Institution: THE UNIVERSITY OF MANCHESTER (UoM)

Unit of Assessment: 1 Clinical Medicine
(Returned staff members are shown in bold, those in other UoA, honorary or former staff in italics)

a. Context

Research carried out in UoA1 links discovery science to translational clinical research and patient benefit, and aims to improve health and patient care both in the UK and internationally. The research has impact in the overlapping areas of:

i. clinical diagnosis;
ii. therapy;
iii. evidence base for clinical management, health screening and prevention.

The key audiences for our research impact are national and international health care providers and users including: (i) Department of Health (policy makers), (ii) commissioners, (iii) provider organisations (especially NHS) (iv) medical and scientific research professionals, (v) professional and statutory regulatory and representative bodies, (vi) international commerce in the health field, (vii) health charities, and (viii) patients and the public.

The key beneficiaries of our research are patients and the public, and wider society. Our work is intended to improve the health and well-being of the population through research that impacts at all levels of the translational medical science pathway. We therefore aim to have beneficial effects on (a) quality of patient care, (b) carers, (c) care-givers, (d) effective use of resources to reduce the burden of health and social care on the tax payer, and (e) support for innovation and economic competitiveness for commercial partners in the health field.

As outlined below, we possess and have invested in all of the elements that are required to develop biomedicine research in Manchester, from basic discovery science to applied clinical research. In order to enhance impact and add value we have aligned and synchronised all of these elements through the Manchester Academic Health Science Centre such that there is now a single, coherent pipeline.

b. Approach to impact

UoM has invested strategically in all aspects of the translational research infrastructure required for developing better delivery of medicine to the patient. It hosts a broad portfolio of discovery science and studies of disease mechanisms spanning the breadth of medical disorders, and has effective means to capture and exploit IP for future commercialisation/adoption (see section 3 below) and widening business engagement and partnership. Cases have been selected in UoA1 in which the impact has led to innovations affecting clinical diagnosis and therapy, and has developed the evidence base of the specialties concerned, with the ultimate goal of delivering improvements in patient care. To deliver on this impact, we have focussed on four main areas:

1. Providing the infrastructure to support impact

The core partnership of academic staff in UoA1 with NHS care providers across Greater Manchester (GM) is supported through **Manchester Academic Health Science Centre** (MAHSC). The four key research themes represented in UoA1, described in detail in REF5, are Cancer Sciences, Cardiovascular Sciences, Human Development, and Inflammation and Repair, and these map directly onto four of the six domains that structure MAHSC. Many of the academic staff in UoA1 hold clinical contracts, and the major research themes are embedded in the teaching hospital sites of Greater Manchester. The Trusts, as part of MAHSC, are committed strongly to patient focused research activity and alongside NIHR have facilitated clinical trials to move rapidly to impactful observations which are altering practice in areas including cancer (**Blackhall**, lung cancer; **Bundred** and **Howell**, breast cancer; **Saha**, leukaemia; **Kitchener**, cervical cancer), heart

disease (**Heagerty**, cardiovascular risk), stroke (**Hamdy**, dysphagia after stroke) and inflammatory disorders (**Denning**, fungal diseases; **Symmons**, rheumatoid arthritis; **Woodcock**, chronic lung disease). Infrastructure developments designed to focus on diagnostics and therapeutics include:

a. The **Manchester Centre for Genomic Medicine** (MCGM) is based in Central Manchester University Hospitals NHS Foundation Trust (CMFT), applying research-based diagnostics testing using an in-house next-generation sequencing facility (SOLiD and Illumina platforms). This has grown from a structure of genetics research embedded for many years within an NHS organisation delivering a major regional and national service. The sequencing and analysis platform is aligned differently from many organisations which rely upon University-based sequencing and computing, and places the MCGM in a unique position to develop research impact directly in the hospital setting. Cases that have benefitted include; **Crow** 'The global impact of gene identification in Manchester'; **Denning** 'Diagnostics and novel life-saving therapies for aspergillosis'; and **Clayton** 'Defining the Phenotype of Severe Growth Disorders, Discovering New Genes that Control Human Growth and Enhancing Clinical Practice'.
b. Three **Clinical Research Facilities** for experimental medicine and early phase clinical studies were awarded NIHR funding in 2012 after submissions made through MAHSC: the Wellcome Trust CRF and Children's CRF based at CMFT (£5.5m), to support all experimental medicine studies with a focus on arthritis, psoriasis, depression, addiction, and diabetes; the Cancer CRF at the Christie (£4.5m), to support early-stage trials of treatments for people with cancer; and the Respiratory CRF at University Hospital South Manchester (£2.5m), to support studies on asthma, fungal infection, chronic obstructive pulmonary disease (COPD), and food allergies. Cases directly benefitting from this strategy include: those of **Woodcock**, **Denning** and **Symmons** mentioned above, as well as **Bigger** 'Improved clinical management of lysosomal disorders'; and **Griffiths** 'Fibrillin-rich microfibrils & efficacy of anti-ageing cosmetics'.
c. **Manchester Cancer Research Centre (MCRC)** is a partnership between the University, the Christie NHS Foundation Trust and its partner trusts and CRUK. It brings together world-class expertise in cancer research in Manchester which includes the CRUK funded Paterson Institute for Cancer Research (renamed CRUK Manchester Cancer Institute from October 2013). The Christie treats 17,000 new cancer patients per year. The MCRC has recruited 4,000 volunteer patients engaged in 70 phase I and 130 phase II cancer trials over the last three years. 200 clinical studies are currently open on the site, and clinical trial programmes are currently in place in collaboration with AstraZeneca, Novartis, Roche, Abbott Laboratories, and GSK. Cancer-based cases (**Blackhall**, **Bundred**, **Howell**, **Kitchener**) have been strongly facilitated by this engagement with the MCRC. The AstraZeneca-funded cancer tissue bank contains 55,000 samples from 5,000 donors and 2,000 patients, covering 13 different tumour types.

2. Patient and public involvement and engagement (PPI/E)

Engagement and involvement has been a critical component of how the research groupings in UoA1 approach impact. UoM aims to create a culture of public and community engagement as part of everyday University life, with a series of public events at venues, such as our Whitworth Art Gallery, Manchester Museum, and Jodrell Bank. Relevant to research carried out in UoA1, Nowgen (based in UoA1, *Starling, Dack*) represents a partnership between UoM and CMFT with funding through Wellcome Trust ISSF, CMFT, R&I Division, consultancy and grants. It was initially part-funded by the Northwest Regional Development Agency and the European Regional Development Fund, and acts as a centre of excellence in public engagement, education and professional training in biomedicine, with a focus on genetics. Examples of activity during 2012-13 include:

- Working with schools: Over 1,000 GCSE & A level students attended curriculum-based laboratory workshops at Nowgen, run with input early career researchers; postgraduate students were trained to deliver the workshops; CPD workshops in genomics were delivered to 80 science teachers; Nowgen coordinated input from FMHS research to the 'Science

Extravaganza' event; 15 students (aged 17-19) were supported to undertake a practical investigation for their Extended Project Qualification, as part of the RCUK-funded programme 'Schools University Partnership Initiative'.

- Creative engagement: Nowgen supported 28 medical researchers to give short public talks at venues around the city, 'Manchester Minute Microlectures' (M-cubed) attended by 180 people; the first FMHS Community Open Day attracted >700 members of the local community; the 'Science Spectacular' event (>4,000 members of the public); and a public dialogue event as part of Manchester Science Festival 2012.
- Support and training for researchers: training workshops delivered to 89 biomedical researchers, 'Engagement@Manchester' monthly events attended by approximately 180 Faculty members, role in the development of the University's Engagement website, '10 ways to get involved in Social Responsibility' for UoM staff and students; individual advice on engagement and involvement given to ~30 researchers/students/staff from FMHS.
- Patient involvement in research: workshops for staff, facilitating involvement of patients in clinical study steering groups, advisory research panels and research user groups. Examples include: **Black**, Fight for Sight-funded ocular genetics study; **Clayton, Davis** & *Callery* (UoA3), NIHR RfPB-funded study on communication in transition clinics; **Symmons/Thomson** Musculoskeletal BRU); and the Stroke network of patients and carers, one of the largest in the UK (**Tyrrell** & *Rothwell*, UoA5). Nowgen has taken a lead role in the establishment of a working group on 'Payment for Involvement' to develop a Faculty-wide policy on payments for patient and public involvement in research and teaching.
- Research: work package leadership of the IMI-funded EUPATI project, investigating knowledge, attitudes and beliefs to patient involvement in pharmaceutical R&D, including largest ever survey of patient attitudes to medicines development; research into adolescents' information needs when taking part in genetic research (**Clayton**, *Callery* (UoA3) *Starling*).

Other examples include the generation of evidence-based guidelines for rare genetic syndromes, where parents and members of lay support groups were involved as partners in the working groups for each condition (see case studies: **Bigger** Improved clinical management of lysosomal disorders; **Hamdy** Design and implementation of a new treatment for dysphagia after stroke; **Evans** The University of Manchester's role in establishing nationally funded forefront services for neurofibromatoses).

3. Technology development and transfer

Development: UoM business engagement teams have developed a strong capability, recognised internationally, in 'health technology' as evidenced by application of e-health (**Dixon W**), Med Tech (**Hamdy**, **Denning**) and the innovation and technology hub (MIMIT: Manchester: Integrating Medicine & Innovative Technology), m-health, regenerative medicine (**Freemont**, **Hoyland**), enabled by the identification of unmet clinical need and supported by coordinated commercialisation groups, UMI^3 and TRUSTECH (NHS). For example:

- The Salford integrated e-health record has developed a clinical information system providing a single, integrated electronic patient record across both primary and secondary care. This infrastructure has allowed major investment £30m from GSK in the Salford Lung Study, testing safety and efficacy of therapy for asthma and COPD, applying expertise in respiratory clinical research to understand patient outcomes across populations.
- UoM and Greater Manchester NHS and Primary Care Organisations jointly work through MIMIT to facilitate collaborations between clinicians, scientists, engineers and industry to develop new technology for patient benefit. An example of success is a new device for treatment of dysphagia in stroke (**Hamdy**, see case study), developed by a start-up company using the MedTECH Centre, established in partnership between CMFT and Manchester Science Parks, and supported by MIMIT. This has now achieved £12m in venture capital investment, CE marking, and sales totalling £3m in UK, Europe and the Middle East.

Transfer: UoM is widely recognised for excellence in technology transfer. UMI^3 Ltd (inspire, invent, innovate) is the University's wholly-owned innovation company. It has responsibility for intellectual

property (IP, see UMIP below) management and commercialisation and operates the University's campus-based incubator facilities:

- the UMIP Division is dedicated to dealing with IP, invention disclosure assessment, patenting, proof-of-principle funding, project management, and industry partnership services for academics;
- the UMIC Division operates the Innovation Centre with extensive physical incubator premises and innovation-related events, and graduation of spin-outs to the Manchester Science Park.

12 spin-out companies relevant to work in UoA1 are currently active which form part of a portfolio of some 50 spin-out companies across UoM. In the last 4 years, these companies have successfully licensed over 100 inventions to commercial parties, including: *F2G* (lead academic **Denning**); *Myconostica* (**Denning**); *Phagenesis* (**Hamdy**, **Thompson**); *Vibio* (**Hampson**); *Renephra* (*Brenchley*); *Cellular Therapeutics* (**Hawkins**); *CG Ceutics* (**Griffiths**); *Gelexir* (**Freemont**); *Iduron* (**Gallagher**); *IF Sensing* (*Brenchley*); *Karus*, **Townsend**; and *Curapel* (*Gibbs*).

4. Academic staff incentivisation

The University's promotion criteria recognise knowledge and technology transfer activity as one of four key criteria (with research, teaching and service/leadership) up to Professorial level. This and the generous academic inventor/UoM share split for IP (at least 85% of net income goes directly to the inventor) has led to strong buy-in by staff to consider impact and innovation as part of any research programme so driving success and a range of areas of direct and indirect impact.

c. Strategy and plans

Impact in research and other activities is integral to UoM's strategy, formalised in the Manchester 2020 Vision document (http://documents.manchester.ac.uk/display.aspx?DocID=14744). The University is committed to achieving impact beyond academia which yields economic, social and cultural benefits. Within FMHS, a major component of the Faculty's Five Year Strategic Plan focuses on social responsibility (Priority 3) and the Faculty's commitment to utilise expertise and opportunities in medicine and health to have a positive impact on others. The systematic capture and documentation of impacts arising from research in UoA1 will be facilitated by a dedicated research administrator in FMHS, appointed to this post in 2013.

Our forward strategy in UoA1 will continue to focus on:

1. Recruitment:
A major recruitment process started in 2011, targeted to fill roles that we have identified as areas of translational strength for future development. Many of the new appointments have already brought impactful research activity from their previous positions, e.g. **Keavney** and cardiac genetics, **Bignell** and fungal drug treatments, **Hussell** and inflammation drug targets (based in Manchester Collaborative Centre for Inflammation Research, a new cross-Faculty centre funded by UoM, GSK and AstraZeneca, detailed in REF5).

2. Industrial collaboration:

Major industrial-research collaborations have been crucial to developing impact by supporting translational research with new diagnostic and predictive testing (e.g. skin care with Boots); development and evaluation of endocrine therapies for breast cancer (with AstraZeneca); evaluation of therapy for airways disease (with GSK). Specific partnerships include strong links with GSK and AstraZeneca (for example MCCIR (above), including long-term secondments from GSK to UoM, the Salford Lung study, and the AZ Alliance. These interactions have brought in over £50m income and are planned to continue through the next 5 years, and will be facilitated by the recent appointment of **Townsend** (Cancer Sciences) as Associate Dean for Business Development, leading on combining enterprise and academic research in strategic partnerships.

3. NHS collaboration:

This will develop further integration of academic staff in UoA1 within NHS clinical care in the MAHSC partnership. There is continuing extensive collaboration with NHS Research and Innovation, and several academic staff hold key roles in MAHSC and Trusts including **Sibley** (MAHSC Research Director and Head of Research & Innovation for CMFT), **Radford** (Director or R&D for Christie Hospital), **Ollier** (Director of R&D for SRFT). Our academics also play a significant role in the NIHR Clinical Research Network: **Clayton** is Director of the Greater Manchester NIHR Medicines for Children Research Network and Associate Director of the Greater Manchester CLRN. The GM CLRN has a £15m budget, with 50,000 participants recruited into 850 studies and is consistently in the top 2 recruiting networks in England over the last 5 years; 40% of our Local Specialty Groups are in the top 5 for national recruitment and UoM academic staff involved as Local Specialty Group leads include **Bundred** (Cancer), **Custovic** (Respiratory), **Griffiths** (Skin & wound healing), **Herrick** (Immunology & Inflammation), **McLaughlin** (Gastrointestinal), **Newman** (Genetics), **Symmons** (Musculoskeletal), **Tyrrell** (Stroke). This close integration of clinical trials infrastructure and UoM academic staff will be continued in the next 5 years as the GM CLRN transitions into the GM LCRN.

4. Innovation and technology transfer:

The main UoM bio-incubator facility sits between the Faculty and Trusts and serves one of the largest integrated clinical academic campuses in Europe, this places it ideally to rapidly undertake first-into-man studies. CMFT is currently investing £25m in a new research and innovation centre (City Labs), including a medical technology incubator to create the same sort of conducive environment for MedTECH as the University has for biotech. This is already creating a pipeline of NHS-developed IP spin-outs that benefit from access to the UoM science base (examples included in section b(3) above). Our capacity to accelerate good science along the translational pathway is facilitated by access to both adult and children's NIHR CRFs in CMFT, and the presence on site of ICON plc, a world leader in early phase studies, gives us added ability to develop new drug discovery models.

5. Strengthening our relationships with national and international policy makers:

Through direct academic participation, we have strengthened our relationships with policy makers and government agencies such as NICE, professional regulatory bodies, MHRA, Health Education England, NHS England and PHE. Senior academic staff within UoA1 have been supported by the University to engage not only with national and international research peer review, but also with a wide variety of national and international advisory bodies and specialist professional societies involved in the clinical translation of research. This places UoM staff in positions of influence to facilitate rapid application of the translational impacts that are highlighted in the submitted case studies. A fuller list of such positions is provided in REF5, but selected examples directly relevant to development of research impact in UoA1 include the following staff who have contributed impact case studies submitted here: **Clayton**: co-author NICE Guidelines, use of GH in children, 2010; **Griffiths**: President, International Psoriasis Council 2013; **Heagerty**: President, British Hypertension Society, (2011-13); President, International Society of Hypertension (2008-10); **Saha**: Chair, International BFM Study Group (for paediatric leukaemia and lymphoma) Resistant Disease Committee; **Symmons**: Chair UKCRN National Musculoskeletal Specialty Group (2009-date); **Woodcock**: President, British Thoracic Society (2012-13).

6. Enhancing public engagement:

As part of the UoM's Social Responsibility strategic aim, FMHS has developed a strategy and action plan on public engagement and involvement to be introduced and implemented from 2013 (*Starling*, *Cutts,* UoA3). This will include recruiting leads for academic engagement and involvement and establishing a coordinating centre (as part of Nowgen, based in UoA1), working together to:

- support researchers and educators to involve and engage patients and the public;

- support patients and members of the public who are, or wish to become, involved in health research and education;
- share learning, skills and solutions about PPI/E in research/education, and develop knowledge and understanding if the value and impact of PPI/E.

Nowgen (*Starling, Dack*) continues to be involved in major regional, national and international public engagement initiatives (e.g. Manchester Science Festival, North West People in Research Forum, MHRA Patient and Public Engagement Expert Advisory Committee). Nowgen will also develop its engagement and involvement support for the Faculty's global health agenda (through Starling's previous work, and as co-applicant on a recently successful Wellcome Trust Global Health Research Centre grant) and its engagement and involvement research portfolio. Nowgen also leads a work-package in the European Patients' Academy on Therapeutic Innovation (EUPATI) aiming to inform and involve patients and public on pharmaceuticals development (detailed in REF5).

Training in engagement and involvement is provided for existing staff in UoA1 through Nowgen and the University's Staff Training and Development Unit. The New Academics Programme includes courses on public engagement and media engagement, in order to raise awareness and skills in these areas. Development of further training in engagement and involvement is a specific focus of the Faculty's engagement strategy.

d. Relationship to case studies

Cases have been selected, as indicated above, as those in which the impact has led to tangible and far-reaching innovations affecting clinical diagnosis and therapy, and have developed the evidence base of the specialties concerned, with the ultimate goal of delivering improvements in patient care.

We present 15 case studies for this submission to demonstrate the variety and scale of research impact across this UoA. Impact does not arise spontaneously from publishing world-leading research, and the UoM, FMHS and the four constituent Faculty Research Institutes represented in UoA1 have committed time and resources to facilitating the transfer of research to produce impacts in our key target areas of:

- Cancer, including cervical, lung and breast cancers, and paediatric leukaemias (**Blackhall**, **Bundred**, **Howell**, **Kitchener**, **Saha**);
- Cardiovascular risk, stroke and dysphagia (**Hamdy**, **Heagerty**);
- Genetic and metabolic disease, gene identification and service development, and phenotypic and genetic definition of growth disorders (**Bigger**, **Clayton**, **Crow**, **Evans**);
- Infective and inflammatory disease, including rheumatoid arthritis, antifungal therapy, respiratory disease and skin health (**Denning**, **Griffiths**, **Symmons**, **Woodcock**).

In each of these cases, clinical academic staff and biomedical scientists have developed the work in direct contact with their NHS clinical practice over many years, in most cases before the current support mechanisms were put in place. The range of differing cases demonstrate the broad and diverse interests in UoM with strengths ranging from new policies to stratifying diseases, to improved cancer management, development of successful spin out companies, and direct changes to patient care.