Institution: University of Nottingham

Unit of Assessment: UoA1

a. Context

The **research themes** within the School of Medicine (Cancer & Stem Cells, Clinical Neurosciences, Respiratory Medicine, Child Health, Obstetrics & Gynaecology, Digestive Diseases, Musculoskeletal & Dermatology and Vascular & Renal Medicine) comprise UOA1 and this diversity is reflected in the very broad impact of our research. This draws upon critical mass exemplified by our relationship with Nottingham University Hospitals and our NIHR Biomedical Research Units (BRUs) in Digestive Diseases and Hearing.

Our research **benefits** patients, health professionals, service providers, charities, commerce and the public with an overall goal of improving health and quality of life. Our research allows practitioners to deliver safe and effective healthcare; has reduced healthcare costs; has opened up market opportunities for our commercial partners (both SMEs and global) and has informed the choices of key research priorities made by the research councils, the NIHR and medical research charities. The **impact** of our research spans both economic impact and patient benefit.

Patient Benefit

Our research has **defined and informed national guidelines** through pivotal trials and systematic reviews. Where the evidence is missing, we have obtained funding for definitive trials. Musculoskeletal systematic reviews and clinical trials have informed European (EULAR) and international osteoarthritis guidelines (specifically avoidance of paracetamol, the important role of exercise). Our portfolio of reviews and trials in dermatology have informed NICE guidance as well as guidelines elsewhere (Europe, South Africa and Japan). Child Health research has changed the recommendations for aminoglycoside dosing in cystic fibrosis both nationally and internationally, with a resulting change in practice, reducing the risk of acute kidney injury. Children's Brain Tumour researchers developed an evidence-based clinical referral guideline for suspected cases (NHS Evidence-standard accredited 2010) and the "HeadSmart" public awareness campaign. Since the programme began, time to diagnosis has been halved. Our school have also developed and disseminated stratified medicine techniques, to allow therapy tailored to the individual. For instance, the Nottingham Prognostic Index for breast cancer stratification is mandated by RCPath and DoH for all UK patients and is used worldwide.

Our research has **decreased morbidity and mortality** through better prescribing, screening and surgical intervention. Digestive Diseases research showed that proton-pump inhibitors can reduce dyspepsia, ulcers and hospitalisation, attributable to NSAID use. Co-prescription of these drugs with NSAIDs was recommended by NICE in 2009 for patients >55 years. Co-prescription has increased (from 27.6% in 2008 to 44.1% in 2012), reducing hospitalisation by 54% and preventing hundreds of deaths each year in the UK. The national rollout (2010) of the Nottingham Bowel Cancer Screening trial saves 3,500 lives / year, at a benefit of £1,600 per quality adjusted life year (QALY). The programme allows removal of pre-cancerous polyps in some patients.

We have **enhanced patient experience** through innovation. Lymphangioleiomyomatosis (LAM) is a progressive, rare disease where patients die of respiratory failure. It predominantly affects women. Through our research, patients are now offered non-invasive diagnosis; effective treatments; the opportunity to take part in clinical trials; earlier treatment for complications and they are no longer advised to avoid pregnancy. Our researchers established the LAM Action charity which has raised £400K since 2008 to provide peer-support. In 2012 we established the CF Unite web platform to establish a dialogue about research with cystic fibrosis patients – who cannot meet together due to cross infection risks. The unique web resource www.nottinghameczema.org.uk has been cited as an example of best practice for patient support information by DoH in 2012.

Commercial and economic impact

We have long contributed to, and benefited from, Nottingham's strong commercialisation culture. Our school has grown new businesses (market capitalization £130M), created jobs and contributed to the success of over 20 medicines and medical devices.

Much of our basic science underpins **drug development**, the focus of three spin-outs since 2008. PRECOS (2010) offers predictive cancer modelling and has contracts with 35 companies. PRECOS was acquired by Crown Bioscience, an international drug development company, in

2013. Platelet Solutions (2012) has commercialised platelet function testing technologies and has contracts with AstraZeneca (AZ), Daiichi, Eli Lilly, Unilever, decode Genetics and GSK. Scancell (2009), with its portfolio of anti-cancer antibodies and DNA vaccines, reached market capitalisation of nearly £100M and delivered a tenfold return for investors.

Clinical research and trials in the School have attracted £16M investment from industry since 2008. This includes £1.6M from Janssen for Pre-Clinical Oncology and a partnership with AZ that has enabled Fulvestrant to be the only new endocrine therapy to be registered in the last 10 years.

Our research has also been developed into other products such as **surgical devices and screening tests**. With Cook Medical our surgeon academics evaluated the Nottingham graft for emergency endovascular aortic aneurysm repair. These Zenith AAA devices have been used in over 250,000 patients worldwide over the last 5 years. Licensing of antimicrobial materials technology to Codman, with ongoing expert advice, led to regulatory approval such that 70% of shunts used annually in England now comprise our Bactiseal® shunt. Through the Oncimmune spin-out (value £30.5M July 2013), the world's first autoantibody blood test for detecting early stage lung cancer, '*Early*CDT-Lung', has been in use internationally since 2010 with further investment (in Scotland) to prepare for a screening programme.

Reducing healthcare costs is also a key impact. Digestive Diseases research led to a novel faecal occult blood screening programme used nationally for the earlier detection of colorectal cancers and has detected 15,000+ early cancers since 2008. This saves the costs inherent in the treatment of advanced disease. Zenith device use for aortic aneurism treatment has reduced average bed stay from 10 days to 48 hours**.** Our research on optimising perioperative fluid therapy has reduced hospital stays by 3 days saving £1,000 per patient.

b. Approach to impact

We have used key strategies to realise impact from our research. These are described below.

Developing an engagement and impact culture

From our undergraduates through to senior academic staff, the School has been pro-active in stimulating an impact culture. This starts at third-year undergraduate level by placing BMedSci students in research projects within impact-driven teams. New clinical translation, protecting IP and business plan writing modules have been introduced for Masters students. The N-Trans Doctoral Training Centre (launched 2009) trains students in healthcare economics and our Graduate School provides enterprise resources for our PhDs/DMs.

The School's Research Committee (est. 2009) drives strategy for impact. Its membership includes senior clinical and basic scientist co-chairs, a Business Development Executive (BDE) and experts in industrial liaison, clinical translation and engagement. It organises workshops led by impact champions, promotes knowledge exchange events, encourages new collaborations and closer engagement with the NHS. Key features include the review and facilitation of impact development and highlighting successful impact approaches. Workshops include sessions on: maximising research impact, industrial collaboration, translational research, intellectual property (IP), patient involvement and impact surgeries. Annual research days highlight University support for knowledge exchange, through Business Engagement & Innovation Services (BEIS), and knowledge exchange funding schemes. Since 2008 our school has been awarded 12 MRC DPFS/Confidence in Concept awards, 5 HEIF-funded Hermes/Innovation Fellowships, plus an NIHRi4i award, a Wellcome Trust Translational Award and CRUK DC funding (a total of £5.2M).

Our strategy is to translate our basic science findings into an investable product, through attracting innovation funding. For instance our spin out company Platelet Solutions which was awarded the following funding: pathway of investment from HEIF (2008), MRC DPFS (£258k, 2009), University Innovation Board (£100k, 2011), TSB Stratified Medicines and a Hermes Fellowship (2012). Similarly, MRC DPFS (2009) and a University Innovation Fellowship (2010) funding have been used to develop the Nottingham Prognostic Index. This has allowed a spin out company to be set up "Nottingham Prognostics", in collaboration with Nottingham Trent University and Nottingham University Hospitals NHS Trust (NUHT). In 2012 both companies secured 20% of the national Small Business Research Innovation Competition budget.

School support for impact

We support staff engagement with industry, healthcare and the charitable sector through paying for staff travel and time, protection of IP and securing MHRA approvals. One of our early career researchers has developed an amniotic membrane "ophthalmic bandage" ("Omnigen" patented in the UK and the US). We facilitated HTA approval and HTA-licensed laboratory facilities for initial patient treatments, drew on BEIS support and secured two University fellowships that leveraged £500k from Ministry of Defence.

We recognise 'impactful' staff achievements. We communicate clinical trial recruitment successes (citing teams) to all staff and reward new innovations which have impact through annual Performance Reviews and the promotions process.

We encourage our staff to use their 20% time entitlement (University Policy on External Work) to engage with external partners, take on leadership roles and provide expert advice. Three clinical academics have used this time to direct key NHS Clinical Research Networks, contributing to NUHT being one of the top 4 trusts in England for research activity. http://www.theguardian.com/healthcare-network-nihr-clinical-research-zone/table/2013-portfolio-activity-league-table Consultancy from our academics allowed Lombard to obtain FDA approval for Aorfix surgical devices. Other leadership roles include National Bowel Cancer Screening Advisory Board Chair, President of Royal College of Opthalmologists and three NIHR Senior Investigators.

Consolidating expertise to underpin impact

Interdisciplinary and international collaborations, particularly between academics and clinicians, underpin our wide impact in society. We are partnering with clinicians and industry to deliver Phase 3 clinical trials (300+ trials in progress in NUHT). In 2008, we established NIHR Biomedical Research Units with NUHT to enable impact from research in Digestive Diseases, Respiratory Medicine and Hearing followed by the £5.5M Arthritis UK Pain Centre a year later. Our systematic reviews of 50+ treatments for osteoarthritis have informed guidelines in the UK and worldwide. Strategic investments feed into research impact. These include one of only two UK 7 Tesla MRI National facilities, a £3M novel hyperpolarised Xenon MRI scanner for lung disease, 4 dedicated Clinical Research Facilities (including facility for Children) and a UKCRC-registered Clinical Trials Unit (CTU). Professor Lelia Duley, with a proven track record in clinical trials research was recruited as Director of the Nottingham CTU in 2011. Investment of a total of £6.5M from the University and private sector has allowed our school to set up the two centres of excellence - for Autoimmunity in Cancer and for Therapeutic Antibodies.

Effective engagement with the NHS

We work closely with the NHS, particularly NUHT, to deliver clinical benefit. NUHT, a major clinical research partner for the School, has 300+ clinical trials in its portfolio, and we have been instrumental in placing NUHT in the top 4 in England for clinical research. More than 40 NHS employees currently have Honorary contracts with the University. RCTs in our Clinical Trials Unit are delivered by our research networks, predominantly led by our clinical academics. Drug discovery is dependent on having appropriate human tissue samples, linked to patient data and so NUHT and our school established the Nottingham Health Science Biobank in 2011. Donated tissue, surplus to routine diagnostic testing requirements, is stored in a single, quality assured, facility. A novel patient informatics system (ORCHID) connects the stored tissue to phenotyping information in the routine patient record. This is now the major tissue source for AZ.

Engagement and involving patients and the public

Our public and patient engagement programme is embedded within research strategies, and at all stages: design, delivery, dissemination and uptake of research, going beyond simply 'informing' the public. The Centre for Evidence Based Dermatology's Priority Setting Partnership (PSP) with the James Lind Alliance (for vitiligo, acne and eczema) and Hearing Biomedical Research Unit PSP (for tinnitus) exemplify this. Patients are involved as partners in prioritising research questions, applications for funding, trial steering committees and in dissemination of research findings.
We undertake extensive outreach activities, notably through conferences for schools, A-level masterclasses, Sutton Trust residential courses and presentation at the BHF 'Mending Broken Hearts' 2013 event. A £29k Wellcome Trust people award developed the CF-Unite website, where

patients benefit from bespoke webinars. Awards include Breast Cancer Charity Research Team of the Year (2012) and Raising and Giving Group of the Year by our students generating £45k for the University's Karnival. The 'HeadSmart: Be Brain Tumour Aware' campaign has led to an informed public awareness of brain tumour symptoms. Through our specialist training, we have introduced improvements in clinical practice (1,000+ surgeons, anaesthetists, nurses and operating department staff have attended our fluid prescribing course).

Commercial innovation and partnership

We contribute to 4 of the 13 University Research and Knowledge Transfer Priority Areas (Drug Discovery, Biomedical Imaging, Clinical Translational Research and Science, Technology and Society). These were established in 2009 to deliver excellence in research and knowledge transfer. Our extensive experience of commercialisation, IP protection and translation into clinical practice from four new spin out companies has shaped our strategies (see section c). Senior spin out company staff drive further innovation within the School. Business Engagement & Innovation Services (BEIS) was formed in 2010 through the University's Strategic Plan to deliver IP management, build relationships with industry and support consultancy. Business Development Executives have fostered relationships with industry (AZ, Roche, Pfizer, Johnson & Johnson) which have led to R&D contracts and increased industry awareness of our research. We have used novel means of pump-priming translational research, such as a £50k regional (Healthcare and Bioscience iNet) award in 2011 (with University of Leicester and genomics company, Source Bioscience) which unlocked £900k from Pfizer to uncover genetic causes of respiratory disease. Our partnership with Johnson & Johnson (Pre-clinical Oncology) developed *in vivo* models and has also led to commercialisation of this technology. Relationships with industry have contributed to a high proportion of industry studies in local NIHR research networks (over one third).

c. Strategy and plans

A 2013 review of our Research strength and weaknesses has shaped our goals for the next 5 years. We consider our strengths to include close partnership with NHS organisations in the East Midlands (including the new Academic Health Sciences Network, hosted by NUHT), partnership in two current NIHR Biomedical Research Units, excellent infrastructure and expertise for clinical trials and strong industrial liaison. Our experience with Scancell Holdings has shown we can use a novel approach to attracting investment and show good financial performance in the biotech sector, despite a difficult economic climate. Our future strategy will seek innovative ways to consolidate relationships with the NHS and Pharma partners. Opportunities to increase research quality and resulting impact will focus on further growing the culture of impact in our school. UoN campuses in China and Malaysia are providing significant new opportunities to extend our partnerships in Asia. Threats include diluted engagement across a large School spanning diverse disciplines and at multiple sites across Nottingham and Derby. Our strategy for delivering our impact potential has three main aims: 1) to provide clear leadership and responsibility through a Knowledge Transfer and Outreach Champions Group, 2) to engage and empower staff through fully embedding impact into our organisational culture and 3) further consolidating our areas of research strength into influential groups of critical mass.

1. Leadership. In 2013 our academics have been consolidated into 11 Divisions and each has established a Research Committee (DRC). All DRC Chairs sit on the School of Medicine Research Committee (SMRC) for improved bidirectional dissemination of practices, ideas and opportunities. Concurrently we have established a Knowledge Transfer and Outreach Champions Group (KTOG) with overall responsibility for Impact. The Chair is a senior academic with a track record of promoting both clinical and commercial impacts. This role assumes responsibility for impact development at all levels and for representing the KTOG on the School Research Committee. KTOG leaders have been appointed with responsibility for formulating and promoting strategic policies across each of our three identified impact themes: **Translation into Practice, Commercial Innovation and Patient and Public Engagement.** They will be joined by our School Business Development Executives, and external advisers from NHS, Technology Strategy Board, and Association of Medical Research Charities.

2. Engaging and Empowering Staff. At an individual level, academics and researchers will be challenged to consider impact in their annual performance review. Divisional Research Committees will support Line Managers in implementation and will develop impact specific sections on their websites. For all levels of staff and students, KTOG will deliver and further expand the impact-related training programmes that we have developed in recent years as an enabling mechanism. In particular, training schemes developed for one sector, such as graduate students or senior researchers will be adapted to ensure widest possible dissemination. A new initiative will require BMedSci and MSc students to include impact in progress reports and final assessments.

3. Consolidating Areas of Research Strength: We recognise that impacts occur more readily in excellent research teams, with a critical mass of expertise. We have learned how we can support translational research at every level from our excellent basic scientists and our patient partnerships, to our BRUs (which deliver early stage clinical trials) and also through our Networks (which deliver phase 3 work and beyond). Successful strengthening of our existing BRUs in required areas is being continued by attracting new funding and increasing our engagement with the NHS and NIHR. We aim to further partner with discipline-specific stakeholders, as we have with Arthritis Research UK and the Stroke Association. Support for our relatively new Stem Cell Biology Unit has been increasing from British Heart Foundation and we aim to enhance such partnerships through continued investment. The School is currently supporting a number of initiatives which are expected to lead to significant Impact within a 10-year period. A new Nottingham Translational Cancer Research Centre will focus on early detection and treatment stratification to promote better survival in cancer patients. This will be underpinned by CEAC, the Ex-Vivo Cancer Pharmacology Centre of Excellence; our world leading research in pathology; the University spin out companies Scancell and Oncimmune and our extensive experience in antibody and drug development. The recent recruitment of Prof David Bates with his experience in translational anti-vascular therapies will enhance this Centre. Through the University's campuses in Malaysia and China, there is the potential for this Centre to become a Global Cancer Institute. In the next twenty years the number of cancer cases in the world per annum will double. In China, the major killer, lung cancer will become 7 times more prevalent. Our key blood test for early diagnosis of lung cancer will be pivotal in fighting this disease but patient stratification for rational treatment with our vaccines, antibodies and drugs aims to be vital in the effective control of this epidemic.

d. Relationship to case studies

Our submitted case studies illustrate how we have delivered the key types of Impact described. Case Studies 36 (proton pump inhibitors) and 28 (Fulvestrant) show how we have encouraged our academics to follow through, from the first scientific and early phase clinical studies, to randomised controlled trials which change practice and save lives throughout the world. Strong links to AZ in both of these studies, shows the benefit of developing long-term partnerships with major Pharma in expediting registration and treatments. Case Studies 29 (EarlyCDT-Lung) and 27 (bowel cancer screening) show our commitment to disease prevention. We have followed a pathway from early stage immunochemical screening of cancers, leading to RCTs and implementation into national screening programmes. Both cases show the benefit of linking academics with diverse expertise. Case studies 38 (antimicrobial implantable devices), 37 (Scancell), 28 and 29 demonstrate how IP protection of technology has enabled us to commercialise product development, both through spin-out and licensing. This would not have been achieved without the expertise and calibre of the University Business Engagement staff. Studies 37 and 29 also show how capital raised through stock market flotation can be used to fund later Phase Clinical Studies. Studies 35 (lymphangioleiomyomatosis), 32 (aminoglycoside safety) and 30 (childhood eczema) show how systematic reviews can inform international treatment guidelines and how patients can be involved at each stage of the research process. Study 31 (children's brain tumour) has shown us the power of a public awareness campaign involving professional media staff in improving outcomes for poor prognostic groups. Studies 33 (perioperative fluid therapy) and 28 reinforce the importance of academics disseminating their work widely in order to change practice and improve patient care.