Institution: University of Exeter

Unit of Assessment: UoA1 Clinical Medicine

a. Context : Translationally relevant biomedical and clinical research in the University of Exeter Medical School (UEMS) is undertaken within the Institute of Biomedical and Clinical Sciences (IBCS). IBCS maintains a portfolio of people-focussed research delivering direct benefit to the NHS, the pharmaceutical industry and to patients. Our research is centred around four principal themes, of which two ("Diabetes, Cardiovascular Risk & Aging" and "Neuroscience & Mental Health") feature within Unit of Assessment 1. All of our research programmes aim to generate outputs which make a difference to people and we achieve reach and significance within the local region, across the UK and on the global stage.

Impact on patient stakeholder groups: The most important stakeholders for our research are patients and we aim to improve their quality of life. To underpin this goal, a key priority has been to establish and maintain public trust in, and support of, our research agenda. To achieve this, we ensure that our research objectives are explained carefully and that public information is provided in a readily accessible, user-friendly, format (see, for example, http://www.exeter.crf.nihr.ac.uk/). We recognise that recruitment of subjects with no particular medical history poses a particular challenge and we take pride in our ability to reach and attract such people. As an example, we are compiling a unique biobank of tissue from up to 10000 local donors (designated "EXTEND"; see http://www.exeter.crf.nihr.ac.uk/node/155) who have consented to its use in on-going and future clinical studies. This population provides a unique opportunity to undertake physiological studies in defined individuals using a genotype-recall approach. As such, we believe that truly personalised medicine is an achievable objective and our associated case studies illustrate this point forcibly. In addition, work within IBCS has contributed seminally to a wide range of further, patient-focussed, impacts such as:

- Establishment of an internationally-recognised centre for genetic testing (and thereby, optimised therapy), based in Exeter, which receives referrals globally and offers advice and guidance for the development of equivalent facilities across the world (www.diabetesgenes.org).
- Fundamental studies on the control of eye movement yielding a new understanding of Duane's syndrome in humans (*Chilton* & *Ellard*) and suggesting an alternative therapeutic approach (Science, 321, 839-843, 2008).
- Development and patenting of novel, slow-release, reagents for the delivery of vasoactive hydrogen sulphide in a physiologically relevant manner (*Whiteman*; see e.g. Exp Rev Clin Pharmacol 4: 13-32, 2011)
- Collaboration with NHS Trusts regionally to form the South West Peninsula Academic Health Science Network (AHSN). Established in 2013, this AHSN has a primary aim to impact positively on the health and well-being of the region's 2.2 million inhabitants.

Impact on industry and commerce: We work closely with industrial partners to exploit opportunities for innovation. The University of Exeter has a well-established intellectual property rights (IPR) policy (available via the staff intranet) and supports a proof of concept fund that can be accessed to advance the commercialisation of existing or new intellectual property (IP). Grants of up to £15000 are available via this scheme, which is managed by the IP & Commercialisation team within the University's Research and Knowledge Transfer department. Examples of Medical School projects which have received recent support include the development and validation of a novel diagnostic assay to detect early signs of sepsis (in collaboration with Meso Scale Discovery Ltd. (www.mesoscale.com)); development and testing of a novel enhanced photosensitizer for use in the photodynamic therapy of certain skin cancers (*Curnow*; in collaboration with Galderma; www.galderma.co.uk) and the patenting and marketing of novel hydrogen sulphide donor molecules with applications in the treatment of cardiovascular disease and other microvascular related diseases (*Whiteman*; with Viva Chemicals; www.vivachemicals.com). In addition, novel nitrate donors have been developed that have applications extending beyond the realm of healthcare into agrochemicals (patents have been licensed to a leading agrochemical company who will now carry out field trials). Additional patents have also been filed (October 2013) to protect novel fatty acid derivatives identified as being potentially useful for the treatment of patients with type 2 diabetes (*Morgan*; in collaboration with CNRS (France)).

As part of our commitment to economic growth and development, and to the training of a new generation of innovative translational biomedical scientists, we have supervised a cohort of PhD and MD studentships in collaboration with industrial partners within the UK and Europe (including Astra Zeneca, Lilly, Shell, Dyamid, Vactech, Boehringer Ingelheim, Onyx). Throughout the REF period, we have also nurtured a continuous tranche of Early Career Researchers holding competitive Fellowship support from Wellcome Trust (including two Sir Henry Wellcome Fellowships), MRC (clinical fellowships) Diabetes UK and the Diabetes Research and Wellness Foundation. Our training programmes are underpinned by an ethos of interdisciplinarity and by the provision of state-of-the-art platform technologies across our research facilities. We also provide access to purpose-designed clinical research facilities via the NIHR-funded Exeter CRF which has received continuous funding from 2010 to 2018, at a total value of £10 million.

Extending these objectives, we have recently entered into partnership with Quntiles (www.quintiles.com) the world's leading biopharmaceutical service organisation, to develop a Prime Site for clinical trials in the South West. This alliance will further enhance our ability to recruit patients and clinical investigators, both of whom are critical to an efficient and effective drug development process. As a result, an increased number of clinical trials across a wide range of disease areas will be conducted in the region, bringing on-going benefits to the community, the economy and to our research programmes.

Impact on public policy and on society: Our work has informed public policy within the UK and overseas. *Hattersley* served on the World Health Organisation Expert committee on the diagnosis and classification of diabetes which concluded that HbA1c could be used to diagnose diabetes and led to changes in clinical diagnosis. *Hattersley* also informed public debate on genomic medicine, contributing to the House of Lord's Select Committee on Science and Technology enquiry into genomic evidence 2009. He also contributed to the international guidelines on genetic testing of patients with neonatal diabetes (www.ispad.org/content/ispad-clinical-practice-consensus-guidelines-2009). *Melzer* provided evidence to the US Food and Drug Administration Scientific Advisory Committee on the environmental effects of pro-oestrogenic chemicals such as Bisphenol A. *Ellard* provides evidence to ensure the NHS embraces genomics appropriately as a member of the Chief Medical Officer Genomics Board and the NHS commissioning Board Clinical Reference Group for Genetics. *Mill* contributes expert advice to the Department of Health Emerging Sciences and Bioethics Advisory Committee (ESBAC). *Thornton* provided expert advice to the All-Party Parliamentary Group on Umbilical Cord Blood and Adult Stem Cells. *Morgan, Shore & Frayling* participated in the formulation of the "type 1 diabetes research roadmap" presented to the UK government in June 2013 (www.jdrf.org.uk/research/type-1-diabetes-research-roadmap).

b. Approach to impact : We work closely with the University's Research and Knowledge Transfer team (RKT) who provide expert advice on achieving research impact. This has helped us to foster a culture of impact within IBCS and has ensured that people consider impact carefully at all stages of the research process. RKT has established a programme of bi-annual impact awards to reward individuals achieving important impact externally, and teams within IBCS (*Hattersley, Ellard*) were winners in 2011 while two more groups have been shortlisted for the 2013 round. In addition, we have also developed other, in-house, approaches which have included:

- Delivery of a programme of interactive workshops on an annual basis. These are open to all members of staff (including early career researchers and PhD students) and provide a forum in which impact cases (real and imagined) are scrutinised in small group discussion and the conclusions then considered openly across the wider group.

- Incorporation of a section about "achieving impact" within the annual Performance Development Review process for established academic staff and early career researchers. This provides an opportunity for a focussed discussion about both impact strategy and business engagement and, for clinical colleagues, includes an evaluation of recruitment targets to NIHR-funded clinical trials.

- Training in consideration of how pathways to impact can be achieved including via the sharing of best-practice in drafting "impact pathway" statements within research grant

applications.

c. Strategy and plans: A fundamental principle which underpins the research undertaken in UEMS (and which has driven our priorities since the inception of Peninsula Medical School) is that it should remain patient-focussed. Thus, our research aims to deliver early and direct patient benefit while also enhancing the knowledge base and economic development of the UK. The infrastructure and support mechanisms operating across the Medical School have been developed with this in view. Our on-going strategy is designed to embed a culture of impact across the Medical School by placing a consistent emphasis on the importance of impact at the level of individual research projects (achieved, for example, by focussed discussions during the annual performance development review of academic staff and by engagement of doctoral students and early career researchers in impact seminars). Active encouragement of industrial collaboration as a means to generate impact, also features strongly.

We believe that centralisation of research support activities is essential to the efficient exploitation of research outcomes and we achieve this in a number of ways. For example, a dedicated NIHR Clinical Research Facility (CRF) provides a purpose-designed location for the conduct of clinical research projects, streamlined mechanisms to secure ethical approval for relevant projects, as well as a centralised collection and storage point for patient samples. Since its creation in 2007, more than 100 different projects have been conducted under the auspices of the NIHR CRF and the HTA licensed facility now holds organ tissue samples from almost 1000 patients as well as DNA, serum and plasma from the EXTEND (Exeter 10000) cohort. The tissue bank steering committee includes patient representatives and provides an opportunity for them to influence whether a proposed project, using samples gifted by others, should be approved. Thus patients play a direct role in determining the direction and impact of this research.

Provision of enhanced capital facilities and new state-of-the-art equipment, as well as increased staff recruitment within targeted areas, remain vital to the success of our research mission. In November 2013, we opened a £27.5M Wellcome Wolfson Medical Research Centre providing enhanced laboratory and clinical research facilities on the Exeter Wonford site to promote our translational research agenda. We also play a central role in a new multidisciplinary initiative to create a state-of-the-art "Living Systems Institute" within the University where a systems approach will be employed to achieve solutions to medical problems. This £50M investment will also enhance the capacity to house experimental animals; a goal which is seen as critical to the Unit's ability to deliver globally-relevant impact in the future.

d. Relationship to case studies: Our case studies were selected as prime examples of high quality and high impact research undertaken within the Unit and they represent a paradigm of excellence to which the whole Unit aspires. They illustrate our ethos clearly by showing how a fundamental understanding of key biological processes can be translated into early beneficial changes at the level of individuals and populations. Two of the impact cases reveal that truly personalised medicine is an attainable goal, by demonstrating that the accurate diagnosis of genetic abnormalities can lead to improved therapy and to a much enhanced quality of life for individuals with particular forms of diabetes. The third demonstrates that global impacts can be achieved across whole populations by providing a rigorous evidence base to support policy decisions.

The impacts achieved by probing the genetics of neonatal and early-onset forms of diabetes have been transformative for individual patients and their families and have spawned a revolution in the diagnosis and treatment of this illness across the world. Our goals are to expand this approach to allow more detailed physiological analysis of the effects of specific combinations of genetic polymorphisms (rather than overt mutations) to provide an improved understanding and more informed treatment options for those suffering from chronic diseases with a polygenic aetiology, such as type 2 diabetes. We also expect that these approaches will impact on the control of neurological conditions such as depression, anxiety and neurodegenerative disorders. As such, we will continue to improve the lives of individuals while also providing underpinning evidence to inform government and policymakers in the development of strategies that will influence millions.