Institution: University of Bath

Unit of Assessment: 3: Allied Health Professions, Dentistry, Nursing and Pharmacy

a. Context

Preamble: Bath's submission encompasses research from the Departments of Pharmacy & Pharmacology and Biology & Biochemistry (Faculty of Science), and from the Dept. of Psychology and the Dept. for Health (Faculty of Humanities & Social Sciences). Research in this UoA is by definition centred very much on applied science, and all projects have at least one eye firmly on their future translation into practical applications. Going forward, this focus will be retained and intensified. The culture of working with 'stake-holder' partners, whether from industry, the regulatory agencies, the NHS or professional bodies, pervades the research ethos of the UoA.

Principal non-academic user groups, beneficiaries of research: Broadly speaking, the pharmaceutical and biotechnology industries (large established companies, middle-market enterprises, small and medium enterprises, and start-ups); the NHS and other international healthcare systems; the UK Medicines and Healthcare products Regulatory Agency (MHRA), the European Medicines Agency (EMA), the U.S. Food & Drug Administration (FDA) and other regulatory bodies; the patient (in its broadest terms), the economy and the general public.

Main types of impact and relation to research activity: Four principal paths underpin the UoA's approach to impact during the REF period, and its future strategy and plans for supporting impact:

- Generation and exploitation of intellectual property (IP) has resulted in (a) the creation of new enterprises that are generating significant revenues, (b) the design of new chemical entities, which are undergoing clinical trials, and (c) new healthcare (drug delivery) technologies.
- Sustainable interactions with key users/beneficiaries of research have led to obvious patient and societal benefit, to new innovations already being exploited via TSB-funded Knowledge Transfer Partnerships (KTPs), and to symbiotic relationships with the pharma/biotech sector.
- Relationships with governmental and professional bodies involve substantial research support to enhance regulatory science and the provision of expert advice to key organisations.
- Public and alumni engagement is an emerging pathway to impact facilitating broader dissemination of the UoA's research to schools, health professionals and the general public.

b. Approach to impact

The UoA's research demonstrates both **reach**, in terms of regional, national and global impact, and **significance**, insofar as it has produced new medicines, created new enterprises, realised important societal and economic benefits, and enabled translation of basic biological, chemical, physical and psychosocial understanding into obvious benefit for the public.

Interaction/engagement/relationships with key user groups and research beneficiaries to develop impact: The applied nature of research in this UoA ensures relevance to real-world problems, the solutions to which lead inevitably to tangible impact.

1. *Generation and exploitation of intellectual property (IP)* characterises a pathway to impact that flows directly from the UoA's research strengths. Resulting directly from Bath IP, this approach is illustrated by 3 specific examples of the translation of academic research to the industrial setting: (a) Vectura, now a publicly traded company, specialising in the development of inhaled drug delivery systems based on Bath innovation to treat pulmonary diseases, that has continued and growing economical and societal impact; (b) development and transfer to the Italian pharmaceutical company, Chiesi, of a distinctly different approach to deliver drugs to the lung; and (c) the spin-out of Sterix, its subsequent acquisition by Ipsen (a major French pharmaceutical company), and the entry of Bath-invented compounds into clinical trials during the REF period.

This strategy has been sustained during 2008-13 and IP generation/exploitation remains a central objective. For example, following refocusing of Ipsen's R&D strategy, Bath acquired in 2012 sole intellectual property rights to a clinical trial-ready anticancer drug developed (and originally designed at Bath) during Potter's collaboration with the company, and to other earlier stage programmes. These have been packaged into a business plan and venture capital investment for a new spin-out company (EstryX Pharma) is being sought to exploit these technologies. Glythera, Ltd., which was co-founded by MacKenzie and Watts, has already been successfully spun-out from the University, receiving its first round of investment in 2008. The

company is developing novel protein/peptide functionalization and glycosylation technologies to impart improved pharmacokinetic properties for the next generation of biotherapeutics. In 2012, Glythera received a further £2M in external venture capital funding enabling dedicated laboratories in the NE of England to be set up with 6 full-time employees. Likewise, Delgado-Charro and Guy have licensed US and European patents on reverse iontophoresis to Nemaura Pharma, a UK-based SME, which is exploring incorporation of the technology into a novel, non-invasive glucose monitoring device for diabetics. Relatedly, Delgado-Charro received funding from the NHS-National Innovation Centre to develop a universal sampling pad for application of reverse iontophoresis in paediatrics.

2. *Sustainable interactions with key users/beneficiaries* are a logical consequence of the applied nature of the UoA's research. Impact has been developed in this way in the areas of adolescent pain, the 'dose-banding' of cytotoxic agents (Bath ASU, founded and initially based at the University), and the provision of safer injecting equipment for users of illicit drugs. These wide-ranging projects illustrate clearly how research informed by end-user/beneficiary stakeholders can result in impact related to quality-of-life, to improved patient care at lower cost, and to societal benefit and, in each case, the interactions continue to strengthen. The Centre for Pain Research (Eccleston) is generously funded by Reckitt Benkiser and a novel test of patients' attention to pain, and its continued improvement, is the target for the development of new products. In parallel, Rodham runs a clinic supporting and treating patients with Complex Regional Pain Syndrome at Bath's Royal United Hospital; complementary online resources have also been developed. The UoA's relationship with Bath ASU is expanding by developing protocols to evaluate and improve the stability of therapeutic monoclonal antibodies upon prolonged storage (Watts). This approach has successfully extended the shelf-life of Herceptin resulting in a substantial new contract (~£0.5M/yr) to Bath ASU. Interaction continues with Exchange Supplies, a unique social enterprise striving to improve the harm reduction response to drug use by developing innovative products (Scott). A project funded by Exchange aims to refine injecting paraphernalia so as to reduce local inflammation. Scott has also consulted 4 hr/week with Turning Point (a drug treatment provider) since 2010 and this primarily clinical work feeds directly into her research.

Further examples include: **[1]** A TSB-supported KTP (~£190K) with Prosonix, Ltd., to develop manufacturing process technology of pharmaceutical co-crystals and binary drug crystals suitable for inhaled and oral medicines (Price). The company will contribute additional funding of *ca.* £150K in pilot plant and analytical equipment and raw materials. **[2]** Research funding from Genentech to explore the variable bioavailability of subcutaneously (SC) injected protein drugs, and from the TSB, with Sirius Analytical, Ltd., to commercialise an instrument modelling the SC site (Mrsny). **[3]** *NextGenSeq*, a company (Lindsay, co-founder) providing training in next generation genome sequencing, a method predicted to facilitate the development of personalised medicine. **[4]** Substantial funding from the EU Innovative Medicines Initiative, FP7 and industrial partners to accelerate the development of better and safer medicines (e.g., evaluating safety of medicines use in pregnancy) (De Vries). **[5]** Creation of a regional NHS centre of excellence to treat anxiety disorders (Salkovskis). **[6]** The South West Autism Group works with schools to support children with autism (including a summer school to support the transition from home to university for autistic students) (Brosnan); an EPSRC project that involved children with autism as design partners in developing educational aides is an excellent example of engagement with end users (Brosnan).

The manifold interactions of the UoA with industry are reflected by the level of research funding awarded during the REF period (~£7.2M out of a total of >£23M, including £4.5M from Ipsen); the close association of academics with industry, such as Potter's secondment to Sterix for 12 years (ending 2010) and Ward's Royal Society Industrial Fellowship with Novartis (2006-10); and the engagement of many academics as consultants and scientific advisory board members of pharmaceutical, biotech, cosmetic, and personal care companies, including GSK, Pfizer, AZ, Novartis, Roche, Genentech, Novozymes, Sanofi-Aventis, Ipsen, L'Oréal, Boots, Reckitt-Benkiser.

3. *Relationships with governmental and professional bodies* provide a further route to impact of the UoA's research, such as: [1] U.S. FDA funding (Price, Fotaki, Delgado-Charro, Guy) to develop and validate new approaches to determine bioequivalence between innovator and generic drug products for treating lung and skin diseases. [2] De Vries (now at the European Medicines Agency (EMA)) was an EMA Expert Advisory Group Member (2009-12) and Rapporteur to the Research Executive Agency for the European Commission. [3] Guy and Weiss are members of the

pharmaceutical science expert advisory and pharmacy practice research panels, respectively, of the Royal Pharmaceutical Society. [4] Fotaki regularly speaks on her research involving *in vivo-in vitro* correlations at outreach workshops organised by the American Association of Pharmaceutical Scientists. [5] Jones and Mrsny continue to fill leadership positions in the British Pharmacological Society and the Controlled Release Society, respectively.

4. *Public and alumni engagement* is an evolving pathway to impact. As a consultant to Bath ASU, Watts has disseminated his research to key user groups via (e.g.) invited lectures at the national NHS Quality Control meeting (2012) and at an NHS training course for aseptic manufacturers (2013). Watts also contributed to the establishment of http://mabstalk.com/, a website dedicated to critiquing academic literature against NHS compliance guidelines to assist user groups in the application of extended shelf-lives to monoclonal antibody therapeutics. MacKenzie, with a collaborator in Cardiff, has launched the "P2X7 interactome" website (www.P2X7.co.uk), which is funded by the BBSRC for public communication of their recently awarded project grant. Welham and De Bank participated in the *Patients Participate! Workshop* organised by UKOLN, The British Library and the Association of Medical Research Charities to explore the development of a body of literature for patients interested in biomedical research, and to improve patient/public engagement by making biomedical science more accessible (http://blogs.ukoln.ac.uk/patientsparticipate/). Brosnan's book 'Technophobia: The Psychological Impact of Information Technology' (Routledge) discusses how technology impacts upon how we learn, work and play. The UoA enjoys close relationships with alumni, such as Raymond Schinazi (Emory University, USA), a renowned chemist/virologist and entrepreneur, who has donated >£0.5M to Bath to support exchange fellowships with Emory (Mrsny and Threadgill have participated). An alumnus of Pharmacy & Pharmacology, Christopher Jones, is Vice President and Global Head of Pharmaceutical Development at AstraZeneca, and was appointed, in 2013, to the University's Ventures Board.

Support/enablement of staff to achieve impact and use of institutional facilities, expertise, resources: Impact, knowledge transfer and public engagement are essential criteria considered in annual staff development and performance reviews at Bath, in promotions, in the selection, mentoring and monitoring of new members of academic staff, and in departmental workload models for all staff engaged in translational research. Impact is a focal point for the Institution's research infrastructure, overseen by the Impact sub-group of the University Research Committee. The Research Development & Support Office (RDSO) facilitates commercialisation of Bath's research and played a pivotal role in protecting the IP, upon which Sterix and Glythera were created as spin-outs, and then catalysing the development of business plans, and the acquisition of venture capital (as it is now undertaking for EstryX Pharma). RDSO also administers the University Enterprise Development Fund providing grants for proof-of-concept of patentable IP, such as Pourzand and Eggleston's caged-iron chelators for skin photoprotection (£134K in total). The Enterprise and Knowledge Exploitation team (EKE) within RDSO is responsible for establishing and supporting Bath-associated KTPs, and acting as liaison between the industrial partners and the funding bodies. EKE was intimately involved in setting up the KTP with Prosonix, Ltd. (Price) and in the successful funding proposals to TSB for this project and that with Sirius Analytical, Ltd. (Mrsny). EKE interacts closely with the UoA, represented by its "KT Champion" (Price), who is able to support colleagues in collaborative activities with funds to kick-start such initiatives. Broader dissemination of impact is enabled by University Corporate Communications, the Researcher & Staff Development Units and the Public Engagement Unit, which actively engages with researchers to communicate the significance of their work beyond academia (e.g., outreach to local high schools (Caggiano, Lloyd, Thompson), and summer studentship research placements (Bailey, Pula, Ward)). A further key role of these institutional resources is to provide training and workshops in impact for early career researchers and postgraduate research students, developing the skills necessary to engage with external organisations – business, government, hospitals, schools – via promotion of research in different formats and to different audiences.

c. Strategy and plans

Strategy for achieving impact: Research is firmly focussed on applied science and its translation into practical applications. As a consequence, the strategy for achieving impact is directly and inexorably linked to the future research goals of the UoA's academic staff. Specifically, the research groups in drug target optimisation, drug synthesis and optimisation, and drug formulation and delivery have evolved a strategy to create a drug design and development facility alongside

the existing "Research in Medicines Design" (*ReMedDes*) initiative to provide a critical mass of expertise to engage with the pharmaceutical and biotech industries, and with the regulatory agencies, at multiple points along the drug development and approval process. Impact is envisaged at manifold entry points, such as the discovery of novel structures and mechanisms to target diseases such as cancer, solving drug delivery problems through a deeper understanding of the formulation-biological barrier interface, and developing new and practical *in silico* and *in vitro* methods to facilitate assessments of *in vivo* bioavailability and its quantification. A senior pharmaceutical scientist from Pfizer (French) has been recruited to lead biopharmaceutical development activities in *ReMedDes*, and to cross-fertilize research impact throughout the UoA.

Research in drug use, pharmacoepidemiology and health and clinical psychology has enhanced clinical translation as its overarching aim. The new and strengthened team in psychology, and the psychosocial research in medicines use and adherence, are geared to impact on how decisions about medicines and treatments are communicated, between pharmacists, clinicians and patients. The overlap with drug safety research and methods development in pharmacoepidemiology is clear and expands the path for translation of basic science to the clinical setting. In sum, therefore, the principal objective of the UoA is to facilitate the flow of discoveries in the laboratory to a tangible impact on the patient, the economy and society in general.

Goals/plans for supporting/enabling impact from current/future research: Key objectives are to identify the potential for impact from research projects at the earliest possible stage, to target potential sponsors of future work, to protect intellectual property, and to horizon-scan for those situations in which the outcomes may have greatest effect. The shift of emphasis towards impact in the research evaluation process has already "sensitised" academic staff to think deeply about the wider implications of their work, and the Research Committees of the UoA are boosting sensitivity at every opportunity; for example, built into all departmental annual 'away-day' activities are dedicated sessions in which impact cases can be discussed and refined, and potential ideas related to impact developed for the future. With respect to the post-REF period, ongoing activities clearly provide significant potential for future impact, including the development of Glythera, the expansion of Bath ASU's business into the provision of stabilised biotherapeutics, Potter's new initiatives with Bath IP and the clinical evaluation of new drugs for cancer and other diseases, the development of the KTP between Price and Prosonix, Ltd. (and Mrsny's relationship with Sirius Analytical, Ltd.), and the role of research from *ReMedDes* to influence methods development for the approval of generic drug products by regulatory agencies (including, specifically, the FDA).

d. Relationship to case studies

The 6 case studies span the breadth of research in the UoA, both when the underpinning work was performed and at the present time. The strategy of engagement and sustained close contact with relevant stakeholders has been instrumental in each of the impact cases. (i) The Vectura story exemplifies the drug delivery group's approach towards innovative solutions to challenging problems and exemplifies the UoA's aim to generate and exploit patentable technology. (ii) The impact on the development of inhaled medicines at Chiesi is a similar example, although achieved with a different technology to that of Vectura; in this case, research was translated to an existing EU industrial partner, rather than via a Bath-originated start-up company. (iii) The case study on safer injecting equipment for illicit drug users again demonstrates close and sustained contact with stakeholders leading to impact in terms of reduced healthcare costs and societal benefit. Research in progress promises to generate additional impact on the problems associated with drug addiction (there is also overlap here with an MRC-funded project striving to deliver a buprenorphine-naltrexone combination for the treatment of polydrug abuse). (iv) The drug discovery case history reflects another successful spin-out (Sterix), its subsequent acquisition by Ipsen, and secondment of Potter for a sustained period during which numerous compounds of potential therapeutic benefit were designed, synthesised and developed. (v) Bath ASU's path to impact capitalised on novel research to create a thriving and growing business in the SW. This case is a model example of a sustainable interaction, which is meeting key needs of the NHS nationally and having direct benefit on patient care – i.e., the key users and beneficiaries of the research. (vi) Lastly, the case study on paediatric chronic pain has had sustained impact both nationally and internationally, and is well evidenced with respect to assessment, treatment, policy and advocacy. Patients and healthcare providers (from clinical staff to the pharma industry) are, respectively, the beneficiaries and users of this work.