Institution: University of Liverpool and Liverpool School of Tropical Medicine

Unit of Assessment: 1 - Clinical Medicine

a. Context

Our Unit has made major contributions to the pipeline of translational research from discovery science in biology, which underpins disease mechanisms, through to clinical studies of disease processes, and interventions. This has led to new approaches to prevention and treatment of disease with industry engagement in biomarkers, diagnostics, and therapeutics Our research impacts directly on patients, policy makers, clinicians, and the biomedical industry. These impacts are generated both in the UK and overseas. The latter has a specific focus on our Global health agenda by directly improving health outcomes, as well as health policies and economic benefit.

The Liverpool School of Tropical Medicine (LSTM) and the four University research institutes in this Unit work with the NHS and Department of Health at local and national levels, and with overseas Ministries of Health and international health organizations such as the World Health Organisation (WHO). Reflecting our contribution to global health problems, our staff serve on key bodies such as the WHO, the Bill and Melinda Gates Foundation (BMGF) and Department for International Development (DFID) in areas such as Drug Resistance and Vector Control), and our work has contributed to significant improvements in the prevention, control and treatment of major health problems, such as HIV, neglected tropical diseases, malaria and rotavirus infections. Contributions such as those with rotavirus immunisation have also led to change in UK health policy with the introduction of a UK immunisation programme, illustrating the synergy between the Global and UK health agendas.

Nationally, we have impacted on Government research policy through research and strategy board involvement with the research councils and major UK charities. Examples of these influences include **Lalloo** (MRC Global Health Group); Greer (Chair, MRC Regenerative Medicine Committee and UK Regenerative Medicine Programme for MRC, BBSRC, EPSRC), **Jackson** (MRC ME/CFS Expert Group and LLHW advisory board) **Pirmohamed** (UK Human Genomics Strategy Group) and **Neoptolemos** (Cancer Research UK science strategy advisory group). They have extensive research interactions and partnerships with pharmaceutical and health products industries and have made significant contributions to the regulation of the safety of medicines and use of medicines in the NHS through membership of the Commission on Human Medicines and NICE.

In Merseyside, we led the development of Liverpool Health Partners (the Academic Health Sciences System for Merseyside), establishing an integrated agenda for heath research, education and service delivery with a functional Joint Research Office. This is facilitated by the close links on Liverpool campus between academic and teaching hospital facilities.

b. Approach to impact

Policies and Processes

Both the University's Strategic Plan 2009-2014 and LSTM's Strategic Plan 2012-2017 set an expectation of 100% staff engagement in knowledge exchange (KE) activities, including consultancy, collaborative research, CPD and public engagement. This activity is supported by the maximum HEIF allocation, which funds a dedicated Directorate of Partnerships and Innovation within the University and KE and impact infrastructure in LSTM. As part of our research planning process consideration at institute level is given to the impact plans of all our researchers. For example, Integrative Biology's strategy is directed by an Impact Working Group which comprises senior and junior academics, PDRAs and PGRs. These colleagues are supported by an Impact Officer who helps develop our strategies and processes designed to enhance synergy, planning and rewards for impact activities. Impact activity is discussed at the annual Professional Development Review (PDR) for each member of staff and is reviewed throughout the year at both Faculty and institute level. Each institute has representation on the Faculty KE strategy group (Chair, **Burgoyne**) that oversees planning, promotion, implementation, monitoring and evaluation of KE activity, including the identification of cross-institute and cross-institutional opportunities.

LSTM is a translational research institute, using research findings to deliver product development and put policy into practice. These two phases of translation are delivered through partnerships

with government departments, NGOs, industry, global health organisations and funding agencies. Our Research Support Office coordinates business and partnership activity, handling more than 600 external contracts each year that form a major part of LSTM's core business. LSTM's research support infrastructure has expanded since 2008, with staff increasing from three to 12, and the introduction of a new communications department (2012), to support KE activities. In 2013, it launched two new Research Centres for Drugs and Diagnostics, and Applied Health Research and Delivery. LSTM's policy is to ensure that senior staff increase their interactions and working with key decision makers at international agencies such as the WHO, and funders, such as BMGF, DFID and USAID to enable LSTM to influence and respond to changing international and national priorities. By supporting, and where appropriate, leading these efforts alongside the private sector, charitable foundations and within partnerships (see examples below), LSTM is able to maintain a robust portfolio of projects from early stage discovery to development and clinical trials. Throughout the REF period, LSTM and the University institutes have participated in a variety of local, regional and national activities designed to promote public engagement with our research, ranging from science festivals (e.g. Brighton and Edinburgh) to TV documentaries (e.g. ITV1 documentary "Help! I Caught It Abroad") that focused on research at LSTM and their Well-Travelled clinic. Staff from this UoA have also engaged with the local community by organising exhibitions at Liverpool's National Museums and Galleries, including celebrations for the Wellcome Trust 75th anniversary and the MRC Centenary, as well as LSTM providing free treatment and public information sessions in support of WHO 'world days'. LSTM were also awarded an International Public Engagement Award by the Wellcome Trust to establish a science exhibition and staff worked with Liverpool schoolchildren and Liverpool Museum, interacting with pupils in Malawi to learn about tropical diseases.

Partnership Development

To initiate new collaborations that maximise potential impact, the Unit has benefited from institutional KE vouchers, funded from the University's HEIF allocation. £90K has been invested in 12 feasibility or translational projects with external partners, including work on novel pneumococcal vaccines with Novartis Vaccines and validation of a lateral flow device for biomarkers of infection with Foresight Diagnostics. In addition to the project outcomes, these vouchers help lever additional funding, facilities or expertise, and enable ongoing collaborations for larger-scale projects. To facilitate this activity three dedicated staff from the University's Business Gateway team work with us to seek partners and negotiate new agreements for collaborative research and KE projects. The Unit has also developed innovative ways of engaging with industry partners which provide impact on skills. For example, the MRC Clinical Pharmacology Training Scheme allows 'training without walls' for 12 clinical fellows with companies such as Astra Zeneca and GlaxoSmithKline. This improves interactions between academia and Industry, providing researchers with access to technologies and expertise, and our industry partners the opportunity to work closely with clinical and pharmacological expertise and patients/patient materials. Our **Technology Directorate** enables external companies to access outstanding analytical expertise and offers our researchers further opportunities to engage with new partners. It has contributed significantly to the development of the new Materials Innovation Factory with *Unilever* that will provide staff from this Unit with access to state-of-the-art biomaterials expertise from the commercial environment.

LSTM and partners work to define, evaluate and support the implementation of effective interventions across a broad range of disease areas including NTDs, maternal and child health, and respiratory and vector borne diseases. LSTM is a partner of choice for many global collaborations and is, for example, currently hosting two virtual Product Development Pathways (PDPs) in vector control, funded by BMGF and DFID, and a filariasis drug development PDP funded by BMGF. Impact collaborations are frequently associated with the 'delivery' aspects of our research, in particular the policy into practice elements, but also encompass significant levels of product development as shown by the award of the Prix de l'Innovation 2013 to **Pleass** for work on developing a biomimetic for IVIG. Additionally, in health delivery, an example is the Global Alliance to Eliminate Lymphatic Filariasis based in the WHO with major contributions from LSTM and academic links and partnerships with Ministries of Health in 83 countries, pharmaceutical companies and funding agencies.

Bridging the translational gap

During the REF period, staff have been supported by the Business Gateway to secure funding for collaborative translational projects. Schemes have included TSB (six projects including one with Unilever to develop instrumental and bioinformatic pipelines to accelerate commercial applications of metagenomics approaches), and NIHR i4i (for example, a Point-of-Care test for Sepsis based on calcium-induced turbidity in blood). LSTM was successful in securing a £250K MRC 'Confidence in Concept' (CIC) award to accelerate the transition from discovery science into the early/late stages of therapeutic/diagnostic development. Five awards were made in 2012 through an open, competitive, peer-review process. Early-stage clinical translational projects have also been supported through a £100K CIC fund established jointly between the Universities of Liverpool and Manchester. This allowed the funding of 3 joint projects involving staff from UoA1 that fostered inter-University collaboration prior to seeking external funding in line with a strategic agreement to exploit complementary areas of expertise. The University is participating in the BBSRC 'Excellence with Impact' competition and the Faculty was awarded £100K by BBSRC as a 'Sparking Impact' award to support new impact-related activities linked to early stage preparation for commercialisation. These funds were distributed on a competitive basis during 2013.

Commercialisation of research

In addition to facilitating applications for project-based funding to accelerate the realisation of impact of research, the University's Partnerships and Innovation staff support its commercial application, demonstrated by the case study of the spin-out company for sepsis diagnosis (**Toh**). The University's IP specialists provided support with the development of patents, the formation of Toh's spin-out company (Sepsis Ltd) and further IP exploitation.

LSTM runs several PDP's (e.g. Insecticide development, malaria drug development) in collaboration with industrial partners. These include two long lasting formulations for indoor residual spraying for malaria control that completed development in 2012 and 2013 with Syngenta and Bayer respectively. These have halved the cost of malaria prevention in African settings. A new insecticide quantification diagnostic for quality assurance at the point of use has gone into commercial manufacture. The WHO, CDC and the US President's Malaria Initiative have undertaken an evaluation of the diagnostic and a WHO recommendation for formal adoption by disease control programmes is expected in 2014. Our Decision Support System software for malaria and dengue control is in use in four countries and BMGF has awarded LSTM a further $2.4M to extend the system for Visceral Leishmaniasis control. The updated system will go into operational use in 2014 in India, where 80% of the world's cases occur.

Use of Major Research Centres

Infrastructure support for facilitating impact generation within this UoA has been enhanced by the major Research Centres described in REF5. These provide a critical mass of researchers, facilities and support structures to enable an integrated and multi-faceted approach. For example, the MRC Centre for Drug Safety Science Industry Programme Manager (funded by the Association of British Pharmaceutical Industries) runs a framework of workshops involving industry and regulators and the Centre plays a leading role in UK and international collaborations that maximise reach and significance of drug safety research, e.g. leading a €32M IMI project to develop better pre-clinical tests to predict drug-induced liver injury. The Centre established a patient/user group on drug safety to advise on study design, patient information leaflets and dissemination and has developed a public information booklet 'Making Sense of Drug Safety' with the charity, Sense About Science (launched November 2013). Other public engagement activities led by Centres have included presentations at the BA and regional Science Festivals. The Wolfson Centre for Personalised Medicines also advised the Y-touring theatre company on a play to raise awareness about personalised medicine, which was performed in schools and at the Royal Albert Hall.

The Malawi-Liverpool-Wellcome (MLW) Programme provides a focus for clinical impact with major research themes centred on malaria, HIV & TB, NCDs and microbial infection and immunity. The strong laboratory infrastructure embedded within a tertiary referral hospital in a disease endemic setting provides an excellent platform for research. Contributions to impact from research conducted at MLW on pneumococcal and rotavirus vaccines have influenced international

policy and malaria and meningitis work fed into regional and international guidelines. MLW also undertakes local public engagement activities with (for instance) a regular radio programme in Malawi "Ubwenzi pa Umpoyo" (Friends in Health) discussing relevant local health issues.

NHS Partnerships

Over the REF period, the University and LSTM strengthened their relationship with local NHS partners through the establishment of Liverpool Health Partners and are part of the North West Coast AHSN. Major research programmes with NHS Trusts have resulted in significant impact in the REF period. For example, in infection, new drugs have been discovered for tuberculosis and a novel vaccine against *Neisseria meningitidis* was evaluated in the Royal Liverpool and Broadgreen University Hospitals Trust (RLBUHT).In pharmacology, drug-drug interaction databases for HIV and Hepatitis C developed in Liverpool are now widely available in NHS clinics. In musculoskeletal diseases, new interventions are tested to delay musculoskeletal degeneration, while novel guidelines have arisen from work newly defining the impact of these diseases on others (e.g. rheumatoid arthritis as a risk factor in cardiovascular disease). The NIHR Pancreas Biomedical Research unit (PBRU) is the only UK centre carrying out translational research into pancreatic disease and is a partnership between RLBUHT and the University (**Sutton**). The PBRU builds on basic and applied research with a range of collaborations with international research institutions and works with companies such as Astra Zeneca, Boehringer, Merck, Roche and smaller companies to develop and validate healthcare products including new therapeutics, and diagnostic methodologies.

Policy Impact

We have contributed to the development of national and international guidelines through engagement with NICE, DoH, MHRA, WHO and other policy agencies. Example changes to DoH policies include HIV Treatment Guidelines that now ensure clinic letters carry standard advice to check for drug interactions and links to resources (**Khoo**), and new encephalitis management guidelines for adults and children (**Solomon**). For MHRA, **Pirmohamed,** as Chair of the Pharmacovigilance Expert Advisory Group led changes in prescribing and withdrawal of drugs to protect public health. For WHO guidelines, LSTM impacted international policy on HIV testing and counselling (HTC) in WHO and the US Centres for Disease Control (CDC). Taegtmeyer was a member of the CDC Counselling and testing team (2007-12) and the main writer of the WHO Handbook for Improving HIV Testing and Counselling Services (2011). LSTM led the CDC and WHO Practical handbook on home-based HTC and was core to the development of the WHO ART guidelines (2013). LSTM contributed to the WHO guidelines on malaria and dengue control through WHO expert panels (**Ranson,** McCall), WHO commissioned reports and reviews (**Ranson** 2011). LSTM technical input was sought for the WHO Global Plan for Insecticide Resistance Management in Malaria Vectors (**Hemingway, Ranson,** McLean, **Coleman**). The 2012 WHO update on intermittent preventive treatment (IPTp) for the prevention of malaria in pregnant women is policy in 39 sub-Saharan countries and based on a meta-analysis led by **ter Kuile**.

c. Strategy and plans

Our Impact Strategy is designed to deliver improvements to health in the UK and globally with a focus on developing countries. Within this broad objective, the Unit will make key contributions to economic development, with health and life sciences being a key strength in the North West, and contribute to UK industry, particularly pharmaceutics.

The key elements of our strategy are:

- Investment in structures to support translation (e.g. IP, Joint Research Office, protection, contracts and partnerships).
- Recognition of impact in rewarding staff and promotion, as well as in recruitment.
- Development of Research Centres as a focus for translation.
- Communication with partners to support impact as well as public engagement to raise awareness or our research findings.

Significant progress has been made over the REF period in terms of raising awareness of the value of **impact planning and generation** supported by KE strategies which provide multiple routes for interactions with research users. We work with Corporate Communications and

Business Gateway to increase further the levels of awareness of KE and impact with our many stakeholder groups. We have a 'one-stop' intranet site to provide information for staff that includes practical advice about applying for funding, establishing new collaborations, preparing business plans, engaging in consultancy and obtaining support from research and KE leads and Professional Services staff. We continue to prioritise marketing of our strengths and expertise through traditional and social media and supporting academic staff to organise and attend key conferences and symposia to raise the profile of our work. A bi-annual magazine, *Realise*, promotes the research strengths and collaborations of our scientists and clinicians to more than 3,000 contacts in industry, local and national governments, funding councils, the higher education sector and media, and will be increasingly used to showcase our research outcomes and impacts.

Our research institutes include impact strategies within their three-year plans, and these inform PDR discussions with staff. Success in generating impact is a key criterion in staff promotion cases. We are integrating impact into our research culture through focusing on Early Career Researchers (ECRs), including PGRs. The Institute for Integrative Biology, for example, has designed a new module for impact that is taken by all Masters and first year PhD students, and our Postgraduate Group organises impact events and training. We support internships and placements for PhD students with non-HEI partners, particularly through our CASE studentships, the BBSRC DTP, and a new institutional scheme offering short-term placements or events and funded by HEIF (awards in 2012/13, for example, allowed us to further develop our work with AstraZeneca on CLL).

We will further use our **major Research Centres and Institutes** to generate increasing impact on multiple sectors and users, by providing a leadership role and a sustainable infrastructure to plan and implement impact activities. For example, the MRC-Arthritis Research UK Centre for Integrated Research into Musculoskeletal Ageing will generate impact to address medical and social challenges through lifestyle interventions to maintain independence and mobility of older people, the Wellcome Trust-Liverpool-Glasgow Centre for Global Health Research will facilitate access to relevant health-based research questions in low and middle-income countries and communities in which to test new diagnostics and interventions. In addition to existing Centres, the Unit is contributing to new Centres in bioengineering and the Materials Innovation Factory to extend the reach of this approach into new areas such as novel anti-microbial surfaces.

A major opportunity for **translation of research into health benefit** for the local population is encompassed in Liverpool Health Partners' (LHP) five-year strategy with Clinical Academic Programmes in Drugs (lead: **Pirmohamed**), Musculoskeletal Disorders (lead: **Moots**), Infection (lead: **French**) and Cancer (lead: **Johnson**). Researchers will receive professional support from a LHP Directorate, including a strategic projects coordinator to facilitate new cross-organisational projects, and a new Joint Research Office. The region has substantial health inequalities and Liverpool residents have life expectancy >seven years less than SE England and the worst cancer mortality in Western Europe. Annual costs from ill health associated with social deprivation are >£2B (lost income and incapacity benefit). The integration through LHP of specialist NHS Trusts and tertiary services gives unparalleled access to patient cohorts with extremes of morbidity facilitating clinical and translational research. Implementation in the NHS will be linked to the unit's role within the North West Coast AHSN and the North West Coast 'Collaborations for Leadership in Applied Health Research and Care' (CLAHRC), awarded in 2013 (£9M from NIHR) with a specific focus on health inequalities. Researchers in this UoA lead improvements in public health, reducing health inequalities within this multidisciplinary team, with themes on managing complex needs and delivering personalised health care (**Pirmohamed**).

The Unit is extending the reach of research across LHP with planned new developments, e.g. investment from the University, RLBUHT and Alder Hey will create a **Liverpool Biomedical Research Centre in Personalised Health** based on the NIHR BRC paradigm and aligned to LHP's Clinical Academic Programmes. This will be enhanced by the formation of a **Liverpool Bioinnovation Hub (LBIH)**: This £12M ERDF bid includes a new build (completion 2015) with a National Biobank, genomics and shared facilities and occupied by the anchor tenant, RedX Pharma and other SMEs to work in Personalised Medicines. In Global Health, the research

strengths of LSTM and the institutes (with continued support from the Wellcome Trust for the Centres in Liverpool and Malawi, and the clinical PhD programme) will enhance existing activities and engage new partners to expand the research base and geographical coverage of our work.

Enhance translation of basic bioscience into clinical benefit

Both LSTM and the institutes are structured to facilitate translation of basic science through to patient benefit. Recent appointments in the institutes enhance this capacity. For instance, appointments in statistical genetics, systems pharmacology and modelling provide world leading expertise in complex analysis and modelling in translational research. LSTM will pursue its strategies of 'product discovery and development' and 'policy into practice' to deliver our mission to reduce the burden of sickness and mortality in disease endemic countries through the provision of interventions to improve human health that are relevant to the poorest communities. This is supported by new appointments in diagnostics, epidemiology, clinical microbiology, statistics and health economics, and new facilities for major activities such as the Maternal and Newborn Health Unit, Centre for Applied Health and Delivery, and the Centre for Neglected Tropical Diseases.

d. Relationship to case studies

Most of the submitted case studies relate to research and dissemination undertaken before 2008 and demonstrate the time, effort and perseverance required to realise true impact on clinical practice or health outcomes. We recognise the core elements of cases as sustained high quality research targeted at priority areas, the effective dissemination of findings and representation of researchers on key groups. For example, improvements in therapy for the *river blindness and elephantitis* study track back to the initial establishment of a new laboratory and research team, research breakthroughs from laboratory studies and community trials and the later establishment of the 'Anti-Wolbachia' (A•WOL) consortium; the reach of improvements in *meningococcal disease diagnosis* was enhanced through HPA dissemination; recognition of **Calverley**'s group's work on *COPD* led to his contribution to multiple studies and guideline groups, generating an impact on clinical practice in the UK and Europe; **Clark**'s specialist expertise led to his involvement with NICE reviews on appropriate clinical practice in treatment of *Chronic Myeloid Leukaemia*.

In all case studies, collaboration with a diverse range of partners and beneficiaries has been crucial. For example, the control of *Japanese Encephalitis* and introduction of the *rotavirus vaccine* involved engagement with other academic groups, government, industry, and policy makers including WHO; improvements to treatment of *Crohn's Disease* and *Pancreatitis* crucially involved NHS partners, clinical associations, charities and patient groups; the *control of malaria in pregnancy* involved a consortium of 41 organisations from 29 countries; the study on *malaria prevention* exemplifies the PDP approach successfully developed by LSTM.

Nine of the case studies reflect the Unit's distinctive expertise in Global Health and its access to research facilities and hospitals in developing countries. The *rotavirus vaccine*, *malarial retinopathy* and *malaria in pregnancy* case studies all resulted from exploitation of the Malawi-Liverpool-Wellcome (MLW) programme, one of the Unit's major Centres. Similarly, in the UK, the case studies on *therapeutic drug monitoring in HIV* and *HLA alleles as genetic predictors* derive directly from the Centre for Drug Safety Science. These issues have informed the strategic approach to invest in major research centres of excellence and the prioritisation of partnership development, including the NHS and industry. Investment in the infrastructure supporting these partnerships will allow greater alignment of research activity and the needs of beneficiaries and other users, and accelerate impact generation.

The case studies have also demonstrated how our impact strategy can be further enhanced by exploiting successful processes and mechanisms on a broader scale. Staff are continuing to develop some of these areas through increased use of the University's pump-priming KE voucher scheme and Innovation Vouchers from the Technology Strategy Board. **Carrol**'s use of a £10K KE voucher to pump-prime development of a point of care device for diagnosis of serious bacterial infection led to award of £600K from the TSB to translate the approach with commercial partners, with subsequent additional support from NIHR. As indicated above by the example of the spin-out Sepsis Ltd and associated activity, support is being provided through all stages of impact development through dedicated staff in Business Gateway and Liverpool IP.