Institution: University of Bristol

Unit of Assessment: 1 – Clinical Medicine

a. Context

Research in this Unit of Assessment derives from three Schools in two of the University's six Faculties: the School of Clinical Sciences in the Faculty of Medicine and Dentistry; the School of Cellular and Molecular Medicine and the School of Physiology and Pharmacology in the Faculty of Medical and Veterinary Sciences. Fundamental to our research is its potential impact on patient care and outcomes, health care delivery and commercial enterprise. Our research is conducted across six research groups with critical mass and close links with industry and excellence in the delivery of health care locally (Infection and Immunity; Cardiovascular Science; Regenerative Medicine; Musculoskeletal Research; Metabolism and Renal Medicine; Cancer Biology), and in many cases the impact of our research has connections with at least two of these six groups.

The research strategy for this Unit of Assessment is to deliver ground-breaking discoveries in basic science and pioneering treatments for patients across a wide range of specialties and conditions. This is achieved through fundamental, translational and clinical research, focussing on our areas of strength in collaboration with colleagues in the NHS and other Units of Assessment, and on fully exploiting our close links with industry including spin-out companies. The strategy covers the translational gaps relating to driving fundamental scientific discovery through to clinical testing in first-in-human studies, and from taking evidence of efficacy derived from such early studies through to large-scale phase III randomised trials.

In addition to substantial laboratory facilities in each of the three Schools for fundamental research, we have the following key centres and collaborative initiatives that underpin our translational research: the Bristol Heart Institute (BHI), a leading centre of clinical and basic science cardiovascular research; an NIHR Biomedical Research Unit (BRU) in Cardiovascular Disease and leadership of part of another BRU within the University of Bristol in Nutrition, Diet and Lifestyle; leading on inflammation and immunotherapeutics within a Biomedical Research Centre (BRC) in Ophthalmology led overall by Moorfields Eye Hospital/UCL; a formal research and training agreement focussing on ocular immunology between the United States NIH and the NHS (under the auspices of the BRC); spin-out companies covering for example musculoskeletal medicine, regenerative medicine, and infection and immunity; the Royal College of Surgeons-funded Bristol Surgical Trials Centre. Through these activities and University-level structures we have impact on patients and their care, national and international policy and practice and the wider economy.

Non-academic beneficiaries and types of impact

Patients have benefited from our research on surgery, medicine and disease prevention. For instance, the substantial uptake of off-pump coronary artery bypass surgery has resulted in fewer complications compared with standard surgical methods. Other examples are: realisation of harm caused by metal-on-metal hip replacement has greatly reduced the use of this type of artificial joint; the PROMPT low-resource obstetric training programme has improved obstetric and infant outcomes in many different health care systems and socio-economic circumstances. Our research in regenerative medicine has also brought tangible progress – for example, a tissue-engineered human airway, and first-in-human clinical trials of stem cell treatment for knee joint cartilage trauma. Our research is also progressing towards clinical trials of progenitor cells for vascular regeneration. The need for alternatives to bone grafts, especially in osteoporosis, has led to development of an artificial bone graft substitute (Bonesave), now in routine use worldwide. With population health sciences colleagues, research on the Avon Longitudinal Study of Parents and Children (a population-based multigenerational cohort) led to greater understanding of the role of adiposity in bone development, and demonstration of the effect of high impact exercise.

We have made major scientific advances leading to novel immunotherapies for allergic and autoimmune diseases such as multiple sclerosis and uveitis. For example, our research underpins the development of new therapeutic strategies involving ocular retinal imaging techniques for treating and imaging the immune system in ocular inflammatory disease. We are conducting clinical trials of new treatments for high blood pressure, including a novel surgical approach to drug resistant hypertension. We pioneered the world's first service for the treatment of Barth syndrome.

For the future, the recently-launched £12m EPSRC-funded SPHERE collaboration led by the University of Bristol is investigating a platform for remote healthcare monitoring for patients with chronic conditions or following discharge from major complex surgery. In particular, we have developed technology for in-home cardiac monitoring to facilitate the early identification of events.

Health care services have benefited from our research in NHS priority areas including disease prevention, patient-focussed care and mechanisms of infection and resistance. Specific advances include: tests for tracking low-level leukaemia ('minimal residual disease'); causes of infection in joint replacement surgery; patient perspectives on the delivery of joint replacement surgery; and new, validated islet autoantibody assays to study the pathogenesis, prediction and prevention of type 1 diabetes. We were the first to provide scientific evidence for the mechanism by which dietary fibre and aspirin are preventative for colon cancer (apoptosis), which was a large factor in the 'five-a-day' public health campaign, and were part of the first international study showing that aspirin reduces bowel cancer incidence in high risk (hereditary nonpolyposis) patients. Our research on hERG potassium channel bioassays has led to major changes in cardiac safety testing for new drugs. We have also led key initiatives in health care delivery models, such as vaccine strategies in paediatrics and analysis of the National Joint Registry of England and Wales.

Commercial enterprises have benefited from our research through partnerships with established companies and spin-out companies including Apitope, Azellon Cell Therapeutics, KWS BioTest and Trident. One such major advance is discovery of the Epstein-Barr virus (gp350) antigen used to generate vaccines for various diseases, which justified the acquisition of patents by GSK to produce recombinant gp350 for vaccine trials. In renal medicine, our cell-cultured glomerulus and tubule models have been licensed by several companies for drug development testing, in terms of both new targets and drug safety. We have identified new approaches to target testing in urology – specifically, pharmacological targets in bladder conditions and drainage stents for the ureter. We have led multinational trials for pharmaceutical companies such as Astellas and Novartis.

National and international health policy has been influenced through our contributions to the evidence base on which such policy is derived and also through individuals' chairing and membership of several key panels. For example, our research into metal-on-metal joint replacements and hERG have led to changes in health policy, driven by the National Institute for Health and Care Excellence (NICE) and/or the Medicines and Healthcare Products Regulatory Agency (MHRA). Our research into low dose glucocorticoid treatment has also contributed to its routine use and is included in NICE guidelines as first-line combined therapy to prevent the progression of joint damage in rheumatoid arthritis. Our staff have chaired the Academy of Medical Sciences (AMS) Wellcome Trust-funded INSPIRE programme, the AMS Academic Careers Committee and the NIHR Comprehensive Clinical Research Network Urogenital Specialty Group.

b. Approach to impact

The University of Bristol engages actively with the NHS and other strategic partners in the region. The Bristol Research and Innovation Group for Health was a partnership between the University of Bristol, the four NHS Trusts in Bristol and the University of the West of England, Bristol. From 2007 to 2012, the six organisations developed a shared research strategy, coordinated infrastructure to enable joint research and agreed common goals for translational and applied health services research. In 2012 this was formally constituted to become Bristol Health Partners, also incorporating the local social care services. Bristol Health Partners is a legal academic health sciences partnership for research and innovation, creating Health Integration Teams (HITs) as inter-organisational groups of commissioners, academics, health and social care practitioners, to

harness research, innovation, education, patient care and prevention pathways. Researchers in this Unit of Assessment lead HITs on retinal and musculoskeletal diseases and, together with other collaborations, these formal relationships provide a strong platform for the impact of our research.

Interaction with key beneficiaries, users and public audiences

We are committed to engaging with patients, clinicians, voluntary organisations, Royal Colleges, specialist associations and policy-makers, with stakeholders involved at all stages of research from inception onwards. We have contributed substantially to campaigns for awareness of health issues and the benefits of research. We have collaborated fully with the NHS to maximise the proximity (and, where possible, co-location and even organisational integration) of our researchers with practicing clinicians. This assists bench to bedside research, and also the identification of clinical problems requiring basic research so as to achieve back-translation of research. This enables staff to exploit wider opportunities such as access to the NHS Trust patient panels and Clinical Research Networks. In particular, major research bases are housed on-site at both of the two local acute NHS Trusts (North Bristol NHS Trust (NBT) and University Hospitals Bristol NHS Foundation Trust (UHB)), so that non-clinical and clinical University staff interact directly with NHS colleagues.

An exemplar of this is the Bristol Heart Institute (BHI) located at UHB, which incorporates basic as well as clinical researchers, and facilitates clinically relevant cardiovascular science research and clinical trials. For instance, *Paton*'s basic science research on hypertension has now moved to phase I clinical trials as a direct result of the interaction between clinicians and researchers within the BHI. In 2012 a partnership of UHB, charity and industry invested £2m in a Retinal Treatment and Research Unit in the Bristol Eye Hospital, embedding research into a clinic and imaging facility to deliver care for patients and facilitate point-of-care and surveillance studies as well as phase I, II and III trials to bring tangible benefits to patients, academia and commercial organisations.

To foster cardiovascular translational research, UHB is also developing the Cardiovascular Regeneration Laboratories. This facility will be in close proximity to the adult and paediatric cardiac surgery, vascular surgery and the Clinical Research and Imaging Centre (CRIC-Bristol). In addition, NBT's new hospital at Southmead, Bristol opening in May 2014 will include dedicated clinical research facilities alongside an extension (co-funded by the University) to its on-site academic laboratory facility, already housing part of the University's School of Clinical Sciences.

In addition to regular mainstream press releases, articles and interviews, coordinated through the University Public Relations Office, staff are encouraged to undertake a wide range of public engagement activities facilitated as needed by the University's Centre for Public Engagement. These include: 'Engage', an annual event to celebrate and share best practice in public engagement; 'Brain Awareness Week' run by the University; 'Science Café' talks, sponsored by the British Science Association; and the 'I'm a Scientist, Get Me Out of Here' outreach programme. We use social media including ResearchGate and Twitter to inform debate, and maintain links with our alumni through, for example, the University's Facebook page. In April 2013 Bristol Health Partners hosted one of the first medical versions of the Technology Entertainment Design (TED) event in the UK (TEDMED), at which five staff connected with this Unit of Assessment gave presentations. We will continue our active engagement with this enterprise in future.

An example of outreach activity specifically for children is the STEM Ambassador Scheme, funded by the Department for Business, Innovation and Skills, Department for Education and The Gatsby Charitable Foundation. The Discover Science Festival, visited by hundreds of school children and members of the public, is facilitated by our linkage to the dedicated science museum @Bristol. We also make full use of the Bristol Mobile Teaching Unit – a lorry that expands into a seminar room for 20 students at a time. *Cannell* is a judge for the national school science fairs called the 'Big Bang'. As well as making extensive use of patient participant groups for specific projects, we have established a number of long-term user-involvement groups. For example, People and Research South West gives advice on involving people in health research and maintains databases of interested local people, and we have close links with NBT's Patient Involvement Panel, particularly in the context of the musculoskeletal research led by *Blom* and *Gooberman-Hill*.

Supporting staff to achieve impact

We have appointed School Impact Directors to review impact at the individual and research group level, and to generate impact strategy. Staff are encouraged to undertake impact-driven research to improve patient health and clinical practice, contribute to the development of new therapeutic approaches, to inform policymakers and raise public awareness of our research. These activities form an important part of the annual Staff Review and Development of all staff. Moreover, success of individuals and groups in terms of achieving excellence in activities relevant to impact are fully recognised by School- and Faculty-level communications – for example, on our intranet sites, in Faculty newsletters, by showcasing presentations by Schools to senior University staff, as well as through the Vice-Chancellor's Impact Award and the University Engagement Award that have been presented since 2011 and 2007 respectively. We also encourage attachments to industry, for example through a Knowledge Transfer Partnership with the biotech company ImmunoBiology.

Use of University resources to achieve impact

The University's Research and Enterprise Development (RED) Division supports seed funding, innovation, impact and commercial contacts. RED have been instrumental in creating University Academic Business Fellows appointed from academic staff with specific remits to establish new academic industry linkages for their respective Faculties; in the case of this Unit of Assessment there are three such individuals. An example of a project that directly benefitted from RED's support is the NIHR HTA-funded IVAN trial (a randomised controlled trial of treatments to Inhibit VEGF in Age-related choroidal Neovascularisation). In addition to a complicated sub-contracting process, RED helped to ensure indemnity cover for a trial that would potentially be opposed by the pharmaceutical industry due to use of generic medications. This trial has been lauded as a model of its kind, including overcoming such difficulties, in an independent review of highlights of the HTA programme over the last 20 years (Raftery and Powell, Lancet 2013;382:1278-85).

Other University initiatives to maximise impact include the Severnside Alliance for Translational Research (SARTRE) and SETsquared. With Cardiff University, we formed SARTRE in 2009 as a focus for translational research and interactions with external partners such as bio-pharmaceutical companies. For example, SARTRE facilitated the formation of a screening partnership by KWS BioTest for research in immunotherapy, and has generated a collaboration to develop systems for point-of-contact diagnosis. SETsquared is a partnership between the Universities of Bath, Bristol, Exeter, Southampton and Surrey to support the growth of new business opportunities through spin-outs, licensing and incubation; it facilitates enterprise development and won the UKBI 'Established Business Incubator of the Year' award. The Bristol Centre of SETsquared organised the 'Changing Worlds Showcase – Impact of University Research', to which we contributed substantially.

c. Strategy and plans

The University's Research and Enterprise Strategy identifies development of a portfolio of high impact research as a priority. The aim is to promote research that generates impact and to develop a tailored platform for impact, which is reflected in the strategic and operational plans of Faculties and Schools. In particular, there are two initiatives directly relevant to the future delivery of this priority: the Elizabeth Blackwell Institute for Health Research (EBI) and Bristol Health Partners. Our staff have very close links with these structures: *Mathieson* is Director of Bristol Health Partners, *Dick* and *N Williams* are the Faculty Research Directors for Medicine and Dentistry, and Medicial and Veterinary Sciences respectively; and *Dick* is an Executive Group member of the EBI.

Launched in 2013, the EBI is supported by a Wellcome Trust Institutional Strategic Support Fund with matched University funding to a total of £1.5m per year for various schemes to promote interdisciplinary health research and direct University resources for this purpose. The schemes include an innovative Clinical Primer Scheme offering active clinicians 3 to 9 months' experience in an academic environment to see if research could be part of their future career, and Translational Acceleration and Knowledge Transfer Awards to help secure commercial or translational funding. The EBI covers research from the basic sciences underpinning knowledge of health and disease to

clinical, social and population health sciences, focussing on translation to effective health outcomes, patient and public involvement and commercial partnerships. It specifically facilitates engagement with engineers, mathematicians and physical scientists. Given the importance of industrial partnerships, SARTRE activities in Bristol have been subsumed within the EBI, and the Director of SARTRE is now both Deputy Director of the EBI and the Director for Partnership.

In addition to driving implementation of our research generally, Bristol Health Partners has formed Health Integration Teams (HITs) as inter-organisational groups of academics, clinicians and commisioners to target major health priorities. To achieve our strategic aims in relation to impact, we will build on the two existing HITs led by our staff, facilitated by the recent award of £9m from the NIHR (with matched funding from the Universities and Bristol NHS organisations) to establish an NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC*west*) as the focus for connecting health research with service organisation and delivery, primarily through the established and further HITs. For example, we are fully involved in the formation of a Bristol-wide Cancer Group that may lead to the creation of a cancer HIT. CLAHRC*west* will work closely with the West of England Academic Health Sciences Network to provide a coherent and well-resourced structure for patient and public involvement as well as capacity for the implementation of research evidence, service enhancement, health improvement and wealth generation.

The School Impact Directors will develop a coordinated overview of activities and ensure an ongoing focus on impact. They will achieve this by working closely with the School Heads of Research supporting individuals and groups to develop impact, brokering linkages and facilitating the gathering of metrics for impact success. The Impact Directors' role will increasingly foster linkages between academics and infrastructural support for innovation and impact within the University and the above partnerships. They will identify potential 'innovation push' at an early stage, foster research in accordance with 'innovation pull' and signpost researchers to the relevant University resources. Where relevant, the latter includes the three University Academic Business Fellows whose remit covers staff in this Unit of Assessment.

We will also develop our approach to the communication of impact. Alongside the University Public Relations office and open-access publishing in international journals, we will expand our use of social media within schools to broker professional and stakeholder interaction, and engage public interest. We will continue to engage with delivering local talks, seminars and meetings within and outwith the University, with science activities in schools remaining a particular priority and focus.

d. Relationship to case studies

RED has fully supported the impacts in our case studies, including the three spin-out companies. Apitope, from research by *Wraith* showing that peptides can be used to stimulate T-regulatory cells and block pathology in autoimmunity, is developing pharmaceutical agents for treating allergy and autoimmune diseases, and has conducted clinical trials in multiple sclerosis. Azellon Cell Therapeutics developed from research by *Hollander* into autologous (the patient's own) stem cell technology; it is conducting a clinical trial of a novel stem cell product for use in meniscal tears of the knee. Trident, a drug discovery company, and KWS BioTest, a contract research organisation specialising in drug efficacy trials for immune diseases, both derive from research by *N Williams*. Trident has conducted clinical trials and KWS BioTest contributes to the design and implementation of pre-clinical pharmacology programmes to test the efficacy of lead compounds.

RED and the Centre for Public Engagement promoted the public health campaign on aspirin and high dietary fibre to reduce deaths from bowel and other cancers, as well as the outreach aspects of the study on the advantages of beating heart surgery. The improvement of maternal and infant safety has benefitted from public health and public relations campaigns promoted through the University. Organisations such as NICE, MHRA and UK Biobank have also been instrumental in our research having an impact on policy and practice, for instance in terms of metal-on-metal arthroplasty, hERG-based drug safety testing and tests for tracking low-level leukaemia.