Institution: University of Leeds

Unit of Assessment: UOA1 Clinical Medicine

a. Context

Our UoA1 research at Leeds is largely delivered within the School of Medicine. Our research strategy is predicated on selectivity, focusing on areas of International Excellence that encompass the full translational pathway, from discovery science to applied health research with the collective aim of improving patient and population health and wealth creation. To achieve this, we need to understand and identify our end users' needs and map these onto our internal, interdisciplinary strengths. Our main beneficiaries are Governments and Healthcare Policy makers who determine the configuration and funding of health services; Health Intervention assessors such as NICE in the UK and equivalent bodies globally; Healthcare Practitioners delivering care; Patients and Users of health services; and Healthcare Related Industries, especially the pharmaceutical and devices sector. Our main impacts are on the clinical and cost effective delivery of health services and on the economy and commercial activities of healthcare related industries. Our strategic approach to impact recognises that our strongest potential for impact arises where our strengths in biomedical, applied health and clinical research converge with technology and physical engineering science to address clinical challenges. Our UoA1 research groups in **Musculoskeletal, Cardiovascular, Cancer & Pathology** and **Genes & Development** reflect these areas of cross-disciplinary strength and are co-located with NHS sites to accelerate delivery of impact. They have strong links with other University Schools: Engineering, Biological Sciences, Chemistry & Physics, reflecting our strategy for multidisciplinary translational research as set out in the University's Biomedicine & Health Strategy which seeks to "address global grand challenges through distinctive, focused, world-leading translational research".

Impacts on **Health & Welfare** have been achieved through **clinical trials** and the introduction and evaluation of **novel diagnostic technologies** to deliver improved patient outcomes in myocardial infarction (**Kearney, CS1**), breast cancer, colorectal cancer and myeloma (**Twelves, CS2; Jayne, CS3; Quirke, CS5; Selby, CS6; Sebag, CS4**); rheumatoid arthritis (**Keenan, CS7**), and early diagnosis of rare genetic disorders (**Sheridan, CS8**). This research has been used to inform government best practice **guidelines**, which in turn has led to changes in the training of health practitioners (**Jayne, CS3; Quirke, CS5**) and the delivery of services (**Keenan, CS7; Selby, CS9; Sebag, CS4**). Impacts on **Health Practitioners and Services** have followed from professional body guidelines incorporating Leeds research findings, leading to changes in professional standards, guidelines and training (**Quirke, CS5; Jayne, CS3; Keenan, CS7**). Impacts on **Public Policy and Services** have been achieved through the evaluation and development of i**nnovative service strategies** for the early management of rheumatoid arthritis (**Keenan, CS7**), and colorectal cancer surgery and pathology (**Jayne, CS3; Quirke, CS5; Sebag, CS4**). Implementation of research at Leeds into health service delivery has shown significant **Economic** benefits, for example, through reduction of local recurrence in Cancer (**Quirke, CS5**) or reducing the costs of late care through early intervention in rheumatoid arthritis (**Keenan, CS7**). Increased use of therapeutic agents shown to be effective by Leeds researchers have made significant positive contributions to **Commerce**, for example increased use of eribulin in breast cancer (**Twelves, CS2**) and eculizumab in haemoglobinuria (**Hillmen, CS10)**.

b. Approach to impact

Our approach to impact has been informed by our understanding of the challenges/ needs of our research beneficiaries and by our research strategy. We have focused resource where external needs map to internal strengths. Health services need to make timely and accurate diagnoses and deliver cost effective treatments of proven clinical benefit. Evidence of effectiveness requires methodological skills, and involvement with health care providers so that we can deliver research led interventions that are not just effective but affordable, feasible and acceptable. Our strategy has therefore prioritised investment in staff and facilities and in promoting strong links between basic scientists and clinicians to bridge the first translational gap (bench to bedside), and between these groups and applied health researchers and clinical trialists to cross the second translational gap (bedside to community). In addition, our approach has included investment in knowledge transfer and commercialisation to build links with industry, particularly medical technology SMEs and pharmaceutical companies. In both cases, the development of partnership working has underpinned our strategy to impact on **health services, health policy and practitioners, health**

economics and commerce.

A close **Strategic Partnership with Healthcare Providers and Users** is essential to deliver our strategy and we have thus established formal partnerships with Trusts across Leeds and Bradford, with NIHR (we host NIHR IS, INVOLVE, CRN CC, and NCN CC), and with the NHS Information Centre for Health and Social Care and TPP SystmOne (http://www.tpp-uk.com). However, for research within UoA1 the **Leeds Teaching Hospitals Trust (LTHT)** is our key partner in delivering patient focused research. A **Joint Partnership Board (JPB)** between the University & LTHT was established in 2008, chaired (jointly) by the University Vice-Chancellor and the LTHT Chief Executive. Across this partnership, LTHT receives over £10m pa NHS R&D funding for a wide range of clinical research programmes and oversees 200+ drug trials. It is one of the highest recruiting Trusts for patients into NIHR portfolio trials in the UK. The **JPB** has delivered a shared research strategy with LTHT with joint investment in the four UoA1 research groups and co-location of research and clinical activities. Examples include the St James's Institute of Oncology, the third largest cancer centre in the UK, with protected research beds and a Clinical Research Facility for early phase trials of oncology drugs in cancer, but also supporting other UoA1 research groups; the NIHR Leeds Musculoskeletal Biomedical Research Unit (BRU); and the Cardiovascular imaging facility. The proximity of our research to the patient base is a key factor in delivering impact that has transformed cancer, cardiovascular and musculoskeletal services locally, nationally and internationally (**Emery, CS7; Jayne, CS3; Kearney, CS1; Quirke, CS5**). This relationship was recently strengthened with the expansion of clinical research facilities to include experimental medicine activities in musculoskeletal medicine and cardiovascular diseases. A joint approach to research governance has deployed LTHT flexibility support funding to a research design service (RDS) that accelerates clinical research and embeds statistical, design and health economics expertise from the outset. Partnership with LTHT led to the creation, in 2009, of the **Leeds Biomedical & Health Research Centre (BHRC**) http://www.bhrc.ac.uk/, a strategic partnership between the four science Faculties of the University of Leeds and LTHT to promote collaboration between scientific, applied health and clinical research (£10M investment, UoL; £3M, LTHT). The BHRC vision is to bring benefit to patients through excellence in translational research. It facilitates new ways of integrating the work of scientists and clinicians, focusing on the discovery and development of novel diagnostics, therapeutic modalities and other clinical applications thus meeting our strategic translational research aims. It has focused on the UoA strengths in cardiovascular, musculoskeletal and cancer research but also supported emerging strengths in neurosciences, genetics and gastroenterology. The BHRC has created:

- 15 **Senior Translational Research Fellows,** 5 of whom are returned here in UoA1, with cumulative £3.5m grant income since 2010 -11 (see environment statement);
- Chemical Biology/Medicinal Chemistry and Bio-Screening platform Technology Groups facilitating proof-of-principle studies in drug discovery, biomarker detection and design, and translational genetics, for example, target validation and drug discovery such as the FcγRs, IL-7 and its receptor (EU-FP7 funded; patent application pending); and
- a Problem Solving Fund, to unblock obstacles in translational research (15-fold return, total external awards £15m e.g. **Del Galdo** EUR286k as PI on DeSSCipher).
- Building on the RDS above, investment in Applied Health Research skills (eg new chairs in health economics, health informatics, clinical trials and statistics) giving clinicians with clinical problems access to appropriate methodological expertise in research design and implementation science to develop high quality applications to deliver impactful research (total value of Trust/ University submissions: £20.8m, total awarded: £5.9m).

User engagement in research is supported across all activities, eg, patients on the Leeds Musculoskeletal BRU patient and public advocacy unit, and Leeds based Patient and Public Involvement Groups sit on local and national research and governance committees ensuring the patient voice is heard by commissioners of research. We host NIHR INVOLVE.

Our approach to Strategic Partnerships with Industry has been supported by WELMEC, the IKC and HEIF funding. Researchers in UoA1 research groups (**Conaghan; Emery; Jones; McGonagle; Quirke**) are Co-Is in the £11.2m **WELMEC Centre of Excellence in Medical Engineering** funded by the Wellcome Trust and the EPSRC http://www.welmec.leeds.ac.uk, one of four UK Centres of Excellence in Medical Engineering, It brings together over 200 engineering,

physical and life science and medical researchers from Leeds with clinicians and industrialists to deliver a series of clinical innovation challenges focused on improving the quality of life of older people. It supports impact in this UoA through work on longer lasting joint replacements; novel biological scaffolds for joint tissues and cardiovascular surgery; and advanced medical imaging to improve diagnosis and treatment.

Leeds EPSRC_BBSRC-TSB **Medical Technologies Innovation & Knowledge Centre (MT IKC)** http://www.medical-technologies.co.uk/ brings together teams of research and clinical experts to work with industry on specific projects supported by professional innovation managers (£9.7m over 5 years, 35 products translated into clinical use from Leeds-centred research). UoA staff who have drawn down funds from IKC include **Jayne** (Intra-Abdominal Platform with Neville [Engineering] £142k) and **McGonagle** (Development of a medical device for intra-operative stimulation of synovial mesenchymal stem cells for improved joint repair, £88k). IKC actively encourages young researchers to understand and value their role in delivering innovation with a targeted programme for PDRAs and Doctoral Trainees. It also includes a leadership development programme for senior staff.

HEIF funding has been used to develop innovation, enterprise and impact including consultancy projects, KT partnerships (eg Leeds Teaching Hospitals, £234k, 2009; Phoenix Partnership, £142k, 2011; Philips Electronics,£175k, 2012), and a joint venture between the Business School and Medicine & Health to improve health outcomes by improving the effectiveness of health management. Intellectual Property disclosures rose from 1 in 2009/10 to 3 in 2011/12. 3 license applications granted, 11 patent applications, 8 active and successful spin outs since 2008 (eg Aptuscan, IVMD, RDInfo). 3 CASE studentships and 192 FTE of industrial/ commercially funded HE students associated with the UoA. A virtual health informatics network was transformed into the *Yorkshire Centre for Health Informatics (YCHI)* that has (supported by the Health Services Hub) forged significant partnerships with The Phoenix Partnership, a local SME and one of the leading UK suppliers of electronic medical record systems to primary and community care in the UK.

c. Strategy and plans

We will continue to target our end users' needs through focussed translational research and the establishment of strategic partnerships. We will target resource in Musculoskeletal, Cardiovascular and Cancer research whilst simultaneously capacity building in core technologies/ cross cutting activities including imaging, pathology, clinical trials, genetics and informatics and engage more with industry/ biotechnology partners to drive wealth creation locally through the AHSN.

Our strategy for partnerships with Healthcare Providers and Users: The impact of close working between the CTRU and UoA1 researchers based upon innovative trials design is exemplified by our case studies (see case studies **CS2, CS4, CS6** and **CS10**). Ongoing collaborative work with CTRU focuses on trials, biomarkers and devices and methodology development, further illustrating our strategy of bringing together researchers and clinicians to deliver translational research with impact for patients. Through the Joint Partnership Board and BHRC (see section b) we will invest £4m from 2011-15 in Applied Health Research through the **Clinical Trials Research Unit (CTRU)** and the **Leeds Institute for Health Sciences (LIHS).** NIHR programme directors have emphasised the primary reason for proposals being refused is the lack of high quality methodological input. This investment will appoint qualitative researchers, statisticians including a chair, data scientists, systematic reviewers, trial managers and research co-ordinators and allow clinical and industry partners access to the expertise to develop high quality research. Health economic expertise will help decide whether the market can accommodate new technologies/ drugs early in the translational pathway. **CTRU** http://ctru.leeds.ac.uk/ is UKCRC Registered and specialises in early phase trials, biomarker and device research, and complex phase III trials. **LIHS,** http://www.leeds.ac.uk/hsphr/index.html provides applied health research design, implementation science, social science, health economics, informatics and statistics.

We will expand existing clinical research facilities at LTHT to incorporate experimental medicine activities in musculoskeletal and cardiovascular diseases adjacent to clinical areas, and we will target investment to ensure renewal of existing musculoskeletal NIHR BRU, and enable us to bid for a second such unit in cardiovascular medicine (£150k already identified to support CV CRF at LTHT).

Organise more public engagement events, eg in 2013, the Stratified Medicine Hub (see below) with Leeds CRUK Centre, organised a public engagement event as part of Leeds Festival of Science on **Personalised Medicine and the Future of Cancer Care** that included Leeds cancer researchers and scientists from Astra Zeneca.

Our strategy for partnerships with Industry. We will continue to work with BHRC, WELMEC and Medical Technologies IKC (section b). Through **BHRC** we have established two technology platforms, Medicinal Chemistry & Chemical Biology (MCCB) and BioScreening (BSTG) Technology Groups (TGs) that provide cross faculty access to drug development, biomarker discovery and target validation pathways. This is central to interdisciplinary biomedical translational research and aims to create economic impact and patient benefit, aligned with the University's biomedical and health research strategy. MCCB is working with **Phillipou** on novel anti-clotting factors and **Burchill** on compounds for treatment of Ewings Sarcoma. BSTG is working with **Ajjan** (modulators of clotting) and **Morgan** (targets for treatment of rheumatoid arthritis). The TGs are important contributors to the hubs described below and provide shared infrastructure/facilities (cf RCUK/ Wakeham).

We will continue to invest in our distinctive approach to HE Innovation Funding via the creation of interconnected, externally facing sector-specific hubs. Senior academics have been appointed Hub Directors, supported by industry experienced Innovation Managers and external stakeholders. Health is identified as a key sector with an allocation of over £1m to provide staff and funding for strategies to bring academic strengths to the external market. All Hubs will work with industrial partners in the pharmaceutical, biotechnology, diagnostic, imaging and bioinformatics sectors, as well as with other sector hubs at the University, eg, the pharmaceutical, food security and social care hubs, and with **Yorkshire & Humber Academic Health Science Network (Y&H AHSN)**

The **Stratified Medicine Hub** supports the development of novel drugs, diagnostics, technological platforms for biomarker discovery, biosensor development and drug discovery. It works with the Proteomics Facility (**Banks**) to help grow contract and collaborative research and supports the Biotechnology Screening Group to manage licence and contract service agreements with SMEs. It has supported a successful application for Business Engagement funds and consultancy contracts undertaken by academics via the hub have grown from £2.2k in 2009/10 to £441k in 2011/12.

The **Medical Technologies Hub** aligns closely with the IKC (see section b), providing a regional and international platform to address the creation and accelerated adoption of new medical technologies and regenerative therapies. Successful collaborations across the University, NHS and Industry that have arisen from our investments include:

A) The Healthcare Technologies Cooperative, (CoNNeCT, **Jayne,** £790k), which aims to develop and promote novel concepts in medical technologies for colorectal disease for research funding and translation into clinical practice. The HTC brings together a national network of key stakeholders operating in the biotechnologies area, including clinicians, academics, commercial partners, funders, charities, and PPI. The HTC already has active partnerships with many SMEs including **Covidien, Ethicon, Shire Medical, Brandon Medical, Intuitive Surgical Inc and Medtronic.**

B) The NIHR Programme Grant ELUCIDATE, (**Selby**, £2m) funded to develop a robust approach to protein biomarker evaluation in liver and renal diseases, through research in methodology, clinical biochemistry and a randomised control trial.

C) The Leeds Diagnostic Evidence Cooperative (£1m) a consortium that will generate clinical research into protein and cellular biomarker-based in-vitro diagnostic devices for the management of renal, liver and musculoskeletal diseases. Devising and refining methods in IVD study design, using health economics and health informatics to improve and speed up IVD evaluation – a core mission of the recently designated **Y&H AHSN**.

The **Health Services Innovation Hub** covers the planning, delivery and evaluation of healthcare services, supporting knowledge exchange and partnership for patient benefit. It has close links with new health and social care commissioners and a wide range of local NHS, social care and 3rd sector partners (LeedsActs!). Examples of impact include: An **innovative patient informatics** platform initially in oncology, but now extending to gastroenterology and other areas that integrates diverse clinical data including patient reported outcome measures **(Velikova)** with clinical trials and

genomic data from Leeds research generated by the Cancer Research UK Stratified Medicine Programme. This has delivered important **population based outcome measures** including early deaths following radiotherapy, cancer relapse patterns and improved patient outcomes. The hub is supporting the application of this technology by GPs assessing the health of carers of people with dementia, and an EPSRC Patient Led Innovation project with commercial partners, patients, NHS staff and researchers to develop digital stories to support product development. A partnership with TPP and SystmOne (http://www.tpp-uk.com/latest-news-stories/tpp-launches-researchone/) has produced a combined health informatics initiative and pump-primed a recent MRC- Farr Institute Bioinformatics submission. Leeds health informatics expertise will contribute to an ambitious AHSN plan for regional health records linkage.

Our Staffing Strategy: It is essential that our staffing structures reflect our ambitions. Clinical academics lead our research groups working with biomedical and applied health scientists and NHS clinical colleagues. We will:

1. Invest in senior academic leadership chairs in UoA1 groups and in applied health research (informatics and trials). With LTHT, create 40 NHS Honorary Clinical Associate Professors, linked with UoA1 research groups to develop translational research addressing clinical challenges. They will be have protected time, training and mentoring to become Cat. C returnees of the future and contribute to BHRC sponsored scientist/clinician engagement events, enabling basic scientists to be aware of and aligned to clinical challenges,

2. Work with the University **Staff and Departmental Development Unit (SDDU)** www.sddu.leeds.ac.uk to enhance staff development and appraisal with clearer expectations of staff plus developmental opportunities to assist understanding of partnership working, the needs of beneficiaries, IP protection and commercialisation.

3. Build on our strategy for clinical academic training that is aligned to our 4 research groups and includes a pathway from UG research (Inspire and LURE http://www.leeds.ac.uk/medicine/lure/index.html), through academic foundation posts, Academic Clinical Fellows and Clinical Lecturers to senior fellowships. In national competition we have increased our NIHR funding for academic clinical trainees by 50% in five years and are creating an additional 10 locally funded posts to complement this.

4. Develop new Postgraduate taught programmes (PGT) to disseminate findings from our research excellence, and new undergraduate science programmes alongside the MBChB to attract students onto a pathway to PGT and then Postgraduate Research

d. Relationship to case studies

The ten case studies submitted illustrate our approach to impact and are drawn from all four UoA1 research groups. A key part of that approach was to build link s and partnerships with potential beneficiaries and to invest in infrastructure and expertise that would allow biomedical research to be translated into benefits for patients. Nine of the studies involve clinical trials demonstrating improved clinical outcomes that have then led in turn to changes in national guidelines, and health practice and policy (**Kearney, CS1; Twelves, CS2; Jayne, CS3; Quirke, CS5; Selby, CS6; Keenan, CS7; Hillmen, CS10; Sebag, CS4**). This would not have been possible without joint investments with the NHS in clinical research facilities and in applied health research and trials methodology and expertise in LIHS and CTRU. Internal approaches linking biomedical researchers with applied health researchers then enabled high quality research to take place. Promoting links with industry has resulted in significant impact on commerce in two of these studies (**Twelves, CS2; Hillmen, CS10**). **Sheridan, CS8** illustrates the benefits of our approach to working with patients and the public (in Bradford and Pakistan) and our investment in these areas to develop new technologies that deliver improved outcomes/ experience to patients. A particular strength has been embedding the shortage areas of surgical and pathological sciences into our Cancer programme (**CS3,5,9**). The importance of close links between the NHS, research in Leeds, and the outputs from that research, led to work commissioned by the Department of Health that influenced the establishment of clinical networks and later clinical research networks in England (**Selby CS9**), and to the UK Clinical Research Networks being hosted by Leeds University. These have been notable for their impact on NHS research intensity, their wide NHS participation and their patient centred emphasis and patient involvement and have in turn reinforced our local approaches to impact.