MEDICAL RESEARCH COUNCIL

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Paper SB/13/22

PROTECT: MGMT

Minute of the 46th Strategy Board (SB) meeting held on 12th March 2013 at MRC Head Office (One Kemble Street)

Attendees

Strategy Board
Sir John Savill (Chair)
Professor Doreen Cantrell (IIB)
Dr Wendy Ewart (MRC)
Professor Amanda Fisher (CSC)
Professor Stephen Hill (MCMB)
Professor Patrick Johnston (TRG)
Professor David Lomas (PSMB)
Dr Declan Mulkeen (MRC)
Professor Stephen O'Rahilly
Professor Jill Pell (PHSG)
Professor Hugh Perry (NMHB)
Professor Paul Stewart (TCG)

Office
Dr Claire Newland – item 1-5
Dr Anne-Marie Coriat - item 1-11
Dr Nathan Richardson – item 1-4
Dr Ghada Zoubiane – item 1-4
Dr Janet Valentine – item 1-5
Dr Rhoswyn Walker – item 1-4
Dr Tom Foulkes – item 1-3.2
Dr Joe McNamara – item 4-11
Dr Catherine Elliott – item 5-8.2
Dr Catherine Moody – item 5-6
Mrs Jill Jones – item 7
Dr David Crosby – item 7-8.2
Dr Jacqui Oakley – item 7-9
Dr Des Walsh – item 7-9
Dr Rebecca Hodges – item 8.2-9

Secretariat
Dr Heike Weber
Ms Krisztina Kamper

Apologies

Professor Peter Piot (GHG)

1. Welcome and introductions

Sir John welcomed members to the meeting.

2. Minutes

SB confirmed the minutes of the February 2013 SB meeting and December 2012 Joint Council/SB meeting as accurate records of the meetings.

3. Matters arising and updates

3.1 Strategic budget

Dr Weber gave an update on the strategic budget. She informed members that the remaining balance to commit for the 2012/13 financial year was £0.8m and led members through the items for a funding decision at the meeting (blood test for vCJD, MRC-LSHTM West African fellowship programme).

Turning to next year's resources Dr Weber let members know that the 2013/14 strategic budget would be £52.5m. This included £15m earmarked for medical bioinformatics and £8m ring-fenced for dementia to be developed and delivered by the TCG/MCMB and NHMB, respectively. These earmarked budget headings were now shown within the strategic budget. Funding against next year's budget had already been committed for Phase 2 of the European Developmental Clinical Trials Partnership (£10m) and the renewal of the joint MRC-Wellcome Trust-DFID Global Health Trials Scheme (£6m) leaving a remaining balance to commit of £13.5m. A major expected demand on next year's strategic budget would be funding for novel industry partnerships.

Dr Mulkeen informed members of likely underspends and overspends in different areas of the MRC's portfolio and let members know that a budget reconciliation exercise would take place at the end of the financial year. Sir John updated members that discussions with a number of companies in relation to novel industry partnerships were progressing well and that these would be brought to SB for consideration once they were at a sufficiently mature stage.

3.2 Experimental Medicine Challenge Grants Round 1

Professor Johnston updated members on the Experimental Medicine Challenge Grants competition. Six proposals had been funded at a total level of £16m addressing a range of areas such as obesity, psychiatric disorders, and vaccination strategies. A further study might be supported if issues identified by the Panel could be addressed by the applicants.

Looking to the future, the Experimental Medicine Panel had recommended that the focus should remain on human studies that target big questions centring on mechanistic understanding of disease pathology. Members had also noted opportunities for the repurposing of drugs and the increasing overlap with the stratified medicine agenda. The Panel had advised that in the future it would be important to encourage applicants to improve risk mitigation, including the adoption of mile-stoned approaches. Smaller initial awards of up to £1m could be considered that would form part of a larger funding package once critical milestones had been met. Sufficient time between the shortlisting of outlines and the preparation of full proposals and a workshop with applicants to clarify expectations at this stage, were also considered helpful.

SB welcomed the funding decisions of the Panel and agreed that a strong set of experimental medicine proposals had been supported across the breadth of the MRC's portfolio. Members were impressed by the range of collaborations fostered by the initiative, including two consortia with industry and one with the British Heart Foundation. For the future, SB endorsed the Panel's recommendations for the adoption of step-wise approaches to mitigate risks. Members thanked Professor Johnston and Dr Foulkes for leading and implementing this successful initiative.

3.3 Update on the Renewal of the UKCRC Public Health Research Centres and the Scottish Collaboration for Public Health Research and Policy

Dr Valentine gave an update on the renewal of the UKCRC Public Health Research Centres. She reminded members that these had been established to provide a platform for high quality public health research, capacity building, engagement with policy and practice, and knowledge exchange and translation. MRC had taken over the management of the UKCRC Centres from ESRC at the renewal stage.

The International Scientific Assessment Panel had recommended that all five UKCRC Centres and the Scottish Collaboration for Public Health Research and Policy should receive renewal funding. The Panel had also conducted a light touch review of the UKCRC Centres initiative. Members had agreed that a complimentary portfolio of Centres with diverse strengths had been established with further value being added through effective collaborations. The accomplishments of the Centres had been considered impressive in terms of scientific progress, translation, and capacity building and members had recommended that the Centres disseminate good practice and models for engagement with policy makers.

SB noted the funding decisions and outcomes of the light touch review. Members agreed with the International Panel that this had been a highly successful initiative that had demonstrated UK leadership in public health research. Members thanked Professor Pell and Dr Valentine for their efforts in delivering the programme.

3.4 EPSRC Interdisciplinary Research Collaborations in Sensing Systems for Healthcare Call Outcome

Dr Mulkeen updated members in confidence on the outcomes of the EPSRC call for interdisciplinary research collaborations in sensing systems for healthcare. Three awards would be announced:

- A Sensor Platform for Healthcare in a Residential Environment at the University of Bristol (co-applicant: George Davey-Smith) Video technologies would be applied to track people at home analysing factors such as eating behaviours and the risks of falls.
- 'Touch and Tell' Optical Molecular Sensing and Imaging at the University of Edinburgh (co-applicant: Chris Haslett) the delivery of a fibre-based sensing device for pathological events in the distal lung and blood of critically ill patients.
- Early-Warning Sensing Systems for Infectious Diseases at University College London (co-applicant: Anne Johnson) the application of novel coating techniques for the development of mobile diagnostic systems for 'point of care' testing and the monitoring of infections in real time.

SB noted the awards. Members welcomed EPSRC's investment in this area and engagement with MRC scientists to tackle medical problems.

3.5 High throughput science call

Dr Newland introduced a draft call text for expressions of interest in high throughput 'omic' science and imaging to enrich existing MRC investments in human cohorts, tissue and animal model collections. The call would enable the development of a roadmap for high throughput science that would add significant value to existing MRC cohorts, tissue and animal model collections, and where investments could be spent rapidly and be adjusted year on year in the light of changing income. It was expected that up to £20-£30m might be available over the next 2-2.5 years. In response to the discussions at the last SB meeting an expression of interest stage had been introduced to help shape the call for full proposals, focussing on proposals that were likely to have high impact and could be feasibly delivered.

SB considered that this was a well-specified call for expressions of interests and approved the call text. Members recognised that some successful proposals might be held over until a later date for a confirmed award decision. It was noted that the call would be launched on 13th March.

3.6 Medical Bioinformatics

SB received updates on the implementation of MRC's strategy in medical bioinformatics.

Package 1
Dr Valentine gave an update on progress with the establishment of a new UK institute for e-health research, building on the recently established e-Health Informatics Research Centres. She reminded members that £20m capital for spend in 2013/14 was available to the Centres for increasing access to NHS and other health-related data, the development of informatics platforms, improving data storage and processing, and enhancing connectivity. The Centres were working together on a joined bid made up of separate component parts. The bid was expected by the end of March and would be evaluated by an Interview Panel on 7th May to determine the added value of the institute as a whole.

Members were informed that the name of the Centre was still under discussion and that an update would be provided at the next SB meeting.

Package 2
Dr Coriat informed members that the Medical Bioinformatics call had been launched on 11th March. The deadline for expressions of interest would be on 22nd April and the Shortlisting Panel would meet on 20th May 2013 with final decisions being taken in October/November 2013. The time lines would ensure that any possible underspend in Package 1 could be used in Package 2.

SB noted the proposed time frames for the initiative and agreed that it was important to ensure sufficient time between shortlisting and the deadline for full proposals so that applicants could accommodate the feedback received at the expression of interest stage. Alignment with existing investments such as the European Bioinformatics Institute (EBI) and ELIXIR would be key and members suggested that the call should be drawn to the attention of key stakeholders, including the Directors of EBI and the Wellcome Trust Sanger Institute.

4. Round table

TCG
Professor Stewart let members know that items for discussion at the next TCG meeting included career support for basic science trainees and enhancing industry partnerships. Views from industry would be sought to inform the discussions. He also drew SB's attention to the programme of the next MRC Fellows' meeting on 21st May 2013 encouraging members to attend.

PSHG
Professor Pell updated members on the development of the MRC strategy for population cohorts. She explained that a portfolio analysis had been conducted based on data collected from 32 MRC and non-MRC supported cohorts and summarised key messages from the recent MRC population cohort strategy workshop:

- Since 1990 UK funders had supported one major new cohort each year
- Gaps in the cohort portfolio included ethnic minority groups, men between 20 and 40 years, women without children, data on infectious diseases and environmental exposures
- Key opportunities for the future included improved communication with policy makers and the basic research community, enhanced data linkage, and the use of new technologies for deep phenotyping

The MRC strategy for population cohorts would be presented to SB in the autumn following further development by the PSHG.

NHMB
Professor Perry reported that NHMB had supported 19 proposals at the recent Board meeting, including 4 strong New Investigator Research Grants. Only few proposals in the areas of dementia and neurodegenerative diseases had been received.

PSMB

Professor Lomas informed members of a £3m underspend in this financial year due to the delay of the quinquennial review of the MRC Biostatistics Unit into the next financial year. Dr Mulkeen confirmed that this would be considered in the budget setting for 2013/14.

TCG

Professor Johnston reported that the Technology Strategy Board (TSB) was close to having committed its £90m budget for the Biomedical Catalyst and would take a pause after the third funding round to consider opportunities for the future.

SB noted the success of the Biomedical Catalyst and the strong support the scheme had received from companies and the BioIndustry Association. It was hoped that TSB could secure further Government funding to continue the programme.

MCMB

Professor Hill informed members that MCMB had considered a developing proposal from the Wellcome Trust to build UK excellence at the interface between biology and chemistry. The Wellcome Trust would commit £6m to the programme and was looking for partners to be able to support 5 awards at a level of £2.5m each. MCMB had been strongly supportive of a £3m MRC contribution to the initiative. The Board had tried to encourage proposals in chemical biology through a highlight notice with only limited success and members had considered a national initiative in this field timely.

SB agreed that this was a very important area of science with a range of applications relevant to MRC strategy. Members considered that MRC influence in shaping the initiative was critical and would be facilitated through a substantial stake in the programme. Members therefore supported a £3m MRC contribution from the science budget and noted that Dr Richardson would represent MRC on the Steering Committee.

Sir John informed members that discussions were ongoing with Imperial College in relation to a proposal applying chemistry in clinical research. An outline might be presented to SB in due course.

IIB

Professor Cantrell let members know that pressure at the last Board meeting had been high with less than half of the score 8 (out of 10) applications being funded. She asked SB to consider support of a collaborative proposal led by the London School of Hygiene and Tropical Medicine (LSTHM), and involving the MRC/UVRI Research Unit on AIDS in Uganda to investigate the impact of maternal tuberculosis infection on the infant response to tuberculosis immunisation. The funding request for this 8-scored proposal was £1m.

SB noted that across the Research Boards only a small proportion of score 8 applications were normally funded. Members recognised the strategic alignment of the proposal with *Research Changes Lives*, the relevance to the remit of the MRC-DFID concordat budget, and the partnership between the MRC Uganda Unit and LSTHM. SB supported funding the application at a level of £1m shared equally between the science budget and DFID concordat funding.

Synthetic Biology

Dr Richardson updated SB on the joint BBSRC/EPSRC-led investment strategy for Synthetic Biology. He informed members that £50m capital was available for spend in 2013/14 and 2014/15 with the aim to align this budget with £23.5m resource funding (£11m confirmed by BBSRC, £12.5m expected from EPSRC and others). Key opportunities included support for multi-disciplinary centres of excellence, DNA synthesis capability, PhD training, and commercialisation seed funding.

SB noted MRC's commitment to synthetic biology, including the recent enhancement of the Centre for Chemical and Synthetic Biology at LMB. Whilst it was important to remain engaged with the initiative, members were not persuaded that there was sufficient research strength and leadership in UK biomedicine for further Centre investment or PhD training activities at the proposed level. SB therefore agreed that a financial contribution

to the joint BBSRC/EPSRC initiative was not justified. However, members noted opportunities for closer engagement between LMB and the Babraham Institute, and alignment of Doctoral Training Grants with the area.

5. Integrative Epidemiology Unit, Bristol

Dr McNamara updated members on progress with the development of a new MRC University Unit in Integrative Epidemiology (IEU) in partnership with the University of Bristol. The *de novo* University Unit would be led by Professor George Davey-Smith and capitalise on the successful MRC Centre in Causal Analyses in Translational Epidemiology (CAiTE) with the aim of addressing major public health issues relevant to the UK and global agendas. This would include extending the Mendelian randomisation framework pioneered by CAiTE to incorporate whole genome sequence data and the use of data on 'omic' and epigenetic mediators to better understand the links between modifiable exposures and health outcomes.

Dr McNamara reminded members that in 2011 SB had approved an in principle budget commitment of £10m for the new University Unit, subject to peer review. The aim was to consolidate MRC investments in CAiTE, secure key resources such as the Avon Longitudinal Study of Parents and Children to ensure maximum impact, and increase critical mass in partnership with Bristol University. An International Board Advisory Group (BAG), chaired by Professor Dave Leon (PSMB Deputy Chair), had guided the development of the proposals and these had been assessed by PSMB in February 2013. PSMB had considered that the application represented a well-integrated scientific and training package of significant strength and had scored the proposals 9 (out of 10).

SB endorsed PSMB's assessment and recommended the establishment of a *de novo* University Unit in Integrative Epidemiology at the University of Bristol. Members agreed that the Unit brought together a strong team of scientists conducting highly innovative research at the leading edge of the field. Professor George Davey-Smith was a greatly respected and very visionary leader and Professor Debbie Lawlor was an excellent researcher in her own right and well placed for the role of Deputy Director. Members were impressed by the partnership with the University of Bristol and the strong commitments made by the University, including in particular contributions to staff salaries and new posts.

Turning to the financial implications, SB approved a funding package of £10.8m for the Unit comprising a £10m commitment from the strategic budget, £249k capital funding for 2013/14, and a PSMB contribution of £560k. Members noted that the case for the establishment of the de novo University Unit in Bristol would be considered for final approval by Council in May.

6. Blood testing to estimate UK vCJD prion infection prevalence

Professor Lomas flagged up his interests as the Dean of the Faculty of Medicine at University College London. He remained in the room on the Chairman's invitation.

Dr Elliot introduced proposals from Professor John Collinge (MRC Prion Unit, UCL) for the application of a vCJD blood test developed at the Unit to determine the prevalence of prionaemia (prions in blood) in samples of 20,000 UK Biobank participants and up to 20,000 US control donors. She explained that whilst there had only been a total of 173 clinical cases of vCJD in the UK and no new cases diagnosed since 2010, Health Protection Agency data from appendix surveillance studies had indicated a possible prevalence of silent prion infection in the UK of about 1 in 2000. There could therefore conceivably be a risk of a second wave of infections through blood transfusion or other same species routes. The epidemiological results and evidence gained on the performance characteristics of the current test could inform any further decisions on progressing towards routine screening of blood samples.

SB recognised the high quality science that had led to the development of the vCJD blood test and the excellent publications relating to it. However, members were concerned that the parameters of the current test, including in particular the sensitivity, were not good enough for its adoption as a valid screening tool. SB considered that the test characteristics were not robust enough to have confidence that the proposed approach would provide a significant step forward in understanding the prevalence or implications of prionaemia in the UK population.

SB expressed secondary concerns about the use of the UK Biobank cohort in relation to the generalisability to the wider UK population and the ethical issues relating to feedback. It was noted that the Department of Health and the Blood Transfusion Service had a strong position that, for public health reasons, positive test results must be fed back if the individual can be identified, accepting the lack of knowledge as to the implications of positive testing for individuals. SB expressed reservations about the use of UK Biobank if such feedback was mandated, but noted that this would be a matter for discussion by the UK Biobank Ethics and Governance Council.

Members decided to decline the proposal for blood testing to estimate UK vCJD prion infection prevalence. Whilst recognising that the MRC Prion Unit's test was a front runner of current tests in development, SB advised that further development work was needed to improve the sensitivity of the test. Initially such work would be expected to be supported from within the Unit budget.

Finally, SB highlighted the potential value of the technique underlying the test and it was recommended that the Unit consider application of this approach to other neurodegenerative diseases involving protein misfolding. Different methodological approaches might also be considered. For instance, it was noted that UCL hosted an EPSRC supported team leading on nanotechnologies, including adherence of proteins to metals, and that the Unit might want to explore collaboration with this group or others with similar expertise.

7. MRC-LSHTM West African Global Health Research Fellowship Programme

Dr Jones introduced a fellowship programme to be jointly managed by the MRC Unit, The Gambia and the London School of Hygiene and Tropical Medicine (LSHTM) with the aim of supporting trainees to undertake a fellowship at the MRC Unit, The Gambia including a maximum stay of 9 months at LSHTM.

SB expressed strong support of the aims of the proposal, both in terms of developing global health research capacity and strengthening the partnership between MRC Unit, The Gambia and LSHTM. However, whilst recognising the importance of the initiative, members had concerns that the proposal was over-budgeted with respect to the number of fellows to be supported and the costs associated with each fellow.

SB agreed to allocate £1m from the strategic budget to support a pilot funding phase of the scheme. Members suggested that up to four research fellows might be supported from this budget and invited the applicants to submit revised costings for Office consideration.

8. Systems Biology for Medicine

Dr Crosby gave an overview of the current status of MRC-funded research in systems biology applied to biomedicine, and its place in the wider UK and International context. He reminded members that following SB discussions in 2008 a cross-Board highlight notice in systems biology for medicine had been published with the aim of encouraging collaborative programmes using systems approaches to address medical research questions. Portfolio analysis had indicated that the highlight notice had failed to deliver a significant increase in ambitious, challenge-led research programmes applying systems approaches in particular outside the remit of neurosciences research. Members were informed that major BBSRC and EPSRC initiatives in systems biology, such as Centre

investments and training programmes were coming to fruition providing opportunities for MRC to build on the capacity created. There was also re-emerging industry interest using quantitative computational models to identify new drug targets and predict off-target effects.

Dr Oakley updated members on the MRC/BBSRC call for proposals on Systems Immunology of the Human Life Course. The call had been launched with a workshop in December 2012 with the aim of stimulating multidisciplinary consortia applying integrative and computational approaches to study immunological pathways and how these relate to diseases over the life course. The response had exceeded expectations. 27 outlines had been received from a strong field of applicants with a total funding request of £47m. The outlines included six collaborative proposals with industry and a large number of challenge-led, ambitious, programme-level applications for instance addressing responses to vaccines and host pathogen interactions.

SB noted that the current highlight notice, whilst incorporating computational approaches, had adopted a broad definition of systems biology for medicine and that the Delivery Plan had deliberately promoted a cautious approach. Members considered that it was timely to provide further clarification on MRC's expectations in systems biology for medicine and highlighted key principles such as quantification, a dynamic range, computational/mathematical modelling to enable prediction, and iterative cycles of modelling and experiments. Based on these principles, members endorsed the following definition: "Systems biology describes the study of complex systems, with emphasis on how interactions between components of biological systems (as characterised by reductionist approaches) underlie the behaviour of the system as a whole. It can predict and explain emergent, systems-level properties and phenomena. It involves the integration of multiple pathways, and the generation and testing of dynamic, quantitative, computational/mathematical models of complex processes, and requires iterative cycles of theory, modelling and experiments."

SB recognised existing strengths in systems biology at the subcellular level such as the study of molecular assemblies, and intercellular interactions. Whilst the integration of models across levels, e.g. from molecules to cells to tissues/organs and whole organisms was an important ambition, this field was at a very early evolutionary stage due to the complexity of the systems and challenges associated with multi-scale modelling. Members highlighted the following opportunities in systems biology for medicine:

- Systems immunology was an important focus for the MRC and the outcome of the IIB-led initiative was awaited with interest.
- Pharmacology/toxicology, such as PK/PD modelling to predict responses to drug doses, was a tractable example of multi-scale modelling with the opportunity of partnerships with industry
- A broad-based systems approach to cardiovascular disease could be pursued in partnership with the British Heart Foundation for instance integrating data and understanding interactions between ageing, inflammation, and metabolic processes

Members advised that the current highlight notice should be withdrawn and be reshaped and re-launched in the light of the discussions at SB and further discussion by the Research Boards. It was noted that BBSRC had ambitious plans in systems biology at the whole organism level, most likely involving simple organisms such as bacteria.

9. Translational Bacteriology and antimicrobial resistance – Future challenges and opportunities for MRC

Dr Walsh updated members on the outcome of IIB's Translational Bacteriology Centre competition and the Board's discussion on potential future directions in antimicrobial resistance and translational bacteriology. He explained that two proposed Centres in Translational Bacteriology had been considered by IIB at its last meeting. Both had been declined as they had not articulated how they would deliver their translational aspirations and bring the fruits of their on-going basic science to the clinic. IIB had agreed that there

remained major areas of need, such as drug discovery, improved diagnostics, vaccine development and capacity building, but had considered that one centre would not be able to address the full spectrum of these activities. Members had recommended a consortia-based approach involving partnerships with industry from the outset.

SB noted the major health threats associated with antimicrobial resistance and the need to encourage the development of novel antibiotics to fill the discovery void in this area, a key challenge articulated in the joint NIHR/MRC Strategy for Public Health Research (2010). Members endorsed IIB's recommendations, recognising the barriers that needed to be overcome including the lack of innovation in antimicrobial development, the dearth of clinical bacteriologists, and the scarcity of effective collaborations. A major opportunity was presented by public-private partnerships to stimulate product development.

Noting the challenges associated with the establishment of a single MRC Centre in Translational Bacteriology, and recognising the interest of major pharmaceutical companies and the biotechnology sector, SB considered that the establishment of a distributed network of experts/centres closely associated with industry would be the most effective way forward. The networks should build on existing strengths and forge stronger partnerships around them. A niche for the MRC could be the mechanisms by which antimicrobial resistance arises and disseminates, including molecular mechanisms operating at the level of individual bacteria or quorum-sensing mechanisms in bacterial populations, and understanding virulence and pathogenicity with a view of identifying new targets for drugs and vaccines. A key issue would be to ensure that new investments dovetail with existing and new initiatives set up by pharma/biotech for rapid translation such as the IMI European Lead Factory.

10. Update on University Units' developments

Dr Ewart updated members on progress with the University Units programme. She explained that transfer papers for 9 MRC Units had been considered by Council at their meeting on 6th March and all had passed their respective Gateways. It was anticipated that by October 15 MRC Units would have been transferred into University Units plus 2 *de novo* Units created, involving approx. 1000 staff.

SB noted the enormous added value achieved by the transfer programme and thanked Dr Ewart and her small team for the efficient and effective delivery. The branding of MRC Units was an important area that needed further consideration.

11. Any Other Business

Dr Mulkeen informed members that Professors Douglas Kell (BBSRC CEO) and Melanie Welham (BBSRC Director of Strategy) would attend the April SB meeting to discuss engagement and opportunities for partnership working between both organisations. He let members know that in consultation with BBSRC nutrition research had been identified as a key area for discussion.

SB noted the breadth of synergies between MRC and BBSRC and agreed that the following areas should be explored in more detail at the meeting:

- Bioinformatics
- Synthetic Biology
- Vaccinology
- Antimicrobial resistance
- Nutrition research
- Fellowship support for basic science

The next SB meeting is 23 April.