Institution: University College London

Unit of Assessment: 1 – Clinical Medicine

A. Context

UCL's UoA1 submission spans eight Divisions/Institutes from three Faculties of UCL's School of Life and Medical Sciences (SLMS) and includes 449.8 WTE. Our impact generation depends on the close partnerships between each Institute/Division of the submission and NHS hospitals, principally University College London Hospitals (UCLH) the Royal Free Hospital (RFL), Great Ormond Street Hospital (GOSH), The Royal National Orthopaedic Hospital (RNOH), and Moorfield's Eye Hospital (MEH). Three NIHR–supported Biomedical Research Centres provide a critical translational interface between the University and UCLH, GOSH, and MEH (investment of £162M in 2012). Importantly, UoA1 represents the majority contribution of UCL to UCL Partners (UCLP) Academic Health Sciences Centre (AHSC). In addition, our strategic alliances with Industry and the University sector are key components for impact. Appreciation of the health needs of the patients served by our partner hospitals drives our basic science along a pathway to impact. In turn, our NHS, industrial and academic relationships enable us to exploit our inventions to achieve both advances in health-care that have been implemented nationally and internationally, and success in commercialisation. The main beneficiaries of our research reflect this context and include:

- **Populations at risk of disease, nationally and globally**, who benefit from our success in identifying emerging patterns of disease, their causes, risk factors, and predictive markers. Our research has transformed the diagnosis of inherited metabolic diseases, the prevention of keratitis, risk prediction for angle-closure glaucoma, the outcome of scleroderma and amyloidosis, HIV resistance, the assessment of lung development, and childhood nutrition.
- **Patients** with cancer, infection, immune, cardiovascular, renal, gastrointestinal, rheumatological, orthopaedic, respiratory, ophthalmic and neurological disease. We have improved diagnosis and disease monitoring, developed new drug and device treatments and biomarkers of treatment response, enhanced the effectiveness of existing treatments, and established more effective ways of implementing best practice.
- **Providers of health-care** in London and nationally, who are affected by the influence of our research on NHS referral patterns. Approximately 50% of patients seen at our partner hospitals come from outside our local catchment areas and we host 27 National Specialist Services for rare diseases, through which we have made important advances in the investigation and treatment of 19 rare conditions. In addition, our therapeutic advances have directly reduced the cost of treatment in 20 disease areas, including rheumatoid arthritis, haemophilia, leukaemia, lymphoma, inherited immunodeficiency, thyroid cancer, and breast cancer.
- **The UK economy**, wherein we support wealth creation through the establishment of new businesses, and the adoption of new technologies and processes in biotech sectors. This results from our many partnerships with small and medium sized enterprises, and our licensing, spin-outs, and knowledge transfer activities. We estimate the total income directly to UCL arising from our commercialisation during the REF assessment period to be £20.6M.
- **The biopharmaceutical industry**, with which we enjoy numerous partnerships. Companies include GSK and Pfizer, with which we engage in all phases of drug development in order to bring new therapies to market and to repurpose existing medications for new licensed indications.
- **Government**, with whom we share expertise (particularly related to our research strengths in gene and cellular therapy), influencing policy on health-care, business and the environment through NIHR, All Party Parliamentary Groups, House of Commons Select Committees, Department of Business, the Food and Environment Research Agency, the MHRA, and EMA.
- **The Public**, our engagement with whom is facilitated by Public and Patient involvement initiatives conducted via the BRCs, the HEFCE-funded Beacon for Public Engagement

programme, media engagement, membership of charity committees, and school outreach work.

B. Approach to impact

Our wide-ranging approach is underpinned by a common aim to achieve clinical impact through **partnerships with the NHS, Industry, and other HEIs.**

B1. Creating an environment for impact

We capitalise on UCL-wide infrastructure designed to enhance impact on the nation's health and wealth, as highlighted in UCL's research and enterprise strategies. This includes the Office of the Vice-Provost (Enterprise), which oversees enterprise and impact, UCL Advances (our centre for entrepreneurship), UCL Business PLC (UCLB; technology transfer company), and UCL Consultants Ltd (UCLC; consultancy services). To further ensure the existence of an appropriate structure to support our researchers' engagement with the enterprise agenda, a SLMS Knowledge Transfer and Enterprise Board was established in 2008 and assimilates information on Divisional/Institute and Faculty initiatives to share best practice and foster strategic alignment.

Three Vice Deans for Enterprise, each representing a different Faculty in SLMS are being returned in this unit (**Chambers**, **Moss**, **Humphries**), as are three Knowledge Transfer (KT) Champions (**Beales**, **Abraham**, **Daniels**) appointed in their support. These leaders have managed a dedicated budget of £175K in the REF period to stimulate KT and enterprise activities. The Vice-Deans for Enterprise are increasingly proactive, and have organised workshops on intellectual property, working with industry, point-of-care technologies, and effective consulting, with over 100 attendees. Training in the recognition and protection of intellectual property is also part of the induction for new staff and students. UCL's commitment to academic staff engagement in Knowledge Exchange and Enterprise is unequivocal (www.ucl.ac.uk/excellence/). Accordingly, enterprise and KT are given equal weighting to research and teaching in appraisal and academic promotion. Some staff have been recruited in major part because of their previous commercial expertise (**Shima**, **Ng**) and the commercialisation successes of our academics (**Coffey**, **Pepys**, **Shima**) has been recognised at the annual UCL Awards for Enterprise.

B2 Structures for commercialisation and entrepreneurship

The principal route to the commercialisation of UCL research is UCLB, which also handles the technology transfer for UCLH, the RFL, MEH, and GOSH. Seven of UCLB's dedicated business managers are assigned to UoA1 Divisions/Institutes. As a single technology transfer office for UCL and its related hospitals, UCLB ensures that commercial agreements accelerate rather than stifle the efficient translation of our technologies, whilst ensuring appropriate revenue sharing with UCL and the NHS. It invests in the costs of developing inventions to a commercialisable stage via patenting and proof-of-concept (PoC) awards. Revenue sharing agreements incentivise commercialisation by allowing the inventor and department to share in the profits (www.ucl.ac.uk/library/scholarly-communication/ipr.shtml). The licensing route to commercialisation is UCLB's preferred option in the biomedical area, since it provides an undilutable revenue stream for UCL through the development (and ultimately the sale) of the technology. This is achieved through a typical licence structure of an upfront payment, development-related milestone payments and a royalty on sales. The strong track record of technology transfer from UoA1 researchers during the period of REF assessment is evidenced by:

- 242 Invention Disclosures, 98 Priority IP protection filings, and 202 instances of IP protection granted (amounting to over 40% of all the patent activity in UCL)
- The recent sale of the UCL spin-out Spirogen to Astra-Zeneca for $200M.
- 75 licensing deals. In addition to those described in impact case studies, recent examples include [text removed for publication]. These projects have generated total developmental milestone payments to UCL of £20.6M, including a royalty income stream based on sales of the products.

Since 2008, UCLB has also provided proof-of-concept funds to 61 commercially-viable research projects (including software and devices) totalling £1.9M. Funds available to our projects include £500K per annum from Higher Education Innovation Fund, a partnership with the pharmaceutical company Johnson and Johnson ($0.8M), and separate proof-of-concept (PoC) funds from each of the NIHR-funded Biomedical Research Centres (BRCs) totalling £0.7M. Furthermore, venture

capital and early stage investment funding is available from a range of other sources, including the Bloomsbury Bioseed Fund, and the Orion fund (a partnership between UCLB, the venture capital group MTI and the technology transfer offices of the Universities of Manchester and Edinburgh).

B3 Maximising the scale and pace of translation of basic science

B3.1 Translational Research Office (TRO)

The SLMS Translational Research Office (TRO), established in 2009 with MRC pump-priming funds, manages a pipeline of biomarkers, devices, surgical techniques, biotherapeutics, and small molecule translational projects. Its highly experienced, industry-background research support staff (eight WTE) has been pivotal in securing grant funding approaching £40M from many sources, including the MRC, Wellcome Trust, NIHR, TSB, and charities, and in managing a growing portfolio of 30 major translational projects, 25 of which are led by investigators in UoA1. 12 of these projects are funded by the MRC Developmental Pathway Funding Scheme (DPFS); this is the largest portfolio of DPFS-funded projects in the UK (value £7.2M). In UoA1 there are also six MRC Developmental Clinical Studies awards (£11.6M) and three Wellcome Trust Translational Awards (£5.6M).

Recognising that a gap in funding between basic research and the main translational schemes was hindering the progression of exploratory research into therapeutic development, UCL established its Therapeutic Innovation Fund (TIF) in 2010. Funded in part through the BRCs and managed by the TRO, the TIF began with a three-year pilot scheme, providing seed funding to support emerging, therapeutically focussed projects across UCL with the aim of setting them up to attract significant further funding. £650K has since been distributed through this scheme to projects in UoA1, with 13 out of TIF's 16 funded projects being led by UoA1 investigators. [text removed for publication]. 10 of the 13 UoA1 projects funded by the TIF have secured follow-on funding (including major translational grants or industrial collaboration) amounting to >£2M as of 2013; this included [text removed for publication] and a major MRC DPFS award to the **Gaspar** gene-therapy project.

Experience with this pioneering fund laid the groundwork for UCL's successful application in 2012 to the newly launched MRC Confidence in Concept scheme for a devolved fund of £700K. This has been supplemented in 2013 with an additional £450K investment in the TIF from the UCLH/UCL BRC. The TRO has also been supported by £300K from UCL's EPSRC Impact Acceleration Account; this has been used to provide project consultancy support and academic training on regulatory requirements in developing health-care devices. Investigators in UoA1 have unrivalled experience of clinical research using **Advanced Therapeutic Medicinal Products (**ATMPs), either gene- or stem cell-based treatments. The TRO currently supports nine clinical projects, all led by UoA1 investigators, representing approximately £10M of active grants. The projects range from research on RNA editing approaches to hypercholesterolaemia, inherited immunodeficiency, and rare forms of blindness, to cell based approaches to cancer immunotherapy.

B3.2 Clinical trial and related infrastructure to support impact

The Clinical Research Facilities (CRFs) at UCLH, GOSH, and MEH together provide clinical space (51 rooms), 44 research nurses, six research Fellows, 12 data managers, 14 research co-ordinators, 11 laboratory technicians, two pharmacists and nine administrators. The remit of the CRFs is experimental medicine; much of their activity relates to early phase clinical trials and a range of other interventional and non-interventional studies designed to better understand the origins of human disease. A key advantage is their location in NHS premises, which permits safe patient-based research, and attracts contracts from industry. The UCLH CRF, which is NIHR-funded (£5.5M in 2012), has housed over 150 clinical trials since 2009. It has a current active portfolio of over 60 trials, and an annual commercial income of £600K: GOSH alone hosts 60 active trials per year and the CRF at MEH has 171 open clinical studies. UoA1 investigators (**Brocklehurst**, **Lederman**) direct two of UCL's three Clinical Trials Units (CTU), which are essential for the prosecution of investigator-led clinical trials in UoA1, particularly in later phase research.

B3.3 Streamlining clinical research approvals

To minimise the time taken to approve human research, we have instituted joint research offices between UCL and its partner hospitals to co-ordinate all clinical research led by UCL academics.

These are the Joint Research Office (partnership of UCLH, RFL and UCL) and the Joint Research and Development Office (partnership of UCL and GOSH), which grant research approvals to over 400 clinical projects per year. We have recently harmonised R+D approvals across the North London sector, streamlining the approval process for trials by conducting review, costing and contracting undertaken within one 'permission centre' on behalf of all hospital sites. The project has reduced review time from an average of 104 days in 2012 to 17 days in 2013.

B4 Engagement with patients and the NHS

Close integration with the NHS across the entire UoA serves to remind us of the scale of unmet clinical need in our patients, and of the requirement to prosecute biomedical research to address this. At the same time, it gives us access to patient populations for experimental medicine studies and clinical trials facilitating our impacts on and benefits for the NHS and its patients.

B4.1 Partnership with the NHS

232 of our academics are clinicians directly engaged in clinical care. In addition, our clinical academics hold leadership positions in the NHS locally: **Bellingan** and **Powis**, for example, are Medical Directors at UCLH and RFL respectively, and six more staff occupy non-executive or executive positions on Trust Boards (**Isenberg** - RNOH; **Goldblatt** and **Smyth** - GOSH; **Tooke** - UCLH; **Luthert** and **Khaw** - MEH). UoA1 academics are also represented in regional NHS bodies (**Pritchard-Jones** - Chief Medical Officer For London Cancer; **Janes** - Pathway Director for Lung Cancer; **Ardeshna** - Pathway Director for Haematological cancers; and **MacAllister** - Chair of the North Central London Joint Formulary Committee). These positions provide important conduits for our transfer to the local NHS of expert knowledge transfer and subsequent treatment advances pioneered at UCL. This is also achieved through our membership of NICE Guideline Committees (**Micali**, **Williams**, **Pereira**, **Humphries**, **Williams**, **Shafran**, **Wedzicha**), with **Hochhauser** serving on NICE Technology Appraisal Committee B. We interface extensively with NIHR - 15 UoA1 staff are NIHR Senior Investigators - and work closely with NOCRI (NIHR Office for Clinical Research Infrastructure - **Rosenberg**). Our expertise in the rapid dissemination of research findings accelerates the establishment of standards of prevention, investigation, diagnosis, and treatment for patients nationally and internationally.

B4.2 Expertise in rare diseases

Many nationally commissioned NHS services are led by UCL academics in UoA1. Their expertise in the pathobiology of disease facilitates drug target validation, and clinical trials are enabled by availability of cohorts of individuals with rare conditions. Three such services at GOSH (which has more nationally commissioned services than any other hospital in the UK), are led by UoA1 Cat A; these are services for Bardet-Biedl syndrome (**Beales**), congenital hyperinsulinism (**Hussain**) and rare neuromuscular disorders (**Muntoni**). The 14 others in which our academics play leading roles include the Complex Tracheal Disease Service, which assesses and treats children with severe and rare conditions affecting the upper airways of the lung, including a complex condition known as long segment tracheal stenosis. Led by Martin Elliott and with input from **De Coppi**, it was responsible for first tracheal transplant. The National Amyloidosis Centre (**Pepys**, **Hawkins**) sees 70% of patients in the UK with this condition via specialist commissioning hosted at the RFL and using a network of outreach clinics. Its close association with UoA1 staff allows the Centre to promote the adoption of research findings that advance the management of this condition in the UK and internationally, including the invention of SAP scanning for monitoring of amyloid burden, now a standard investigation world-wide. The RFL also hosts nationally commissioned clinical services in scleroderma and pulmonary hypertension (**Denton**, **Abraham**), haemophilia (**Nathwani**), kidney/liver transplantation (**Burroughs**), and lysosomal storage disease (**Metha**). The nationally commissioned London Sarcoma Service (**Flanagan**) at UCLH and RNOH represents the largest sarcoma service in the UK and the largest single group worldwide contributing to international clinical studies in bone sarcoma. It treats ~50% of UK patients with this disease annually and is the most research-active sarcoma unit in the UK, leading the genomic characterisation of sarcoma in collaboration with the Wellcome Trust Sanger Institute. At MEH, highly specialised services include ocular pathology (**Luthert**), ocular oncology and retinoblastoma (**Sagoo**). In total, of the 31 National Specialist Services hosted by UCL partner hospitals, 27 are in UoA1 and of these, seven are directed by UoA1 academics.

B5 Capitalising on our clinical research strategy for impact

B5.1 Providing early phase capacity for first-in-human studies

Although most first-in-human studies within UoA1 have explored new chemical entities (NCE) arising out of the drug industry, our research also generates NCEs, some of which proceed to clinical investigation. A prime example is **basiliximab**, invented at UCL in the late 1980s and commercialised by Novartis in collaboration with **Akbar** [text removed for publication]. Since 2008, **Pepys** has been investigating a molecule (CPHPC) generated from his own research as an adjunct to a HIV DNA vaccine. We led the first gene therapy trial for retinal degeneration (**Ali**, **Bainbridge**), have started first-in-human studies in retinal cellular therapy (ACT–**Bainbridge**) and have worked with regulators to obtain approval for human embryonic stem cell (hES) therapy for age-related macular degeneration using a patch delivery system. UoA1 researchers (**Morris**, **Pule**, **Amrolia**) are also leading first-in-human trials using gene engineered immune cells for the treatment of cancer and opportunistic infection.

B5.2 Repurposing of existing medicines

Repurposing of existing medications for new indications avoids the prolonged preclinical testing required of new compounds. We take a number of approaches to achieving impact via this route. The first is the use of our research to established the pathogenic mechanism and, thereby, to open up the prospects for using an existing drug for a new indication. In UoA1, seven active repurposing trials are ongoing, including perhexiline in cardiomyopathy (**Elliot**), and racecadotril in pulmonary hypertension (**MacAllister**); seven of our impact case studies describe the success of this approach. Secondly, UoA1 academics use genetic studies in populations as natural randomised trials to validate drug targets. This approach has identified a causal role for the interleukin-6 receptor in cardiovascular disease, providing an opportunity to repurpose the interleukin-6 receptor blocker toculizumab, currently used in rheumatoid arthritis. The UCLH/UCL BRC awarded £600K in 2013 to fund a systematic approach to identifying the likeliest candidates for repurposing (**Hingorani**). Thirdly, a major component of our commercial partnering portfolio addresses preclinical re-profiling (see section B6.1). [text removed for publication]. Finally, our work has allowed the repurposing of medicines via their reformulation into a novel preparation of greater acceptability to patients.

B5.3 Refining the dose, schedule of administration or combinations of therapies

This has been an important approach to our delivery of clinical impact, particularly in cancer therapy. It was the basis of treatment advances for ovarian cancer (**Lederman**) and anal cancer (**Lederman**) and the identification (using a novel biomarker) of a subgroup of juvenile idiopathic arthritis patients who respond well to methotrexate (**Wedderburn**).

B5.4 Non-pharmacological treatments

These are principally advances in surgery, radiotherapy, and ATMPs, our understanding of the impact of lifestyle on health, and the deployment of devices. Twelve of these are described in our impact case studies.

B5.5 Improved diagnosis and monitoring of disease

Our approach to improving disease diagnosis and monitoring has particularly involved the use of genetics to improve the diagnosis of inherited disease, and imaging for better disease detection and monitoring, including new end points for clinical trials. For example, **Moon** has developed non-invasive MRI imaging for the detection of tissue amyloid deposits that has been incorporated as an outcome measure in clinical trails. **Peggs** has recently defined the role of PET to stratify patients with relapsed lymphoma, combining it with a novel chemotherapy regime.

B6. Working with industry

Our academics collaborate widely with biotech companies, the pharmaceutical industry, and medical device manufacturers. 82 academics received industry funding totalling £47M for research between 2008 and 2013, and GSK was UCL's Enterprise Partner of the Year in 2009.

B6.1 Collaboration with industry in early phase development

We encourage an approach that builds on the strengths of either partner, with early engagement at the drug discovery phase. We are, for example, working with GSK to develop novel anti-fibrotic agents through preclinical target validation (**Chambers**) and via the development of

imaging biomarkers in humans (**Groves**). This partnership has delivered findings critical to supporting a Phase II study of a novel PI3 kinase inhibitor in lung fibrosis (clinicaltrials.gov/ct2/show/NCT01725139) and the selection of a candidate molecule targeted against the αvβ6 integrin for human testing. Importantly, our collaborative work (on IL-13 and EP4) has also generated reliable negative data ensuring that two other compounds have not progressed to clinical testing. [text removed for publication].

Collaboration with the devices industries is extensive, and includes developmental work in prostate imaging and early Phase I and Phase II work, for example in vascular-targeted phototherapy in prostate cancer (**Emberton**) in collaboration with Tookad Soluble™, which led to a randomised phase III study (€100M investment) that has completed recruitment within the EU (CI **Emberton**). Similarly, Sonacare invested over $1M in a phase II study of high intensity focused ultrasound for early prostate cancer (**Emberton**); this was followed up by Wellcome Trust/DoH Health Innovation Challenge Fund (two awards totalling £3.5M) to perform phase 3 studies of this technology.

B6.2 Industrial studentships

UoA1 has prioritised - and subsequently seen a substantial increase in the number of - industrial studentships since 2008. Currently 60 of our academics have RCUK CASE studentships part-funded by industry. The UCL IMPACT Award scheme, which was launched in 2010 to boost PhD student numbers and engage external organisations, provides 50% (£32,535 for a three year studentship) funding, this to be matched by a non-Research Council funder. While the scheme targets industry and charities, some awards have been made to partnerships with government and overseas universities; 78 studentships have been awarded to our investigators since the scheme started.

B6.3 Job-exchange programmes

Examples have included a visiting Professor scheme for senior scientists from GSK to spend six months at UCL (Birault) and a BBSRC-funded secondment of a Pfizer executive (Eveleth).

B6.4 Bioincubator space

In 2013 funding of approximately £2M was secured from the HEFCE Catalyst and UCL/UCLH NIHR BRC to allow UCL to take office and laboratory space in the Stevenage Bioscience Catalyst (SBC). The SBC is a unique bioscience community, created to provide small biotech and life sciences companies and start-ups with access to the expertise, networks, and scientific facilities traditionally only accessible from within multinational pharmaceutical companies. The site will encourage interaction between tenant university projects and companies, with the expectation that the combination of opportunity and cooperation will breed innovation and commercial success. The UCL/UCLH NIHR BRC has allocated a £600K fund for three “Vanguard Projects”, including one belonging to this UoA [text removed for publication]. The University of Cambridge (UoC) has also taken space at the SBC and it is envisaged that joint UCL-UoC projects will be developed, funded and based at the SBC.

B6.5 Consultancy

UCL allows academic staff to undertake up to 40 days of remunerated consultancy per annum, facilitated by UCL Consultants Ltd (UCLC), and since 2008 73 UoA1 academics have been active in consultancy work with industry. There are 15 who sit on the Scientific Advisory Boards of major Pharmaceutical companies (**Bellingan**, **Cheetham**, **Foster**, **Greenwood**, **Lightman**, **Lomas**, **Luthert**, **Muntoni**, **Ng**, **Peggs**, **Shima**, **Singhal**, **Stauss**, **Unwin**, **Wedzicha**). 37 have acted as expert witnesses, sometimes in complex areas of patent law. [text removed for publication]..

B6.6 Contract research with industry

This has expanded since 2008, much of it early phase research conducted in the UCL CRFs. that have provided the pharmaceutical industry with access to the patient cohorts necessary to conduct phase 1 and 2 clinical trials in cancer, hepatology, gastroenterology, cardiovascular, infection and rheumatology. Since 2008, 92 industry-funded trials have been hosted at UCLH and 71 at MEH.

B7. Commercialisation through spin-out companies

Examples of this strand of our approach include: Abcodia, set up to commercialise the UKCTOCS Biobank resource, which has been developed through the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) clinical trial. Nanogenic Solutions, who have developed a set of non-viral vectors that have shown outstanding transfection capabilities both *in vitro* (e.g. primary

cell lines) and *in vivo* (transfection of blood vessels and respiratory tract). Nanogenic is now selling its vector for lab reagent applications and has an in-house therapeutic vector in development for cardiovascular indications. This work has been developed at the UCL Institute of Child Health. Neurexpert provides neurophysiology solutions to industry. [text removed for publication].

B8. Provision of expert advice to policy makers

We have a track record of early engagement with regulators of the development of gene therapy for retinal disease (**Ali**) and hES therapy for age-related macular degeneration (**Coffey**), and have worked very effectively to streamline regulatory approval in these novel areas. Nonetheless, we realise that regulatory blocks present an on-going risk to impact, and several investigators (**Coffey**, **Khaw**, **Tooke**) have given evidence to the recent House of Lords Review of Regenerative Medicine to help ensure that government is well-informed. **Thrasher** has advised the US Recombinant DNA Advisory Committee, the US Federal Drugs Administration, the UK Gene Therapy Advisory Committee, the Medicines Control Agency and the European Medicines Evaluation Agency on matters related to human trials of gene therapy. **Bitner-Glindzicz** advised the DoH on amendments to Clause 14(4) of the Human Fertilization and Embryology Bill regarding embryo selection, particularly as it applied to deafness and the culturally deaf community. In addition **Bitner-Glindzicz** presented to the All-Party Parliamentary Group in July 2012 at the House of Commons on the subject of Consent for Consent. **Zumla** chairs and **Lipman** is a member of the International Scientific Advisory Expert Committee to the All Party Parliamentary Group on Global TB. **Malone-Lee** serves on the All Party Parliamentary Group on Incontinence, and **Kingston** and **MacAllister** have advised the MHRA, and **Forbes** the EMEA on drug licensing issues. The following have all advised Department of Health Committees in the REF period; **Lomas** (Chair, Scientific Priorities Committee, 100k Genomes and Respiratory and Allergy Expert Advisory Group to the Commission on Human Medicines 2006-9), **Taylor A** (Sub-Group of the Department of Health Post Mortem, Forensic and Disaster Imaging Group), **Brocklehurst** (Co-Director of DoH Policy Research Unit), **Griffiths** (Joint Committee on Vaccination and Immunisation), **Towers** (National Expert Panel on New and Emerging Infections), **Brown** (Committees on bronchiectasis, pneumonia, pandemic flu), and **Taylor S** (Advisory Committee on COMARE). **Waddington** has advised the Food and Environment Research Agency on the risk to the environment of GMOs and the risk of agro-terrorism using gene transfer vectors, **Sen Gupta** advised the Human Fertilisation and Embryology Authority on pre-implantation genetic diagnosis, and **Griffiths** Chaired the UK National Certification Committee for Polio Eradication. **Williams** is a member of the NIHR Strategy Board.

B9. Engagement of health-care users, the media and the public

Each of the BRCs is active in Patient and Public Involvement (PPI). They are supported in this by the PPI unit in UCL's Joint Research Office, which provides a dedicated officer to give advice and organises PPI workshops. During the REF period academics in UoA1 have organised 11 exhibitions (including the annual Cheltenham Science Festival; **Lythgoe**) and 47 open days, delivered 61 public lectures including two TED talks (**Lotto**; 2.4M viewings), and used the media to publicise research findings on 84 occasions. Highlights include events related to the coverage of rare eye diseases, stem cell research, inherited cardiovascular disease, and kidney disease. Innovative facets of this strand of our approach have included the creation, execution, and publication of a research project on bees within Blackawton School, Devon (**Lotto**: http://vimeo.com/22582869). **Bitner-Glindzicz** has used Information Days and worked with the deafblind charity Sense to engage hard-to-reach groups at risk of genetic deafness to improve the uptake of genetic tests invented at UCL. UCL's Public Engagement Unit was created in 2008 as one of six in the United Kingdom funded by the Beacons for Public Engagement Programme set up by HEFCE, Research Councils UK and the Wellcome Trust. It has awarded nine Beacon Bursaries to UoA1 investigators to engage patients in Ophthalmology, Child Health, and Women's Health.

C Strategy and plans

C1. Overarching strategy

The key components of our future approach will be to maintain and enhance successful aspects of our current impact strategy founded on **partnership with the NHS, industry and other HEIs**.

C1.1 Estates and Facilities

Co-location of a critical mass of clinical academics in an appropriate health-care environment with state-of-the-art facilities and technology has been critical to impact. Major estates renewal is anticipated in the next REF period and to enhance and accelerate our ability to translate exploitable research into clinical advances and patient benefit, we plan to make provision for bioincubator space in all new buildings or major refurbishments. We will, for example complete the partnership project between UCL and the RFL and deliver a research building for the Institute of Immunity & Transplantation to achieve full integration of research and clinical excellence for the benefit of patients. Another major project is the Bloomsbury Research Institute, which will bring together researchers from UoA1 and from the London School of Hygiene and Tropical Medicine to create a leading centre in infectious disease research. In some instances early stage translational work can be done off-site (such as at the SBC), but academics and industrial partners frequently need direct access and close proximity to clinical research facilities and specialist platform technologies. This will be particularly important in areas where UoA1 staff work closely with our BRCs, AHSC, and Academic Health Sciences Network (AHSN; see C2), where the triangulation of hospital, UCL research department and bioincubator will enhance our capacity for innovation, development, and downstream commercialisation.

C1.2 Incentivisation and Training

A second key strategic goal is to embed impact into the research and teaching objectives of every member of academic staff. To achieve this we will ensure that: i) new staff inductions include sessions on technology and knowledge transfer; ii) enterprise and knowledge transfer feature regularly on the agendas for staff meetings; iii) our academics make better use of institutional resources to document impact-related activity (http://www.iris.ucl.ac.uk); iv) sabbaticals are offered to academics who wish to create spin-out companies; and iv) knowledge transfer and enterprise activity are properly assessed and recognised in promotion and appraisal. Vice-Deans for Enterprise will work with Faculty Tutors to incorporate enterprise training into our postgraduate programmes to ensure the sustainability of this approach. At School level, the Knowledge Transfer and Enterprise Board will monitor a core set of five KPIs (industrial research income, invention disclosures, consultancies, industrial studentships, and snapshot value of technology transfer portfolio) to ensure that we are achieving our strategic objectives.

C1.3 The interface with Industry

Thirdly, we recognise that it is difficult for potential industrial partners to fully appreciate the extent of the research conducted across all parts of UoA1, and that this is a barrier to their effective engagement with our academics. To address this we will develop outward facing ‘one stop’ web portals to clarify the types of technology transfer activities in which we wish to engage. In support of this initiative UCL Consultants has recently initiated a series of thematic pilot projects across UCL, one of which includes the Institute of Ophthalmology. As part of these projects, newly appointed Consultancy Managers will be tasked with reaching out to industry to maximise our potential in areas such as analysis and testing, continual professional development (CPD) and short courses, expert witness and academic consultancy. In addition, our Enterprise Vice-Deans, KT Champions and BRC Business Development Managers are working together to develop a portfolio of sector-specific ‘industry days’ to bring selected external companies, investors, and funders (including MRC, Wellcome Trust, and TSB) into the unit to hear short presentations on research activity of potential interest to them. As part of our ‘outreach’ activities we will also promote ‘Reverse Showcase’ events, where individual companies are invited to meet with expert UoA1 staff to talk about the challenges they face in order to identify possible areas for future collaborative partnerships. For companies where we have an existing strategic relationship, we will devote resources and develop business models that facilitate sustained interaction.

C2. Local health impact through an AHSN for North London

The UCLP AHSN aims to span the second translational gap of implementing best clinical practice for the 6.3 million population of North London. Four of its five programmes (integrated Cancer, Cardiovascular Health, Comorbidities, and Life Course for Women and Children) map onto our research and we will make substantial contributions to achieving health and wealth impact over the next four-five years. Programme boards for each of these areas will be set up, with UoA1 investigators contributing as Programme leads and board members. In this way we will maximise the chances of both our own research and that of the UK University sector more broadly achieving

its full health impact.

C3 Continued focus on rare diseases
The Centre for Children's Rare Disease Research is a major capital project timetabled for 2015-2016. £10M of HEFCE capital funding has been committed and a further £50M is being raised by the GOSH charity to support the creation of a new purpose-built research centre housing 5,500 m^2 of laboratories, manufacturing facilities, clinical offices, and high quality space for patient engagement activities which are crucial to best progressing the academic mission in rare diseases. The GOSH charity has already purchased land for the building.

C4 Progression of current research portfolio to achieve impact as rapidly as possible
UCLB will continue to promote commercialisation through licensing and/or spin-out formation. [text removed for publication].

C5 Continued investment in Good Manufacturing Practice (GMP) laboratories for ATMPs
UCL researchers conduct more gene and cellular therapy human studies than those at any other centre in the UK. There are four dedicated GMP Facilities for gene and cellular therapies in UoA1 (see REF5 section D2.2.1 for a full description).

C6 Centre for Drug Discovery
The UCL-wide Centre for Drug Discovery is being developed to exploit the therapeutic potential of our basic biomedical and clinical sciences across a range of therapeutic areas, including cardiovascular diseases, inflammation, infectious diseases, and oncology. The Centre will be focused on the School of Pharmacy (which has recently become part of UCL), with significant contributions from the TRO, Division of Medicine, and Department of Chemistry. Professorial appointments in medicinal chemistry (Paul Fish) and chemical biology (Frank Kozielski) have been made in the School of Pharmacy. Two medicinal chemists (Drs Richard Angell and Sally Oxenford) with over 30 years' cumulative industrial experience between them have been appointed to start up a new TRO drug discovery facility. Alongside established UCL facilities such as Chemibank (compound collection and screening) and LMCB Translational Research Resource Centre (high content phenotypic screening), the Centre for Drug Discovery play a central role in bridging the development gap between target identification and robust lead molecules allowing successful drug discovery projects.

C7 Institute of Clinical Trials
The incorporation of the MRC Clinical Trials Unit into UCL in August 2013, and the setting up of a new Institute of Clinical Trials and Methodology (with the MRC CTU at its core), delivers expertise in early and late phase clinical trials governance and management is unparalleled among UK universities.

C8 Informatics for large data sets
We are working closely with the new **Farr Institute**, computer science and statistics researchers within other UCL Faculties, the **Francis Crick Institute** (see C10), EBI, the Wellcome Trust Sanger Institute, and partner NHS Trusts to generate new health informatics platforms. These bring direct benefits to patients but also make it possible for us to identify highly specific, stratified cohorts of patients for clinical studies. This is of particular interest to pharma and biotech companies working in areas from drug discovery through to post-licensing surveillance.

C9 The Centre for Advanced Sustainable Medical Innovation (CASMI)
Founded in 2013, CASMI is a joint venture between Oxford University and UCL, hosting experts from industry and government agencies. Its focus is the decline in R&D productivity, which it aims to address by driving the development of new innovation models for drug and device discovery, with inputs from experts in medicine, bioscience, social science, law, government, and ethics, as well as from patients. The approach will develop new models that will accelerate medical innovation and promote their uptake by policy makers, industry, and the public. The concept of **adaptive licensing** is being pursued in collaboration with GSK, for the more rapid development of drugs for amyloidosis (**Pepys**).

C10 The Crick Institute
The £700M **Francis Crick Institute** will open in 2015 with 1,250 researchers working on the

biological bases of a wide range of diseases. UCL was chosen as a founding academic partner for the Crick because of its broad research excellence in Life and Medical Sciences. Over the next five years we will invest in collaborations with the Crick by making joint appointments and allowing researchers to move their labs there to promote the application of our basic science approaches to address clinical problems. We are currently appointing UCL Crick Chairs of Clinical Science who will be UCL staff based in the Crick (**Swanton** and **Stockinger** are already in post).

C11 Promoting industrial partnerships

Recognising the importance of relationships with the biopharmaceutical sector, SLMS has recently (July 2013) used co-funding from UCL Enterprise and the UCLH/UCL NIHR BRC to establish an Industrial Partnerships Group in the TRO, with the express intention of supporting growth in this area. The recruitment of a group of dedicated Industrial Partnership Managers is already accelerating these initiatives and opening up new avenues for industrial engagement, for example by taking the lead in UCL establishing an academic hub at the Stevenage BioScience Catalyst.

D. Relationship to case studies

Our case studies demonstrate many of the impacts on and benefits to non-academic populations identified in section A. Thus they provide examples of improvements in the diagnosis of 14 and in the monitoring of 13 diseases, 17 new drug treatments (or drug combinations), two new devices, 10 examples where we have introduced novel non-drug treatments, three examples of commercialisation of our discovery science and 20 diseases areas where our advances have reduced health-care costs. They also exemplify many of the approaches we have taken to achieving described in B1-B3. The examples below highlight case studies of impacts arising from the pathways described in sections B4-B9.

D1 Engagement with patients and the NHS

Partnership with the NHS wherein the dual role of UoA1 staff as leading clinicians at NHS centres of excellence allows our research results to be directly applied in practice, is a vital means of extending the reach and significance of our impact. Examples of such impact include the provision of tools and testing facilities such as lung function equations and calculators through a dedicated website (UCL01-STO) and roll out of genetic testing for deafness (UCL01-BIT), safer surgery for glaucoma (UCL01-KHA), and provision of national services for prenatal diagnosis (UCL01-CHI) and the diagnosis of rare metabolic conditions (UCL01-CLA). We used our UCLP networks to accelerate local uptake of oesophageal monitoring in intensive care in N. London (UCL01-SIN1), and were influential in having this advance taken up as six National High Impact Innovations.

Expertise in rare diseases shared through our nationally commissioned services has enabled us to identify the cause of cryopyrin associated periodic syndrome (CAPS), identify a drug target, ***repurpose an existing monoclonal antibody*** as an effective treatment, provide data to support licencing, and then establish a national service for the treatment of patients throughout the UK with this condition (UCL01-HAW). A similar process of discovery and invention accounts for the progress made in the treatment of digital ulcers in scleroderma (UCL01-DEN1) with bosentan.

D2 Clinical research strategy for impact

Examples of our ***repurposing of existing medicines*** include the use of rituximab to treat rheumatoid arthritis (UCL01-EDW), several immunosupressants for uveitis (UCL01-LIG) and toculizumab in the treatment of juvenile chronic arthritis (UCL01-WED).

Expertise in ATMPs have been applied in ***early phase trials*** and include gene therapy for haemophilia (UCL01-NAT), and immunodeficiency (UCL01-KIN).

Our work on ***refining the dosing schedule of existing treatments*** led to the reformulation of midazolam, used in childhood epilepsy (UCL01-SCO), and of cytotoxic drugs in glaucoma surgery (UCL01-KHA). Reduction in the dose of radioactive iodine (UCL01-HAC1) and targeted radiotherapy after surgery for breast cancer (UCL01-VAI) reduced the toxicity but not effectiveness of these therapies. We achieved simplified childhood vaccination schedules (UCL01-GOL) and a range of advances in treating leukaemia (UCL01-KHW), lymphoma (UCL01-LIN; UCL01-PEG).

Novel combinations of drugs explored in later-phase clinical trials were used to demonstrate

improvements in outcomes of liver transplantation (UCL01-BUR), biliary tract cancer (UCL01-HAC2), and in lung cancer therapy (UCL01-HAC3).

Non-pharmacological treatments have included complex interventions such as the use of dietary manipulation and surgery to treat resistant seizures in children (UCL01-CRO), and self-management to improve symptom control in prostatic hyperplasia (UCL01-EMB). Other examples include the invention of a percutaneous pulmonary arterial valve for use in in children (UCL01-TAY), and use of hypothermia to prevent ischaemic brain damage in neonates (UCL01-ROB).

Improved diagnosis and monitoring of disease has been achieved via the use of our research to produce better genetic diagnosis and counselling in childhood deafness (UCL01-BIT), inborn errors of metabolism (UCL01-CLA), hypercholesterolaemia (UCL01-HUM), prenatal testing (UCL01-CHI), and sudden cardiac death (UCL01-MCK). Advances in monitoring include the use of oesophageal Doppler probes in intensive care (UCL01-SIN1). The many imaging advances arising from our research include fundus autofluorescence imaging as a novel read-out for clinical trials in age-related macular degeneration (UCL01-FIT), novel approaches to optic nerve head imaging for glaucoma (UCL01-GAR), and a better method of colonic cancer detection (UCL01-HAL).

D3 Collaboration with industry has been key to many of the impacts described in case studies (including UCL01-HAW, UCL01-DEN1, UCL01-ROB and UCL01-TAY), including the collaboration with GSK in amyloidosis drug development (UCL01PEP1) and breast cancer treatment, (UCL01TOB).

D4 Commercialisation and entrepreneurship is evident in four of the submitted studies. Licensing of technology for commercialisation was achieved in haemophilia (UCL01-NAT) and infant formula feeding (UCL01-SIN2), and spin-out companies were established to exploit intellectual property relating to small molecule development in cancer (UCL01-HAR) and amyloidosis (UCL01-PEP1).

D5. Provision of expert advice to policy makers: **Humphries** has contributed directly to NICE guidance (UCL01-HUM); **Halligan** gave advice on bowel cancer screening (UCL01-HAL) both in the UK and internationally; **Pillay** has provided advice to the WHO (UCL01-PIL*)*, as has **Goldblatt** (UCL01-GOL). **Bitner-Glindzicz** has advised the Department of Health on legislation (UCL01-BIT).