Trust Board Meeting: Wednesday 10 September 2014
TB2014.105

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<th>Title</th>
<th>Annual Research and Development Governance and Performance Report</th>
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<th>Board Lead(s)</th>
<th>Dr Tony Berendt, Interim Medical Director</th>
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Executive Summary

Clinical research is of major strategic and reputational importance to the Trust. OUH is highly active in clinical research, with ongoing clinical research studies in all Divisions. The Trust has a close partnership with the University of Oxford in clinical research, exemplified by the NIHR Biomedical Research Centre (BRC) and Biomedical Research Unit (BRU), and hosts the NIHR Local Comprehensive Research Network and the Academic Health Sciences Network. Through the recently-designated Academic Health Sciences Centre the NHS Trust has formal joint working agreements with the University of Oxford and with Oxford Brookes University. The BRC and BRU expect to compete in the next NIHR competition for renewal in 2016. Major areas of new endeavour include genomics and clinical informatics, based on strong links with Genomics England and the NIHR Health Informatics Collaborative (HIC), respectively.

The OUH hosts more than 1400 clinical research studies, including approximately 300 clinical trials. OUH R&D activities are supported by annual revenues approaching £50m. Operationally, the Joint Research Office, comprising over 80 members of staff from both OUH and University of Oxford, supports all joint research across the partnership.

Against this background of major strategic successes and increasing clinical research activity, there is a need to meet the challenges of performance benchmarks set by the National Institute of Health Research (NIHR), and ensure robust governance and effective delivery of clinical research.

Recommendation

The Board is asked:

- To note this report; and

- To approve the proposed research governance and support plan, as outlined in Section 9 of the report.
1. Strategic Importance of Research to Oxford University Hospitals

Enabling and undertaking research in Oxford University Hospitals (OUH) aligns the Trust with regional and national agendas to deliver evidence-based medicine in the NHS, and to create health and wealth through research and innovation. Supporting clinical research meets the obligations placed on NHS organisations to promote research and the use of research evidence when providing their services. Moreover, the scale, scope and quality of clinical research activity across the Trust adds national profile to the OUH as one of England’s leading University Hospital Trusts, and has important beneficial impacts on clinical services, quality of care, and the recruitment and retention of clinical staff.

OUHT is a highly active research organisation, with clinical research taking place in every Clinical Division – including both OUH-initiated studies and studies in close partnership with the University of Oxford. OUHT receives a wide spectrum of funding to support clinical research, and either hosts or is a partner in key local and regional research infrastructure. The OUHT R&D revenues, approximately £50m per annum, come from a variety of sources including charities, industry and public sector funders and this budget is proportionately distributed across the clinical divisions. The budget supports clinicians, nursing staff and allied health professionals across the organisation. Maintaining a vibrant and growing research environment within OUHT is central to our involvement in the initiatives listed above and to securing a leading position in the region. Moreover, the scale of our activities attracts world-class clinicians, clinician scientists and other clinical and non-clinical staff to Oxford, and contributes significantly to retention and career development.

Key partnerships for OUH in clinical research include:

**The NIHR Oxford Biomedical Research Centre (BRC).** The Oxford BRC is hosted by OUHT in partnership with Oxford University and was awarded £98m over five years (2012-2017) following the NIHR competition in 2011. The BRC supports ‘translational research’, taking laboratory research into a clinical setting. The BRC supports research across many clinical areas, spanning all OUH Divisions, focussing on innovations to improve diagnosis, treatments and healthcare delivery for the benefit of NHS patients. The BRC is currently undertaking a detailed and systematic Mid-Term Review of progress, through an external panel of advisors, in order to begin preparation for the anticipated BRC renewal competition in 2016. A detailed report on the BRC’s progress and research highlights is provided in a separate paper for the Board (NIHR Oxford Biomedical Research Centre (BRC) report, Paper reference TB2014.104).

**The NIHR Oxford Musculoskeletal Biomedical Research Unit (BRU).** The Oxford BRU is hosted by OUHT in partnership with Oxford University and was awarded £9.8m over five years from 2012-2017 and undertakes translational research in three key musculoskeletal areas: (a) epidemiology and risk factors for osteoarthritis and osteoporosis; (b) orthopaedic surgery; and (c) inflammatory arthritis (rheumatology).

**The Thames Valley and South Midlands Local Comprehensive Research Network (LCRN).** The new LCRN replaces the former Thames Valley Local Comprehensive Research Network (TVCLRN) and topic-specific networks in Diabetes, Stroke, Cancer and
Neurodegeneration (DENDRON), incorporating these activities into 6 new clinical research divisions covering all therapeutic areas. The OUHT was successful in the 2013 competition to host the new LCRNs, and was awarded £13.5m/year for 5 years, from April 2014, to support the LCRN activity across the Region. The LCRN depends on participation from all NHS Trusts across the LCRN region, which is coincident with the Oxford AHSN, but the governance and responsibility for the management and performance of the LCRN rests with the Board of Host Organisation, working through a designated Executive Director (the OUH Medical Director), and the recently-appointed LCRN Clinical Director and Chief Operating Officer.

The National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (NIHR CLAHRC) Oxford. Although hosted by Oxford Health Foundation Trust, OUHT is a partner in, and contributor to, the Oxford CLAHRC. Through strong collaborative leadership, the NIHR CLAHRC Oxford aims to address areas of high importance and relevance for patients as well as key NHS priorities: delivering the most effective and best value services and focussing on those with greatest need – the frail elderly presenting to acute medical services, people with dementia in care homes, and those with chronic enduring illnesses and comorbidities; the highest users of NHS services.

The Oxford Academic Health Science Centre (AHSC). The Oxford AHSC received its designation in 2013 and was launched in early 2014. The AHSC is a partnership comprising OUHT, Oxford Health Foundation Trust, University of Oxford and Oxford Brooks to bring together research, teaching and clinical care activities in the four organisations to address some of the greatest strategic challenges to health care systems here in the UK and globally. Core to this programme will be six interconnected themes that will focus on strategic issues which the partners believe are central to sustaining a successful healthcare system:

- Big Data: Delivering the Digital Medicine Revolution
- Building Novel NHS, University and Industry Relationships
- Modulating the Immune Response for Patient Benefit
- Managing the Epidemic of Chronic Disease
- Emerging Infections and Antimicrobial Resistance
- Cognitive Health: Maintaining Cognitive Function in Health and Disease.

The Oxford Academic Health Science Network (AHSN). The Oxford Academic Health Science Network is one of 15 AHSNs licensed for five years by NHS, with the vision of ‘Best health for our population and prosperity for our region’. The Oxford AHSN will support collaboration, research and innovation across the NHS, universities and business, building on our strengths to deliver exemplary care and create the strongest life science cluster. The Oxford AHSN area covers a population of 3.3 million living in Berkshire, Buckinghamshire, Milton Keynes, Oxfordshire and Bedfordshire. The NHS spends £5bn a year in this region and employs 65,000 people. The Oxford AHSN will:

- Focus on the needs of patients and local populations – support and work in partnership with commissioners and public health bodies to identify and address unmet health and social care needs, whilst promoting health equality and best practice.
• Speed up adoption of innovation into practice to improve clinical outcomes and patient experience – support the identification and more rapid uptake and spread of research evidence and innovation at pace and scale to improve patient care and local population health.
• Build a culture of partnership and collaboration – promote inclusivity, partnership and collaboration to consider and address local, regional and national priorities.
• Create wealth through co-development, testing, evaluation and early adoption and spread of new products and services.

2. Clinical Research Activity

The volume of active research studies has increased progressively in recent years, with more than 1400 active research studies in 2014.

This number can be analysed according to the nature of the research and whether it is hosted or sponsored, and whether the study is a clinical trial of an investigational medicinal product (CTIMP), or other interventional trial.
The OUHT sponsored CTIMPs are the most resource intensive to the Governance team; with all interventional trials (sponsored and hosted) being the primary focus for reporting of OUHT performance to NIHR.

3. Clinical Research Performance

3.1 Background
The Government’s Plan for Growth, published in March 2011, aims to increase efficiency in initiation and delivery of clinical research, focusing on recruitment of the first patient to clinical trials within 70 days of receiving a valid protocol; and delivery of commercial clinical trials to time and target.

NIHR has placed renewed emphasis on reporting metrics for the approvals and initiation of clinical studies, which will be used for monitoring the R&D performance of NHS Trusts. Since June 2012, the NIHR has required that the Trust report on performance to these targets on a quarterly basis. Attainment of key metrics is a requirement for NIHR funding, including BRCs/BRUs, and performance metrics are published for each NHS Trust receiving NIHR funding. The Trust is now required to publish the information regarding its performance to these metrics in a readily accessible page on the website.

The Chief Medical Officer has recently notified NHS Trusts that significant financial penalties will be imposed on Trusts that fail to meet the performance targets, and show little improvement over time. The OUH performance requires improvement, and sustained work by the R&D Teams and Joint Research Office has now reduced the average time taken to review and grant approval to new clinical trials to 14 days. However, there is an urgent need for us to improve our recruitment to clinical trials following TMA, to achieve the initiation of clinical trials within the NIHR target, and to maintain recruitment of commercially-sponsored studies to time and target.

The ninth quarterly report of required data was submitted to NIHR in July 2014, and are reported to the OUH Trust Management Executive on a quarterly basis.

3.2 NIHR Clinical Trials Performance Indicators

70 day Benchmark for initiation of clinical trials: This metric applies to all clinical and interventional trials and relates to the time taken to set up a study and grant permission within a Trust; and, once permission is granted, the time taken to recruit the first patient. Specifically, the first patient must be recruited within 70 days of receipt of a valid research application (VRA). The R&D Teams must review the VRA for Trust Management Approval (TMA) within 15 days, following which the PI must recruit the first patient into the trial within the remaining portion of the 70 days.

Recent changes to the OUH’s policy for Trust Management Approval, and the introduction of a new software system for monitoring clinical research studies through the approvals process have led to an improvement in our time to grant of TMA. From April to June 2014 the mean period of TMA approval reduced to 11 days, from approximately 40 days in 2013.
Although our performance in granting TMA is improving, there remains a problem with failure to identify and successfully recruit eligible patients; suggesting a lack of readiness or capacity for conducting the research, or conflicts with other on-going studies. Studies with rare diseases still have the same target as those with a larger target population. If a set of studies are approved that have dependent recruitment, later studies will all fail if the first fails to recruit. Recruitment of the first patient remains a challenge that needs to be addressed on a Trust-wide basis.

3.3 Commercial Trials’ Recruitment to Time and Target

The delivery metric is based specifically on commercially-sponsored clinical trials, which must recruit to time and target, calculated from the total number of patients and the duration of the recruitment period, as set out in the study contract. The number of trials reaching target recruitment by or before the target date has shown no significant improvement over the past four quarters.

The R&D Governance team are focusing attention on the identifying those trials where performance must be addressed to achieve compliance. Areas for improvement, in order to meet both the first patient recruitment target and the commercial study recruitment to time and target include:

- More realistic expectations of performance at the contractual stage.
- Early identification of eligible patients who may be willing to participate.
- Improved readiness or capacity for conducting the research, including study teams and infrastructure fully in place.
- Ensuring no competition with other on-going research studies.
- Better communication and ‘buy-in’ from clinical colleagues to support the trial in a timely fashion

4. Strategies to Enhance and Accelerate Clinical Trials Performance

A number of measures have been implemented, and are proposed, to improve the OUH performance in respect of the NIHR metrics for the initiation and delivery of clinical research:

4.1 Measures to improve rapid data management and tracking

The very large scale of the OUH clinical research portfolio requires systems that can track and alert both R&D teams and investigators within the short timelines required by the NIHR metrics. A new Portfolio Management System (PMS) has been developed within the JRO and was launched in March 2014. This is proving to be an invaluable tool for the management of clinical research performance, by more rapidly highlighting timelines in the performance of the JRO and clinical research teams. The PMS facilitates a proactive approach to the management of data, so that outliers can be identified and addressed, within a time period that will impact upon the data submitted to NIHR.

The PMS is subject to on-going development, with the intention to expand access to relevant data across the Trust, so that real time data can be monitored and potential breaches of time targets highlighted promptly to the relevant PI and Divisional Director. Thus, prompt action to rectify the situation can be implemented by the research teams.
This will affect both the 70 day benchmark and the recruitment to time and target metric. Such a development will also serve to create a shared sense of ownership of clinical research performance across the Trust.

The R&D staff have developed a proactive and outward facing approach to research; the JRO ethos is of an integrated team to support clinical research across the Trust. R&D team members attend steering committees and individuals are identified as key contacts for the various Divisional groups and Clinical Trials Units.

4.2 Measures to improve specific components of the Trial Initiation Timeline

*The time taken by the R&D team to approve the research project:* The R&D teams continue to identify improvements in their systems for review of research applications, thereby increasing their success in meeting the national targets. This includes streamlining of governance reviews, the costing process and the processing of model agreements, wherever possible. There has been a dramatic improvement in the time taken to deliver Trust Management Approval by the OUH R&D teams within the JRO.

*The time taken for the research team to recruit the first participant:* Without prompt recruitment of trial participants, even substantial reductions in the time taken for Trust Management Approval will have limited impact on the overall performance of the Trust in respect of the ‘70 day’ metric.

The importance of recruitment of the first patient is highlighted within the NHS Permission letter and the R&D Governance team have systems in place to flag to Principal Investigators that the deadline is approaching. A greater emphasis is being placed on feasibility and logistics, in the process of Trust Management Approval for new clinical trials.

4.3 Commercial Trials: recruitment to time and target

PI awareness, readiness and motivation, on behalf of both research and clinical care teams are key to achieving effective and timely recruitment. The importance of accurate feasibility assessment is emphasised by R&D, during contract negotiation and governance review. Recruitment targets agreed with commercial companies, need to be realistic and achievable.

4.4 Prioritising Clinical Research Performance in the OUH Clinical Divisions

The OUH Clinical Divisions are crucial to effective clinical research management, governance and performance, since the clinical activity and patient flows are embedded within Divisions, and research study PIs work as either substantive or Honorary Contract holders within the Clinical Division. Work is underway to appoint Divisional R&D Managers, who will take responsibility for coordinating the Divisional clinical research portfolio and ensuring overall satisfactory performance in feasibility, study initiation and recruitment. Embedded within, and professionally accountable to the Divisions, there will be a reporting line into the Joint Research Office. The increasing
importance and demands on clinical research performance monitoring and management will also require additional support and responsibilities to be identified with the JRO R&D teams. It is envisaged that the finances to cover these roles would be generated through increased research activity, including commercial studies, and grants awards to the Trust.

All performance data are summarised by Division and Directorate, which will allow individual Divisions/Directorates to review and act on their performance data in the context of core audit and performance activities.

The prioritisation of clinical research performance by the OUH is reflected in the recent decision by TME to receive a formal report of OUH Clinical research performance every quarter, and to recommend that a similar report is made the OUH Board every 6 months.

4.5 Improved Communication of Research Performance Priorities

Much effort is put into communication of the importance of Trust performance to these metrics. Where training of any kind is delivered to researchers; whether formal in good clinical practice training and audits, or informal in the course of business, the issues of both first patient recruitment and recruitment to time and target is highlighted. However, more systematic work can be done. Opportunities include: introducing clinical research into staff induction briefings; highlighting clinical research performance at clinical team meetings, within Clinical Research Facilities and Clinical Trials Units, BRC Themes, and in collaboration with University Departments, through the University’s MSD Research Committee and the MSD Board. These communications will be made through letters, papers and presentations from the OUH Director of R&D, and more widely by other members of the R&D teams and JRO, for example through ‘road shows’ and workshops to reinforce the message with PIs, research teams and clinical staff.

4.6 Incorporation of Clinical Research Performance in Statutory & Mandatory Training, and in Consultant Appraisal

The R&D Team provide both face-to-face and on-line training modules in Good Clinical Practice (GCP) for all clinical research PIs and for other researchers, to be undertaken in accordance with OUH policies. Greater ‘visibility’ for GCP training, and the opportunity to introduce specific aspects of clinical research performance that are relevant to both PIs and to wider groups of OUH clinical staff, could be achieved by including research training modules in the OUH Statutory & Mandatory Training requirements.

In the last year the OUH local requirements for consultant medical appraisal have incorporated some aspects of reporting and assessing clinical research activity, for example evidence of up-to-date training in GCP. Working with the Medical Director, there is an opportunity to modify these local requirements to include more systematic and objective information on clinical research performance for all consultants who are PIs in research studies, for example by a requirement to include listings of all studies, with performance metrics, which could be made available through the JRO’s Portfolio Management System.
5. Research Governance

5.1 Research Governance in the NHS

Research governance refers to the framework in OUH to manage the research process from end to end, to ensure that research is undertaken in a safe, appropriate and ethical manner, in accordance with national guidance and applicable laws to ensure that maximum benefit is derived from research of public and patients. These include:

- **The Health Research Authority (HRA)** that has responsibility for the National Research Ethics Service (NRES), which is responsible for all Research Ethics Committees (RECs).
- **The NHS Research Governance Framework (RGF)** that sets out a framework for the governance of research in health and social care. This includes clinical and non-clinical research; research undertaken by NHS or social care staff using the resources of health and social care organisations; and any research undertaken by industry, charities, research councils and universities within the health and social care systems that might have an impact on the quality of those services. The HRA intends to replace the RGF late 2014 with a new simplified framework.
- **EU Clinical Trials Directive** (2001/20/EC) provides a framework which sets out how clinical trials investigating the safety or efficacy of a medicinal product in humans must be conducted. The EU Clinical Trials Directive was transposed into UK Law as the Medicines for Human Use (Clinical Trials) Regulations 2004 and came into force on 1st May 2004, forming the basis for the UK Clinical Trials Regulations 2004.

5.2 Local Frameworks for R&D Governance, Training and Monitoring

Locally, clinical research is governed by a number of OUH Trust polices:

- Safety Reporting in Clinical Research
- Sponsorship of Clinical Research Studies
- Trust Management Approval for Clinical Research
- Research Protocol Amendments
- Monitoring and Audit of Research Studies
- Research Grants Policy and Procedures
- Management of Intellectual Property
- Integrity in Research
- Receipt, Storage and Handling of Investigational Medicinal Products

These policies are underpinned by a suite of Standard Operating Procedures (SOP) within R&D. Policies and SOPs are updated in response to national and local developments.

The policies are all available on the OUH website and specific attention is drawn to them during Good Clinical Practice (GCP) training. The content and requirements of the policies are also covered within this training. Through collaboration with the University of Oxford Clinical Trials and Research Governance team (CTRG), GCP training is provided to cover all research-related legislation and GCP; courses being designed for both staff new to trials and an update for experienced researchers. GCP training is a legal requirement of the Regulations and the Research Governance Framework. All researchers, in the Trust and the University, are required to have undertaken this training every three years as a minimum.

A training course is provided for clinical researchers, specifically designed for those not engaged in the conduct of a CTIMP. Informal training is provided in the form of advice and support to researchers and their teams.
The R&D Governance team ensure that all Clinical Trials of Investigational Medicinal Products (CTIMP) and device trials, for which the Trust has taken on the role of Sponsor, are monitored, to assure the Trust of compliance with the relevant regulations. In addition, a number of hosted CTIMPs are selected for audit, either where concerns have been raised, or according to a risk assessment.

6. Strengthening Research Governance in OUHT

OUHT has a very large research portfolio and has established a robust approach to governance in accordance with national standards.

Despite this positive environment there is a need for all members of staff involved in research to maintain a high level of awareness of the need to comply with the policies and procedures for research governance in the Trust. This is most easily achieved by ensuring that R&D activities are fully integrated, reported and monitored in the Clinical Divisions. Currently, the OUHT Director of R&D is in discussion with Divisional Directors and the OUHT Board to establish the roles of Divisional R&D directors supported by a senior R&D manager/coordinator.

These dedicated individuals would be mandated to promote research, oversee performance and ensure that research active staff have adequate training to undertake trials and studies in a safe manner. This effective local/divisional implementation and monitoring of governance policies will promote patient safety in OUHT.

Greater awareness of R&D governance, for training in GCP and the requirements of R&D SOPs and policies could be achieved through Statutory and Mandatory Training, through Appraisal and through Divisional audit and training activities, the goal being to ensure that the vast majority of clinicians are able to support well governed research by understanding the processes that should be demonstrable by investigators in the clinical environment.

9. Conclusions

Continued focus on clinical research activity and delivery will be achieved through the OUH’s key research programmes and programmes. The Joint Research Office has established a research governance and support plan with prioritised objectives to include:

i. Working with all OUH Divisions and partner University Departments to provide support for research and development

ii. Continuing review and setting of standards in research design, approval and conduct of research

iii. Development, through consultation, of a research governance and delivery scorecard based on key performance indicators, and its incorporation into Divisional and Trust performance review processes

iv. Development of a learning package to disseminate broad understanding of basic principles of research governance (and how ethically to promote and support clinical research) among the vast majority of front line clinical staff

v. A programme of audit of compliance with key policies and standards

vi. Quarterly reporting to TME and annual reporting to the Board
Dr Tony Berendt
Interim Medical Director

Paper prepared by:

Professor Keith Channon
OUH Director of R&D,

September 2014