Department of Health

ACADEMIC HEALTH SCIENCE CENTRES
FULL STAGE APPLICATION

Note: The accompanying *"Academic Health Science Centres – Full Application Guidance"* contains essential guidance on the information you need to provide when completing this proforma.

Please adhere to the page limits stated within each box. Only information submitted up to this page limit can be assessed. Please do not alter the margins of this proforma.

Please note this form should be completed in font no smaller than 10-point Arial.

All fields must be completed.

Please insert your unique Reference Number into the Footer space provided.

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership:

Imperial College Academic Health Science Centre

Name, email and telephone number of the Lead Contact for the proposed AHSC:
Note: This will be the contact for all correspondence relating to this application.

Professor David Taube, AHSC Director
david.taube@imperial.nhs.uk Phone : 020 3313 1371

Please list the members of the partnership involved in the proposed AHSC, including names of NHS Provider(s) and university(ies) involved:

Imperial College Healthcare NHS Trust

- Hammersmith Hospitals
- St Mary's Hospital
- Charing Cross Hospital
- Queen Charlotte's and Chelsea Hospital
- Western Eye Hospital

Imperial College London

- Faculty of Medicine
- Faculty of Engineering
- Faculty of Natural Sciences
- Business School

2. ABSTRACT (250 words)

In plain English, present the specific aims, goals and objectives of the proposed AHSC.

Imperial College AHSC is a highly successful partnership established in 2007, between Imperial College Healthcare NHS Trust (ICHT) and Imperial College (IC), with the vision to measurably improve the quality of life of patients and populations by taking the discoveries that we make and translating them into advances, new therapies and techniques in as fast a timeframe as possible. The patient is central to our goals and objectives; enhancing research through the pre-eminence of IC's discovery science and the critical mass of ICHT, bioengineering, informatics, developing a cadre of healthcare leaders through education and training programmes, translating research into new patient focussed policies and wealth generation through innovation. Over 5 years, we will make significant improvements in the management and outcomes of some of the commonest causes of morbidity and mortality including obesity, diabetes, neurodegeneration and stroke, infection and antibiotic resistance as well as improving patient safety and patient experience. We are committed to making discoveries in the understanding and treatment of rarer diseases and in the design and implementation of novel surgical technologies and real time diagnostics. Our ability to deliver benefits for patients locally and globally will be substantially enhanced by (i) a service reconfiguration of our hospitals, (ii) our close relationship with the Academic Health Science Network (AHSN) which expedites the adoption and diffusion of our discoveries to address unmet health needs, (iii) by development of Imperial West, a 34 acre translational hub for research and innovation and (iv) internationally through our global partnerships in healthcare.

3. STRATEGY (4 pages)

Please provide the strategy for how the alignment of strategic objectives will continue to improve health and healthcare delivery including:

- A restatement of the partnership's goals, vision and purpose;
- Specific overall short (1-2 years), medium (2-3 years) and long term (4-5 years) objectives for the AHSC;
- A summary of the partnership's top six specific themes or work programmes of focus and how they fit into the overall strategy and goals of the proposed AHSC;
- An outline of the expected specific deliverables of the AHSC over the 5 years of designation that could not be achieved through another type of partnership;
- How success of the proposed AHSC will be evaluated, including success against specified objectives and deliverables;
- Evidence that the partnership has a strong clinical informatics platform to underpin the delivery of the proposed AHSC objectives;
- How the partnership will further align NHS provider and university strategic objectives in order to harness and integrate world-class research, excellence in health education, and excellence in patient care over the 5 years of designation. How this will lead to improved health and healthcare delivery, including through increased translation of discoveries from basic science into benefits for patients.

Imperial College Healthcare NHS Trust (ICHT) was created in 2007, by merging Hammersmith Hospitals NHS Trust and St Mary's NHS Trust to form one of the country's largest acute Hospital Trusts. It has a total operating budget £971m and c.10,000 staff serving a population of 2m with over 1m annual patient episodes and includes designated regional centres; Hyper Acute Stroke Centre, Major Trauma Centre and Heart Attack Centre. ICHT linked with **Imperial College** (IC) in 2007 created the UK's first Academic Health Science Centre (AHSC), **Imperial College AHSC** (referred to henceforth as the AHSC), was designated in 2009. ICHT is consistently rated as one of the safest hospitals in the UK with significantly low mortality rates [HSMR, 70, SHMI, 0.76 and the lowest death rates in low risk conditions, 0.17, (*Dr Foster, Hospital Guide*, 2012)].The metrics outlined in the Pre-Qualifying Questionnaire (PQQ) clearly demonstrate the strengths of IC and its Faculty of Medicine (FoM). IC is ranked 8th in the world, 3rd in Europe and 4th in the UK in The Times Higher Education World (THE) University Rankings, and has 14 Nobel Prize winners within its alumni. The FoM is one of Europe's largest, with a THE World University ranking of 3rd in the UK and 5th in the world for 'clinical, pre-clinical and health' subject areas. It has 470 academic staff (with equivalent numbers holding honorary contracts), c1300 under-and postgraduate students admitted per annum and a research income of c£161m in 2011/12. FoM has 20 Wellcome Trust (WT) Investigators (highest in the UK) and 20 National Institute for Health Research (NIHR) Senior Investigators among its staff and contains 29 externally funded, peer reviewed research centres. The AHSC partners have pioneered many of the major medical advances of the 20th century including vaccines; (Wright, 1913, typhoid vaccine), antibiotics (Fleming, 1927, Penicillin), clinical imaging (Bydder and Young, 1990) and biological therapy (Maini and Feldman, 1998, anti-TNF). The AHSC is nested with unity of vision within the North West London (NWL) Academic Health Science Network (AHSN). This network is co-ordinated by IC Health Partners (ICHP), licensed as the AHSN, comprising 20 partners including IC, (for clarity, this is referred to henceforth as the AHSN).

Our **purpose** as an AHSC is to utilise excellence in research and education across all Faculties at IC to transform health outcomes and to support the UK's globally competitive position in healthcare related industries by increasing societal and economic gain. The AHSC's **vision** is that the quality of life of our patients and populations will be measurably improved by translating our discoveries into medical advances, new therapies and techniques, and by promoting their application in the NHS and around the world, in as fast a timeframe as is possible. Through our vision, we will make advances in the prevention, diagnosis and treatment of diseases: both common diseases with large societal burdens and rarer diseases afflicting individuals and families where insights contribute to developmental and pathogenic mechanisms.

The **strategy** has the **patient as central** to all we seek to achieve and encompasses the following **goals:**

(i) To utilise the research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations, **(ii)** To create powerful new interdisciplinary synergies spanning the IC, AHSC and the AHSN to transform healthcare through translational science, bioengineering and informatics, **(iii)** To educate and train the future generation of multidisciplinary clinical scientists capable of utilising new technologies for enhanced healthcare, **(iv)**To translate research into new policies for the benefit of patients nationally and internationally, **(v)** To create new wealth through innovation in healthcare in discovery science and in population-based translation.

Our strategy is built around 3 major components: **(1)** programmatic excellence, **(2)** strategic reconfiguration and **(3)** a bold spatial strategy arising from the alignment of the AHSC and the AHSN objectives**.** These are described below;

1. Programmatic Excellence: Our strategic goals are delivered through programmes directed at improving patient care, including our Centres for Translational Medicine (CTMs), combining the full strength of IC

Faculties, ICHT and our close alignment with the AHSN and the **Collaboration for Leadership in Applied Health Research and Care (CLAHRC)** for NW London. Through these we will transform healthcare, develop a cohort of future academic and clinical leaders, provide an evidence base for healthcare policy and contributing significantly to the knowledge economy. Our programmes are further outlined in **Section 5.**

2. Strategic Re-configuration: Over the next 5 years, in conjunction with our hospitals and primary care partners in NW London and explicitly in the context of an AHSC, we will undertake a strategic reconfiguration of services within ICHT to deliver one acute site (St. Mary's Hospital), a specialist site (Hammersmith Hospital) and an elective site (Charing Cross Hospital), all co-located with cognate research disciplines and facilities. We will apply the well-established research and education culture of all the Faculties at IC in conjunction with the AHSN, Clinical Commissioning Groups (CCGs) and the clinical expertise of ICHT to create new strategies for out-of-hospital care and to provide the evidence base for transformative change in health outcomes and the emergence of new insights into the policy and economics of health care focussed on maximal societal benefit.

3. Spatial Strategy: IC has acquired a site of 35 acres at White City located contiguous to the Hammersmith Hospital site - the location of our recently opened c£70m **Imperial Centre for Translational and Experimental Medicine (ICTEM),** with the intention of breaking ground on a £150m **Research and Translation Hub (RATH**) funded by UK Research Partnership Investment Fund (£35m), private investment of £90m and IC investment of £25m, as part of **Imperial West's** centrepiece, launched in 2013. With space for 1,000 researchers alongside 50 spin-out companies, the Hub can support innovation on an unprecedented scale in London. **Within 5 years** through integrated **strategic planning,** we will develop this site to create the basis for a globally-leading **biomedical quarter** in London, integrating the AHSC and the AHSN with a network of biotechnology facilities, clinical research facilities (CRFs) encompassing both academic and commercial Clinical Research Organisations (CROs), a data centre with the capacity to handle large complex data sets, large scale incubator facilities for biomedical start-ups and engagement of big pharma on the site. We will maximise the translation of discovery science with complementary major infrastructural developments such as the **CRICK Institute**. This is a partnership between the UK's 3 largest funders of biomedical research: the Medical Research Council (MRC), Cancer Research UK (CRUK) and the Wellcome Trust (WT), and 3 leading universities: IC, University College London (UCL) and King's College London (KCL). This Institute will encourage ground-breaking translational research across a range of scientific disciplines and Higher Education Institute (HEI) partnerships intended to ensure that laboratory discoveries are translated as quickly as possible. A total of around £650m will be invested in the institute, due to open in 2015.

We outline herein a **strategic plan with clear objectives and deliverables over a 5 year period** to achieve this bold vision with all activities outlined overseen by the Joint Executive Group (JEG) of the AHSC which is the strategic delivery mechanism that has met consistently since the inception of the AHSC. Additionally, joint capital investment, estates and people strategies are required to deliver these components and require close planning between ICHT and IC which we believe is best delivered as an AHSC. These activities are explicitly fully dependent both on the AHSC and on its integration in the AHSN. Within the context of our overall strategic plan, we intend to achieve the following objectives;

***Within Years 1-2*: i)** To further develop our position as a leading, **international AHSC for translational research** feeding through to patient care at a tertiary and quaternary level, with significant numbers of patients entered into early-stage clinical trials and with supporting bioengineering, computing and informatics technologies to ensure that we are at the cutting edge of translation and innovation. This ambition will strongly be supported by the **NIHR-funded Biomedical Research Centre (BRC),** the translational capacity at the **Imperial College Centre for Translational and Experimental Medicine (ICTEM)** facility including the **WT** funded **Clinical Research Facility (CRF)**, and by relocation of cognate disciplines such as **Chemistry in the Clinic** and Bioengineering to the contiguous RATH at Imperial West. This will be supported by **key academic appointments** in translational disciplines. **ii)** Capitalising on our unique position in metabonomics, we intend to develop as the **leading global hub for stratified medicine**. We have substantial expertise in genetics, genomics and imaging (including the **Imanova** facility) and this is further amplified through our powerful new capacity in metabonomics as exemplified in the **MRC NIHR National Phenome Centre**. Relational analyses of data from imaging, genetics, genomics and metabonomics, with the emerging science of exposomics as illustrated by the EU €8.7m grant led by Dr Paolo Vineis of IC **School of Public Health (SPH)** strongly positions us as a world-leading centre for the stratification of medical and surgical patient care pathways and the discovery of new therapeutic targets for exploitation with our partners in chemistry and structural biology. Our plans extend to the development of **networked synergistic capacities** in imaging, metabonomics and metagenomics with partners at the **Lee Kong Chian (LKC) School of Medicine**, and our joint venture in Singapore with **Nanyang Technological University (NTU)**. **iii)** To further utilise the strengths of IC as a bridge between the AHSC and the AHSN and in particular the SPH (within IC), to be strengthened through **new strategic appointments** focussed on delivery of evidence-based care pathways. This interface with the AHSN provides a union of early stage T1 and T2 translation, with later stage T3 and T4 translation diffusing innovation in healthcare into the community. Strategic appointments will focus on the development of interventional capacity at a population level, bringing

the resources of SPH in population health data, mathematical modelling and statistical management to the population of NW London through the interface with the AHSN. This relationship encompasses the recently awarded **Local Clinical Research Network (LCRN), CLAHRC and the IC Business School** which will focus on the development of **research-led pathways for the reduction of the burden of common diseases**. **iv)** During this period we will continue to develop **Imperial Clinical Trials Unit (ICTU)** within SPH, and its relationships with both pharma and CROs, to achieve further improvement in the recruitment of patients to clinical trials, the time taken from application to launch of trials, and the quality of research undertaken in partnership with industry. **v)** The nesting of the AHSC within the AHSN will be strategically facilitated by the **AHSN Research Committee**, chaired by Prof Jonathon Weber (Director of Research, AHSC), which includes membership of all the NIHR Research structures in NW London, effectively acting as the engine of integrated research management. The membership comprises the Directors of the IC and Royal Marsden Hospital (RMH), BRC, the Respiratory and Cardiovascular Biomedical Research Units (BRU), the CLAHRC, ICTU, the Research Design Service (an NIHR funded pan-London programme) and the LCRN. This committee creates an integrated research strategy across NW London, aligns the NIHR funding streams in support of this strategy and enables pull-through of translation from the research centres and translation across the entire sector. Initial projects include respiratory rare diseases, integration of patient experience research and public engagement, rationalisation of local approvals of multicentre projects, and a sector-wide assent process to allow patients to be approached directly regarding targeted clinical information.

***Within Years 2-3*: i)** Within the context of all of these developments, recognising that excellence in patient outcomes must be matched by the quality of patient experience, it is crucial that the AHSC becomes a **leading centre for the enhancement of the patient experience**. In 3 years' time, through **Imperial Centre for Patient Experience Research (ICPER)**, we anticipate that our programmatic approach to improved care pathways, enhanced use of technology and formal delivery of patient-focused care will result in substantial improvements in the patient reported experience at the AHSC. We intend to agree a **Heads of Terms** between **IC, ICHT, Institute Cancer Research (ICR) and Royal Marsden Hospital (RMH)** in relation to exploring the integration of cancer service and research between the institutions. It is expected that we will incorporate RMH models of care in the management of our cancer patients. We will also work closely with international healthcare partners, such as the **Cleveland Clinic**, to ensure that at the end of the 5 year period we will be in the top10 percentile for patient experience across all areas and metrics. **ii)** The emerging complexity of data analysis, as exemplified in the strategic plan, requires an ability to generate and analyse large volumes of data in increasingly complex algorithms, focused on improvements in health and patient care. Our capacities are greatly enhanced through working with our Faculty of Engineering (FoE) e.g. within the EU funded **e-triks programme**, we are developing integrated approaches to capture, store and manage large datasets with potential to interface with machine-learning technologies. With a 3-5 year horizon, IC is committed to the development of a **data centre for large-scale data analysis on the Imperial West campus.** Such a centre, coupled to our expertise in computing within engineering, will allow our positioning at the forefront of academic development in this field, collaborating with national and international partners focussed on enhancing patient care through data-based evidence. **iii)** The development of new models of out-of-hospital care, coupled to expertise in tertiary and quaternary stratified care delivery and population-based management of chronic disease pathways, will enable us to co-develop with our partners in education, including IC Business School, **modular programmatic educational and training opportunities** designed to address future challenges in healthcare; the development of better models for translating research from the laboratory to the clinic; the creation of educational strategies for the delivery of out-of-hospital care; stimulation of a culture of healthcare innovation in ICHT and the community; creating a cadre of leaders equipped with the skills to meet future challenges. **iv)** We are creating an **international network of education, research and service** with the AHSC at its centre. This network will include: (a) **NTU at Singapore**, with our partners, the National Healthcare Group associated Novena Health City, (b) **The IC Diabetes Centre (ICDC)** in Abu Dhabi with associated biobank capacity and population-based research, and (c) **The Qatar Biobank** with its capacity for powerful research into common diseases, such as diabetes mellitus and metabolic syndrome. The strategy includes integration with our partners in International Health through the **WT Global Health Centre** and the **Institute for Global Health Innovation (IGHI). (v)** In partnership with the AHSN we aim to provide the international benchmark for development and implementation of health policy within the next 3 years. This will be achieved through the continued work on population health statistics and modelling in SPH, health economics with the Business School, specific policy vehicles such as the **Global Health Summit** and through the clear vision exemplified in a **joint clinical leadership programme** with the Business School that includes leadership for policy, an integral component of an AHSC/N.

***Within Years 3-5*: i)** Building on the increased delivery focus of the SPH, our intention is to strategically position SPH by placing it at the centre of a new build, which is a purpose-built hub (with bespoke facilities and infrastructure) centred on the **Imperial West** site, allied to our specialist Hammersmith Hospital site. This development will facilitate co-ordinated activity and promote synergistic outputs from activities of the AHSC and AHSN within an innovation environment that will encompass a data centre, an incubator facility and medical biotech and pharma commercial enterprises. This spatial strategy coupled with our radical health

services reconfiguration, will powerfully catalyse an integrated capacity for a major step change in our ability to influence healthcare delivery for maximal societal benefit. **ii)** Within the 5 year period of the project, we anticipate that we will have a powerhouse of activity, generating economic benefits as outlined in **section 7** including **ICTU** and the creation of new links with CROs and the pharmaceutical industry. A further core element of the mission will be to enable work through physical co-location across academic and healthcare partners within NW London to promote economic growth and ensure that national initiatives in health, implemented locally, will enhance the local innovation landscape. **iii)** Co-incident with changes outlined above and consistent with our intention to reduce hospital admissions through enhanced care pathways, we intend to proceed over the 5 year period with a **strategic academically co-ordinated physical re-configuration of clinical service provision** across the AHSC as outlined. This reconfiguration demands a new approach to out-of-hospital care and chronic disease management actively being planned with our partners in healthcare in NW London.

Translational Work Programmes: We have selected examples of our programmes to illustrate aspects of future development. 4 programmes are selected as CTMs from our AHSC work programme; the 5th, **Population Health and Primary Care**, is an enabling programme for late stage translation and represents a key driving force of AHSC-AHSN interactions. For the 6th, Surgery and Technology is selected as an example of a Programme of Excellence within a CTM which builds on the translational interface of the FoM and the FoNS and FoE (with design capabilities of the Royal College of Art) in the creation of inventive solutions with global application through the IGHI. Global innovation is also exemplified in the **Programme on Metabolic Medicine** which has resulted in the generation of new drug-based and technology-based therapeutic approaches and which is influencing treatment for metabolic conditions in ICLDC in Abu Dhabi. **Our Infectious Diseases** work programme**,** backed by a strong IT platform and encompassing evidence-based infection control pathways and basic research on anti-microbial resistance is directly focused on the improvement of patient outcomes, from prevention and therapy. The work programme on **Inflammatory Diseases** focuses on the development of new approaches to vascular inflammation encompassing conditions such as glomerulonephritis and other forms of renal disease driving clinical trials of new and innovative diagnostic and therapeutic approaches. **Brain Sciences and Diseases** illustrates clear evidence of translation from research to practice in improved outcomes for brain injury and stroke**.** Although not one of our selected programmes for this application**, Cancer** is illustrated in a number of examples in **Section 8** and we are moving rapidly to enhance the quality of cancer research and care through substantial integrated approaches with AHSN partners at the RMH and through enhanced collaboration agreements with the Institute for Cancer Research. Not included due to application constraints, is **Cardiovascular** research which represents significant partnerships between the AHSC, AHSN, Royal Brompton Hospital (RBH) and the National Heart and Lung Institute (NHLI).

Clinical Informatics: We are further strengthening our clinical informatics platform through the development and full deployment of **CERNER PAS and Maternity Systems** to go live April 2014, closely followed by a **clinical documentation and electronic prescribing system**. Plans include generating an electronic **Health Care Portal and Health Information Exchange with primary care** to deliver a more integrated healthcare system. We envisage the system will connect with all other NW London Trusts and with the appropriate governance; it will be extended to allow patient access to records. As part of our role in the IT forum involving primary care, 8 NW London **Clinical Commissioning Groups (CCGs)**, we seek to deliver improvement in information use and exchange with the CCGs. As part of our spatial strategy, we will co-align the Trust ICT Dept. at Imperial West. Through these plans we will align systems to the extensive phenotyping and epidemiological IC resources, and use e-health approaches for data linkage, data extraction and follow up of cohorts. Our capabilities are further enhanced by significant infrastructure resources in the shape of the £20m EU IMI initiative **European Translational Information and Knowledge Management Services (e-triks**) led by FoE and the planned afore mentioned **Data Centre at Imperial West** which will greatly increase our ability to perform complex analysis of multi-source large scale data. Additional capabilities will be developed through the **MRC Centre for Outbreak Analysis and Modelling**, the stratified medicine approaches of the **MRC-NIHR Phenome Centre** in partnership with KCL and the **Clinical Phenotyping Centre** with analytical technology companies providing capacity in metabolomics. We will ensure that there are effective governance arrangements in place to support the clinical informatics platform, such as the **AHSC Research Informatics Subcommittee** which reports to the **AHSC Research Committee**. The Committee's focus is the implementation of a comprehensive informatics strategy driven by the **NIHR Health Informatics Collaborative (NHIC)** programme, a challenge to the 5 NHS Trusts with the largest BRCs i.e. IC, Oxford, Cambridge, University College Hospitals and Guy's and St Thomas' Hospital to collaborate and share NHS clinical information to facilitate more effective research, lead to benefits for patients and the public, researchers and NHS staff. Our plans further include developing **training for all health professionals in clinical informatics and genomics,** building on our statistical courses, informatics modules within the Integrated Academic Training Scheme and workshops for technology enhanced learning.

Specific deliverables of the AHSC over the next 5 years, which we believe could not be achieved through another type of partnership include**: (i)** The AHSC partnership provides the catalyst in ensuring that full utilisation of the NIHR BRC provides a solid platform from which to bridge the gaps in translational research.

(ii) A joint approach to investment resulting in new infrastructure opportunities, attracting private and commercial sector investors and joint strategic appointments such as academic clinicians of the highest calibre. We will continue to jointly review all Trust Consultant posts to ensure that new posts are aligned with the AHSC strategic direction. **(iii)** Our unified approach to Shaping a Healthier Future (SaHF) provides opportunities to further co-locate clinicians and academics, aligning service provision with education and research capabilities. **(iv)**The partnership is predicated on the AHSC Joint Working Agreement (JWA) which provides the capacity to translate new discoveries for exploitation, implementation and wealth generation through a single commercialisation partner, Imperial Innovations Limited. We anticipate increased exploitation of IP year-on-year. **We will measure our success** using an integrated **AHSC scorecard** which brings together KPIs under 5 headings as a unified approach to performance management; KPI's include **Research**, **Education**, **Clinical Service Innovation and Impact**, **Strategic Priorities**. Progress is measured quarterly and reported to the JEG with scrutiny and oversight by the Strategic Partnership Board (SPB). Research and education KPIs are integrated into the Trust Board performance scorecard.

4. GOVERNANCE AND LEADERSHIP (2 pages plus an Organogram)

Detail the governance and leadership arrangements for the proposed AHSC including:

- Details of the organisational model and governance arrangements of the proposed AHSC. This should include an organogram outlining lines of accountability within the governance arrangements;
- Evidence of the functionality and effectiveness of the governance arrangements;
- A summary of how effectiveness of the governance arrangements of the partnership will be measured over the term of AHSC designation;
- Detail of the leadership of the proposed AHSC including key posts and post holders, illustrating how the posts will contribute to the delivery of the goals, visions and purpose of the proposed AHSC.

The **IC AHSC is the formal partnership between IC and ICHT,** designated as one of the UK's first AHSCs in 2009. The partnership follows a contractual model and is formalised in a **Joint Working Agreement (JWA)**, a legally-binding deed upon which the framework for the original partnership was built. The JWA creates a framework for the activities of the AHSC and incorporates agreements on protection of intellectual property (IP) and data protection and sets out the priority areas of work as: **(i)** to provide world class patient care, **(ii)** to provide internationally excellent research, **(iii)** to provide internationally excellent healthcare education, **(iv)** to enhance the translation of research into safe practice, and **(v)** to attract, develop and retain highly qualified talented and motivated staff and students at all levels.

The initial AHSC governance arrangements in 2009 were operated around a single leadership governance model in which the CEO of ICHT was also Dean of the FoM. Issues relating to separate funding systems and reporting structures within the NHS hindered the development of this model, which was later reviewed by Prof Lord Darzi in 2012. Arising from this review, the AHSC was reconfigured as an overlapping governance model in which the activities of the **Joint Executive Group (JEG)** were overseen by a **Strategic Partnership Board (SPB)** with joint IC/ICHT representation and an independent chairman. The Darzi review also suggested the appointment of an AHSC Director with overall administrative responsibility for the AHSC and with responsibility for the generation of links with **AHSN.** The designated executive lead for the AHSC and Chair of JEG is the Dean of the FoM. The **SPB** is chaired by Prof Sir Gordon Duff, and includes the IC President and Rector and ICHT Chairman, thus providing a direct line to the executive and governance fora in each partner organisation as outlined e.g. IC Council, IC Cabinet and ICHT Board. The **JEG,** chaired by the Dean of the FoM, meets fortnightly and is the body directly responsible for the operational management of the AHSC, for developing the AHSC strategy, the research and educational strategies, monitoring progress against key deliverables and allows for the creation of sub-committees. The JEG ratifies the **Chairs of the Centres for Translational Medicine (CTMs)** and approves their local work programmes. Lines of accountability and reporting are shown in the organogram. Of note, the AHSC Director and the AHSC Director of Research are both members of the Faculty Cabinet, the primary executive group of the FoM, and the Trust Management Board, the most senior ICHT executive forum.

To co-ordinate the delivery of the research mission of the AHSC, we have established the **Joint Research Office (JRO)** and the **Joint Research Compliance Office (JRCO)** as the single vehicles through which strategic, budgetary, operational, regulatory and oversight issues relating to AHSC research are administered. The relationship between the AHSC and AHSN is consolidated in our formal governance structures. To co-ordinate the activities of our many partners in healthcare, IC instigated the establishment of **Imperial College Healthcare Partners (ICHP)** representing 20 partners. This body, set up as a limited company and chaired by Prof Lord Darzi, has overseen and operates the Department of Health designated NW London AHSN. The ICHP appointed Dr Adrian Bull as CEO and in this capacity he functions as Director of the AHSN. The AHSC and AHSN Directors are cross-represented in attendance at the JEG and the ICHP Board respectively to facilitate maximal collaboration and mission integration. The Vice Dean for Research at IC is the AHSC Director of Research and also the BRC Director thus ensuring a single route for co-ordination of all research activities. The **AHSC Research Committee**, chaired by the AHSC Research Director has representation from the affiliated **Biomedical Research Units (BRUs)** at the Royal Brompton Hospital and representation from other Faculties represented at IC. This committee reports to the JEG on matters of research strategy, financial and regulatory governance, and comprises full IC, ICHTand AHSN membership. The recently configured **AHSN Research Committee** is also chaired by the AHSC Research Director, thus ensuring convergence of the missions of both AHSC and AHSN. The **AHSC Education Committee**, also reporting to the JEG and brings together IC and ICHT education leads. It receives reports from the **Health Education Board** and oversees the **AHSC Health Science Academy (HSA)** in addition to co-ordinating communication and activities with **Higher Education NW London (HENWL).**

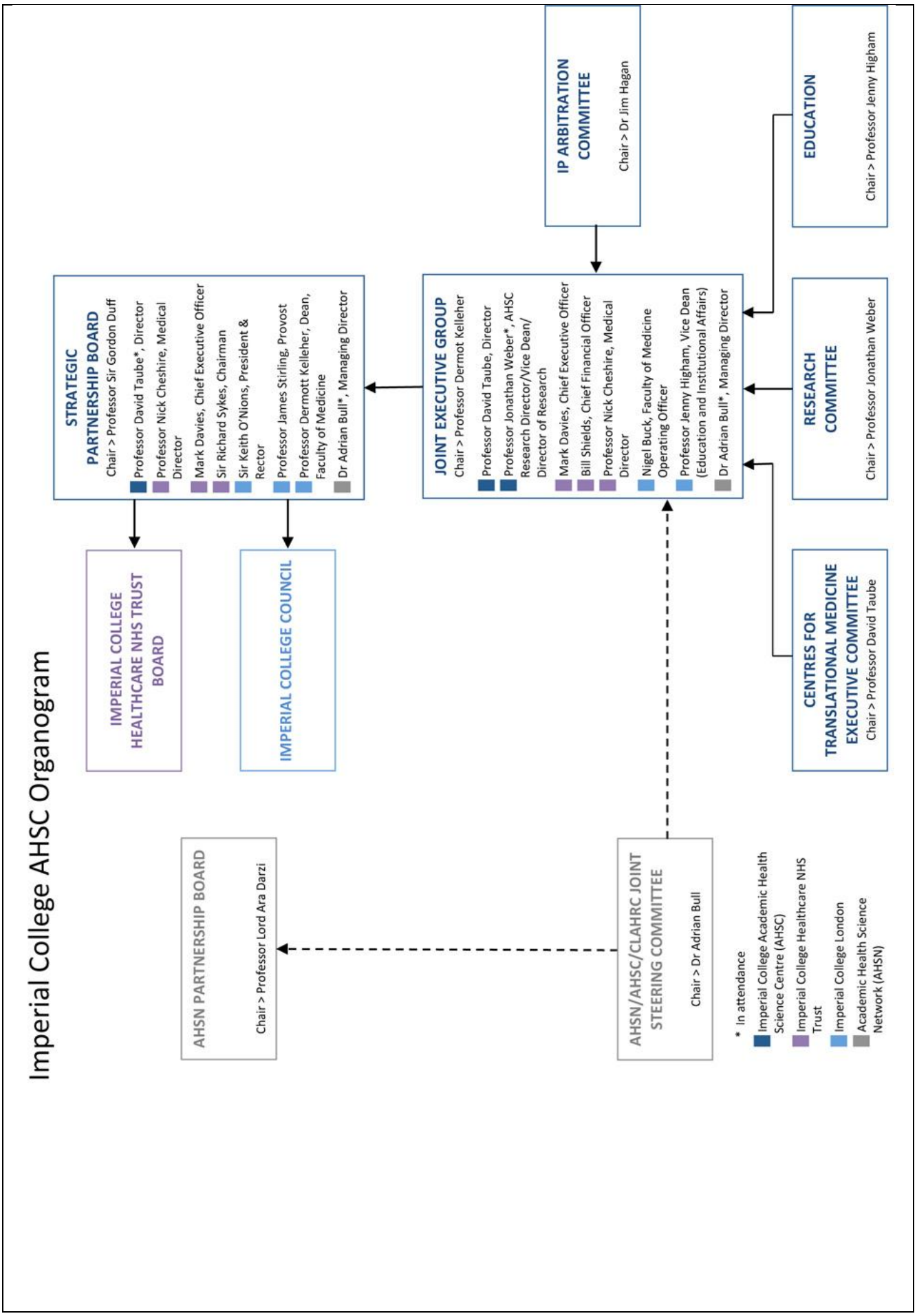
The governance arrangements described have operated effectively to deliver the goals of the AHSC. Through the integration of the roles of research director AHSC and BRC Director, the research activities funded

through NIHR are directly linked to the formal activities of the AHSC. During its operation, since 2009, the AHSC has provided the integrative governance function for many major initiatives, such as substantial capital investments including the **Imperial Centre for Translational and Experimental Medicine (ICTEM) c£70m AHSC flagship centre** for research and education at the Hammersmith site; the **Surgical Innovation Centre (SIC) at St Mary's Hospital (£15m**), designed for high turnover minimally invasive surgery, housing **IC's Clinical Skills Laboratory** for undergraduate and postgraduate teaching; the **Robotic Assisted Microsurgery Laboratory;** the establishment of the **JRO** and **JRCO,** responsible for the management of research, its governance, regulatory compliance and harmonisation of research policy and the establishment of and recruitment to the key joint posts of AHSC Director and the AHSC Director of Research. We have engaged the entire University, Engineering, Natural Sciences, and Business School, with the FoM and ICHT, supported by the **Biomedical Research Centre (BRC)**, to pull through basic science to the clinic. **Decisions have been taken in accordance with and within the scope of the JWA.** We have managed the **IP** of the AHSC on an integrated basis as per the JWA and established an **IP Arbitration Committee** to manage potential conflicts of interest. The JEG also maintains budgetary oversight for AHSC offices and the JRO. A further key component of the JEG function is the review of all consultant appointments, with right of veto to ensure that new posts are aligned with the AHSC strategic mission.

The AHSC's governance arrangements are subject to **annual review for effectiveness** by the partners. The most recent review and changes were made in 2012, following the extensive review by Lord Darzi. The next review is scheduled for January 2014.The purpose of these reviews, which are conducted jointly by ICHT and the IC, are to consider and evaluate the governance and operational arrangements. Additionally, in-year measurement and scrutiny are provided through the AHSC Director who reports to each public meeting of the ICHT Board and the FoM Cabinet. Real time review of **financial internal control processes** is carried out through regular budgetary management reports from the AHSC and JRO/JRCO directorates to the JEG, with issues reported to the SPB. The **AHSC objectives** have been risk assessed and the principal risks and their mitigating actions are reported to the JEG with an escalation process for serious concerns through to the SPB. The JEG also receives **6 monthly IP reports**, including any **arbitration issues**, which flow upwards to the SPB through the JEG regular reports. We feel it is essential to include **patient and stakeholder views** in the effectiveness of our governance arrangements and are building processes to facilitate this, such as the attendance of patient representatives from the enabling programme of **Patient Safety and Experience** on a defined basis at the JEG and through developments using the expertise of the **CLAHRC** and the **ICPER** based within the SPH. We intend to publish the results of our governance reviews, in addition to progress on our objectives, in the **AHSC Annual Report.**

Senior leaders of the AHSC include:
The senior leaders of the AHSC are the senior leaders of IC, ICHT and the AHSN. The majority hold important external appointments, and several are frontline researchers, clinicians and educators directly involved in the delivery of the tripartite mission of the AHSC. In addition, there is a wealth of financial and operational experience with a strong track record in delivery.

Sir Gordon Duff, FRSE, FMedSci, FRCP is Chairman of AHSC SPB.
Sir Richard Sykes, FRS, FMedSci, Hon.FREng is Chairman of ICHT.
Sir Keith O'Nions, FRS, Hon.FREng is President and Rector of IC.
Professor Dermot Kelleher, FMedSci, FRCP, FRCPI, is the Chairman of the JEG, Dean of the FoM and Dean of Lee Kong Chian School of Medicine, Singapore.
Mr Mark Davies is the Chief Executive Officer of ICHT.
Professor David Taube, FRCP is Director of AHSC and Professor of Transplant Medicine.
Professor Jonathan Weber, FMedSci, FRCP is the Vice Dean FoM, AHSC Director of Research, BRC Director and Chair of AHSC and AHSN Research Committees, and Jeferriss Professor of Communicable Diseases and GU Medicine.
Professor Jenny Higham, FRCOG, FHEA is Director of Education and Vice Dean, FoM and Senior Vice Dean of Lee Kong Chian School of Medicine, Singapore.
Professor the Lord Ara Darzi, KBE, PC, FRS, FMedSci, Hon.FREng is the Chairman of IC AHSP and NW London AHSN, Vice Dean FoM, and holds the Paul Hamlyn Chair of Surgery at IC.
Professor Nick Cheshire, **FRCS** is Medical Director of the Trust and Professor of Vascular Surgery at IC.
Professor Janice Sigsworth, RN BSc, MSc. is the Trust Director of Nursing,
Mr Bill Shields, M.A., CIPFA. is the Trust Chief Financial Officer,
Mr Nigel Buck is FoM Operating Officer.
Dr Adrian Bull, MD is Managing Director of IC ICHP and the AHSN**.**
Professor Anthony Bull, FoE is Head of Department of Bioengineering, IC, provides cross Faculty input**.**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RESEARCH COMMITTEE
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AHSN PARTNERSHIP BOARD
Chair > Professor Lord Ara Darzi
AHSN/AHSC/CLAHRC JOINT STEERING COMMITTEE
Chair > Dr Adrian Bull
* In attendance
Imperial College Academic Health Science Centre (AHSC)
Imperial College Healthcare NHS Trust
Imperial College London
Academic Health Science Network (AHSN)

Department of Health

ACADEMIC HEALTH SCIENCE CENTRES

SPECIFIC THEME / WORK PROGRAMME

Note: The accompanying *"Academic Health Science Centres – Full Application Guidance"* contains essential guidance on the information you need to provide when completing this proforma.

Please use this form to provide details on one of the six specific Themes / Work Programmes of focus for the proposed AHSC.

Please use a separate form for each of the Theme / Work Programme. Please complete no more than four pages for each theme; only information submitted up to this page limit can be assessed.

Please note this should be completed in a font no smaller than 10-point Arial.

Please insert your unique Reference Number into the Footer space provided.

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership: Imperial College AHSC

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work programme.

Surgery and Technology (within CTM: Surgery, Technology, Cancer Haematology)

2.2 Aims and objective of the theme/work programme.

Our strategy continues to build on incremental and disruptive innovation in surgical practice with the ultimate aim of enhancing the safety and quality of surgical care. The Surgery and Technology theme embraces the innovation pathway in surgical practice from invention to adoption and diffusion via: (i) translational research in areas of novel and smart surgical instruments and devices including Robotic Surgery, Surgical Imaging and Sensing, and original surgical technology platforms such as Single Incision Laparoscopy (SILS) and Natural Orifice Translumenal Endoscopic Surgery (NOTES); (ii) effective and safe introduction of new innovations into clinical practice. This will be achieved through the design and validation of novel training tools such as surgical simulators, and building safety resilience in complex environment and health systems; and (iii) addressing the main challenges in technology adoption and diffusion through evidence based synthesis, policy translation and entrepreneurial commercialisation of technology.

2.3 Description of how the proposed theme or work programme will contribute to the aims of the AHSC.

(i) To utilise the research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations. This theme combines the research excellence in science and technology at IC and the pioneering surgery and translation at ICHT. This is achieved through convergence of the strengths of IC in science and technology, engineering, physics, computer science with the academic surgical team at ICHT. The theme is led by the Division of Surgery and its constituent research centres: NIHR Centre for Patient Safety and Service Quality (CPSSQ), the recently constituted Centre for Health Policy, Institute of Global Health Innovation (IGHI), and The Hamlyn Centre, Faculty of Engineering.

(ii) To create powerful new interdisciplinary synergies spanning the IC, IC AHSC and the AHSN to transform health care through translational science, bioengineering and informatics. Our main research areas are: **1. Surgical technology - research platforms and pathways**. Our MDT leads research into technological platforms that are incremental or disruptive throughout the surgical pathway. The main technology platforms we will focus on are: ***Sensing:*** Through collaboration with engineering, we will develop smart technologies for improving pre-operative care, surgical risk monitoring and risk mitigation, and early detection of complications. ***Surgical metabonomics:*** An NMR machine has been installed in St Mary's Hospital (SMH) as part of the new Clinical Phenotyping Centre in collaboration with Stratified Medicine (Prof Jeremy Nicholson). This will provide a new approach to real-time (RT), on site surgical diagnostics. SMH is the only hospital in the world to use this advanced technology for RT diagnosis of direct benefit to patients in the operating theatre. ***Surgical imaging****:* This will bring cellular and molecular imaging modalities from the laboratory to an *in vivo–in situ* surgical setting to expand the functional capabilities of surgical intervention through improved tissue detection, labelling and targeting, using technologies such as confocal imaging and optical biopsy (*Newton R et al. Lung 2011; 189: 111*). Collaborating with Stratified Medicine, we aim to couple electro-surgery to mass spectroscopy to develop RT surgical diagnostics and new decision capabilities, using the 'Intelligent Knife' (*Balog J et al. Sci Transl Med 2013; 5: 194*; *Takats Z et al. Future Oncology 2012; 8: 113*). This will be applicable to many surgical procedures ensuring safer dissection and improved adherence to oncological surgical principles in tumour excision. ***Surgical devices and instrumentation****:* We intend to transform existing instrument design to allow for flexible access with integrated imaging and sensing, combined with intelligent mechatronic control and robotic assistance; and to facilitate new surgical strategies such as cell-based therapy and endovascular intervention. Our leadership in surgical robotics research has been recognised internationally in areas of image augmentation, gaze contingent motion compensation, and force constraint (*Mylonas G et al. Med Image Ana. 2012; 16: 612*) we will continue to build on this success. **2. Translation research platforms in surgery:** We will translate the technology platforms into clinical practice to reduce trauma of access and transform endoscopic surgery from intra-cavity to endo - or trans-luminal surgery. Robotic surgery is a priority research area in basic and translation research, with an established track record in this area achieved through disruptive innovation. Since 2008, we have developed several robotic platforms, mainly i-Snake® (ICRA best medical robotics paper award), which will drive translation in surgery from a trans-cavity robotic approach to endo- and trans-luminal robotic surgery. We have led development of NOTES surgery; and conducted the first UK human cases of trans-vaginal cholecystectomy (TVC). We are developing approaches for trans-gastric access to the peritoneal cavity. The same principles and technologies developed for NOTES will be utilised to further develop SILS. These novel platforms will create translational research opportunities in the following areas. ***Bio-surgery:*** Focus will be on development and translation of biomaterials and new prostheses, e.g. partial knee replacements (robotic insertion). We will continue our collaboration with industry in biocompatible prosthetics in areas of reconstructive surgery such as abdominal hernias (*Cobb J et al. Clin Orthop Relat Res 2010; 468: 2143*). ***Surgical oncology:*** Imperial has a presence at the Royal Marsden Hospital (RMH) (Darzi, Tekkis). We will continue convergence in areas of translational research in surgical oncology with the BRC, the CRUK Cancer Centre and joint appointments at the RMH/ICR. ***Endovascular surgery:*** We have led the largest clinical trials in endovascular surgery, e.g. EV Aneurysm Repair (EVAR) in patients with abdominal aortic aneurysm (*Greenhalgh et al. NEJM 2010; 362:1863*). Innovation through collaboration with Hansen Medical produced a smaller system better suited to optimise use in the arterial tree. We aim to improve visualisation of the robotic catheter tip to align with live 3D CT and ultra-sound intra-operative images, making EV therapy safer and complex procedures easier. ***Metabolic surgery:*** In collaboration with Metabolic Medicine, we have studied the physiological changes in gut hormones after surgery. In our planned RCT of Surgery versus Best Medical Therapy in diabetes, we aim to understand the gut hormones responsible for insulin sensitivity and secretion, to facilitate new drug discovery in order to deliver the benefits of bariatric surgery without the surgery, the so-called 'medical bypass'. ***Endoscopic surgery:*** The team has integrated its expertise in minimally invasive endoscopic techniques (*Sodergren M et al. Ann Sur 2010; 252: 1027*) and metabolic surgery to develop procedures for treating obesity and co-morbidities (*Ashrafian H et al. Obes Rev 2010; 11: 907*). We are running the UK's first multicentre RCT on the benefits of the EndoBarrier® GI Liner as an endoscopic bariatric procedure to offer patients new surgical options for obesity management, which fits with our mechanistic research to understand and enhance the next generation of metabolic procedures. This will continue through a proposal to perform the world's first RCT comparing endoscopic and laparoscopic metabolic surgical interventions. **3. Diffusion of innovation through incentives and evidence synthesis**: This group consists of clinical academics, health economists, psychologists, and epidemiologists. ***Dynamic measurement of clinical outcomes and patient experience:*** We have successfully released Wellnote, an iPhone app by Prof Darzi, to provide access to high quality health services. We aim to engage in design and implementation of innovative smart-phone based tools that synchronise with the patient pathway to improve outcomes and quality (at the IC Weight Loss centre with bariatric surgeons and allied health professionals). ***Incentives and behavioural economics:*** Behavioural economics incorporates principles from psychology and economics applied to

healthcare, with implications for public health and clinical safety (*Dolan P et al. BMJ 2009; 339: b2577*). Members produced the influential MINDSPACE report for the Institute for Government, which provided a framework for behavioural change and will be used to test incentives required to change behaviours and attitudes, e.g. the first investigation into the role of targeted incentives on uptake of screening for abdominal aortic aneurysms. We will examine if behavioural economics in the design of patient clinic invitations can reduce non-attendance for clinic follow up and outpatient consultations, in what will be the largest trial of behavioural cues in a healthcare setting. ***Evidence synthesis:*** Research includes development, improvement and dissemination of value-based technologies to enhance the quality of healthcare delivery by applying world class scientific methods. This has led to analysis of surgical data to improve treatment strategies and enhance patient outcomes through statistical techniques (*Mayer E et al. BMJ 2010; 340: 1128*). The Centre for Health Policy will drive translational research in this field to generate the evidence base in areas of innovation in surgery and allied technologies. Future projects include working with NICE on evidence base gaps, to drive comparative effectiveness research, lead a programme with the Health Foundation on costs and quality in health, and on-going work with National Cancer Intelligence Network, Public Health Education, to study effectiveness and cost-effectiveness of alternative care pathways.

(iii) To educate and train the future generation of multidisciplinary clinical scientists capable of utilising new technologies for enhanced healthcare. Team performance, simulation and the reduction of error: The Hamlyn Centre is one of the most advanced research and teaching facilities for surgical robotics. Within the Hamlyn Centre, a Robotic Assisted Microsurgery Laboratory has been established. This is the UK's first robotic assisted microsurgery laboratory with a clear focus on technological innovation, direct clinical translation and patient benefit. We have pioneered a number of virtual-reality simulations (*Kassab E. et al. Ann Surg 2011, 254, 1059)*, allowing common surgical procedures to be practised repeatedly in a non-patient, safe simulated environment, and mapping care pathways to ensure optimal service provision. We are investigating optimisation of pre-procedural preparation for operating theatre (OT) personnel to increase alertness to error, help diagnose safety concerns, and enhance mental readiness. Initial findings in simulated settings are positive; we will translate this to OTs locally and across the NHS using the AHSN as a means for adoption in the first instance, following completion of the pilot study. Aligned with the AHSC vision, the Hamlyn Centre and Surgical Skills Laboratories are based within the Surgical Innovation Centre (SIC). Research will be focused on validating methods of education and continue to underpin the development of programmes of education, teaching in surgical skills within the SIC, playing a central role in surgical training of all London Deanery ST3 and higher trainees.

(iv) To translate research into new policies for the benefit of patients nationally and internationally.

Safety and quality of adoption of innovation in surgical practice: We will expand on the novel systems approach to surgical safety research, which has led to direct improvement of the OT environment, efficiency and length of stay at national and international levels. Our multidisciplinary group composed of clinical academics and psychologists will focus on further safe adoption and diffusion of innovations in surgical practice, thereby aiming to increase safety and efficiencies such as length of stay. This programme is linked with the NIHR CPSSQ, led by Profs Darzi and Vincent. ***Safety in surgery, safety dashboards and electronic checklists:*** We are evaluating adoption and wider impact of the WHO Surgical Safety Checklist in the NHS (*de Vries E et al. NEJM 2010; 363: 1928*), examining clinical outcomes, barriers and enablers of adoption to develop a model of best practice. We will develop the basic checklist by: a) customising to different specialties; b) developing checklists for surgical emergencies; c) developing e-versions to be integrated with the patient record; and d) developing a full 'safety dashboard' that captures critical information in real time for the theatre team and can be seamlessly integrated into clinical pathways. This will be trialled at IC first, and then rolled out across the AHSN. ***Assessment of surgical outcomes and surgical improvement initiatives:*** We aim to examine how high performing units achieve their results through use of innovative technologies, training and teamwork. We will work with organisations to evaluate impact of large scale improvement initiatives, e.g. WHO Checklist, and of new technologies to establish a prolife of successful implementation and guidelines for best practice. **Translational research platforms in surgery:** ***Surgical epidemiology and screening: reducing the burden of surgically treated disease:*** Building on Prof Wendy Atkin's RCT demonstrating efficacy of endoscopic screening, with adenoma removal, in reducing distal colorectal cancer incidence and mortality rates, further screening platforms and trials will be explored to prevent disease, reduce need for surgery and improve earlier detection in patients.

(v) To create new wealth through innovation in healthcare in discovery science and in population-based translation. Working with the AHSN and partners in both Faculty of Engineering (FoE) and industry, we will continue to expand our existing IP portfolio, particularly in the arena of surgical instrumentation and design. This will be enhanced by the establishment of the HELIX, a joint initiative between the Royal College of Arts (RCA) and IC. HELIX combines the user-centred design expertise of the RCA with the clinical and engineering expertise of IC to design high impact, low cost solutions in healthcare. It will bring together designers, clinicians, technologists and frontline staff within a hospital setting to conduct research for the generation of novel IP in the area of frugal innovation for health. HELIX will have a mix of research projects, Masters programmes, PhD training and international collaborations with leading academic institutions such as Stanford University and Singapore University of Technology and Design (SUDT), as

well as commercial organisations.

2.4 Description of how the proposed theme or work programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

We will continue to develop both incremental and disruptive innovation in surgical practice to reduce both the burden of disease and the physical/psychological trauma of surgery. We will also address the safe translation of novel technology into clinical practice (*Kneebone R et al. BMJ 2009; 338: b1001; Kneebone R et al. BMJ 2012; 345: e8135; Kneebone R JAMA 2009; 302: 1336*.) and attempt to close the gap between evidence and practice in terms of surgery. This will be facilitated through the SIC, which integrates patient services, research and educational facilities in one setting at SMH over 4 floors, 10 clinic pods, 2 operating theatres and research facilities, including the first UK Microsurgery Robotics Lab and the Hamlyn Centre for advanced surgical robotics, the Centre allows direct translation of research into the clinical pathway. A unique strength of this Theme is its policy research and platform for diffusion of innovation through health policy. The Centre's focus will be to promote innovative evidence-based policies among decision-makers worldwide, through both academic research and applied policy analysis emerging in this Theme and across the AHSC. We will examine the science of incentives, uptake and diffusion of evidence based clinical practice. Public engagement and outreach are also priorities; we have a high and rising profile, including Royal Society Summer Science Exhibitions, Science Museum events, Cheltenham Science Festival and WT public engagement portfolio events. We host annual research meetings e.g. London Surgical Symposium and the international Hamlyn Symposium on Medical Robotics.

2.5 Description of how the theme/work programme will involve and enhance multi-disciplinary and multi-professional working.

Our research is led by the Division of Surgery and constituent research centres: NIHR CPSSQ, Centre for Health Policy, Institute of Global Health Innovation (IGHI), and The Hamlyn Centre, FoE. Our team consists of both academic and NHS staff, supported by the AHSC facilitating an innovation culture and clinical translation. The teams are aligned to the innovation pathway, with basic scientists driving technological inventions through to clinical academics which translate outputs in surgical disciplines. Our social scientists, epidemiologists, and health care economists address the challenges of safe adoption, policies of diffusion and socioeconomic impact. Our newly commissioned SIC, an innovative facility that utilises NHS space to provide clinical services tailored to the needs of patients, has adjacent research facilities to further drive translational research and increase staff and patient involvement. This is a partnership with the AHSC, NIHR, Wolfson Foundation, and Helen Hamlyn Trust.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work programme.

CTM Chair for Surgery and Technology, Prof the Lord Ara Darzi MD KBE PC FRS FMedSci HonFREng. Paul Hamlyn Chair of Surgery at IC, the RMH and ICR, Director of the Institute of Global Health Innovation at IC and Chair of Imperial College Health Partners. NIHR Senior Investigator. A leading voice in the field of global health policy and innovation with research interests in robotic surgery and patient safety. Introduced to the House of Lords as Professor the Lord Darzi of Denham in 2007 and appointed Parliamentary Under-Secretary of State at the Department of Health. UK Global Ambassador for Health and Life Sciences.

Prof Guang-Zhong Yang PhD FREng FIET. Professor of Medical Image Computing, Director of the Hamlyn Centre for Robotic Surgery and Deputy Chairman of the IGHI Director and Founder of the Royal Society/Wolfson Medical Image Computing Laboratory, co-founder of the Wolfson Surgical Technology Laboratory, and Chairman of the Centre for Pervasive Sensing. Research interests in medical imaging, sensing and robotics. Recipient of the Royal Society Wolfson Research Merit Award and the II Rabi Award International Society for Magnetic Resonance in Medicine.

Prof Charles Vincent PhD FACSS. Professor of Clinical Safety Research. Director IC CPSSQ and the Clinical Safety Research Unit. NIHR Senior Investigator. Co-chair of the Patient Experience and Safety CTM with research interests in Patient Safety. Expert Advisor, Parliamentary Health Select Committee on Patient Safety. Advisor on Patient Safety, WHO.

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

This form, together with other requested attachments must be submitted by **1:00pm on 30 September 2013**.

Department of Health

ACADEMIC HEALTH SCIENCE CENTRES

SPECIFIC THEME / WORK PROGRAMME

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1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership: Imperial College AHSC

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work programme.

Brain Sciences and Diseases

2.2 Aims and objective of the theme/work programme.

The theme aims to enhance understanding of brain injury, neuroinflammation and neurodegeneration for the benefit of patient care, focusing on major disorders such as traumatic brain injury (TBI), stroke, multiple sclerosis (MS), Parkinson's (PD) and Alzheimer's diseases (AD). We will build on internationally-recognised strengths in neuroimaging and biomarker discovery: (i) To further the understanding, diagnosis, and treatment of traumatic brain injury; (ii) To validate a bioinformatics-based approach to personalised medicine for more effective delivery of stroke care; and (iii) To pursue trials of innovative treatments for neuroinflammatory and neurodegenerative disorders.

2.3 Description of how the proposed theme or work programme will contribute to the aims of the AHSC.

(i) To utilise the research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations. The Theme will build on our research strengths within the Division of Brain Sciences, drawing on expertise in brain injury (TBI; stroke), neuroinflammation (MS) and neurodegeneration (PD; AD) from IC Centres for Restorative Neuroscience and Neuroinflammation & Neurodegeneration. Our brain sciences research programme (Prof David Sharp), builds on the infrastructure and patient resources at IC and ICHT: the IC TBI Research Group; the St Mary's Major Trauma Centre (MTC); and the IC Royal British Legion Centre for Blast Injury Studies. We are able to study the hyper acute management of TBI via the MTC, which manages around 1000 head injuries per year, over 200 requiring surgery, and through Lead Consultant Neurosurgeon, Mr Mark Wilson, who is a Consultant London's Air Ambulance. Collaborating with the IC for Endocrinology (Prof Tony Goldstone), we have established the UK's only multidisciplinary Neurology/Endocrine TBI clinic, supported by Neuropyschiatry, Radiology and Neurosurgery (Fleminger, Patel, Wilson). Our stroke research programme builds on our clinical stroke services, The Imperial Stroke Centre, including the top ranked Hyper Acute Stroke Unit (HASU), which manages around 2,000 strokes a year. Our research into the understanding of genetics,

genomics, proteomics and stem cell therapy for stroke (*Marjot T et al. Stroke 2011; 42:913*), benefits from the collaboration between IC Cerebrovascular Research Unit (ICCRU) and the Bio-Repository of DNA in Stroke (BRAINS) one of the largest stroke biobanks of South Asian stroke patients.
The Centre for Neuroinflammation and Neurodegeneration investigates MS, AD and PD. We run one of the largest MS clinical services in the UK, having recruited over 1,280 patients on disease modifying therapy since 2004. The MS research group runs the UK MS Society Tissue Bank, led by Profs Richard Reynolds and Paul Matthews, and is one of the major suppliers of human MS tissues for research in the world. We host the MS Trials Collaboration (MSTC), (Dr Richard Nicholas), which aims to provide patients with MS, who are not suitable for current therapies, access to pharmaceutical-sponsored clinical trials. We support a large number of clinical trials within the Imperial Memory Unit (Dr Richard Perry) and the W London Clinical Trials Unit (Dr Craig Ritchie), which includes the developing MRC UK Dementias Platform (Ritchie, Matthews), a major initiative that promises to link all major cohort studies of early risk of neurodegenerative disease across the country. Our neuroimaging expertise benefits from our collaboration with the Imaging theme and access to Imanova a world-class imaging facility based on the Hammersmith Campus. Together with Imanova, the IC Clinical Imaging Facility provides world-leading positron emission tomography (PET) and magnetic resonance imaging (MRI) facilities, focusing on the implementation of novel molecular neuroimaging. Expertise in neuroimaging analysis is supported by the Computational, Cognitive and Clinical Neuroimaging Laboratory and The Biomedical Imaging Analysis Group, IC Department of Computing, led by Prof Daniel Rueckert. Dr Adam Waldman, ICHT, leads our research theme, focusing on basic and translational imaging development in neuro-otology and neurodegenerative dementias.
(ii) To create powerful new interdisciplinary synergies spanning the IC, IC AHSC and the AHSN to transform health care through translational science, bioengineering and informatics. The Theme encompasses brain injury (TBI; stroke), neuroinflammation (MS) and neurodegeneration (AD; PD). **Brain injury (TBI):** IC is leading in research fundamental to improvements in TBI care aiming to identify patients at high risk of poor long-term clinical outcome and evaluate appropriate treatments to restore function (*Ramlackhansingh A et al. Ann Neurol 2011*; *70:374*; *Hellyer P et al. Ann Neurol 2013; 73:489*). We will integrate clinical (Sharp) and vestibular (Seemungal) studies with neuroimaging, genetic, endocrinological (Goldstone, Sharp) (*Bonnelle V et al. PNAS 2012;109:4690*) and neuropathological (Gentleman) measures; focus on advancing methods for patient stratification; use microglial and amyloid PET imaging [18F Florbetapir] to study the link between TBI and late neurodegeneration (including AD); and coordinate acute TBI research, focusing on hyper acute pre-hospital management, novel measures of intracerebral blood flow, and enrolment of patients into Phase III clinical trials (Wilson). With Imanova and Lilly/AVID, we will develop PET Imaging 18FT807 to investigate TBI and AD pathology. We will conduct clinical trials of anti-inflammatory treatment with minocycline and of dopamine replacement. IC has an international reputation in Bioengineering, which combines cutting edge brain and materials science, and has strong links with Ministry of Defence (MoD). In collaboration with Prof MJ Midwinter (Royal Army Medical Corps), we will extend our investigation of blast injury in soldiers in Afghanistan (the BIOSAP project) by investigating the inflammatory effects of blast exposure. In the endocrine field we have (i) defined the optimal method of assessing pituitary function after TBI; and (ii) demonstrated a high prevalence of pituitary dysfunction in soldiers suffering moderate-severe blast TBI (*Baxter D et al. Ann Neurol 2013; Epub*). We will further examine the effects of growth hormone replacement and the metabolic syndrome on recovery. **Brain Injury (Stroke):** We will focus on developing accurate tools for prognosis after stroke and treatments aimed at limiting deterioration restoring function, improving the understanding of biological basis of stroke recovery in the fields of language (Wise) (*Sharp D et al. Ann Neurol 2010; 68:753*; *Warren J et al. Brain 2009; 132:3428*), attention (Malhotra), balance (Bronstein, Seemungal), and neuroimaging to guide or predict rehabilitation therapies (Soto, Malhotra, Bentley). We will develop approaches towards improving cognitive function e.g. the restoration of attentional function. Attention is disrupted in a number of neurological conditions and our strength in this area will allow us to investigate how to treat this (Malhotra, Wise, Soto), TBI (Sharp, Leech, Hampshire) (*Leech R and Sharp D. Brain 2013; Epub*) and AD (Malhotra, Wise) (*Malhotra P et al. Brain 2009; 132:645*). We will expand biobanking resources by building on our stroke database of ~2,500 stroke patients who presented to the HASU. The ICCRU will continue to drive the BRAINS platform to establish a highly characterised DNA repository (currently ~4,000). Stroke research will be strengthened by new appointments, i.e. joint recruitment of Prof Roland Veltkamp, an internationally recognised clinical trialist in stroke (*Liesz A et al. Nat Med 2009;15:192*); Dr Geraghty, a stroke epidemiologist will utilise his experience of large-scale clinical stroke databases to maximise the research opportunities provided by the HASU; and Prof Simone di Giovanni, who will extend fundamental understanding of mechanisms of regeneration in acute central nervous system (CNS) injury. We have established research synergies with the FoE, through establishment of a PhD programme between Brain Sciences and Bioengineering to investigate robotic assistance for stroke rehabilitation (Burdet). **Neuroinflammation (MS):** The MS grouping (Reynolds, Muraro, Nicholas, Matthews) is engaged in fundamental, translational and clinical studies of neuroinflammatory diseases affecting the CNS (*Abrahamsson S et al. Brain 2013; 136:2888*; *Gold R et al. NEJM 2012; 367:1098*) including molecular analysis of signaling pathways involved in the pathogenesis of MS, the development of animal models and

early clinical trials of novel therapy. Led by Dr Paolo Muraro, we are the first to perform a UK Stem Cell Foundation-funded Phase II trial of Mesenchymal Stem Cells in MS, using autologous mesenchymal stem cells. We will investigate mechanisms of neurodegeneration in MS, following our discovery of changes in signaling pathway leading to neuroinflammation-induced neurodegeneration, which is an important factor in the clinical progression of MS (Reynolds) (*Kim J et al. Nature Neuroscience 2010; 13:180*). We will test these ideas in experimental models of MS, validating *in vivo* neuroinflammation measures using PET microglial imaging ([11C]PBR28 and GE-180) before designing early clinical studies. **Neurodegeneration (AD & PD):** An active neuroimaging programme investigates the mechanisms of neurodegeneration applied to AD and PD (*Vandenberghe R et al. Ann Neurol 2010; 68:319*). Building on the success of our prior endeavours (*Politis M et al. Sci Transl Med 2012; 4:128ra141*; *Politis M et al. Sci Transl Med 2010;* 2:38ra46; *Rinne J et al. Lancet Neurol 2010; 9:363*), we will assess mechanisms of neuroinflammation and responses to stem cell therapies in PD; the relationship between inflammation and amyloid deposition in prodromal AD; and the therapeutic efficacy of the GLP-1 agonist liraglutide and the TNF alpha blocker Cimzia (Brooks and Edison). We will develop symptomatic treatments for AD, e.g. planning a trial of combined cholinergic and noradrenergic treatment (Malhotra and Ritchie); investigate the relationship of inflammation and neurodegeneration, focusing on how glial cells may act as mediators of both neurodegeneration and neural repair (Sastre); address basic mechanisms of neuronal cell death, which has translated into a Phase I trial of iron chelation therapy in PD (Dexter and Alavian); explore mechanisms of long-term complications in the treatment of PD (Piccini). We will investigate the pharmacological changes associated with non-motor problems in PD e.g. sleep disorders and dementia, (Prof Piccini). We are one of the main partners of the €11m EU Seventh Framework Programme (FP7) consortium to assess optimisation and clinical application of cell therapies (Piccini). **Cognitive assessment:** We have a good track record in creating a cost-effective way to accurately assess cognitive impairment, having developed a web-based system optimised for large-scale and repeated cognitive assessment (*Hampshire A et al. Neuron 2012; 76:1225*). Building on this success and a recent study testing more than 100,000 individuals using CBS Trials, we will expand technology for large-scale clinical trials.

(iii) To educate and train the future generation of multidisciplinary clinical scientists capable of utilising new technologies for enhanced healthcare. Brain Sciences has a strong track record of training clinical scientists engaged in translational medical research. We have an active NIHR Academic Clinical Fellow (ACF) and Clinical Lecturer in Neurology programme overseen by Prof Sharp. 13 trainees have enrolled in this programme, and all but one are currently in full-time academic positions. 5 ACFs have gone on to obtain Wellcome Trust (WT) or MRC-funded PhD Fellowships and 3 Clinical Lecturers have now obtained an NIHR Senior Lectureship, WT Intermediate Fellowship (Dr Ghandi, UCL) and an MRC Clinician Scientist award and subsequently an NIHR Professorship (Prof Sharp). Our clinical trainees have access to a range of quality training opportunities, and are part of the IC Graduate School. The Division of Brain Sciences organises extensive clinical neuroscience teaching for medical students as part of their core training, and Year 4 students who undertake the Neuroscience BSc. Our Neuroscience MRes provides a range of research experience. The IC School of Medicine Surgical Society will continue to host the annual Imperial Trauma Conference to provide lectures and workshops for medical students and UK and internationally trainee doctors. We will coordinate the Pan-London Neurotrauma Group, Annual Neurotrauma symposium, and a head injury training course at the Royal College of Surgeons.

(iv) To translate research into new policies for the benefit of patients nationally and internationally. Brain Sciences has a strong track record of facilitating the rapid translation of science for patient benefit. Examples are: the demonstration that cooling limits the degree of brain injury caused by lack of oxygen in neonates at birth, which has resulted in changing NICE guidelines (*Azzopardi D et al. NEJM 2009; 361: 1349*); the identification of pituitary dysfunction as a frequent (>30%) complication of blast exposure in military personnel has resulted in revision of military guidelines; the development of DaTSCAN™ imaging as a method for assessing dopamine levels in the brain, is now used routinely in clinical practice for the assessment of PD (Brooks); and the evaluation of the monoclonal antibody Natalizumab to prevent disease progression in MS is resulting in direct patient benefit (Nicholas). Our researchers have influential roles in shaping national and international initiatives in brain sciences, which include NICE panels (Bain) and the Association of British Pharmaceutical Industries (Matthews). Building on our influence and prior successes, our stroke research will expedite the delivery of personalised medicine and create the largest stroke biobank in the world, and expects to facilitate the evaluation of current NHS treatments strategies and identify new therapeutic targets. Our pioneering clinical trials in AD, PD and MS have major potential to develop novel therapies and change clinical guidance for these diseases.

(v) To create new wealth through innovation in healthcare in discovery science and in population-based translation. Brain Sciences will address wealth generation through innovation in healthcare, in discovery science and in population-based translation. We have been actively using IC translational science facilities in delivery of over 20 innovative early phase drug development trials or proof of principle research for companies including GE, Sirtris, GSK, Creabilis, Spinifex and UCB. For example, fundamental research imaging dopaminergic function in PD has led to DaTSCAN™ imaging (GE). We experienced direct commercial impact and new job creation when GSK established a partnership with IC to build on this

expertise. Work on drug distribution and interactions using PET led to joint investment of more than £50m by GSK in an advanced clinical imaging centre, Imanova, now a spinout owned partly by IC. We have contributed key data for over 14 molecules in early development at GSK. New interactions with GE will lead to the evaluation of a novel diagnostic for brain inflammation in TBI and MS, with potential applications in stroke recovery. Brain Sciences will continue to lead in joint appointments with industry, including senior academic staff with pharmaceutical and diagnostics companies, and honorary appointments of full time industry staff. We are also fostering spinouts and encouraging entrepreneurialism in new recruits. Senior Lecturer (Dr Hampshire) has established CBSTrials.com, a company that provides scientifically proven tools for population based cognitive assessment that can be used over the internet. This technology will be developed for healthcare screening and drug study evaluation with Pfizer.

2.4 Description of how the proposed theme or work programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

We will focus specifically on Brain Sciences research into the major neurological disorders which impose an immediate and growing healthcare burden. Around 1.4 million people attend emergency departments in England and Wales each year with head injuries (*Health Service Journal 2013*). Our research on piloting treatment for accelerated neurodegeneration in TBI and understanding patient recovery following TBI will contribute to the improvement of clinical treatment. Stroke is the leading cause of adult disability in the UK, 1:5 being fatal and with associated costs at £3.7b-£8b a year (*British Heart Foundation 2012; DH National Audit Office 2010*). Our work in identifying attention disorder in stroke patients will facilitate targeted approaches with specific pharmacological or behavioural therapies. In the UK, around 100,000 people have MS (*MS Society 2013*); 1:500 people suffer from PD (*European PD Association 2011*); and 800,000 people in the UK developed dementia as a result of AD with current associated costs at over £23b a year (*The Alzheimer's Society 2013*). Our commitment to perform clinical trials and improve treatments for patients with MS, AD and PD will help those unable to access current drug therapies. A particular strength of IC is the basic science expertise in our non-clinical Faculties and the translation of these sciences for patient care. Many researchers within Brain Sciences are actively engaged in public engagement, facilitating health education e.g. Mr Mark Wilson in collaboration with Prof Roger Kneebone has created a head injury simulation model, used for health education and featured at The Big Bang Science Exhibition.

2.5 Description of how the theme/work programme will involve and enhance multi-disciplinary and multi-professional working.

Brain Sciences brings together many disciplines; clinical scientists, specialist neurologists, neuroradiologists, neuro-otologists, endocrinologists, neurosurgeons, nurses, neuropsychiatrists, academics and basic scientists in a common goal to improve patient treatment. Extensive clinical teams are in place within the MTC and ICHT HASU to provide high quality acute care in life-threatening situations. We will continue to contribute to the Neurotechnology Initiative, a cross-faculty Neuroscience Technology Network of Institute of Biomedical Engineering, which aims to foster collaborative research at the interface of neuroscience and engineering across the FoE, FoM and FoNS. We will strengthen the connections between different elements of care to facilitate a seamless transition between clinical care and research.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work programme.

CTM Chair for Brain Sciences, Prof David Sharp PhD MRCP. NIHR Professor of Neurology. Head of the multidisciplinary TBI clinic at Charing Cross Hospital. Expert in the impact of TBI on cognitive function.
Prof Richard Wise MD FMedSci. Professor of Neurology. Head of Cognitive Neuroimaging Group and Computational, Cognitive and Clinical Neuroimaging Laboratory. Focus on language recovery after stroke.
Prof Paul Matthews OBE MD FRCP. Professor of Clinical Neuroscience. Head of Division Brain Sciences. Head of GSK Clinical Imaging Centre. Expert in translational applications of clinical imaging.
Prof Paola Piccini PhD FRCP. Head of Centre Neuroinflammation and Neurodegeneration. Research focuses on movement disorders, use of PET to study new therapies for PD and MS.
Dr Paolo Muraro MD PhD. Clinical Reader Neuroimmunology, Head of Clinical Neuroimmunology Group. Research focuses on effective therapies for neuroinflammatory diseases, Chair Autoimmune Disease Working Committee, the Centre for International Blood and Bone Marrow Transplant Research.

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

This form, together with other requested attachments must be submitted by **1:00pm on 30 September 2013**.

Department of Health

ACADEMIC HEALTH SCIENCE CENTRES

SPECIFIC THEME / WORK PROGRAMME

Note: The accompanying *"Academic Health Science Centres – Full Application Guidance"* contains essential guidance on the information you need to provide when completing this proforma.

Please use this form to provide details on one of the six specific Themes / Work Programmes of focus for the proposed AHSC.

Please use a separate form for each of the Theme / Work Programme. Please complete no more than four pages for each theme; only information submitted up to this page limit can be assessed.

Please note this should be completed in a font no smaller than 10-point Arial.

Please insert your unique Reference Number into the Footer space provided.

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership: Imperial College AHSC

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work programme.

Infectious Diseases

2.2 Aims and objective of the theme/work programme.

We aim to understand the basic pathology of infection, design patient-focused interventions for Human immunodeficiency virus (HIV)**,** Human T-lymphotropic virus (HTLV) and tuberculosis (TB), and study antimicrobial resistance (AMR)**,** leading to the development of diagnostics and therapeutics, as well as targeted health protection interventions. Our translational pipeline includes: (i) Novel drugs, vaccines, treatment strategies for Influenza, RSV, HIV and HTLV-1 infection, leading to new prevention and eradication clinical studies, undertaken nationally and internationally; (ii) New management and treatment strategies, in particular, TB, HIV and Hepatitis co-infections in patients/migrants; (iii) Risks and causes of healthcare associated infection (HCAI) via studies of bacterial persistence and development of approaches to tackle AMR and HCAI, including innovative surveillance and behavioural interventions addressing infection prevention and antibiotic prescribing.

2.3 Description of how the proposed theme or work programme will contribute to the aims of the AHSC.

(i) To utilise the research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations. The control of acute and chronic infection remains a high priority for the UK and internationally. Our theme is focussed on globally important infections where key gaps in knowledge or technology exist: prevention of viral disease including influenza, RSV and HIV; treatment of HTLV, diagnosis of TB; and management of HCAI, particularly addressing the increasing challenge of AMR [MRC Centre for Molecular Bacteriology and Infection (CMBI) led by Prof David Holden] (*Pearson J et al. Nature 2013; 501:247*). Our research on HIV is based on our patient cohorts at ICHT (in partnership with Chelsea and Westminster Hospital as the largest HIV patient cohort in Europe, n=7,500), of whom 80% are in clinical studies. Our research on HTLV benefits from the fact that ICHT houses the DH-funded National Centre for Human Retrovirology, a National Referral Centre for patients with HTLV

infections, which provides services for diagnosis, counseling, research into pathogenesis and treatment of patients with HTLV-associated disease. Research into screening for TB, HIV, Hepatitis B and C in migrants benefits from collaboration with the International Health Unit at IC, and GP practices at Hammersmith and Charing Cross Hospitals. Research in influenza virus and RSV incorporates modelling technologies, immunology and translational approaches to assess intervention. Our multi-centre cohort investigation into new entrant latent TB screening utilises patient cohorts with 177 Primary Care Organisations nationally. Tackling HCAI and AMR is spearheaded by the National Centre for Infection Prevention and Management (CIPM), a UKCRC, NIHR, and WT funded centre. CIPM works with NIHR-accredited centres and uses ICHT as a test platform for their research.

(*ii) To create powerful new interdisciplinary synergies spanning the IC, IC AHSC and the AHSN to transform health care through translational science, bioengineering and informatics.* Infection is a broad theme spanning virology, bacteriology, HCAI, AMR and development of novel diagnostics and vaccines. **HIV:** We have a track record of making pivotal contributions in basic retrovirology, such as resolving the structure of the HIV integration complex (*Gall A et al. Retrovirology 2013; 10:es:8*; *Yager N et al. AIDS 2013; 27:313*; *McKay et al. Retrovirology 2010; 9,O65*; *Maertens G et al. Nature 2010; 468:326*; *Huang K et al. Nature Communications 2010; 1:102*), and have published major international clinical trials on the treatment of HIV infection (DART: *Schouten E et al. Lancet 2011; 378:282*; SPARTAC: *Weber J et al. NEJM 2013; 368:2036*; *SPARTAC Trial Investigators. NEJM 2013; 368:207*) and on HIV prevention (Vaccines: *Harari A et al. J Exp Med 2008; 205:63*; Microbicides: *McCormack S et al. Lancet 2010; 376:1329*). Our current research on preventing HIV infection includes new vaccine and microbicide trials and an HIV eradication trial using HDAC-inhibitor together with an immunotherapy (CHERUB). These studies will take advantage of novel point of care diagnostics for CD4 testing and viral load. We shall study the application of a universal HIV test and treatment strategy on HIV incidence in a cluster randomised trial (PopART) in Zambia and South Africa. Building on the success of our prior work, we aim to understand the effects of HIV cognitive impairment through novel PET/fMRI imaging in collaboration with the Imanova Imaging Centre at the Hammersmith Hospital. **Vaccine Development:** ICHT investigators (Shattock, Weber, Gilmour, Gotch and Xu) have an excellent track record in HIV vaccine development and have trialled 9 novel HIV vaccines since 1995, most recently a DNA-prime, MVA pox-virus boost, protein gp140/GLA adjuvant re-boost, now in Phase I/II trials in London and Tanzania. We have a long-standing partnership with the International AIDS Vaccine Initiative (IAVI) whose Human Immunology Laboratory at IC supports over 20 vaccine studies. AHSC researchers are involved in the Wellcome Trust (WT) funded UK HIV Vaccine Consortium (UK HVC), a collaboration of academic groups studying diverse DNA, pox, and Adeno proteins and adjuvants to produce potential combination HIV vaccine constructs and immunisation strategies. We will build on the strength of our expertise by embarking on a Phase I study of mucosal HIV-gp-140 vaccination and Phase I clinical studies to assess novel routes of mucosal immunisation utilising DNA immunisation and MVA and adenoviral vector immunisation (*Guimaraes-Walker A et al. Vaccine 2008; 29,3511*). These studies have to date focussed on HIV but we will explore potential new targets including *rhinovirus, respiratory syncytial virus* (Johnson, Openshaw) (*Tregoning J et al. PNAS 2013; 110:5576*; *Durrant L et al. J Virol 2013; Epub; Hansel T et al. Lancet 2013; 381:861; Loebbermann J et al. PNAS 2013; 110:2987*), *influenza* (Barclay, Hussell, Openshaw) (*Myles P et al. Eur Resp J 2013; 41:824*; *Bewick T et al. Thorax 2011; 66:247*; *Dunning J et al. BMJ 2011; 343:d1799*), *dengue virus* (Screaton) (*Tsai W et al. J Virol 2013; Epub; Dejnirattisai W et al. Science 2010; 328:745; Duangchinda T et al. PNAS 2010; 107:16922; Weng L et al. Ann Rheum Dis 2010; 69:1519*) and *norovirus* (Goodfellow) as well as non-viral pathogens *Clostridium difficile* (Sriskandan, Fairweather), *Streptococcus pyogenes* (Sriskandan) and *Salmonella* (Holden) (*Santos A et al. J Cell Science 2013; 126:2990; Yu X et al. Science 2010; 328:1040; Helaine S et al. PNAS 2010; 107:3746; Lapaque N et al. PNAS 2009; 106:14052*). Research on influenza (*Sridhar S et al. Nature Medicine 2013; Epub*) has demonstrated the potential for universal vaccination against influenza virus. We have a strong sponsorship record e.g. multinational commercial and charitable partners, including Sanoffi-Pasteur, Novartis, FIT Biotech, the Infectious Disease Research Institute, 3M Drug Delivery Systems, WT and Gates Foundation, many will continue to fund our vaccine studies. **HTLV:** Work on the management of **HTLV** infection includes the provision of diagnostic assays (proviral load, integration site), trials of novel anti-retroviral and immune-modulatory therapy and development of PET imaging biomarkers of HTLV-1-associated disease development. We will build on observations on the effect of ciclosporin (*Martin et al. PLoS Negl Trop Dis 2012; 6:e1675*) and explore anti-CCR4 approaches. **AMR and HCAI**: Tackling these threats, with CIPM, is in line with the call to action to address AMR and develop new antibiotics by Prof Dame Sally Davies (*Castro-Sánchez E and Holmes A. Lancet Infect Dis 2013; Epub*; *Sánchez E and Holmes A. Lancet Infect Dis 2012; 12:819*). We continue to have a local impact on ICHT with the development of an award-winning smartphone application (*Edwards R et al. Lancet Infect Dis 2012; 12:318*; *Charani E et al. J Antimicrob Chemother 2013; 68:960*), through joint-working with IT, application designers and ICHT's communication team, to support point of care decision making on anti-infective treatment. The app has been adopted by junior doctors with android/smartphones, who use it daily to inform practice, and is recognised in the UK strategy document on AMR (September 2013). We will explore the lessons learned from the development and implementation of a smartphone application and 'm-

Health', conducting research involving doctors, pharmacists, nurses and patients. We will develop specialist multiplatform m-Health interventions in infection prevention and management, in collaboration with the FoE as well as Public Health England and the Royal College of General Practitioners. Joint studies between CIPM and Prof Holden (Microbiology) investigating virulence of nosocomial pathogens such as *Klebsiella* and *Acinetobacter* provide the molecular understanding necessary for ICHT translational studies. The collaborative work on *Staphyloccus* (Sriskandan from CIPM and Grundling from Microbiology) aims to develop enzyme-specific inhibitors to prevent growth of MRSA (*Lu D et al. PNAS 2009; 106:1584*). Investigations have started to dissect antibiotic pharmacokinetics and pharmacodynamics in specific patient groups e.g. in the obese (Holmes). Research into virulence factors and clinical features of *Norovirus,* aimed at identifying the genetic factors leading to outbreaks, will assist better understanding of disease transmission (Goodfellow, Cambridge and Holmes). *Norovirus* is a significant HCAI, resulting in 50,000 lost bed days annually; our work will help reduce this. Collaborating with the Interventional Public Health theme, epidemiological study and linkage of existing databases (including microbiology, patient data, staff illnesses) will be utilised to predict outbreaks ahead of surveillance systems (Holmes, Drumright). We plan to develop antibody diagnostics for HCAI, in Gram positive organisms and in *C. difficile*. Translational work in tackling AMR and HCAI will extend to studies of: *C. difficile* and bacterial persistence in collaboration with the Centre for Molecular Microbiology and Infection (CMMI; Holden); development of multiplex assays for enteric infection based on current understanding of noroviruses and enteroviruses; and detection, risk stratification and prevention of *C. difficile* and *Norovirus*. **Diagnostics**. Developing rapid diagnostics to target treatment, optimise care and minimise unnecessary exposure and risk, runs through our theme with capacity to evaluate the impact of diagnostic tests on care delivery and patient pathways, building on our NIHR Diagnostic Evaluation Centre (DEC, Prof Hanna) that has infectious diseases as a major focus.

(iii) To educate and train the future generation of multidisciplinary clinical scientists capable of utilising new technologies for enhanced healthcare. The Department of Infectious Diseases and Immunity, in collaboration with ICHT and Public Health England, offers many short modular and postgraduate courses; the MSc in Infection Management for Pharmacists is the only UK course to provide antimicrobial pharmacists with the knowledge required to work effectively and become influential leaders, addressing local and national challenges of AMR. CIPM collaborates with British Society of Antimicrobial Chemotherapy (BSAC) to offer workshops to microbiologists, infectious disease consultants, scientists, pharmacists, infection control specialists and health professionals. The Centre will continue to develop e-learning packages for NHS staff and offer Postgraduate Certificate, Diploma and Masters in Infection, to develop a strong cohort of healthcare professionals capable of addressing the challenges of HCAI. We run a short course on HIV and sexual health for pharmacists and non-HIV specialist clinicians. The Department of Infectious Disease Epidemiology runs a 10-day course on mathematical models of epidemiology and control of infectious diseases e.g. influenza, TB, SARS, HIV, and vector-borne diseases, for policy makers, researchers, mathematicians, health economists, and public health and disease control professionals.

(iv) To translate research into new policies for the benefit of patients nationally and internationally. We have a strong track record in developing clinical guidelines based on our discovery science, as exemplified by the results of the WT-funded SPARTAC trial, which has the potential to change HIV management (*Weber J et al. NEJM 2013; 368:2036*; *Lichterfeld and Rosenberg. Ann Int Med 2013; 159:425*). We envisage that with our prior successes of contributing to NICE TB guidelines (Lalvani, Wilkinson [Respiratory Theme]) and the development of the low cost MODS test allowing rapid diagnosis of multi-drug resistant TB (Friedland) (*Fitzwater S et al. Eur Resp J 2013; 41:1163; Elkington P et al. Sci Transl Med. 2011; 3:71; Elkington P et al. J Clin Invest 2011; 121:1827; Moore D et al. NEJM 2007; 356:189*), our current work on exploring new treatment strategies for TB will have the potential to change clinical guidelines or policies. The results of our work on the Mechanisms of Severe Influenza Consortium (MOSAIC) study, the largest study performed during the H1N1 influenza pandemic, will lead to targeted vaccines for those with a genetic variant of IFITM3 (*Everitt A et al. Nature 2012; 484:519*), a gene that influences how we respond to influenza infection. This large-scale study will inform interventions and preventative strategies to influence new policies. Based on our prior work on epidemiological and molecular investigations into an emm1 *S. pyogenes* outbreak (*Steer J et al. J Infect 2012; 64:1*), which led to a new diagnostic test being adopted as a HPA standard, a newly-awarded BRC grant SpyVAC project 'Towards a *S. pyogenes* Vaccine' will examine population immunity to *S. pyogenes* and will have the potential to impact on future clinical trials to study Group A *Streptococcus* vaccine candidates. Building on the antibiotic prescribing smartphone app, CIPM will develop specialist multiplatform m-Health interventions in infection prevention and management, with a focus on the DH 5 Year Strategy and Action Plan on AMR to provide surveillance, quality improvement and education, and engage with stakeholders, particularly patients.

(v) To create new wealth through innovation in healthcare in discovery science and in population-based translation. Our collaborations across Faculties and with our industry partners, and our continuous building on intellectual assets, will enable us to generate new wealth through innovation in healthcare. Most notably, our innovations have resulted in the formation of several spin out companies: DNA Electronics, in collaboration with IC Institute of Bioengineering and Infection, will develop technology to detect alleles, i.e., HLA-B5701, with applications in diabetes; Indigix Ltd, will develop novel dendrimer based therapeutics to

treat infectious diarrheal diseases; and IC spinout PolyTherics, will develop a novel, patented pegylation technology for proteins and peptides (*Zloh M et al., Nat Protoc. 2007;2:1070; Shaunak S et al., Nat Chem Biol. 2006;2:312*). Our continued improvement and innovative development of our smartphone application will potentially generate revenue through adoption into the community and other NHS organisations.

2.4 Description of how the proposed theme or work programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

There is significant morbidity and mortality arising from HCAI, with a prevalence rate of 6% of all patients developing a HCAI, costing the NHS more than £1b a year (*HPA 2012*). Our work to understand infection and to develop new diagnostic methods, treatment and prevention strategies will address this concern. Work in infectious diseases often includes working with deprived and vulnerable communities. Our research has resulted in reduced morbidity and mortality from meningococcal sepsis. Studies will facilitate early identification and intervention for those at risk of adverse outcomes from infections such as TB, HIV, and acute respiratory infection. Work on screening for TB, HIV and Hepatitis infections in migrants will provide benefit in early diagnosis and treatment and vaccination. Recognising a gap in antibiotics development highlighted by the CMO, we will continue to develop work streams to tackle AMR. Building on work in behavioural interventions, we will improve the understanding of antibiotic prescribing. We will develop links with public health medicine, primary care, commissioners, education and community health services.

2.5 Description of how the theme/work programme will involve and enhance multi-disciplinary and multi-professional working.

Our experts in HIV and HTLV will work together on vaccine development for the Imperial BRC Vaccine Initiative, which will incorporate researchers and patients from Infection, Paediatrics, Gastroenterology and Hepatology and Respiratory Themes, and include novel imaging of immune responses to create new vaccine constructs for infectious targets (HIV, HCV, TB, Dengue and *N meningiditis* subtype B). CIPM will guide its work-streams towards a sustainable infrastructure for research, national and international partnerships, capacity planning and dissemination of best practice, with aims to provide significant benefits for patients. The Centre brings together biomedical scientists, pharmacists, nurses and experts on infection, benefiting from collaborations across other IC Faculties (psychologists, microbiologists and academics in experimental medicine); the Business school; ICHT (pharmacist researchers, Infection Prevention and Control Service, Microbiology Laboratories); and Public Health England. For example, the further refinement of local m-health application and point of care data to improve antibiotic prescribing brings together expertise from the IC FoE and FoM, pharmaco-epidemiologists and specialist developers. We will continue to run courses on antimicrobial stewardship, the mechanisms, surveillance and epidemiology of infection, and AMR for doctors, nurses, managers, pharmacists and other members of the multidisciplinary team to foster patient safety and quality improvement initiatives. Infection control within ICHT is directly informed by CIPM research and has provided exemplars for international best practice (Oslo and Israel).

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work programme.

CTM Chair for Infectious Diseases, Prof Alison Holmes MD FRCP. Professor of Infectious Diseases. Co - Director of CIPM, Programme Lead CPSSQ. Research into hospital epidemiology and infection prevention and control. Expert member of the Governmental Advisory Committee on AMR and HCAI.
Prof Jonathan Friedland PhD FMedSci. Professor of Infectious Diseases. Head of the Department of Infectious Diseases and Immunity. Lead Clinician Clinical Infection at ICHT. Co-Director of CIPM. Research into the innate immune response to TB and the development of novel diagnostics for TB. Member of the Joint Committee on Vaccination and Immunisation. Department of Health TB advisory group. Member of the MRC/NIHR Public Health Infection Science Strategy Group.
Prof Jonathan Weber PhD FRCP FMedSci. Jefferiss Professor of Communicable Diseases and GU Medicine. Director of Research FoM and IC AHSC. HTLV-I, other PI UK HIV Vaccine Consortium. Member NIHR Efficacy and Mechanism Evaluation Programme, MRC DPFS/DCS Board, MRC Stratified Medicine Panel. NIHR Senior Investigator 2009-12.
Prof Charles Bangham PhD FMedSci. Professor of Immunology. Head of Division of Infectious Diseases. WT Senior Investigator. Research into regulation of retroviral latency and expression in HIV and HTLV-1 and gene therapy with retroviral vectors.

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

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Department of Health

ACADEMIC HEALTH SCIENCE CENTRES

SPECIFIC THEME / WORK PROGRAMME

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Please use this form to provide details on one of the six specific Themes / Work Programmes of focus for the proposed AHSC.

Please use a separate form for each of the Theme / Work Programme. Please complete no more than four pages for each theme; only information submitted up to this page limit can be assessed.

Please note this should be completed in a font no smaller than 10-point Arial.

Please insert your unique Reference Number into the Footer space provided.

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership: Imperial College AHSC

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work programme.

Inflammatory Diseases

2.2 Aims and objective of the theme/work programme.

Our aim is to improve the recognition, management and outcome of patients with inflammatory disease. We will achieve this by: (i) rigorously identifying and developing the clinical utility of research findings within a broad basic inflammation science portfolio; (ii) specific programs in inflammatory disease research cohorts that target unmet clinical needs. Objectives include: development of diagnostic tests to improve recognition of inflammatory disease; development of biomarkers and imaging modalities to optimise patient selection for therapy; assessment of new therapeutic approaches to enhance outcome; development of strategies to address co-morbidities of inflammatory disease e.g. improving vascular access in chronic kidney disease; development of treatment approaches e.g stem cell therapy in kidney and pancreas transplantation.

2.3 Description of how the proposed theme or work programme will contribute to the aims of the AHSC.

(i) To utilise the research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations. We will continue to integrate basic biomedical research with translational research programs in multidisciplinary clinical research groups (Renal Medicine, Rheumatology and Hepatology) e.g. integrating IC and ICHT skills in the development of multidisciplinary Lupus and Vasculitis Centres which pool clinical expertise to enhance patient care and directly link to IC biomedical research laboratories: Centre for Complement and Inflammation Research and Renal and Vascular Inflammation Section respectively. The Robert Hesketh Hepatology Clinical Research Facility links to basic sciences in the Section of Hepatology. These centres attract national referrals and renal medicine has one of the largest patient cohorts in Europe.

(ii) To create powerful new interdisciplinary synergies spanning the IC, IC AHSC and the AHSN to transform health care through translational science, bioengineering and informatics. **1. Systemic**

lupus erythematosus (SLE): We have longstanding research expertise in SLE and an integrated clinical service for lupus patients in the Imperial Lupus Centre, we have pioneered the use of steroid-sparing regimens in lupus nephritis (*Pepper R et al. Nephrol Dial Transplant 2009; 24: 3717*) and plan to improve outcome in SLE by: studying markers of response to anti-B cell therapies (e.g. anti-CD20, anti-BlyS/BAFF) including expression of ITIM/ITAM-motif containing receptors on innate immune cells; the instigation of a multi-centre international trial assessing the role of rituximab without oral steroids in lupus nephritis (The Rituxilup Trial NCT01773616); reducing atherosclerosis in SLE (*Ali F et al. J Biol Chem 2009; 284:18882; Ali F et al. Cardiovasc Res 2010; 85: 701*) through statin therapy: a randomised trial of rosuvastatin [Astra Zeneca] with Prof Dudley Pennell, Royal Brompton Hospital with outcome measures that include endothelial function, cardiac function and atherosclerotic burden. **2. Vasculitis:** We have longstanding research expertise in anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV) and large vessel vasculitis (LVV), and deliver integrated care for vasculitis patients in the Imperial Vasculitis Centre. We plan to improve outcome in AAV by: assessing if changes in cellular immunity in AAV influence disease outcome e.g. role of regulatory T and B lymphocytes, and of CD14+ CD16+ monocyte subsets in disease activity; expand our vasculitis trial portfolio (*de Groot K et al. Ann Intern Med 2009; 150: 670; Jayne D et al. J Am Soc Nephrol 2007; 18: 2180*), which includes efficacy of plasma exchange in severe AAV (NIHR and NIH funded PEXIVAS trial) to novel approaches, including C5a receptor inhibition (Chemocentryx), sequential B cell depletion with rituximab (Arthritis Research UK funded RITAZAREM trial), and spleen tyrosine kinase inhibition; and continue genetic analysis of AAV in the European Vasculitis Genetics Consortium (*Lyons P et al. NEJM 2012; 367: 214*). In LVV, we will prevent severe complications by assessing the ability of novel imaging, modalities to identify early disease e.g. PET ligand PK11195 (*Pugliese F et al. J Am Coll Cardiol 2010; 56: 653*), radiolabelled water and microvascular flow changes; study CT coronary angiography for coronary vasculitis, and MR angiography (Bioengineering and Aeronautics) to model LVV-mediated vessel abnormalities; improve diagnosis and monitoring of LVV by studying temporal artery ultrasound (TABUL study); develop diagnostic tests in Behçet's syndrome (BS) e.g. capsaicin-induced blood flow and neuropeptide release; predict thrombosis and aneurysm risk in BS through coagulation and tissue factor assays, and imaging studies (MR and microbubble contrast ultrasound) to detect venous inflammation **3. Glomerulonephritis (GN):** We aim to improve understanding of IgA nephropathy by characterising: the response of mesangial cells to patient-derived IgA1 (*Kim M et al. J Immunol 2012; 189: 3751*); the pathogenicity of autoantibodies to abnormally glycosylated IgA1 molecules; and genetic factors linked to disease development and progression (MRC grant: MR/K01353X/1). In membranous nephropathy, we will assess how plasma anti-phospholipase A2 receptor (PLA2R) antibodies correlate with PLA2R receptor expression in kidney biopsies and clinical outcome, and contribute to novel genetic studies (with Prof Paul Brenchley, Manchester University). We recently characterised C3 glomerulopathy, a new group of kidney diseases (*Gale D et al. Lancet 2010; 376: 794; Ruseva M et al. J Am Soc Nephrol 2013; 24: 43; Malik T et al. J Am Soc Nephrol 2012; 23: 1155*), and plan to: develop rapid genetic and serological screening tests; establish an International C3 Glomerulopathy Pathology Registry to define clinico-pathological parameters to help stratify patients for appropriate treatments. In diabetic nephropathy we will study urinary biomarkers of disease progression (including chemokines) and participate in trials of emerging therapies: vitamin D analogues, and inhibitors of C5a receptor**. 4. Chronic kidney disease (CKD) and kidney and pancreas transplantation:** In CKD**,** we will study: the effect of dialysis dose on cardiovascular fitness, nutrition and inflammation; risk factors associated with stroke and the role of thrombolysis; the use of ghrelin in preventing malnutrition during dialysis (*Ashby D et al, Kidney Int 2009; 76: 199*); and the use of hepcidin levels in optimising anaemia therapy (*Ashby D et al. Kidney Int 2009; 75: 976*). In transplantation, we will characterise donor specific anti-HLA antibodies and their effects on transplant outcome (*Willicombe M et al. Am J Transplant 2011; 11: 470*); study the effects of anti-blood group antibodies in ABO-incompatible transplantation; develop improved methods of transplant biopsy analysis (mRNA transcript analysis, electron microscopy) and correlate with transplant outcome; study endothelial activation in donor organs prior to transplantation and subsequent immunogenicity of the graft; investigate endothelium-targeted anti-thrombotic fusion proteins in *ex vivo* human kidney and pancreas perfusion studies; continue studies of peripheral blood-derived stem cells in treatment of the failing pancreas in patients with kidney and pancreas transplant, and extend this to examine mesenchymal stem cell therapy in kidney transplant rejection (STELLAR FP7). **5. Hepatic and gastroenterological inflammation.** Our approach examines the mechanisms whereby both intrinsic and extrinsic factors can modulate inflammatory change. We are partners in a Newcastle-led MRC Stratified Medicine Initiative in Primary Biliary Cirrhosis in which new approaches will be developed to address bile salt-mediated hepatic inflammation. In the GI tract, we have also shown that modulation of the secreted factor, fibroblast growth factor 19 (FGF19) is a feature of primary bile acid diarrhoea (PBAD) (Pattni et al. Aliment Pharmacol Ther 2013, Epub ahead of print) and that FGF19 expression in human ileum is highly responsive to bile acid (*Zhang J et al. Am J Physiol Gastrointest Liver Physiol 2013; 304: G940*). We have a large PBAD patient cohort and established links with Metabolic Medicine to study changes after gastric bypass. We will optimise the diagnosis rate of PBAD using FGF and SeHCat analysis, perform early Phase II studies of a new drug that increases FGF19 production, and determine the relationship between changes

in FGF19 following gastric bypass, altered bile acid kinetics and weight loss. We are examining the relationship between Hepatitis C virus (HCV) and systemic disease mediated through changes in gene expression involved in both inflammation and metabolism and identified changes in gene expression patterns of TXNIP and PPARγ, both strongly implicated in the development of hepatic steatosis and diabetes (*Blackham S et al. J Virol 2010; 84: 5404*). We will define the metabolome of patients with chronic HCV infection, before and after treatment, to identify key pathways relating to lipid insulin resistance. We currently lead the NIHR-HTA trial of therapy for alcoholic hepatitis candidates (STOPAH). This trial will give us access to samples from 1200 patients with alcoholic hepatitis (largest collection in Europe). These specimens will be used to conduct a genome wide association study (GWAS), in collaboration with the Genetics and Genomics Theme, of genetic susceptibility to alcoholic hepatitis. On-going work shows macrophages play an important role in the pathogenesis of liver failure secondary to alcoholic liver disease and liver fibrosis. Our investigations demonstrate a profound defect in monocyte function due to endotoxin tolerance and high levels of IL-10 in serum. Using small molecule and antibody mediated inhibition of IL-10 signalling, we will evaluate the restoration of monocyte function in *ex-vivo* experiments with the intention of identifying potential translational strategies.

(iii) To translate research into new policies for the benefit of patients nationally and internationally. This theme represents a focus on rarer diseases which significantly impact patient lives. The introduction of plasma exchange in combination with immunosuppressive drugs improves outcome in rapidly progressive glomerulonephritis due to AAV. This approach, pioneered at IC, is recommended in European and International guidelines. We have characterised a novel complement-mediated familial renal disease (CFHR5 nephropathy) and now offer diagnostic testing. This condition is part of the spectrum of C3 glomerulopathy, and has recently published the first International Consensus Guidelines. We have demonstrated the utility of combined 18F-FDG-PET, MRA and high resolution US in the diagnosis and management of patients with LVV, avoiding invasive imaging and high dose oral cyclophosphamide. We have demonstrated cost effectiveness in patients with mild hepatitis with pegylated interferon and ribavirin leading to a change in NICE guidelines. We identified hepatitis Be antigen (HBeAg) negative mutants caused by a mutation in the pre-core region of the virus (>800 citations) which led to the description of these variant infections as causing a more severe form of HBV infection, which has a distinct clinical phenotype and treatment response. This has led to widespread HBV DNA testing, and optimised management in this previously unidentified sub-group.

(iv) To educate and train the future generation of multidisciplinary clinical scientists capable of utilising new technologies for enhanced healthcare. We run a MSc in Immunology for Scientists and Clinicians, and short courses in immunology, rheumatology, nephrology and hepatology. We provide training for a large cohort of doctors, including NIHR ACFs and CLs, across clinical specialties, with many undertaking PhDs or MDs in our laboratories. A comprehensive clinical training programme for all healthcare professionals includes research, teaching, development of managerial skills and exposure to sub-speciality medicine. In Renal Medicine a state of the art Simulation Unit provides training in common clinical scenarios and renal procedures on manikins which we will use for trainees across London. We contribute to medical undergraduate teaching in specialties, BSc modules in our basic science fields.

(v) To create new wealth through innovation in healthcare in discovery science and in population-based translation. We will address wealth generation through translation of our basic and clinical science. We will engage in clinical trials with several industrial partners including Alexion, Chemocentryx, Roche, GSK and Astra Zeneca with a view to identifying new treatment approaches applicable to our patient populations. We have research collaborations in pre-clinical studies with Baxter, Astra Zeneca and GSK with the potential to develop novel, patentable therapeutics. We are involved with a spin-out company, Riotech Pharmaceuticals Ltd, which is developing novel approaches to the treatment of flaviviral diseases.

2.4 Description of how the proposed theme or work programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

The prevalence of SLE is 15:10, 000 (*Pons-Estel G et al. Semin Arthritis Rheum 2010; 39: 257*), and of vasculitis is 3:10, 000 (*Koldingsnes W et al. Norsk Epidemiologi 2008; 18: 37*). In both SLE and vasculitis, chronic relapsing/remitting diseases with high morbidity, there is a need to understand pathogenic mechanisms, validate biomarkers and evaluate new therapies. Our multidisciplinary Lupus and Vasculitis Centres are well placed to take this forward in collaboration with our basic biomedical research. We have several active collaborations with Immunology and with Cardiovascular Diseases in these areas. In LVV, the development of non-invasive imaging techniques will allow earlier diagnosis and better monitoring of disease progression, and this relies on our collaboration with Imaging. CKD affects 1:10 of Western populations. In the UK, the annual incidence of end stage renal disease has reached over 100 new patients per million of population (*El Nahas A et al. Lancet 2005; 365: 331*) and costs around 2% of the NHS budget. Glomerulonephritis and diabetic nephropathy are the commonest causes of end stage renal disease worldwide. Our research in GN is designed to facilitate early diagnosis and prevention of progression – thus avoiding the need for costly renal replacement therapy. In diabetic nephropathy, we work closely with

the Metabolic Medicine Theme to examine the role of inflammatory mechanisms in development of diabetic nephropathy and investigate new approaches to treatment. In renal transplantation, we work with the Immunogenetics Laboratory to examine the role of anti-HLA and anti-blood group antigen antibodies in acute and chronic allograft rejection. Better understanding of the clinical relevance of these antibodies should allow us to tailor therapy according to risk and expand the pool of potential donors traditionally regarded as "high risk". Despite the success of our transplant programme, the number of patients on maintenance dialysis continues to grow and we need to optimise management of this patient group, concentrating on prevention of cardiovascular events and improved vascular access. This work depends on close collaboration with Cardiovascular, Stroke and Imaging Groups, and for vascular access with Bioengineering and Aeronautics. Chronic liver disease is the 5th commonest cause of mortality in the UK and, in contrast to other EU countries; the mortality rate in the UK is rising. Impacting liver disease will thus have a major effect on the Nation's health in terms of morbidity and mortality. Gastroenterological disorders form a major healthcare burden in the UK (30% of GP consultations e.g. malignancies, such as pancreatic adenocarcinomas, chronic immunological disorders such as coeliac disease, and inflammatory bowel diseases). The microbiome impacts on these diseases, on the development of obesity and other metabolic problems, and on functional disorders of the gastrointestinal tract such as irritable bowel syndrome. New developments in understanding causes, diagnosis and treatments will improve patient outcome.

2.5 Description of how the theme/work programme will involve and enhance multi-disciplinary and multi-professional working.

In Renal Medicine, Rheumatology and Hepatology, we have well established clinical research groups, which include physicians, surgeons, nurses and AHPs. These groups work closely with clinical and basic scientists in our laboratories. Several of our non-medical healthcare professionals have undertaken PhDs supervised by clinical academics in our laboratories. Our Lupus and Vasculitis Centres are based on a multidisciplinary, multiprofessional approach which requires the involvement of experts in several other fields, including Respiratory Medicine, Ophthalmology, Neurology, ENT and Dermatology. We hold regular meetings of these groups to discuss clinical priorities and research, and also hold termly research meetings at which specialist trainees from across North West London can present their work. Since CKD is a major risk factor for cardiovascular disease, including myocardial infarction and stroke, we work very closely with Cardiovascular and Metabolic Medicine Themes. In patients requiring dialysis, there is on-going collaboration in assessing different types of vascular access with Infectious Diseases and with groups in Bioengineering and Aeronautics. Through links with Metabolic Medicine and Surgery Themes, we aim to study changes after gastric bypass, e.g. in progression of diabetic nephropathy. With the Genetics and Genomics Theme we will conduct genome wide association studies to identify genetic factors in alcoholic liver disease, and family studies of IgA nephropathy.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work programme.

CTM Chair for Inflammatory Diseases, Prof Matthew Pickering PhD FRCP. Professor of Rheumatology, Academic Director for the Imperial Lupus Centre, Wellcome Trust Senior Fellow in Clinical Science. Leading researcher in C3 glomerulopathy, complement and SLE. Board member European Complement Network and International Complement Society.

Prof Charles Pusey DSc FMedSci. Professor of Medicine, Head of Renal and Vascular Inflammation Section, Director of Clinical Academic Training at AHSC. NIHR Senior Investigator. Lead Clinician in the Renal, distinguished for work in autoimmune renal disease, including primary systemic vasculitis. Member of 2014 REF Sub Panel for Clinical Medicine.

Prof Dorian Haskard DM FMedSci. Professor of Cardiovascular Medicine. Head of Immunology and Inflammation. BHF Sir John McMichael Chair in Cardiovascular Medicine. NHLI and Deputy Director of the BHF Centre. Head of the Vascular Sciences Section, NHLI. Leading figure in research on vascular inflammation, atherosclerosis and Behçet's syndrome. Member of the MRC Population and Systems Medicine Board and ARUK Strategy and Programme Grant Committees.

Prof Marina Botto MD FMedSci. Professor of Rheumatology, Director of Centre for Complement and Inflammation Research. Research into genetics and immunology of SLE. Member of College of Experts, MRC. Panel Member, Clinical Interview Committee, Wellcome Trust.

Prof Mark Thursz MD FRCP. Professor of Hepatology. Secretary-General, Governing Board, European Association for Study of the Liver. Research into hepatitis C virus and alcoholic hepatitis.

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

This form, together with other requested attachments must be submitted by **1:00pm on 30 September 2013**.

Department of Health

ACADEMIC HEALTH SCIENCE CENTRES

SPECIFIC THEME / WORK PROGRAMME

Note: The accompanying *"Academic Health Science Centres – Full Application Guidance"* contains essential guidance on the information you need to provide when completing this proforma.

Please use this form to provide details on one of the six specific Themes / Work Programmes of focus for the proposed AHSC.

Please use a separate form for each of the Theme / Work Programme. Please complete no more than four pages for each theme; only information submitted up to this page limit can be assessed.

Please note this should be completed in a font no smaller than 10-point Arial.

Please insert your unique Reference Number into the Footer space provided.

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership: Imperial College AHSC

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work programme.

Metabolic Medicine

2.2 Aims and objective of the theme/work programme.

The Theme advances understanding of the basic science of obesity, diabetes and endocrine disorders, and uses new knowledge to develop and test novel targeted therapies. Our research will enhance the function of the failing beta cell, invent and trial novel drugs for obesity and diabetes, such as the gut hormone analogues, develop technologies which mimic the functionality of a healthy pancreas and regulate blood glucose for management of diabetes, manipulate thyroid hormone action for novel targeted therapies in osteoporosis and osteoarthritis, and develop a novel method for treatment of infertility using kisspeptin.

2.3 Description of how the proposed theme or work programme will contribute to the aims of the AHSC.

(i) To utilise the research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations. The Division of Diabetes, Endocrinology & Metabolism at IC, funded by NIHR, DH, MRC, BBSRC and Wellcome Trust (WT), unites strengths in basic science with clinical expertise and infrastructure to translate findings rapidly into the clinic. Our obesity research, led by Prof Sir Stephen Bloom, is pioneering with the discovery of the role of gut hormones in regulating appetite (*De Silva A et al. Cell Metab 2011;14,700*) and human Phase I clinical trials currently underway to assess the pharmacokinetics and safety of 3 peptide hormone analogues for new treatments in obesity. The Phase I clinical trials of our peptide analogues are run in partnership with the NIHR/WT Imperial Clinical Research Facility (ICRF), Imperial Innovations and industrial partners including Wyeth/Pfizer and PAREXEL International. Our work in management of obesity using the Counterweight Scheme, led by Prof Gary Frost, has now been implemented in more than 250 NHS general practices and 30 Primary Care Trusts. IC diabetes investigators work in partnership with ICHT, which hosts the coordinating centre for the NIHR Diabetes Research Network (DRN), Professor Desmond Johnston. The DRN has 8 Local Research Networks (LRNs) spread across the UK, and aims to achieve benefits for those with diabetes or at risk of developing diabetes through excellent clinical research; and to provide world-class health service

infrastructure to support this research. We have a clinical research programme which utilises patient cohorts from ICHT Multidisciplinary Diabetic Foot Service to reduce complications from diabetes (*Valabhji J. Diabetes Care 2011; 34:e135*). Our research in osteoporosis and osteoarthritis has identified thyroid hormone receptors and metabolism enzymes as novel therapeutic targets. Research into developing treatments for infertility, using the hormone kisspeptin, brings together IC clinical academics, trial expertise at ICHT IVF unit and Imperial Clinical Trials Unit (ICTU). We will bring together groups in human genetics, fundamental β-cell biology and control of appetite, to enhance interactions with biological, chemical, physical scientists. We will provide a pipeline of treatment approaches, through stratified medicine, modulating insulin release and the actions of gut hormones.

(ii) To create powerful new interdisciplinary synergies spanning the IC, IC AHSC and the AHSN to transform health care through translational science, bioengineering and informatics. **Obesity:** Our research team are focusing on understanding mechanisms of appetite suppression and, based on the success of gut bypass, developing gut hormone analogues for weekly administration to treat obesity. This fits the Government's strategy to reduce obesity and will use the NHS to enhance entrepreneurship for economic benefit. We have shown that the gut hormones oxyntomodulin (OXM), peptide YY (PYY) and pancreatic polypeptide (PP) can suppress appetite and enhance energy expenditure. Building on the success of our proof of concept studies, we will: (i) test newly-developed glucagon+Glukagon-like peptide-1 (GLP-1) 'dual agonist', currently in GMP manufacture for a Phase 1 trial to start mid-2014, as a next-generation obesity therapy with powerful effects on weight loss and diabetes prevention [MRC Developmental Clinical Studies (DCS)-funded]; (ii) perform a Phase 1b/c clinical trial on PP analogue, PP1420, to investigate its efficacy, tolerability and pharmacokinetics during repeated dosing (WT funded); (iii) perform a Phase 1 clinical trial on PYY analogue, Y3394, to demonstrate its effectiveness when given for extended periods to patients with obesity. PYY analogue, Y242, has been successfully shown to reduce weight in a 5 week Phase I trial; (iv) Prof Bloom (*Murphy K and Bloom S. PNAS 2007; 104:689; Murphy K and Bloom S. Nature 2006; 444: 854; Wynne K, Bloom S. Nat Clin Pract Endocrinol Metab 2006; 2:612*) will collaborate with Prof Chris Toumazou, (*Toumazou C et al. Nature Methods 2013;10:641*) Institute of Biomedical Engineering on a project, called 'Intelligent implantable modulator of Vagus nerve functions for treatment of obesity' (i2MOVE). We will use an 'intelligent' microchip to detect signals in the vagus nerves and instruct the brain and the gut that it is full, and therefore suppress appetite. Imperial Weight Centre, the 1st of 2 centres accredited as International Centre of Excellence for bariatric surgery in the UK, is a crucial resource. Prof Bloom's team have recently been awarded an MRC Experimental Challenge Grant (£2.8m 2013-18) to investigate the mechanisms underlying the effectiveness of bariatric surgery, and to determine if a combination of gut hormones is able to replicate these mechanisms (*Cummings et al. Nature Medicine 2012; 18:358*). We will utilise participants from the Imperial Weight Centre to investigate the place of personalised medicine in the treatment of morbid obesity, and analyse the effect of GPRC6A ligands on appetite suppression. We have had UK-wide success with the Counterweight Programme, now commissioned by over 30 primary care organisations. Building on this work we will investigate methods to manage obesity using dietary interventions with BBSRC-funded investigation of the role of dietary non-digestible carbohydrate (NDC). This has led to a first in human trial and patent of an inulin propionate ester, a safe food ingredient which suppresses appetite.

Diabetes: Research interests in Diabetes include investigations to enhance the function of the failing beta cell, the genetic basis of type 2 diabetes and development of technologies to improve care for patients with diabetes. Research led by Prof Guy Rutter seeks to improve the number and function of beta cells in the context of type 2 diabetes (T2DM), exploiting recent advances in understanding of the genetic landscape of the disease, and mechanisms which control beta cell growth and survival (*Iglesias J et al. J Clin Invest 2012; 12:4105*; *Li D et al. PNAS 2011; 108:21063*). He is developing ways to image beta cell mass *in vivo*, a key diagnostic gap in the understanding of disease progression. We will use genetics to improve diagnosis and devise personalised treatment for patients with T2DM and obesity [led by Prof Philippe Froguel (*Bonnefond A et al. PLOS One 2010; 5:e13630*; *Walters R et al. Nature. 2010; 463:671*)]. Work on this has begun in the Innovative Medicines Initiative (IMI)-funded DIRECT and IMIDIA studies on personalised medicine for diabetes. These projects bring together academia, industry and biotech in the joint development of solutions for improved disease management. Building on these (*Morris A et al. Nat Genet. 2012; 44:981*; *Scott R et al. Nat Genet 2012; 44:991*), we have devised 3 sub-projects: (i) Identifying the genetic tools to enhance diagnosis and treatment options for inherited forms of T2DM, where we will perform Whole Exome Sequencing of families with maturity onset diabetes of the young; (ii) Personalization of the management of T2DM patients with therapies tailored to individual needs, which involves identification of the most informative and predictive biomarkers of progression of T2DM, complication risk and resistance to treatment modalities; (iii) Stratification of patients to identify very high risk individuals who would benefit from early intervention (diet or surgery). We will extend research to the wider population, performing a population study of screening for diabetes to ascertain patients with diabetes, lesser degrees of glucose intolerance and other coronary heart disease (CHD) risk factors. This will provide a framework for genetic epidemiology studies in diabetes and CHD, integrating genetic, conventional physiology and metabonomic approaches; we will exploit the ethnic mix of this population to explore the basis for ethnic

differences in diabetes and CHD risk. Research will focus on development of technologies for management of type 1 diabetes (T1DM) [led by Prof Johnston (*Ramachandran A et al. Lancet Diabetes and Endocrinology 2013; in press*)]. We have a Phase I study currently in place in the ICRF to test the Bio-inspired Artificial Pancreas – a fully closed loop system, which mimics the functionality of a healthy pancreas and aims to tightly regulate blood glucose, minimising the occurrence of serious complications. The Bio-inspired Artificial Pancreas has been evaluated in fasting, overnight and post-prandial states in patients with T1DM; and results indicate highly effective glycaemic control without hypoglycaemia (which has been a serious issue with some other systems). We have an NIHR i4i research programme which will evaluate a novel microneedle-based continuous glucose sensor. This could revolutionise the management of diabetes (no need for finger pricks). Our ultimate aim is to deliver a closed loop device which mimics the function of a healthy pancreas in conjunction with continuous glucose sensors, insulin and glucagon pumps.
Endocrinology: Research in Endocrinology focuses on improving the treatments for endocrine disorders. Current treatments for osteoporosis reduce fracture risk by only 25-50% and there are concerns regarding long-term safety. Patients with early osteoarthritis are asymptomatic and develop problems only after significant cartilage destruction has occurred. There are no drugs available that can prevent or delay disease progression. Thus, there is an urgent need to advance understanding and define molecular pathways for development of new treatments for these common debilitating disorders. A £2.8m WT Strategic Award (2014-2019) to Profs Duncan Bassett and Graham Williams (*Bassett J et al. PNAS 2010; 107:7604*) will characterise genetic determinants of bone and cartilage disease and identify new therapeutic targets. Recognising that current treatments for infertility have limited success and significant side effects, we will develop kisspeptin as a new and more natural therapy for patients with infertility and hypothalamic amenorrhea. We have carried out the first in human studies of novel hormone kisspeptin and shown that kisspeptin potently stimulates reproductive hormone release in healthy men and women, and in patients with infertility due to hypothalamic amenorrhea (*Jayasena C et al. Clin Endocrinol (Oxf). 2013; 79:558*; *Jayasena et al. Clin Pharm Ther 2010; 88:840*). We will now determine if longer term administration of kisspeptin can restore fertility in women with hypothalamic amenorrhea to bring this novel treatment into clinical practice. A recent joint MRC- and NIHR-funded Phase II study has shown that kisspeptin can successfully result in egg maturation in women undergoing IVF, and the first baby has been born using kisspeptin in IVF treatment. By its unique mechanism of action, kisspeptin has the potential to benefit women at risk of developing ovarian hyperstimulation syndrome (OHSS).
(iii) To educate and train the future generation of multidisciplinary clinical scientists capable of utilising new technologies for enhanced healthcare. The Hammersmith Hospital Endocrine Department organises an annual UK Multidisciplinary Endocrine Symposium (MES), bringing together trainees and consultants who manage complex endocrine patients to share best practice and discuss difficult cases. Now in its 8th year, it is attended by patients with pituitary and multiple endocrine neoplasia, and will continue to serve as an update for specialists in the field. Prof Gary Frost is, Deputy Director of the MRes in Clinical Research, which gives doctors, nurses and AHPs grounding in translational research. Research nurses train in the Dept. as part of continuing professional development. The Dept. organises lectures and tutorials for Year 4 BSc students who take the Endocrinology: Type 2 Diabetes, Obesity And Metabolism module. The Theme has 3 NIHR funded PhD/clinical scientists, 3 NIHR post-doctoral award holders, 2 NIHR Career Development Fellows. Clinical scientists are encouraged to undertake the MRes in Translational Medicine, core training in research methodology and trial design with expert supervision.
(iv) To translate research into new policies for the benefit of patients nationally and internationally. Our research on GLP-1 has been used to invent analogues that are used in clinical practice as highly effective treatments for diabetes that, importantly, cause weight loss unlike every other treatment for diabetes. Our research into peptide hormones continues to show that these are capable of reducing food intake which results in weight loss in human volunteers, and improvement in glycaemia in patients with T2DM. Our clinical studies on peptide hormones have the potential to yield novel drugs for treatment of obesity and diabetes. Our work in the practical nutritional management of diabetes (*Bodinham C et al. Br J Nutr 2011:1*; *Jebb S et al. Am J Clin Nutr 2010; 92:748*; *Philippou E et al. Obesity 2009; 17:396*) has already been cited in national guidelines, and we envisage that our work to investigate personalised medicine in morbid obesity will result in translational breakthroughs that affect clinical practice. We have a unique programme investigating novel dietary solutions and have just received BBSRC "super follow-on funding" to translate our recently patented inulin propionate ester into a food ingredient for appetite control.
(v) To create new wealth through innovation in healthcare in discovery science and in population-based translation. We have a track record of producing intellectual assets, sale of spin-out company, Thiakis Ltd., to Wyeth/Pfizer which generated income for IC as a shareholder. We aim to generate wealth through 3 new peptide hormone analogues and 2 novel foods, targeted at gut nutrient receptors, to develop new treatments for obesity.

2.4 Description of how the proposed theme or work programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

Our new therapies focus on patient populations with metabolic/endocrine disorders. **Obese and overweight patients:** England ranks as one of the most obese nations in Europe with around 5-6% of the NHS's total budget spent on the disease consequences of overweight and obesity (DH 2011). Our research will lead to improved public health and a safe and effective pharmacological therapy for obesity with potential to decrease morbidity and mortality and the cost of obesity to the UK. We have a strong track record in proof of concept studies in obesity, with our peptide hormones shown to be safe, well-tolerated, and successful in reducing food intake and resulting in weight loss. We will develop a major new therapy that will reduce the incidence of obesity. This is reflected in our programme of targeting nutrient receptors to suppress appetite. **Patients with diabetes:** Diabetes affects an estimated 2.5 million people in the UK, of which 850,000 are undiagnosed; NHS spending on diabetes is approximately £10b per year (Diabetes UK 2012). We will continue to improve the clinical management and quality of life for people with diabetes, and reduce the cost of treatment of diabetes to the NHS. Our design of The Bio-inspired Artificial Pancreas for subjects with T1DM will progress on a translational pathway, integrating basic science with clinical trials to improve diabetes management. Our Multidisciplinary Diabetes Foot Service will continue as a flagship clinic, driving innovative integrative care across healthcare, reducing complications such as limb amputations in diabetic patients. Internationally, we helped established the IC Diabetes Centre in Abu Dhabi, a state-of-the-art facility specialising in Treatment, Research, Training and Public health. It provides the highest level of specialised patient care, from diagnosis to the management of all complications. **Patients with osteoporosis and osteoarthritis:** Bone and cartilage disorders affect more than 50% of adults over the age of 50 and their prevalence is increasing. Osteoporosis affects 3 million people in the UK, whilst osteoarthritis (OA) affects over 8.5 million people and costs an estimated 1% of gross national product (National Osteoporosis Society 2013). Studies in skeletal disease will lead to identification and development of drugs. **Infertility:** Infertility affects 1 in 6 couples (NHS UK 2013). Currently 45,000 IVF cycles are performed each year at £2,800 per cycle. The cost to the NHS of treating the health risk of IVF, ovarian hyper stimulation syndrome, is £28 million per year, and with NICE approval for IVF treatment this will increase in the future. Investigation of kisspeptin will lead to safer and more cost effective IVF therapy.

2.5 Description of how the theme/work programme will involve and enhance multi-disciplinary and multi-professional working.

To translate early research findings rapidly into patients, our research brings together clinical academics, basic scientists, surgeons, research nurses, students, clinical trial managers and chemical pathology staff. Many staff hold joint IC and ICHT appointments. This ensures a seamless translational pathway towards devising new therapies in proof of concept studies. Prof Bloom is collaborating with Prof Toumazou, the Institute of Biomedical Engineering on a project, called 'Intelligent implantable modulator of Vagus nerve functions for treatment of obesity' (i2MOVE) detailed above (2.3 ii). Nutritech FP7 (Application of technologies and methods in nutrition research, the example of phenotypic flexibility) will bring together European leads to investigate the use of new "omics" platforms in nutrition research. Clinical academics in Diabetes are collaborating with computing, clinical genomics, system genetics and stratified medicine to understand the genetic and metabolic basis of diseases. Work on the Bio-inspired Artificial Pancreas will foster collaborations with engineers, to apply engineering technologies to provide personalised healthcare devices for chronic disease management. The multidisciplinary diabetic team will work with Department of Primary Care and Public Health to test the effectiveness and efficiencies of different approaches in different population subgroups, and to look for primary care determinants in acute admissions for diabetes.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work programme.

CTM Chair for Metabolic Medicine, Prof Waljit Dhillo PhD FRCP. Professor Endocrinology & Metabolism. NIHR Fellow. Research into aspects of endocrine control of obesity and reproductive function.
Prof Sir Stephen Bloom DSc FRS FMedSci. Professor of Endocrinology. Head of Division of Diabetes Endocrinology and Metabolism, Chair Section of Endocrinology and Investigative Medicine. NIHR Senior Investigator. Pioneer in obesity, developed oxyntomodulin a novel treatment for obesity. Advisor to WHO.
Prof Jonathan Valabhji MD FRCP. Adjunct Professor Diabetes and Endocrinology. National ClinicalDirector for Obesity and Diabetes at NHS England. Consultant Diabetologis, Endocrinologist. Research interests diabetic foot disease and MDT services
Prof Desmond Johnston PhD FMedSci. Professor of Clinical Endocrinology. Director of the NIHR Diabetes Research Network. Research into the pathogenesis of type 1 diabetes.

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

This form, together with other requested attachments must be submitted by **1:00pm on 30 September 2013**.

Department of Health

ACADEMIC HEALTH SCIENCE CENTRES

SPECIFIC THEME / WORK PROGRAMME

Note: The accompanying *"Academic Health Science Centres – Full Application Guidance"* contains essential guidance on the information you need to provide when completing this proforma.

Please use this form to provide details on one of the six specific Themes / Work Programmes of focus for the proposed AHSC.

Please use a separate form for each of the Theme / Work Programme. Please complete no more than four pages for each theme; only information submitted up to this page limit can be assessed.

Please note this should be completed in a font no smaller than 10-point Arial.

Please insert your unique Reference Number into the Footer space provided.

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership: Imperial College AHSC

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work programme.

Population Health and Primary Care

2.2 Aims and objective of the theme/work programme.

The Population Health and Primary Care (PHPC) Theme will conduct population-based research aimed at implementing effective approaches to: (i) Understanding mechanisms of disease through characterisation of interactions between exposure and genetics in disease pathogenesis and incorporating modelling of environmental pathogen exposure; (ii) Developing strategies for disease prevention, from primary prevention and immunisation to screening, early diagnosis and treatment; (iii) Re-designing patient pathways, e.g. Integrated Care Interventions and improving health outcomes and experiences by healthcare analytics; (iv) Creation of evidence-based cost-effective care models for maximal societal benefit

2.3 Description of how the proposed theme or work programme will contribute to the aims of the AHSC.

(i) To utilise research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations. The performance of the UK with premature mortality is persistently and significantly below the mean EU15+. Progress in premature mortality from several major causes, e.g. cardiovascular diseases (CVD) and cancers, will require stronger concerted action in public health, prevention, early intervention, and treatment activities. The School of Public Health (SPH), working across AHSC and AHSN, will drive this agenda by strengthening the evidence base and its implementation into interventions. Research from SPH scored in the top 2 of epidemiology and public health submissions to the UK's most recent Research Assessment Exercise. We aim to strengthen SPH's capacity in population based research through the creation of 2 new Chairs to facilitate engagement within the AHSC and AHSN, and augment our ability to create population-based health initiatives in chronic disease prevention, early detection and management, e.g. proposed work includes harnessing the power of large NHS data sets to develop disease prevalence models that allow the gap between diagnosed and predicted disease prevalence to be estimated at different levels (small geographical area, general practice, locality); and strategies for identifying patients with previously undiagnosed chronic diseases, using data linkage and "big

data" analytics. The Imperial College Clinical Trials Unit (ICTU), within SPH, encompasses all stages of clinical trials; generation to delivery. The Unit, led by Profs Neil Poulter and Deborah Ashby, plays a pivotal role in supporting the goal of becoming one of the world's top research centres and improving the quality of life of patients and populations. Our goal over the next 5 years is to co-locate ICTU with SPH on the Imperial West Campus in an innovation- rich environment encompassing engagement with CROs and industry, to facilitate recruitment of patients throughout the AHSN in clinical trials. The NW London NIHR Collaboration for Leadership in Applied Health Research & Care (CLAHRC) an alliance of organisations working to develop and promote a more efficient, accelerated and sustainable uptake of clinically innovative and cost-effective research interventions into patient care. The SPH plays a key role with the CLAHRC, and leads on the public health and primary care activities for its £22M work programme from 2014-2018. Collaborations between SPH and CLAHRC in a 5-year cycle of funding include: improving health during the early years of life; developing models of care to manage the ageing population and patients with frailty (who account for a significant proportion of NHS resources); harnessing the power of large NHS data sets to develop and validate predictive models for improving chronic disease management, limiting demands on unplanned care, and improving health outcomes in vulnerable patients. The Imperial Centre for Patient Experience Research (ICPER) aims to establish a MDT centre to transform the quality of care for patients via research, innovation and translation of evidence into an improved experience for our patient population.

(ii) To create powerful interdisciplinary synergies spanning the IC, IC AHSC and the AHSN to transform healthcare through translational science, bioengineering and informatics. ICHT and IC were the first to establish an Interventional Public Health Clinical Programme closely integrated with the SPH. This visionary step has since been adopted by other acute Trusts and AHSCs which has led to innovations in translational research, integrated care and mainstreaming of Public Health. The work of this group will be fully integrated with ICHT so that public health improvement and enhancement of joint working with primary care teams becomes part of its core activity. The AHSC's strength lies in being able to draw on the critical mass of research expertise found throughout its Departments and other IC Faculties, and integrating with ICHT to deliver world class research, education and service. Such research includes major work on genetics of substantial health problems such as obesity *(Horikoshi M et al. Nat Genet 2013; 45: 76; Bonnefond A et al. J Clin Invest 2013; 123: 3037; Ichimura A et al. Nature 2012; 483: 350*), diabetes (*Kooner J et al. Nat Genet 2011; 43: 753*), red cell function (*van der Harst P et al. Nature 2012; 492: 369*) and cardiovascular disease (*Wain L et al. Nat Genet 2011; 43: 1005*). The departments hosted within the SPH are: Epidemiology and Biostatistics, Infectious Disease Epidemiology, PCPH, Genomics of Common Disease, ICTU, Neuro-epidemiology and Ageing, and eHealth. In addition the School hosts the MRC-HPA Centre for Environment and Health, and the MRC Centre for Outbreak Analysis and Modelling, as well as the World Health Organization (WHO) Collaborating Centre for Public Health Education & Training. The MRC Centre for Outbreak Analysis and Modelling, led by Prof Neil Ferguson has a major role in the analysis of spread of major outbreaks such as H1N1 and H5N1 influenza (Dorigatti I et al. *PNAS 2013; 110: 13422;* Cauchemez S et al. PNAS *2011; 108: 2825;* Cauchemez S et al. *NEJM 2009; 361: 2619; Fraser C et al. Science 2009; 325: 1072;* Fournié G et al. *PNAS 2013; 110: 9177*), malaria (*Bejon P et al. Lancet Infect Dis 2013; 13: 319;* Blagborough A et al. *Nat Comm 2013; 4: 1812*) and HIV (*Cremin I et al. AIDS 2013; 27: 447*) and powerfully informs national and international policy. The Centre works in priority areas for organisations including Public Health England, WHO and the US Centres for Disease Control, thus providing a platform for research translation into policy. The WHO Collaborating Centre for Public Health Education and Training was formally designated in 2007, and since 2008 has been located in the SPH. The Centre works closely with WHO Geneva, the 6 Regional Offices of WHO, Global Fund, the UN and other international agencies. The MRC Centre for Environment and Health, led by Prof Paul Elliott, forms a multi-disciplinary research cluster, covering a wide range of techniques and approaches. It uses advanced geographical information systems (GIS) and statistical modelling techniques, combined with experimental data, biomarker and mechanistic studies, and analyses of large population cohorts, to tackle environmental health problems of key public health and scientific importance including issues like salt intake (*Shay CM et al. Am J Clin Nutr 2012; 96, 483*), hypertension (*Ehret G et al. Nature 2011; 478: 103*), liver function (Chambers J et al. *Nat Genet 2012; 43: 1131*) and metabonomic profiling of environmental contamination (*Behrends V et al. JBC 2013; 288: 15098*). Through the Clean Air for London (ClearfLo) project, measurements are being taken at street level and at elevated sites, to develop integrated measurements of the meteorology, composition and particulate loading of London's urban atmosphere. The Dr Foster Unit at Imperial College London, led by Sir Brian Jarman, known for his work in the Bristol Royal Infirmary and Mid Staffordshire Inquiries, examines variations in quality and safety in healthcare. We build on innovative statistical and computational methods for processing large data sets. Our current studies include further development of indicators for orthopaedics, time trends analysis of diagnosis on admission in children under 10, and examination of primary angioplasty rates. The Unit aims to enhance the international system for comparing benchmarks, used by AHSCs globally. Researchers across the Population Health Theme have assembled a number of large population cohorts that include the collection of biological samples which will allow gene-association studies and/or metabonomic analyses. Interdisciplinary synergies are demonstrated through the following studies: (1) Coordinating centre for the

European Prospective Investigation into Cancer and Nutrition (EPIC) study, established in the mid 90's, led by Prof Elio Riboli, a multicentre multi-national prospective cohort study that includes 520,000 participants based in 10 European Countries containing the first very large biobank designed to investigate the role of nutrition, lifestyle and environmental factors in the aetiology of cancer, cardiovascular disease and diabetes (*Gallo et al. Neurology* 2013; 80: 829). EPIC is currently funded nationally (MRC, BHF, CRUK) and internationally (EU, WCRF and NCI-NIH) for future long term follow-up and disease specific research projects; (2) Data centre for the Northern Finland 1966 and 1986 Birth Cohort Studies, led by Prof Marjio Ritta Jarvelin and leading to a series of publications in Nature Genetics (*Soler Artigas M et al. Nat Genet 2011; 43: 1082; Speliotes E et al. Nat Genet 2010; 42: 937*) Each cohort has around 10,000 participants, followed from pregnancy to the present day. These cohorts provide unique sets of data with which to explore the origins of adult disease, and gene-environment interactions in the evolution of metabolic and CVD (*Wang T et al. Lancet* 2010; 376:180); (3) Data coordination centre for the International Collaborative Study of Macronutrients, Micronutrients and Blood Pressure (INTERMAP) study (led by Prof Paul Elliott), a multi-centre cross-sectional epidemiologic investigation designed to clarify unanswered questions regarding the role of dietary factors in the development of unfavourable blood pressure levels in adults; (4) In collaboration with researchers in cardiovascular medicine, SPH is involved in the London Life Sciences Prospective Population Cohort (LOLIPOP) study (led by Prof Jaspal Kooner), investigating the mechanisms underlying heart disease, stroke, diabetes, and obesity (*Chambers et al. Nat Genet 2010; 42: 373*); (5) AIRWAVE long-term health monitoring study on police users of radiotransmitters (led by Prof Paul Elliott), recruiting a cohort of up to 80,000 users and plans long term follow-up over the next 15 to 20 years. The study will investigate diseases e.g. cancer, CVD and Parkinson's, with sickness absence levels and trends for retirement on health grounds. The PCPH Department led by Prof Azeem Majeed is developing close integration between the AHSC and the AHSN through 3 major research projects: (1) The North-West London Integrated Care Pilot (NWL-ICO) Population Database, which will include information on up to 2,000,000 participants from NW London. This has been developed in an effective partnership between ICHT, local GPs, mental health trusts, community care trusts, commissioners, local authorities and the voluntary sector (Diabetes UK, Age Concern), to enable provision of Integrated Care. This will be extended to cover a greater range of patient groups and innovative models of joint working, e.g. Health Maintenance Organisation or Accountable Care Organisation models of healthcare delivery; (2) The NW London Urgent Care Project investigates trends in unscheduled care utilisation in the local NHS, in primary care and hospital settings in order to develop and evaluate more appropriate models of healthcare delivery, e.g. patients who may benefit from case management or cognitive behavioural therapy; (3) Optimisation of early diagnosis and management of long-term conditions through implementation of diagnostic programmes, use of informatics and new technology (such as smartphone-stored personal health records), and re-design of care pathways, including changes in professional skill-mix. SPH works with the AHSN in areas such as developing use of NHS data for quality improvement; increasing patient participation in clinical research; and delivery of evidence-based practice.

(iii) To educate and train the future generation of multidisciplinary clinical scientists capable of utilising new technologies for enhanced healthcare. The Master of Public Health and MSc in Epidemiology offer high-quality training in quantitative and applied public health research methods. The programmes provide a scientific base for research students who wish to pursue PhD programmes, and provide research training for NHS clinicians and managers. These are complemented by stand-alone courses e.g. biostatistics, data analytics, meta-analysis and systematic reviews. The Imperial GP Specialty Training Programme (Dr Josip Car) supports the development of the next generation of General Practitioners. This programme offers training for GP specialist trainees in areas such as public health, commissioning, primary care research and teaching, leadership and management. A key element is the community rotations that place trainees in local practices across NW London. The scheme has been successful in obtaining funding to support 2 Academic Clinical Fellows (ACFs) per year, in addition to nationally funded posts. The Global eHealth Unit continues to develop a series of courses utilising and developing e-learning delivery approaches. Courses are targeted at NHS, IC staff and students, with the aim of increasing knowledge in informatics, telematics and health technologies. An eHealth MSc course is being developed to recruit students by 2015. Dr Car (an Editor of the Cochrane Collaboration), following an invitation from the WHO, is to lead a state of the art systematic review of eLearning for undergraduate health sciences education and training. The anticipated report will assess the scope for and potential impact of eLearning and act as a catalyst for future work. This builds on recent experience in broad approaches to systematic reviews (*Black A et al. PLoS Med 2011; 8: 1549*). SPH is recognised for training of specialist trainees in public health, including NIHR ACFs and Clinical Lecturers, and will develop clinical academic training programmes to combine specialist training with a PhD programme. Plans include modularisation of postgraduate courses for efficient delivery, and creation of specialist programmes to deliver a skilled workforce for implementation of out-of hospital care and chronic disease management.

(iv) To translate research into new policies for the benefit of patients nationally and internationally. The Government's recent White Paper *Healthy lives, healthy people: Our strategy for public health in England* puts a focus on wellness rather than the traditional approach to "treating disease". It is congruent

with a major paradigm shift that has been occurring over the last 20 years, which has not yet permeated many aspects of practice in medicine and healthcare delivery. Internationally, the UK does not consistently perform at a top level in a number of important clinical outcomes, e.g. survival after treatment in forms of cancer, infant mortality, obesity rates, calling for improvements in prevention, healthcare delivery, and increased focus on public health. Our work programme will generate much-needed evidence through new discoveries and drive the implementation of innovative stratified approaches to community-based prevention and treatment. The comprehensive database of the NWL-PHR will provide a powerful vehicle for testing disease pathways and treatment strategies at unprecedented levels in terms of size, scope, stratification and timeliness, with close to real time data extraction and processing.

(v) To create wealth through innovation in discovery science and in population-based translation.

IP-protected innovation and its diffusion through AHSN partners will create enhanced opportunities to create wealth. Such diffusion will be substantially enhanced by the planned re-location of the SPH and elements of AHSC and AHSN within the Imperial West campus and through population database research based on needs of the population. At a time when radical health services redesign is either planned or underway, driven by the annual £20 billion financial gap in the NHS, the research evidence the AHSC generates will facilitate the development of synergistic approaches between research, clinical and commissioning efforts to improve clinical outcomes, patient experience and cost-effectiveness of care. Population-based clinical trials conducted through ICTU will also result in enhanced relationships with the pharmaceutical industry and CROs which have the potential to co-locate with the AHSC.

2.4 Description of how the proposed theme or work programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

Through the close links between ICHT and IC and the joint mission to improve population health, there will be a focus on developing new integrated models of healthcare, leading the Trust in becoming a health promoting hospital, strengthening collaboration between primary and secondary care, and encouraging care to be more preventive. The close relationship between the AHSN, SPH and the PHPC CTM creates an environment for synergy between research and service, supporting continued opportunities for evidence based medicine and translation of the latest clinically innovative and cost-effective research into patient care. A powerful feature of SPH is its strong engagement with technologies within the AHSC, providing us with powerful new tools for patient stratification in population-based care guidelines.

2.5 Description of how the theme/work programme will involve and enhance multi-disciplinary and multi-professional working.

PHPC has been designated as one of 4 enabling programmes CTMs. This supports Population Health to work across the 7 CTMs, encouraging and enabling multi-disciplinary/professional working, particularly in the development of the Programmes of Excellence (PoE). PoEs are examples of AHSC flagship services delivering excellence across a range of measures such as clinical care, research, education and championing innovation and technology transfer. Population health is a multidisciplinary specialty engaging with professionals from a range of backgrounds including clinical (medicine, dentistry, nursing, AHPs) and non-clinical (usually with a health science or environmental background) and this is reflected in our educational delivery.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work programme.

CTM Chair for Population Health and Primary Care, Prof Elio Riboli MD HonFPH FMedSci. Director IC SPH. Research effects of nutrition, obesity and reproductive life on risk of cancer and premature death.
Prof Deborah Ashby OBE PhD FMedSci. Co-Director of ICTU. NIHR Senior Investigator. Chair Medical Statistics and Clinical Trials. Research interests clinical trials, risk-benefit decision making for medicines, and the utility of Bayesian approaches in these areas.
Prof Paul Elliott PhD FMedSci. Chair Epidemiology and Public Health Medicine. NIHR Senior Investigator. Head of Department of Epidemiology and Biostatistics in the SPH at IC.
Prof Neil Ferguson OBE DPhil FMedSci. Professor of Mathematical Biology, Head Department Infectious Disease Epidemiology. NIHR Senior Investigator. Director MRC Centre for Outbreak Analysis & Modelling.
Prof Azeem Majeed MD FFPH. Professor Primary Care, Head Department of PCPH. Expert in prevention, early diagnosis, management of chronic diseases, new technology and informatics.

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

This form, together with other requested attachments must be submitted by **1:00pm on 30 September 2013**.

6. INCLUSIVITY AND DIVERSITY (2 pages)

Please provide evidence of the proposed AHSC's commitment to equality and diversity including:

- How the partnership will realise the full potential of talent from across the whole workforce including promotion of equality and diversity;
- The partnership's strategy for meaningful patient and public involvement (PPI) in the delivery of the objectives of the proposed AHSC;
- The partnership's strategy for meaningful patient and public engagement (PPE).

We recognise that the workforce of each partner is of great value to the AHSC (staff, volunteers, students). To realise the potential of talent across the workforce and to ensure that it is representative of the communities we serve and has equal access to opportunities, a **staffing mission** has been developed based on achieving excellence in the following areas: **i)** recruitment and human resources (HR) practices are fair, inclusive and transparent, **ii)** structures and processes that recognise and champion diversity, **iii)** career planning and lifelong learning for all staff, **iv)** identifying talent along the full spectrum of the translational pathway, **v)** effective use of workforce data to continuously improve the composition of the workforce at all grades and work conditions. In developing these plans we recognise the strengths and expertise of each partner and aspire to share skills and learning, and to rationalise policies and practices. The plans are central to the development of our **AHSC values** which are **Excellence, Discovery, Innovation and Equity**. We will further build upon IC's significant achievement of **10 Departmental Athena SWAN awards** and a **Silver award** at an institutional level. IC and ICHT are **Equal Opportunities Employers**, fully committed to ensuring fairness in employment through their **Equal Opportunities Policies**. Organisational commitment to equality and diversity (E&D) is further demonstrated through the following actions which seek to develop an enriched and fair culture:

i) All our managers are required to complete E&D training and utilise these skills in ensuring recruitment is based on ability. Each partner complies fully with all statutory duties through the **NHS Equality Delivery System** for ICHT, the **Academic Diversity Task Force** for IC and the **Education and Student Strategy** which sets out equality related priorities. Our policies are equality impact assessed for fairness and regular audits of practice are carried out to facilitate continuous improvements.

ii) Recognising the need to support and to empower all staff we have established a variety of mechanisms which include; **designated staff** leads at operational and Board levels; **Imperial as One** is a joint support network developed by IC and the Trust for black and ethnic minority (BME) groups which has been a key player in establishing a London-based race equality network, **Imperial 600** (Lesbian Gay Bisexual Transgender Network); IC's internal leadership programme for BME staff, **iLead,** has been very successful and supported by Higher Education Funding Council for England (HEFCE). For staff reporting a disability, we introduced the **Calibre Leadership Programme.** We also provide **Elsie Widdowson Fellowships** which allow female academics to concentrate on research on returning from maternity/adoption leave, by relieving teaching or administrative duties for 12 months. The **Ambassadors for Women Scheme** will continue to promote change and provide valuable high profile role models in science.

iii) The importance of our researchers' personal and **career development**, and **lifelong learning**, is recognised and supported at all levels. IC has implemented fully the Concordat to Support the Career Development of Researchers and was awarded the **European HR Excellence in Research Badge** in 2012. Each year, all staff are required to undertake a Personal Review and Development Plan (PRDP) and for ICHT staff an annual appraisal, both involve a two-way discussion aimed at recognising achievement, providing constructive feedback, and assisting with career development. To equip senior academic staff with the practical skills and awareness required for **organisational leadership**, IC runs the **Senior Academic Leadership Programme**. The programme is based on the National Occupational Standards for management and leadership, and is accredited with the Chartered Management Institute. The **Postdoctoral Development Centre** (PDC) offers a tailored programme of support to postdocs, helping them meet professional development needs. The PDC provides skills and career development training, a **personal development programme designed for women** and a range of individual support, including **coaching** and mock interviews.

iv) To facilitate identification of talent, succession planning, increase diversity, support retention and enhance our overall performance, capacity building of middle leaders is delivered through selective and **targeted talent development programmes**; the **Management Training Scheme, Horizon and Pegasus** developed in partnership with our **Business School**. In particular we have developed bespoke programmes in support of the Trust's organisational restructuring, including an **Introduction to Management** through to courses for senior leaders and Board members**.** In recognition of the need to increase the numbers of staff with protected

characteristics in gaining promotions, we introduced **grade specific development programmes** and will continue to run **focus groups** allowing discussion and action planning to further promote equal access to career progression. Our involvement in the **CRICK Institute** provides exceptional opportunities to promote new and emerging talent in translational medicine.

v) We are committed to further utilising **workforce data** to identify priority areas of imbalance across our workforce, be this in relation to ethnic composition, profiles of senior leaders, success in awards and promotions and to monitor experiences related to job satisfaction, reports of harassment and bullying. To this effect we intend to further improve data quality and completeness and increase its use in planning processes and as measures of success in developing the workforce of the future.

In developing our plans for **patient and public involvement and engagement (PPI/PPE)** we have drawn on our expertise, achievements and resources, notably ICHT and IC initiatives and a track record in working with patient and healthcare related groups including: Prof Roger Kneebone's work as the **Wellcome Trust Engagement Fellow** adds expertise to our enabling programme in the **Centre for Translational Medicine for Patient Safety and Experience** alongside the work of Prof Helen Ward, Head of the **Imperial Centre for Patient Experience Research (ICPER)**, in the School of Public Health (SPH), the ICHT's stakeholder engagement plans as part of the Foundation Trust process, the NIHR funded **Centre for Patient Safety and Service Quality (CPSSQ)** and the AHSN and the **Collaboration for Leadership in Applied Health Research and Care (CLAHRC)** which adds considerable value through skills and knowledge in related methodologies and evaluation processes e.g. their contribution to the Public Involvement Impact Assessment Framework and Guidance to Assess the Impact of Public Involvement in Research (PiiAF). Our plans are strengthened by the inclusion of best practice including the work of **NIHR INVOLVE**. The AHSC strategy places patients as central to all we seek to achieve and will be supported by the development of meaningful and effective involvement and engagement of all stakeholders. In order to achieve this we will;

i). Develop and evaluate processes to support inclusion of the patient (and carer) voice in all AHSC core business: We will deliver training to support PPI**/**PPE with ICPER and in association with the CLAHRC to develop skills including qualitative research. We will set standards for each of the BRC Research Themes and the Centres for Translational Medicine (CTMs) in conjunction with **Imperial Clinical Trials Unit (ICTU)** such as: representation on advisory boards; patient feedback systems on research, design of data collection processes and research accessibility; clear policies for the dissemination of results including reporting back to participants, contributors and others. We will continue to develop close collaborations with research teams and patient representatives from charities including the Kidney Patients Association and the British Liver Trust. ICHT will continue to provide 'i-Care' training which centres on attitudes, behaviours and communication to support PPI/PPE and will evaluate its effectiveness.

ii). Ensure that patient activation is supported within pathways and models of care We aim to capitalise on the growing knowledge base which proposes a relationship with patient knowledge and participation in managing their own health and care and improved outcomes. Through the work of our enabling programme for Patient Safety and Experience, chaired by Professor Charles Vincent and Dr Chris Harrison, Trust Deputy Medical Director, we will develop processes designed to increase patient involvement in disease specific groups including chronic conditions and services for older people. We will seek to adopt patient-led peer education projects for symptom management and use the model of a research involvement group which was set up by the **NW London Diabetes Research Network** to help people with diabetes and members of the public get involved in their activities. Through our relationship with the AHSN we will share the learning from these initiatives with a view to possible wider adoption.

iii). We are developing a research programme to better understand the process by which PPI/PPE initiatives influence research, and whether patient involvement in research improves their experience and outcomes. This programme is being developed in partnership with the 3 London BRCs. We will enhance the sophisticated patient feedback mechanisms that have been developed by ICHT, in association with the **Dr Foster Unit** we will seek to understand differences in the patient experience for planned and unscheduled care, at night and at weekends. We will utilise the early findings of our **Health Foundation** funded work stream exploring the relationship between staffing and safety and experience, and will further engage with our Business School and SPH in developing high impact interventions to improve patient experience.

iv). Further develop an understanding of AHSCs and extend engagement in our activities
We will continue to use a multi-method approach to increasing the understanding of the AHSC's purpose and objectives with staff, patients, public and stakeholders. Underpinning our PPI/PPE plan is our pledge to inclusivity, equity and valuing the diversity of our patients and population. We recognise that certain groups or characteristics within stakeholders may affect levels of involvement and engagement and we will tailor our work to distinct needs and approaches. The CTM local Boards include a requirement to involve relevant

stakeholder membership, thus providing involvement and engagement in all aspects of strategic developments, matching stakeholders and constituent parties for maximum impact. A scoping exercise on stakeholders forms the basis of our communication plan to support the AHSC strategy. We will continue to deliver a wide range of stakeholder events e.g. BRC public presentations, workshops and NIHR Showcase Events, IC Festivals, Science Festivals, CLAHRC Collaborative and Learning Delivery events, CTM public engagement programmes, FT Membership activities, and various social media initiatives.

7. CONTRIBUTION TO ECONOMIC GROWTH (2 pages)

Detail of the proposed AHSC's strategy and ambition for contributing to economic growth including:

- The track record of the partnership to contribute to economic growth and the economy, including through improved health outcomes and through collaborations with industry;
- The strategy for how the proposed AHSC will contribute further to economic growth and the economy together with plans to measure this contribution;
- The plans and strategy for identifying, managing and exploiting intellectual property, including the track record of patents filed and granted, the establishment of spin-out companies and income generated from the commercialisation of intellectual assets.

The AHSC has a **strong track record in contributing to both economic growth, and improved health outcomes** through research and exploitation of derived IP, collaborations with industry, (pharmaceutical and biotechnology, medical devices and technology-based), innovative health education and training programmes, use of technological advances and informatics, development of the international brand in education, research and patient service, and our contribution to global health through international partnerships and the IC Institute for Global Health Innovation (IGHI). Engagement with industry is underpinned by **our rich research base, clinical networks, and primer fund portfolio** (through corporate level interaction, strategic co-investment, and person-to-person engagement) and has fostered fertile collaborations**.** Such relationships have been further exemplified in major pharma purchasing IC start-up companies (e.g. Merck with Thiakis and J&J with Respivert). Recent examples of corporate level interactions include **Johnson & Johnson** engagement via the **J & J London Innovation Centre**, **Astra-Zeneca (AZ) External Discovery Partnerships Initiative** to deliver joint AZ/IC high throughput screening projects in 2013 and the **Pfizer, £2.3M respiratory collaboration.** A notable example of improving health outcomes in partnership with industry and generating wealth is the introduction of anti-TNF agents which has profoundly changed the management of severe rheumatoid arthritis and which were developed from the first clinical study at Charing Cross Hospital; over 1m patients have received treatment and the global sales of the 3 licensed TNF inhibitors amount to over $9b.

Over the next 5 years, our strategic focus will be on enhancing physical and human infrastructure, programmes and processes to respond to industry need, effectively marketing our existing strengths and supporting staff to engage strategically and successfully with pharma and more widely with industry. Our strategy includes the **establishment of a globally-leading biomedical quarter at Imperial West,** outlined in **Section 3,** with significant capacity to contribute to the national health and wealth agenda. This hub will act as an anchor for industry, businesses and universities in the UK and beyond. It represents investment in the **local regeneration** of the White City area, providing homes, jobs, accessible green space, pedestrian subways and leisure and retail facilities. **Our objectives for economic growth and health improvement** align to existing and developing infrastructure and include the following: **(i)** to review and benchmark the AHSC portfolio in areas of interest to industry and explore new potential development areas such as cell-based therapies and stem-cell research through the work of the Centres for Translational Medicine (CTMs) and collaborations e.g. with Birmingham University, **(ii)** to continue the support of rapid trial initiation and delivery of studies to time and NIHR performance benchmarks, **(iii)** to continue to build alliances with MedTech/equipment manufacturers and develop pro-active proposals to pharma in which our expertise matches Industry strategic intent, **(iv)** to work with the AHSN to capitalise on UK government funding to encourage private/public sector collaborations and to disseminate innovation in the community, **(v)** to work strategically through pan-London consortia such as **AHSC Executive** and **London Life Sciences** together with **Global Medical Excellence Cluster (GMEC)** (capturing the South East) to maximise economic impact, **(vi)** to diversify the provision of educational programmes through the **Health Science Academy (vii)** to support cost-effective out-of-hospital delivery programmes, educate and engage staff on industry needs to ensure our patients have access to newly developing therapies, **(viii)** to explore options to increase the market share of specialised services as AHSC flagship clinical services, **(ix)** to extend our economic global reach, building on the educational and research innovation introduced in Singapore and clinical treatment centres and Biobanks in Abu Dhabi and Qatar respectively.

Successful partnership with industry remains key to realisation of effective development and distribution of many of our discoveries, and to maximise economic and societal impact through translation. **IC is one of the most successful universities in the UK for securing research funding from industry**. Research funding from UK based industry was £18.9m in 2012, a growth of 3.8% over 2011. Our engagement with industry involves supporting rapid trial initiation and delivery of studies to time and target. Research funding from industry outside the UK in 2012 was higher, at over £20.7m (Higher Education Statistics Agency), emphasising the **international reach** of our expertise. **ICHT total research income** was £49.2m in 2012/13 (ICHT annual report 2011/12) and **income from commercially sponsored clinical** studies has doubled from 2011/12 to more than £4m. During 2012/13, ICHT hosted more than 700 individual studies (commercial and non-commercial), including the population-based COSMOS study (47,000 patients and healthy volunteers recruited), which has enabled the NW London Comprehensive Local Research Network (LCRN) to become

the highest performing Network in the UK. ICHT was top in the recruitment of patients to portfolio studies in 2011/12 (Guardian Portfolio Activity League Table, June 2013). The breadth of our on-going AHSC collaborations with industry for 2012-13 covered **Pharma**: 40, **BioTech**: 10, **MedTech/Devices**: 4, **Diagnostics:** 2. The number of other collaboration agreements and Non-Disclosure Agreements **(NDAs**) signed with industry 146. We have extended our reach to development of **substantial international relationships** with the potential to create value-added opportunities e.g. the partnership with NTU in Singapore to create the LKC School of Medicine, IC Diabetes Centres (increased to 3), Abu-Dhabi and a Bio-bank, Qatar.

Specific industry collaboration objectives are embedded within all BRC Theme delivery plans. In 2012/13 the **BRC supported 115 new strategic industrial collaborations,** to the value of £15.3m. To further broaden translatable research, we established an **Imperial BRC/Innovations Fund** which supports pump-priming of basic research towards clinical application. The success of this initiative allowed us to leverage the MRC **Imperial Confidence in Concept Scheme** (ICiC), which gives devolved funds to universities (£700,000 to IC); ICiC currently supports 15 projects (£1.3M). The excellence of projects emerging from our schemes has led to **considerable interest and engagement from industry** (MoU signed with **AZ** for access to all ICiC proposals). Our innovative development alliance with Waters Corporation and Bruker Spectrospin GmbH through the Department of Surgery and Cancer has provided the **Imperial Phenome Centre** with **£20m** for high-spec equipment and staffing to support programme development and training programmes. The collaboration includes a strong training element and joint working on data, analysis, integration, visualisation and interpretation. This alliance is expected to extend internationally with a further £5m allocated to provide a complementary metabonomics facility with new capacity in Singapore which will aid knowledge sharing and dissemination. Our **joint initiatives in computer science, systems medicine/biology, epidemiology, biostatistics, e-Health and medical bioinformatics** with collaborations spanning the FoM, FoNS and FoE have successfully generated income. Highlights include the work of Prof Chris Toumazou that has developed several spin out companies including DNA Electronics Ltd, Toumaz Technology Ltd.

Within the AHSC formal structures, there are a number of specific enablers of economic growth. The **Joint Working Agreement (JWA)** sets out the approach and processes to **identifying, managing and exploiting IP**. Each of the partners has a **nominated lead** individual responsible for IP and an **IP Committee** which meets to review on-going IP matters, activity data, revenue sharing and to communicate successes and identify new opportunities. IP capable of commercial exploitation, subject to the involvement of any third party contract, will be owned and exploited by IC through its **commercialisation partner**, **Imperial Innovations Limited.** Disputes are handled through an independently chaired **IP Arbitration Committee** reporting to the **JEG.** Our plan is to make a strategic contribution to knowledge management, IP and value added to UK growth through: **(i)** Generate income from commercialisation of IP under a revenue share relationship and in the case of IC as a shareholder, to inventors through direct payments, **(ii)** Realise benefits for the wider economy by supporting small businesses, generating employment, training opportunities and transferable skills for students and staff and delivering benefits to healthcare, **(iii)** Further champion and celebrate innovation by developing closer links with commercialisation staff and ICHT/IC staff in order to assess market opportunities in high value/high patient benefit areas, **(iv)** Continue to provide educational sessions in innovation and technology transfer and promote the benefits of commercialisation of assets via a dedicated website, a single innovation portal and through local roadshows, **(v)** Encourage greater commercialisation of NHS led IP through a designated NHS IP manager post within Imperial Innovations, who will support the growth of an entrepreneurial environment within the AHSC and further develop links with the AHSN.
IC has produced **more spin-out businesses than any other UK university**, 142 since 2006 and Imperial Innovations have invested £120m into spinouts which have successfully gone on to collectively raise £370m. The spinout portfolio currently stands at 555 patent families; £22m generated in licence and royalty income; and funding for more than 80 early-stage proof of concept projects. In 2011, Imperial Innovations raised £140m to invest in businesses built on IP developed at and associated with IC, Universities of Cambridge and Oxford, and University College London (UCL). More recently, the company received a £30m 12-year loan from the **European Investment Bank** to specifically invest in Biotech and Therapeutics. One example of particular relevance is an investment by Imperial Innovations of £2m in Abingdon Health, which led to a £3m funding round from other investors. Abingdon Health is focused on commercialising a portfolio of novel clinical diagnostics technologies and they have acquired a controlling stake in the complementary IC spin-out company, Molecular Vision.
The **AHSC IP metrics 2008-13 :** 655 **invention disclosures** received (includes ICHT IP and student IP), 86 **new priority patent applications filed** (with 313 patents pending), 11 **patent applications** successfully proceeded to grant, 7 **spinout companies** formed, 19 **licence deals** signed and >£180k **income generated from licensing**. AHSC projects/IP assets managed by Imperial Innovations over this period received >£34m of **translational funding and Proof of Concept funds**. 76 **grant applications** were supported directly by Imperial Innovations across the ASHC, and 71 **non-disclosure agreements** were entered into by Imperial Innovations for the purpose of industry engagement, of which 58 are still in effect.

As **Lead Provider of Medical Postgraduate Education and Training** in NW London and through our further development of the **Imperial GP Speciality Training Programme**, **Health Science Academy**, schemes such as the **Chain Florey Fellowships** and partnerships with the **Centre for Cancer Research UK** and the **CRICK Institute**, we will develop new models of education and training enabling the diversification and increase of income streams related to education.
Economic impact and improved health outcomes are measured through a series of KPIs within the **AHSC scorecard** (R&D, clinical trials, innovative educational initiatives, industrial collaborations) and are reported quarterly to the **JEG** and **SPB** as part of its performance scorecard.

8. STRATEGIC PARTNERSHIPS & WORKING WITH NIHR-FUNDED RESEARCH INFRASTRUCTURE (2 pages)

Detail of the proposed AHSC's strategy for building meaningful external partnerships including:

- The strategy for linking with NIHR-funded research infrastructure, e.g. Biomedical Research Centres or Units, CLAHRCs, Healthcare Technology Cooperatives, Diagnostic Evidence Cooperatives and Clinical Research Network;
- Other existing strategic partnerships, and the strategy to develop new partnerships, that will enhance the delivery of the proposed AHSC's objectives.

One of the key goals of the AHSC strategy is to **'utilise the research strengths of IC combined with the critical mass of ICHT to enhance healthcare for patients and populations**'. Our strategic plans to link NIHR infrastructure are based on the work of the **Joint Research Office (JRO), ICHT, AHSC and AHSN Research Committees** as the primary vehicles that facilitate linkages between the University and NIHR-funded research infrastructure (outlined in **Section 9**) and enable this to effectively operate to ensure appropriate leverage and exploitation for maximum impact. The recently funded **Local Clinical Research Network (LCRN)** will be incorporated into the AHSC and AHSN governance structures and will benefit from the strategic alignment of other NIHR support infrastructure. NW London has one of the highest concentrations of the full range of research and innovation organisations in the UK, supported by a substantial number of **NIHR Initiatives** hosted by the AHSC or IC as the lead University. We have developed systems, processes and networks to work towards a goal of utilising research and education to improve patient care and outcomes, and will enhance these strengths as the partnership moves forward over the next 5 years.

Our **linked NIHR infrastructure** includes the following centres, units and awards: **(i) NIHR Biomedical Research Centre (BRC):** Our integrated strategy is exemplified of the award of £112m for 5 years (2012), the single largest BRC award. We aim to channel excellence in translational research towards improvements in patient care and patient outcomes through the BRC which covers our 5 hospitals and the multiple sites of IC. There are **21 research themes**: Biobanking, Cancer, Cardiovascular medicine, Gastroenterology and Hepatology, Genetics and Genomics, Haematology, Imaging, Infection, Neonatal Medicine, Neuroscience, Obesity, Diabetes, Endocrinology and Metabolism, Paediatrics, Population Health Laboratory, Renal Medicine and Transplantation, Respiratory disease, Rheumatology, Stratified Medicine, Surgery and Surgical Technology and Women's Health. Research led by the BRC strives to achieve wider impacts; saving more lives, improving quality of life, creating a more productive workforce and leveraging economic benefits to the UK. We are working with the 5 largest BRCs to deliver the **Chief Medical Officer's** clinical informatics '**Grand Challenge'**. Phase I-III clinical trials are coordinated through ICTU operationally within the SPH, accredited with the UK Clinical Research Collaboration. We have recognised expertise in primary and community care research through Prof Azeem Majeed in the SPH, who co-leads the NIHR London Research Design Service and we intend to substantially expand our capacity in this area through the recruitment of senior academic clinicians with expertise in population-based interventional strategies. **(ii) NIHR/Wellcome Trust (WT) Imperial CRF** (formerly named the Sir John McMichael Centre), based at Hammersmith Hospital is the main clinical research centre at ICHT. Funding from the WT and NIHR allowed expansion of the original centre and a move to the new ICTEM building (February 2012). It provides a safe environment for research and comfortable clinical accommodation for healthy volunteers and patients taking part in studies, **(iii) NIHR/MRC Phenome Centre** the first of its kind in the world, is a high throughput, quality controlled analytical facility for large scale metabolic research. The centre opened in April 2013 and will deliver broad access across the UK to world-class metabolic phenotyping to accelerate the translation of medical discoveries into better healthcare. This now provides us with unique opportunities to decipher the interaction between environmental exposure signatures and the genetic basis of common diseases. In the long-term, this will lead to better diagnostic tests and stratification approaches that will benefit the whole UK translational medicine community. The centre is led by IC and Kings College London (KCL) and is funded over 5 years by an investment of £5m each from the MRC and NIHR, and £20m from Bruker and Waters Corporation. A complementary facility is now planned at our partner location NTU Singapore, **(iv) The NIHR Diagnostic Evidence Cooperatives for point-of-care testing (POC)** is focussed on how evidence generated from POC tests will reduce the lead time for adoption into clinical practice and thus realise early benefits from clinical trials and provides direct patient benefit facilitating more care into the community settings, **(v) The NIHR BioResource** is an umbrella organisation borne out of our partnership with five other NIHR BRCs, BioResources and industry (IC, Cambridge, Guy's and St Thomas', South London and Maudsley, Oxford, UCH, and the Leicester Cardiovascular BRU). It represents an integrated central database with well characterised subpopulations and, by collaborating across BRCs, our researchers can target specific patient groups for focussed research projects. **The NIHR Centre for Rare Diseases** is a key and integral part of the BioResource and is funded for the clinical application of next generation sequencing techniques, **(vi) The West London Collaboration for Leadership in Applied Health Research and Care (CLAHRC)** is an essential member of the Joint Steering Group with the AHSN and AHSC. We intend to build on our initiatives with the CLAHRC, for example developing care pathways for children with allergies (Itchy, Sneezy, Wheezy),

with facilitation by the AHSN to identify new joint projects and further opportunities to work together and with other regional and national CLAHRCs, enabling Trust patients to benefit from early involvement in new, improved services. **(vii). The NIHR Patient Safety Translational Research Centre at ICHT** including the **Centre for Patient Safety and Service Quality (CPSSQ),** is 1 of only 2 NIHR funded centres in the country specialising in patient safety, providing essential infrastructure for developing new external partnerships to address safety related challenges across organisations and health sectors, is strongly embedded in our **enabling programme of Patient Safety and Experience** bringing together CPSSQ leaders, CLAHRC, clinical researchers, engineers, clinicians and healthcare managers, **(viii) The IC Experimental Cancer Medicine Centre** (ECMC) is part of the ECMC network across the UK and is jointly funded by CRUK, NIHR in England and the Departments of Health for Scotland, Wales and Northern Ireland. IC ECMC specifically aims to develop novel imaging, biomarkers and therapeutic approaches for cancer, with a particular focus on reversing drug resistance and aiding stratified treatments. Other areas of expertise include metabolomics and epigenetics, **(ix) Clinical Research Networks;** As hosts and participants of numerous networks we play a vital role in bringing together clinicians, researchers and academics to further accelerate the translation of research into practice and to identify and address areas of unmet health need. We intend to build on our extensive experience in regional networks and national networks; e.g. the Polypill - The UMPIRE Clinical Trial published in JAMA (Thom S et al. JAMA 2013; *310,918-929)* led by Prof Thom, NHLI at IC, is one example of a portfolio trial of the Diabetes Research Network, **(x) Local Clinical Research Network (LCRN):** ICHT was recently awarded (Sep.2013) hosting arrangements of the LCRN, supported by the AHSN, North West London Hospitals and Royal Marsden Hospital, (RMH). The network will increase opportunities for patients to take part in clinical research, and will be responsible for ensuring that studies are carried out efficiently. It supports the Government's Strategy for UK Life Sciences by improving the environment for life-sciences research. The **LCRN Executive Committee** includes representation from across the research community with the **AHSN Partnership Group** acting as the driving force for collaboration across the region. We will continue to work closely with the **Respiratory and Cardiovascular BRUs** at the Royal Brompton, primarily through our disease-equivalent Themes, **shared appointments and membership of the AHSC Research Committee**.

In addition we will continue to seek to utilise and enhance the specific **pan-BRC collaborations,** including **CHERUB**, the pan-BRC HIV eradication consortium including the MRC "REACH" trial; the pan-BRC health informatics consortium (NHIC) which includes 5 projects, in acute coronary syndrome (Lead, J Chambers, IC), viral hepatitis (Lead, Oxford), transplantation (Lead Kings), ovarian cancer (Lead Cambridge) and critical care (Lead UCL), and an MoU to work on fatty liver disease and fibrosis with Oxford, Cambridge, King's and UCLH on the NIHR BioResource. The **RMH/ICR BRC** has partnered the MRC IC Confidence in Concept (ICiC) application and will invest directly in the Imperial Joint Translation Fund in order to promote RMH/ICR staff collaborating with IC in discovery science, particularly in Engineering and Natural Sciences. We will further synergise our relationship with the **RMH and ICR** and work to enhance complementarities, improve patient care, and build capacity in translational medicine in cancer. The work of the **IC Bio-Bank** will further develop collaborations with the pan-BRC BioResource and associated sub-groups on infection and immunity, cardiovascular, neurosciences and rarer diseases. Our approach to working with the **Healthcare Technology Cooperatives (HTC)** to develop new devices, technologies and interventions is based on building relationships directly between clinical academics in areas of great synergies such as with the University of Birmingham in their HTC for brain trauma and the Cambridge HTC for brain injury.

Other strategic partnerships that enhance the delivery of the AHSC objectives within London include;

(i) The Global Medical Excellence Cluster (GMEC): a major opportunity for collaborative research working across London and incorporating Oxford and Cambridge, which has served as the vehicle to develop common legal positions to facilitate negotiations with external bodies such as Higher Education Institute, leading to the creation of the **Imanova Imaging Consortium** and the consortium for the **Rare Diseases Initiative (Pfizer)**. **(ii)** The **London AHSC Executive,** involving the London AHSN's has the potential to be the main vehicle to bring together London's AHSCs and AHSNs, coordinating strategic clinical services and associated clinical and translational research for patient benefit, including improvement science, CLAHRC related activity and the strategic educational agenda. It will influence both national and local policy with regard to the translational agenda for London. Together with its "subsidiary", **London Life Sciences,** it has served as a mechanism for integrated AHSC operations, creating and communicating a coherent identity for the life sciences regional community complementary to the **MedCity** proposal of the Greater London Authority to national and international audiences, providing a knowledge interface with industry and academia.

(iii) The CRICK Institute: A high powered collaboration to carry out translatable science in biomedical research and working with HEI partners and AHSCs to find new ways to diagnose, prevent and treat a range of illnesses. IC is financially committed to the CRICK and is represented at all levels within the governance structures. It is expected that there will be a strong working relationship between the CRICK and AHSC, with an emphasis on multi-disciplinary research, fostering emerging talent and novel partnerships. We are committed to placing senior clinical academics into the CRICK, with a clinical base in the AHSC, to developing the careers of younger researchers through PhD studentships or secondments, and to collaborating in biomedicine, engineering and physical sciences to generate new knowledge for the benefit of

human health. **(iv) Institute of Cancer Research (ICR):** IC-ICR MoU, 2012, to develop a **Centre for Systems Oncology** to jointly recruit senior academic positions to develop strategic academic collaboration across a range of disciplines. **(v)** We have extended our **international partnerships** with the opening of the **School of Medicine in Singapore (Aug. 2013).** The innovative medical curriculum is expected to change the education system at IC with broader implications across NW London. We are further developing a global profile in areas such as **Diabetes Treatment Centres**, **Abu-Dhabi**, **Biobank** and **cancer services in Qatar.**

9. WORKING WITH THE NHS ARCHITECTURE (2 pages)

Please describe the proposed AHSC's strategy for engaging with the wider NHS architecture including:

- The strategy for ensuring that:
  - the AHSC is fully nested within the relevant local AHSN;
  - that there is integrated working with the local AHSN, emphasising the complimentary roles of AHSCs and AHSNs;
  - there is appropriate co-working with other AHSNs nationally to deliver improved outcomes for patients and the NHS.
- How the proposed AHSC will engage with primary, secondary and tertiary care sectors, NHS commissioning organisations and social care providers to improve outcomes for patients;
- How the proposed AHSC will work with other AHSCs to improve outcomes for patients and the NHS.

The AHSC is tightly nested within the AHSN and our aligned strategic vision provides for clarity in the roles of the AHSC and AHSN across a continuum of research from discovery science to implementation, dissemination, evaluation and impact. Within this relationship, the AHSC largely, but not exclusively focuses on discovery science and early stage translation (T1-T2) with the AHSN focussing on larger–scale knowledge mobilisation and delivery of evidence based practice into healthcare through dissemination, adoption and diffusion across the partner organisations and beyond (T2-T4). This process is further supported by the **Collaboration for Leadership in Applied Health Research and Care (CLAHRC)** and the **North West London Local Clinical Research Network (LCRN)** at ICHT.

In 2012, IC and its clinical and primary care partners in NW London established a **limited company** with the primary objective of operating as an AHSP, enhancing research and disseminating the benefits of research to patients across the partnership. This partnership comprises (Central London Community Healthcare NHS Trust, Central NW London NHS Foundation Trust, Chelsea and Westminster Hospital NHS Foundation Trust, Ealing Hospital NHS Trust, Hillingdon Hospitals NHS Foundation Trust, NW London Hospitals NHS Trust, Royal Brompton Hospital and Harefield NHS Foundation Trust (RBH), Royal Marsden Hospital (RMH) NHS Foundation Trust, West London Mental Health NHS Trust and West Middlesex University Hospital NHS Trust. Within this membership, IC and ICHT have well established collaborations with a number of organisations such as RBH and Ealing in relation to cardiovascular research, Chelsea and Westminster in relation to infectious diseases with the largest European HIV cohort, and future plans to establish two professorial appointments with the Mental Health Trusts.

In December 2012, **Imperial College Health Partners (ICHP)** was successful awarded the hosting of the AHSN, now embedded in this organisation. Both partners of the AHSC are formal members of the ICHP and since the award of the AHSN have taken formal steps to strengthen the necessary relationships for knowledge generation and dissemination. The **AHSC Joint Executive Group (JEG)** includes the **AHSN Managing Director** who is a contributor to the AHSC strategy and the associated work programmes of the CTMs which ensures that they reflect AHSC and AHSN priorities. The **Dean of the FoM**, Chair of the JEG and **ICHT CEO** are AHSN Board members. In addition the AHSC Director is in attendance. The **AHSC Research Director / Vice Dean of Research FoM** is Chair of the **AHSN Research Committee**. Within this committee there is already broad representation from many of the Healthcare Trusts in NW London including RBH and RMH.

This governance framework ensures that new approaches in research, education and innovation are strategically aligned and prioritised, and provides a systematic and strategic approach to translation research, innovation and adoption. A **Joint Strategic Annual Planning Round** identifies discoveries from the AHSC to be taken forward by the AHSN and CLAHRC and a feedback loop on emerging areas of need/gaps which can be addressed by the AHSCs focus on discovery science. **AHSN Chair, Professor the Lord Ara Darzi** is a Vice Dean at IC, Consultant surgeon at ICHT and Chair of CTM Surgery and Technology, Cancer and Haematology, facilitating close collaborations between service, research, AHSN and AHSC relationships.

The **School of Public Health (SPH)** at IC contains within it two MRC Centres, **MRC-HPA Centre for Environment and Health**, and the **MRC Centre for Outbreak Analysis and Modelling,** a Wellcome Trust PhD programme, and has substantial expertise in combining world-class research at local, national and international level with translational work within the IC AHSC. Together with its research, teaching and evidence-led policy work, SPH addresses the major public health challenges of the 21st century. An example

is the current research across the AHSC and AHSP, co-ordinated by Prof Paul Elliott and Prof Jaspal Kooner, funded by Framework Programme 7 (FP7), examining the relative contributions of data obtained through joint metabonomic/genomic profiling to cardiovascular risk. We see the SPH as a **key enabling capacity linking AHSC and AHSN** in the future in a number of ways. **(i)** We intend to appoint 2 chairs in Public Health focussed on health interventions to be nested within the AHSN for delivery of research led health interventions with the potential to be coupled to genomic and metabonomic stratification. **(ii)** The Imperial College Trials Unit (ICTU) within SPH will expand to be the vehicle for clinical trial dissemination across the network. **(iii)** We intend to create a new physical hub for the SPH at the Imperial West campus, encompassing ICTU providing a co-location hub for AHSC and AHSN with emerging innovation in NW London.

In **working with other AHSCs,** we will continue to identify collaborations to improve health and which play to the strengths of the AHSC, utilising our capacity and capabilities in areas such as genetics and genomics, biomedical engineering, highly advanced imaging and access to and analysis of large data sets supported by clinical informatics – examples of which are contained in **section 8**.

We provide 3 clear examples of **joint AHSC working: (i)** The **MRC-NIHR Phenome Centre** (Prof Nicholson), a collaboration between IC and KCL, is a national resource which provides services to researchers throughout the UK, offering fast, efficient and high-quality analysis of phenomes to support personalised medicine for patient benefit, **(ii)** The collaboration with **Centre for Infection Prevention Management (CIPM),** with Cambridge and St. Georges, funded by the UKCRC Translational Infection Research Initiative (TIRI), promotes high quality collaborative multi-disciplinary research addressing national research priorities in the field of preventive medicine in microbiology and infectious diseases, **(iii) Imanova** represents a unique collaboration between ICL, UCL, KCL and the MRC providing state of the art radiochemistry and imaging facilities on the Hammersmith Hospital site to support generation of new tools with the capacity to shorten the clinical trial process for our patients. In addition, we will continue to work with the aspirant AHSC's e.g. **University Hospitals, Birmingham** and associated BRU, in sharing technology around cell based therapeutics and metabolomics and in innovative training programmes and collaborate with the KCL led Cell Therapy Catapult. We are actively discussing collaborations around clinical informatics with **Oxford University Hospitals NHS Trust** with the potential joint catchment population of c. 5m.

We view engagement with primary, secondary and tertiary care sectors, NHS commissioning organisations and social care providers as crucial to improving care for patients. We will build on our existing links, identify areas for new collaborations and align these endeavours with the Trust's developing clinical strategy which sets out the defining services as: cardiovascular, cancer, emergency services and obstetrics and gynaecology. Examples of specific areas include improving cancer services by working with other education leads, the **Imperial Centre for Patient Experience Research (ICPER)** and our developing relationship with **RMH,** to further improve the trainee experience and increase patient satisfaction, building on strong clinical outcomes to develop new innovative patient pathways and models of care across sectors. Through the work of SPH we are able to support focused interventions to improve health outcomes in challenged areas, for example in seeking 'pioneer status' for the **Integrated Care Organisation within NW London** and in seeking to develop "academic" GP's**.**

We also work closely with the **Clinical Commissioning Groups** (**CCGs)** within NW London in the Shaping a Healthier Future (SaHF) plans in which hospital partners, CCGs, AHSC and AHSN are planning future healthcare in the NW London catchment area. Through regular planning meetings, we are constructing a strategy based on out-of hospital care and new referral patterns to reduce hospital admissions through A&E and develop new patterns of referral and integrated care pathways. CCGs are also members of the AHSN and have worked with us in developing and testing scenarios regarding service reconfiguration in NW London. We anticipate that the engagement of CCGs in the AHSN, coupled to the development of evidence-based pathways though the SPH and ultimate integration of informatics platforms will transform our capacity to generate evidence-based care in NW London. In addition we will develop a **Child Health General Practice Hub Framework** to deliver better out-of-hospital care across a broad spectrum of paediatric conditions. Successful further development of **integrated care pathways for adult patients with chronic disease** will involve **(i)** establishing digital links with primary care through our IT strategy, **(ii)** education of medical and allied health professionals (AHP) in principles of effective healthcare delivery, and **(iii)** effective patient education programmes. We will work closely with CCGs to deliver programmatic approaches in a cost-effective way within an appropriate funding structure. Such delivery is key to the AHSC, as it is absolutely essential for effective reconfiguration of services and physical infrastructure within ICHT. We are committed to further developing relationships with **NHS England** and local **CCGs** and view the AHSN and SPH as playing pivotal roles in developing health prevention strategies and population–based innovations with these partners. ICHT is a member of the **Shelford Group,** which comprises leading NHS multi-specialty academic healthcare organisations, including several AHSCs/AHSNs. We intend to utilise this forum to further develop the profile and impact of AHSCs in improving healthcare. We will build on our membership of the **pan-London Clinical Senate** to collaborate on sector-wide issues. Our membership or hosting of numerous **cross-sector partnerships and clinical research networks** enables us to use these as building blocks to continue to establish new collaborations.

10. INTEGRATION OF RESEARCH, HEALTH EDUCATION AND PATIENT CARE (3 pages)

Detail of the proposed AHSC's strategy over the next five years for the furthering integration of research, health education and patient care including:

- Evidence that the partnership's ability to translate discoveries from basic science into excellent translational, clinical and applied research, and into benefits for patient health and improved health outcomes. Please provide 5 examples from over the past 5 years;
- A description of how the partnership will achieve further integration of research, health education and patient care over the next 5 years as an AHSC;
- How this increased integration will lead to improvement in research, health education and patient care;
- The partnership's vision and strategy for maximising the impact that multi-disciplinary and multi-professional working across the AHSC;
- Details of the partnership's close working with the Local Education and Training Board and how this will further the aims of the AHSC.

We have been successful in establishing and renewing the **infrastructure** essential for producing high quality discovery science, enabling rapid access to clinical trials and furthering synergistic collaborations which support translation and increase the ease with which discoveries translate to both health and education benefits. Specific examples include the **JRO and JRCO, the MRC-NIHR Phenome Centre**, **ICTEM,** the UKCRC registered **ICTU** which delivers world class clinical trials of all phases at national and international levels, the **Surgical Innovation Centre** and **Imanova** (all outlined in previous sections). We present **5 examples of discoveries in basic science that have resulted in improved patient care and outcomes.** Encompassing drug discoveries and surgical innovations the **examples** have each had a national or international impact in clinical practice;

1. Reduction of colorectal cancer (CRC) incidence rates by mass screening once-only flexible sigmoidoscopy (FS). In the English Bowel Cancer Screening Programme (BCSP) randomised clinical trial, Prof Wendy Atkin demonstrated reduction of CRC incidence by a third and mortality by 43%, 11 years after a single FS screening, hence predicting prevention of 5,000 CRC diagnoses and 3,000 deaths in the UK each year. FS screening was approved by the UK National Screening Committee in 2011 with a roll-out of the pilot programme in March 2013 with the aim of achieving 30% coverage by 2014, 60% by 2015 and full coverage by 2016. **(NICE Clinical Guideline 2011** Colorectal cancer: the diagnosis and management of colorectal cancer. **NHS Bowel Screening Programme, 2012** Piloting Flexible Sigmoidoscopy, Advice to the NHS and bidding process. **EU Guidelines for quality assurance in colorectal cancer screening and diagnosis, 2011,** section 1.3.1. **American Society Guidelines for the early detection of cancer, 2013** colorectal cancer and polyps).

2. Hypothermic Neural Rescue: Birth asphyxia occurs in approximately 3:1,000 births (UK). 3 RCTs led by Prof David Edwards and Prof Denis Azzopardi proved that hypothermic neural rescue significantly improves survival for neonatal asphyxia by 50%. This simple cost-effective treatment is used across the developed world, and will make a significant impact in low resource countries where the burden of birth asphyxia is heaviest**. (NICE Interventional procedure guidance 347 (2010)** Therapeutic hypothermia with intracorporeal temperature monitoring for hypoxic perinatal brain injury).

3. Improving the survival of patients with chronic myeloid leukaemia (CML) & Invention and development of a globally recognised molecular method of monitoring disease response in CML

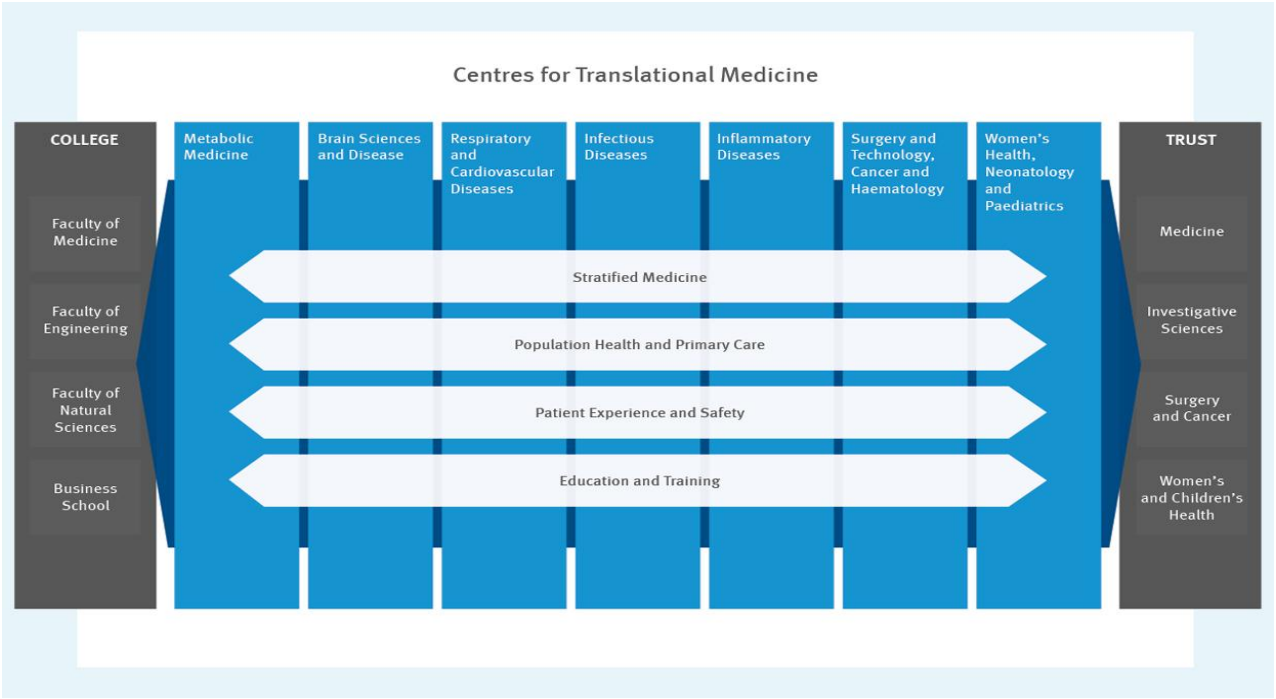
Having pioneered imatinib treatment in CML, Prof Jane Apperley's group demonstrated clinical efficacy of 2nd and 3rd generation third generation tyrosine kinase inhibitors (**NICE technology appraisal guidance 241, 2012)** and identified mechanisms of resistance to these drugs. In addition they have developed methodologies to quantify residual leukaemia, more accurately, assess the disease course and identify early the 10-15% for whom allogeneic stem cell transplantation is still the optimal therapy (**European LeukemiaNet Guidelines, 2009)**.

4. Genetic diagnosis and combined treatment algorithm for novel EMA/CO chemotherapy regime in gestational trophoblastic disease (GTD). Prof Michael Seckl's group has reduced early deaths and significantly improved patient survival rates in patients with high risk GTD. (**RCOG Clinical Guidelines: Green-top Guideline No. 38. 2010,** The management of Gestational Trophoblastic Disease. **Australian guideline for NSW GTD patients 2009,** Gynaecological Oncology Clinical Practice Guidelines**.** Section 6: Gestational Trophoblastic Disease, **Dutch working group guidelines 2013,** Datum Goedkeuring: 2010-12-01, Versie: 1.3, Verantwoording: Werkgroep Oncologische Gynaecologie (WOG)).

5. Radiofrequency in Liver Surgery. Prof Nagy Habib with the FoE developed radiofrequency (RF) devices which facilitate blood-less resection of tumours significantly reducing blood loss, improving functional recovery, reducing length of stay and need for intensive care in liver tumour resection. EMcision Ltd holds 20 patents, with global sales of the devices also used in kidney, spleen, pancreas, uterus and lung surgery. Prof Habib's work in RF has been used in the development of (**NICE interventional procedure guidance 464:**

2013.)

We will achieve further integration of research, health education and patient care over the next 5 years as an AHSC through the following mechanisms: **(i)** Centres for Translational Medicine (CTMs) (See Diagram) and Enabling Programmes, **(ii)** Developing healthcare Leaders of the future, **(iii)** Cross-disciplinary resources.



(i) Recognising a need for structured, close collaborations between BRC theme leads, other researchers, educational and clinical service leads, we established **7 CTMs** as delivery mechanisms to fulfil a central role in integrating research, education, clinical care and innovation through locally developed work programmes. They have an intrinsic focus on use of novel technologies and informatics, new diagnostic and therapeutic approaches to both common and rare diseases, the utilisation of integrated technological approaches in patient stratification, the development of new treatment algorithms and delivery approaches for integrated care pathways, the creation of data at a population level that can inform policy decisions, the development of IP and spin out opportunities in support of knowledge, health and wealth generation. We have established **Enabling Programmes (EPs)** to provide essential expertise in discovery science, epidemiology and large data capabilities, safety and experience, education and training e.g. the **Education and Training EP** (Chair Prof Jenny Higham) with members from all CTMs, including the **Director of Education and Quality, Health Education North West London (HENWL)** fulfils a central role in the education/research interface.

(ii) The **NW Thames Academic Foundation Programme** remains one of the largest such programmes nationally (116 Academic trainees annually, with over 30 training at Imperial) and remains oversubscribed (1:7, 2013). This year, 48 IC students obtained a position on an Academic Foundation programme, the highest of any Medical School. Our Masters courses provide a pipeline of students for PhD programmes, allowing exposure to a specific academic discipline. 1200 students are currently studying for a research degree (PhD, MPhil, MD (Res)) or one of the 34 Masters courses within the FoM, currently being streamlined into a set of modularised programmes. We run **5 clinical PhD programmes**: the Wellcome Trust Clinical PhD Programme, the Wellcome Trust/GSK Translational Medicine and Therapeutics Programme, the MRC/BRC Chain Florey Fellowships, Epidemiology and Control of Infectious Diseases and The Molecular and Cellular Basis of Infection. There are 300+ **Clinical Research Training Fellows (CRTFs)** studying for higher degrees, 30% supported by the MRC, Wellcome Trust or NIHR. We continue to be successful in competing for places on the **NIHR Integrated Academic Training Path** and have been awarded the second highest number of academic trainees in the UK, with 263 **Academic Clinical Fellows (ACFs)** and 95 **Clinical Lecturers (CLs)**. The success of our academic trainees has been outstanding; over 90% of our ACF's, have obtained a competitive CRTF to work for a PhD. We were also successful in bidding for **HEFCE Clinical Senior Lecturers (CSLs)**, with 35 awards (second highest nationally). Our aim to train and educate a cohort of doctors in experimental medicine has resulted in several innovative training programmes and appointments: **Patient Safety Fellows** working across the Education Directorate and the CPSSQ, **Fellowships in Clinical Leadership** ('Darzi' Fellowships'), a **Fellow in Integrated Care** with the **Imperial GP Scheme** and 2 new **Clinical Education Fellowships** to support undergraduate medical teaching. We will further support future healthcare leaders through a new **Clinical Leadership Programme** with the Business

School (inaugural cohort, 2013). An effective working relationship with the **NIHR CLAHRC** and the AHSN supports the adoption and diffusion of our discoveries to the wider population e.g. in **'MyAction',** an innovative family-centred preventive cardiology programme which integrates the care of patients with vascular disease with that of individuals identified at high multi-factorial risk. Working with the SPH, Dr Foster Unit and the Business School we are able to evaluate the impact of the AHSC across metrics for research, education, innovation and economic growth across sectors and use these analytical capabilities to systematically scan for new and diverse opportunities. We are a key partner in **Higher Education North West London (HENWL)** with several staff of ICHT on the **HENWL Board and its Strategic Advisory Council** including Prof Jenny Higham, Vice Dean FoM, who represents Higher Education Institutes (HEIs) and Prof Janice Sigsworth, Director of Nursing, as HENWL Board member and ICHT Associate Director of Education. We continue to work closely on a pan-London basis with other LETBs and Lead Providers to enhance the quality of training through dedicated educational leadership teams and enhanced governance in commissioned specialties. Future initiatives with HENWL across health and social care will include increased focus on providing integrated care and improving the patient experience e.g. **Community Education Provider Networks** in dementia, pressure ulcers and paediatric integrated care.

(iii) Cross-disciplinary resources One of the defining characteristics of our AHSC is the **integration of diverse professional groups** which adds depth and breadth to our portfolio of skills and expertise. Our strategy to maximise the impact that multi-disciplinary and multi-professional working brings to the AHSC is based on the development of academic careers through the **Health Science Academy (HSA)** and interdisciplinary research hubs. **Nursing and Midwifery** (N&M) has a track record of excellence in research and education that supports delivery of high quality patient care and outcomes. We support circa 700 N&M pre-registration students and in 2009 (nursing) and 2011 (midwifery) actively tendered for education partners that could integrate education and research. Close partnership working with our education partners (BNU and KCL) includes the establishment and hosting of 2 Professors of Nursing, a Reader in Nursing and an active approach to the development of **Clinical Academic Careers among N&M and Allied Health Professional (AHPs)** with a growing number of national fellowships investigating clinical issues e.g. safety in theatre, nutrition in ITU, nurse prescribing. **Multi-professional skills exchange** and learning is at the heart of our approach to CPD. We are the most successful Trust in England for **NIHR Fellowships for nurses, midwives and AHPs** with 13 MRes, 2 Post-Doctoral, (Clinical Lecturers), 1 Clinical Senior Lecturer and 5 Doctoral. Prof Christine Norton (Nursing) and Dr Mary Hickson (Therapies) contribute to the **Department of Health (DH) National Working Party Clinical Academic Career Pathways for Nursing and AHPs.** We will further develop research modules for non-medical staff to support the development of confidence and capabilities in research methods and continue to celebrate multi-professional research e.g. through our **NW London Nursing, Midwifery, AHP and Pharmacy Research Symposium,** organised by the HSA. The **IC Adjunct Professor Scheme** enables us to recognise multi-professional AHSC achievements and we will focus on establishing these appointments across the full spectrum of our staff. We will continue to utilise funding for non-medical CPD including development of staff in Bands 1-4, nurses AHPs and biomedical scientists. We will allocate this funding to support the AHSC objectives and improves the patient experience e.g. **NVQ Apprenticeships** for Therapy Assistants and enhanced research skills for nurses; the first cohort of Nursing MRes students graduated 2012. The Global eHealth Unit, SPH, will assist in **developing novel courses in research methodologies, informatics including training in genetics, telematics and health technologies** and through ICTU we will deliver a substantial NHS training function around the design of clinical trials utilising the Statistical Advisory Service, and working Pan-London with the NIHR Research Design Service. **ICHT** has won competitive bids as **Lead Provider of Postgraduate Medical Training for 26 specialities at Core and Higher level** mostly within NW London and some pan- London. In addition, we run the **Imperial GP Scheme** with local practices to develop a new generation of GP's educated and trained to the highest standards as leaders and practitioners.

Our research is supported by **interdisciplinary research hubs** e.g. the **Institute of Biomedical Engineering (IBME) Research Technology Networks**, which includes the Cardiovascular, the Metabolic and Endocrine, Musculoskeletal and Bioinformation Technology Networks. **The Centre for Synthetic Biology and Innovation** is an EPSRC-funded partnership with KCL, focusing on and optimisation of new synthetic biology solutions. **The Wellcome Trust EPSRC Centre for Medical Engineering Solutions in Osteoarthritis,** comprises engineers, surgeons, rehabilitation therapists and basic scientists. The **Royal British Legion Centre for Blast Injury Studies** comprises civil engineers, scientists and military doctors. **The Centre for Bio-Inspired Technology** uses engineering technologies to provide personalised devices for chronic disease management e.g. developments such as the Bio-inspired Artificial Pancreas and diagnostic lab-on-chips for early detection of disease. **The Centre for Infection Prevention Management (CIPM)**, ,brings together biomedical scientists, pharmacists, nurses and experts in a multidisciplinary team, and benefits from collaborations across other faculties within IC (psychologists, microbiologists and academics in experimental medicine); ICHT (pharmacist researchers, Infection Prevention and Control Service, Microbiology Laboratories; and Public Health England. We will maximise multi-professional working with

industry, building on our effective 'Chemistry in the Clinic' discovery science and the MRC-GSK scheme in which we are invited members. We will continue to encourage **multi-professional working in the development of healthcare policy**, be this in the form of NICE or clinical guidelines, e.g. ASCOT trial (Sever) on statins to prevent cardiovascular events in patients with hypertension, the SPARTAC trial of antiretroviral therapy at primary HIV infection or wider developments e.g. the **Institute for Global Health Innovation** (Prof Lord Darzi) to maximise the multi-professional influence within the changing healthcare architecture.

11. FINANCIAL PERFORMANCE (1 page)

Please describe the current and prospective financial performance of the partnership's constituent NHS provider and university organisations.

Table 1 Presents ICHT data. Key risks are delivery of a challenging efficiency programme and impact of Shaping a Healthy Future (SaHF) on service reconfigurations and activity changes. Reducing the risk will be achieved by further developing a culture of efficiency, working to a 5 year planning horizon and pursuing rigorous financial control and investment appraisal, supported by the improved management of clinical pathways, better use of the estate and benchmarked operational efficiencies. Continued strengthening of project management will enable the approaches to deliver demonstrable improvements. Liquid ratio 2012/13, 2013/14 assumes working capital facility is available, in line with TDA reporting.

Table 1 Trust Financial Performance

	2012/13 Outturn	2013/14 Forecast	2014/15 Forecast	2015/16 Forecast	2016/17 Forecast
Income (£m)	971.3	955.9	949.9	953.8	960.5
Costs (£m)	(904.1)	(885.2)	(874.3)	(877.0)	(881.4)
EBITDA (£m)	67.2	70.7	75.6	76.8	79.1
Net Surplus/(Deficit) (£m) before impairments	9.0	14.5	15.6	18.4	20.1
Net Surplus/(Deficit) (£m) after impairments	-40.0	14.5	15.6	18.4	20.1
Cash at bank (£m)	55.3	60.3	56.7	71.5	63.6
EBITDA margin (%)	6.92%	7.40%	8.00%	8.10%	8.20%
Liquid ratio (days)	13.3	10.7	17.3	14.9	22
Financial Risk Ratings	3	3	3	3	4

Table 2 IC Financial Performance

The reduction in cash at bank is a result of the enhanced capital programme, including the additional land acquisition in White City along with the development of the Research and Translation hub; the change in the surplus is reflective of this and of one-off costs involved with the planning of the estates masterplan, IT investments such as the new student system. As these one-off costs are expended, we anticipate an increase in surplus in the later years.

Institution: Imperial College London	**Forecast 2012-13**	**Forecast 2013-14**	**Forecast 2014-15**	**Forecast 2015-16**	**Forecast 2016-17***
Net Income (£m)	795.6	841.1	865.3	903.8	949.0
External borrowing as % of total income	19.4	17.7	16.5	15.2	
Net cash flow as a % of total income	13.1	8.1	7.2	8.6	
Staff costs as a % of total income	48.1	51.1	51.7	51.5	
Net Surplus	79,635	31,573	35,314	50,885	49,373
Cash at Bank	274,371	87,343	44,261	31,067	

***Note:** The College has not provided formal forecasts to HEFCE for 2016/17 but has estimated Net Income and Surplus based on current expectations re activity levels and capital needs. Further information can be provided if required.

12. ADDITIONAL COMMENTS (1 page)

Please use this section to address directly any feedback provided by the Panel on your application at the shortlisting stage, including any highlighted issues with quality of patient care such as adverse Monitor or CQC ratings.

Ratings

The Trust is on plan to submit an FT application in 2014. Currently there are no known concerns in relation to the application that have been raised by those in charge of the process. The Trust is registered 'without conditions' by the Care Quality Commission (CQC) and all inspections have demonstrated that all essential standards are being met.

Multi-disciplinary Training and Informatics Training

In response to feedback from the PQQ submission we have clarified our commitment to providing multi-disciplinary training and training on informatics. Throughout the application, and in particularly in **section 10,** we have outlined the depth and breadth of the training and opportunities we provide to all staff involved in delivering the AHSC vision. We have noted the breadth of undergraduate, post graduate and bespoke training on offer and included in our future plans is the further development of our Health science Academy. We highlight our intentions to develop training programmes from the basic use of patient related information to the understanding of genetics and genomics for all healthcare staff, through to highly sophisticated analytical functions.

Governance Arrangements

We have provided a more comprehensive description of our **governance arrangements** including the contractual foundations underpinning our partnership. We highlight several key structures and posts which facilitate effective information flows, transparency of process and decision making, probity and the effective use of resources. We have crafted our governance framework to be flexible enough to respond to organisational changes in the partners' organisational structures and to ensure optimal inclusivity in decision making.

The College Council receives regular reports on AHSC matters from the Dean FoM as the executive lead for the AHSC.

The Trust Board reviews a report on the AHSC at each of its public meetings.

The Strategic Partnership Board (SPB) has a primary role to ensure that the AHSC's objectives are achieved. The SPB has an independent chair, Sir Gordon Duff, and includes the College President and Rector and Trust Chairman, thus providing a direct line to and from the executive and governance fora in each partner organisation.

The Joint Executive Group (JEG) is the body directly responsible for the successful implementation of AHSC goals and for providing direction to the executive team. The membership of the JEG is 50/50, Trust/College as with the SPB, to balance the interests of the partners. The JEG performance manages the delivery of the AHSC strategy and work programme and the arrangements allow for the creation of sub-committees.

The AHSC Research Committee reports to the JEG on matters of research strategy, financial and regulatory governance and comprises cross College, Trust and stakeholder involvement. It is chaired by the AHSC Research Director

AHSC Research Director is also the Faculty of Medicine (FoM) Vice-Dean Research and the BRC Director. This post is responsible for all research related activities and is operationally accountable for NIHR funded infrastructure through reporting lines to the Dean FoM and the Trust CEO. The Director presents an annual public report on activity and progress.

Faculty of Medicine Cabinet, chaired by the FoM Dean and the Trust Management Board chaired by the Trust CEO both include members of the JEG and facilitate operational alignment of AHSC matters at a divisional level.

13. DECLARATIONS AND SIGNATURES

By signing the declarations the named individual is agreeing that they are authorised to do so on behalf of their organisation.

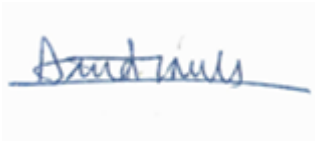
Please print this page, have it authorised and return it by post by 7 October 2013 to the address stated at the bottom of this form.*

The applying English NHS Provider/University Partnership fully endorses the application for an Academic Health Science Centre award and assert that appropriate support will be provided to the AHSC should the application for designation be successful.

English NHS Provider/University Partnership: Imperial College Academic Health Science Centre

Name, job title, address, email and telephone number of the lead contact for the proposed AHSC:
Professor David Taube, AHSC Director, AHSC Directorate, Hammersmith Hospital, Du Cane Road, London, W12 0HS

david.taube@imperial.nhs.uk Phone : 020 3313 1371



Signature **Date: 30th September 2013**

(contact for the proposed AHSC)

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

This form must be submitted by **1:00pm on 30 September 2013**. The 'wet-ink' Declaration and Signatures section of the application from should be received by NIHR CCF on **7 October 2013**, and sent to:

Dr Sonja Tesanovic
NIHR Central Commissioning Facility
Grange House
15 Church Street
Twickenham
TW1 3NL