:

- GM said that this trial got good or excellent reviews.
- NW stated that funding being requested in below the R&D funding envelope of £200K per annum.
- HK said there was a large and unresolved issue in blood transfusion. Standard tests right now are very relevant to find methods if these tests are predictive. He thinks this is the way to go about looking at it and stated that otherwise this was very good study and will achieve its objective as a pilot study.
- EvdS considered that the reagents should be funded by the other party but otherwise agreed it is a good study. JM agreed.
- NW stated that the next step is an agreement, and we should be able to include funding of the reagents in the agreement.
- PV agreed it is entirely appropriate to ask for consumables and that otherwise this is a good pilot study. It should be judged now for size and likelihood that it will achieve what it should achieve. We should go to HTA with this if it is successful to move to a bigger study.
- DC noted that the proposal is different from the initial proposal, as it is now randomised and contamination is an issue.
- CS pointed out other party is picking up consumables and this needs to be out of the budget. PV said we should seek clarification about this point,

Outcome: Committee approved the proposal and funding, subject to clarification regarding the funding being provided by external parties for consumables.

Action: NW to communicate outcome to applicant and confirm arrangements for funding of consumables.

(SS returned to the room at this point)

b. WP15-15 - Defining novel cell intrinsic ways to improve blood cell formation in the laboratory (For approval of scope)

NW provided information about the work package, asking for approval of scope. This work package funds the junior group leader at Cambridge and aims to improve how we can produce blood cells *in vitro*.

During discussions it was noted that:

- The work package is of very good quality and supported by strategy group and there is funding in budget;
- GM noted that this fits with Dr Cedric Ghevaerts' work, with support from Andrew Hadley. This is a reasonably easy decision to agree.
- HK – agrees that it is a nice fit and that the science is good.
- ES stated that it is a very good proposal
- NW said that this is a forward looking proposal with a natural progression of what has been done before.
- PV stated that this doesn't set out clearly what funding she is getting from external sources, and how much time she has set aside to work on this as opposed to what she is doing already.
- PV agreed this is a strategic fit and we would be supportive of this.

Outcome: Committee approved the proposal.

Action: NW to communicate outcome to applicant.

c. 12-01-CSU: TREATT

NW presented this paper and stated that it had been escalated to the Committee because of concerns regarding the change of sample size. Originally the sample size was to be 660 in UK plus 200 in Australia, but funding for the Australia trial was not approved at first, although it subsequently was approved. The current proposal was to reduce the sample size to 600 in totality with 100 from Australia and 500 from the UK. Absolute numbers are not known, but the study will run until there are 616. The TSC and TMG have agreed to those changes. Committee raised the following concerns regarding the changes to the study:

- DC stated his main concern would be to have a study that was powered to detect results in UK alone. He says the power is just over 70% and he considered that clinicians may find it easy to ignore the result. HK agreed that the study may be underpowered, not generally accepted and that homogeneity would not be acceptable;
- PV asked whether it would be possible to combine both studies with the same protocol.
- HK asked why the study does not just add more centres in the UK
- JW noted the sample size was correct in the beginning, and stated it would be disappointing if the trial does not have the power as it should have

In response to these concerns SS stated that homogeneity would be possible and that the clinicians have not raised this as an issue. He also stated that there is a single protocol and unanimity of analysis of results. The reduced sample size is due to the low recruitment rate and an interim analysis could be conducted to assess heterogeneity and power. Maintaining the original sample size might require the study to be extended and therefore require additional funding. SS assured the committee that there is evidence that the recruitment rate is increasing.

Outcome: PV stated that SS is to relay protocol and all governance of the trial to committee including HK for reassurance that it is a single trial, then DC is to think about heterogeneity and an interim analysis. If that assurance is provided, the committee can agree a 616 patient trial across two countries, with revised costings for those patients and increased time for those patients. If the committee is not reassured, then the outcome must be 616 patients in the UK. He stated a scientifically invalid trial cannot work and that Committee should

make a considered decision in November.

Action: NW to request report from SS addressing these issues for November RDC meeting.

d. Behavioural Research – call for proposals

NW presented a proposal to run a competition for studies in behavioural research to support the R&D strategy. Working with academics at a number of Universities we have tried to obtain funding from the Wellcome Trust and the Health Foundation. Unfortunately due to a lack of preliminary date these applications have been unsuccessful. Preliminary data, provided via a feasibility study would support an external application. It was recommended that a competition should be run for feasibility studies in consent for organ donation. During discussion the following points were made:

- GM agreed this is a pragmatic way forward. We will not be funding whole study. We should then move to an open call. She noted that health economics is a large part of this;
- JW stated that there is a difference when approaching living donors or families and said we need to work both avenues. We should make a health economic argument to increase donor pool;
- JM asked why we are just focusing on diseased organ donation and stated that SNODs are not involved in living donors. Focusing on RCTs might be too narrow a perspective;
- JM still approves of a project on living kidney donations, but doesn't feel like it's the same problem because it would lack focus. JM feels we should do both, but separately;
- PV agreed two programs, one for deceased. PV suggested leave the issue of living donors, but in future we may separate calls for research for living donors;
- NW stated the need for external peer review of proposals;

Outcome: Committee approved the external call as proposed, with applications to be considered at the November 2017 meeting.

Action: NW to organise external call for feasibility studies in behavioural research aimed at increasing organ donation consent rates

e. IMPACT – support for a clinical trials network in stem cell transplantation

PV left the room at this point due to a conflict of interest (see above).

HW outlined the IMPACT clinical trials network which is based at Birmingham and started in April. Anthony Nolan, Leuka and NHSBT are providing funding for this initiative, however, NHSBTs' contribution was originally provided by the Department of Health. Unfortunately this stream of funding is no longer available and our contribution is being provided by Diagnostic and Therapeutic Services. Discussions with NIHR and DH are ongoing regarding future funding.

Outcome: Committee agreed to consider a business case for funding for IMPACT at the November 2017 meeting.

Action: NW to add "IMPACT – future funding" to Agenda for November 2017 meeting and request business case from Dr Andrew Hadley, General Manager Specialist Services.

(PV returned to the room at this point)

6. Annual Reports for discussion:

a. Report on PI Activity

NW reported a successful year for our Principal Investigators as measured by the agreed key performance indicators. There has been an increase in the number of publications and external grants obtained. Seven PhDs were awarded during the year. DC noted that the Clinical Trials Unit continues to grow, diversifying to ODT trials, two externally funded studies and a number of grant applications in the pipeline. PI stated this report was outstanding.

Action: NW to pass on Committees' congratulations to PIs

b. Trust Fund Progress Reports

NW reviewed the report and stated that progress on these awards is very good. The paper included the highlights from all active studies.

Outcome: Committee accepted the report

c. Intellectual property report

NW gave an overview of this report, noting a slight reduction in spend on IP advice. He reported that two patents are in national phase. A review of processes at IBGRL had identified deficiencies in how income from licensing agreements was paid. All companies licensing NHSBT cell lines have been contacted and asked for payment.

Action: NW to report back to Committee on the income received from cell lines and antibodies as a result of contacting commercial companies selling these under license

d. Report on Clinical Fellows

GM provided an overview of this report and noted that there was not a lot of change, and there was a very good output. There were two funding sources for clinical fellows (NHSBT and NIHR) and some externally funded fellows. For the NHSBT fellows, 4 were at 100% - one vacant position, but this will be filled – with 50% of another 3 fellows. These fellows were in Virology, PBM, clinical trials and platelets. The annual Clinical Fellow's Day was the day after the RDC.

PV noted that there is a rich seam of trainees for the future of the organisation.

Outcome: Committee accepted the report

7. Workplan for future RDC meetings

NW presented the workplan, stating that this provides a plan for future meetings. The data projects to be reviewed in November. There were no comments.

8. Review of Terms of Reference

NW provided the annual review of ToR. He confirmed there are a small number of changes which were largely around clarifying names of directors. Comments were deleted regarding the video links to conference calls. There were only a few more small changes made.

PV confirmed a general agreement. He said that going forward we should think strategically about the R&D envelope in review process. He stated that where there is no peer review, we are to review the scope and whether we are happy with the results of any research. The committee should think about where money is going to get spent.

Outcome: The revised Terms of Reference were accepted

9. AOB

PV asked for AOB, but there was none. He thanked everyone for attending the meeting. HK commented that the meeting was very efficient and conveyed his thanks.

10. Date of next meeting

7 November 2017 – TBC, London