Agenda
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:30</td>
<td>Meeting Opening</td>
</tr>
<tr>
<td>10:40</td>
<td>MRC Molecular Pathology Review</td>
</tr>
<tr>
<td></td>
<td>Professor Sir Robert Lechler (King’s College London and Chair of Review Steering Group)</td>
</tr>
<tr>
<td>10:55</td>
<td>NIHR support for molecular pathology</td>
</tr>
<tr>
<td></td>
<td>Dr Nathan Moore (Research &amp; Development Directorate, Department of Health)</td>
</tr>
<tr>
<td>11:10</td>
<td>Innovate UK Precision Medicine Catapult</td>
</tr>
<tr>
<td></td>
<td>Dr Penny Wilson (Innovate UK)</td>
</tr>
<tr>
<td>11:30</td>
<td>MRC EPSRC Molecular Pathology Nodes Call</td>
</tr>
<tr>
<td></td>
<td>Dr Jonathan Pearce (MRC), Dr Stephen Oakeshott (MRC) and Dr Victoria Marlow (EPSRC)</td>
</tr>
<tr>
<td>12:30</td>
<td>Networking Lunch</td>
</tr>
<tr>
<td>13:30</td>
<td>Q&amp;A and Open Discussion Session</td>
</tr>
<tr>
<td>14:30</td>
<td>Meeting Close</td>
</tr>
</tbody>
</table>
MRC Molecular Pathology Review

Professor Sir Robert Lechler

Chair of Review Steering Group

MRC EPSRC Nodes Call Workshop: 1st October 2014
Stratified medicine has the potential to deliver improved diagnoses and therapies

**Input**
- Affected population

**Tools**
- Genetic / Molecular
- Clinical Presentation / Phenotype
- Therapeutic Response

**Outputs**
- Disease Strata

**Value**
- Mechanism of disease leading to new therapies
- Diagnostics to better predict disease state, prognosis, response
It is moving beyond its historic bases in oncology/infection and genomics/IHC

- **Disease Area**
  - **Current** - infectious diseases and oncology
  - **Future** - anticoagulants, antipsychotics, autoimmune diseases, asthma, COPD, diabetes, and pain

- **Technology**
  - **Current** – Genomic and immunohistochemistry
  - **Future** – mRNA, proteome, epigenome, metabolome, etc

- **International**
  - **Current** – UK has contributed to development of field, but it is being led by overseas competitors
  - **Future** – Significant investment has established internationally competitive UK stratified medicine discovery engines

If the UK is to capture the opportunity, we need to be able to translate both the therapeutic and diagnostic outputs of stratification to patient and economic benefit
However, compared to therapies, the diagnostics path is complex & poorly linked

<table>
<thead>
<tr>
<th>Modality</th>
<th>Developer</th>
<th>Type</th>
<th>Regulatory Approval</th>
<th>Evaluation</th>
<th>Adoption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>All</td>
<td>All</td>
<td>Yes but efficacy not required</td>
<td>NICE (TAP)</td>
<td>Mandated</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>Commercial</td>
<td>All</td>
<td>Yes but efficacy not required</td>
<td>NICE (DAP)</td>
<td>Not Mandated</td>
</tr>
<tr>
<td>Hospital</td>
<td>Rare Genetic</td>
<td>No</td>
<td>UKGTN</td>
<td>Not Mandated</td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>Non-Rare/Non-Genetic</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The field would benefit from these gaps being addressed and from clear guidance on the path and required evidence for the discovery, development, regulatory approval and evaluation of molecular pathology tests.
... and the diagnostic development landscape is fragmented

Research and Service base has become separated, to the detriment of both

Clinical Research

Pathology Service

Industry

UK IVD companies are not well placed to help bridge the divide

There is a critical need to bring these various parties into closer proximity
Signatures are the future of diagnostic tests and will require close collaboration

<table>
<thead>
<tr>
<th>Time</th>
<th>Test</th>
<th>Biomarker(s) Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current</td>
<td>HercepTest</td>
<td>Level of single biomarker, HER2, to predict response to Herceptin</td>
</tr>
<tr>
<td>Emerging</td>
<td>Oncotype DX</td>
<td>Level of expression of 21 genes, to predict response to adjuvant chemotherapy</td>
</tr>
<tr>
<td>Future</td>
<td>Algorithmic signatures of multiple biomarkers from different classes (protein, metabolite, etc) to identify disease strata</td>
<td></td>
</tr>
</tbody>
</table>

Managing the development challenges of future tests will require close collaboration between researchers, service providers and industry with access to multi platform, data integration and data analysis capabilities
Flux provides opportunities for change

- **Infrastructure**
  - Innovate UK is establishing an industry facing Precision Medicine Catapult (£50m over 5 years)
  - The £175m MRC co-ordinated clinical research infrastructure initiative may help move recommendations forward

- **Regulation**
  - Draft EU Medical Device In Vitro Diagnostic Directive will require clinical evidence
    - Could bring together the research, clinical and industry bases, and align regulation and evaluation

- **Evaluation**
  - Department of Health review of UKGTN

- **Adoption**
  - NHS England commissioning model is under development
Recommendations

- **Path** - Produce clear unified guidance setting out the critical path and required evidence for the discovery, development, approval and evaluation of tests. Address the gaps in the UK’s regulatory, evaluation, adoption and delivery system

- **Proximity** - Establish joint research/clinical service ‘nodes’ aligned with industry and complementing NIHR, TSB and other RC and partner investments

- **People** -
  - Train next generation of research leaders in molecular pathology, potential merit of guaranteed follow through clinical lectureships
  - Further development of UK capacity in statistics, bioinformatics and health-economics
  - Under-graduate medical curriculum to include molecular pathology, to aid adoption and interpretation
MRC EPSRC Nodes Call launched as an initial response to recommendations

• In an initial response, the MRC and EPSRC have launched a joint call to support up to eight molecular pathology nodes

• Each node will be a multidisciplinary centre of innovative molecular diagnostic test discovery and development bringing together the research base, pathology/genetic services and industry
  • Research base to include biomedical, clinical, engineering and physical sciences

• Together the nodes will be expected to complement partner investments and cooperate as a network for the benefit of the UK
National Institute for Health Research

MRC EPSRC Molecular Pathology Nodes Call Workshop

1 October 2014

Nathan Moore
Infrastructure Manager,
Research & Development Directorate, Department of Health
Goals

• Transform research in the NHS
• Increase the volume of applied health research for the benefit of patients and the public
• Develop and support the people who conduct and contribute to applied health research

Principles

• Transparent
• Competitive
• High quality
• Value for money
• Focused on outcomes
The central role of NIHR research in the innovation pathway

INVENTION ➤ EVALUATION ➤ ADOPTION ➤ DIFFUSION

Medical Research Council

- Basic Research
- Development Pathway Funding
- Efficacy Mechanism and Evaluation

National Institute for Health Research

- Invention for Innovation
- Biomedical Research Centres
- Biomedical Research Units
- Experimental Cancer Medicine Centres
- Clinical Research Facilities
- Patient Safety Translational Research Centres
- Healthcare Technology Co-operatives
- Diagnostic Evidence Co-operatives
- Horizon Scanning Centre
- Research Schools
- Research for Patient Benefit
- Public Health Research
- Programme Grants for Applied Research
- Health Services and Delivery Research
- Health Technology Assessment
- Centre for Surgical Reconstruction & Microbiology
- Collaborations for Leadership in Applied Health Research and Care
- Centre for Reviews & Dissemination, Cochrane, TARs
- NHS Supply Chain
- National Institute for Health & Care Excellence
- NHS Evidence
- Academic Health Science Networks
- NHS England
- Providers of NHS Services
- Support for Procurement
- Guidance on Health & Healthcare
- Access to Evidence
- Innovation
- Commissioning
- Patient Care

This pathway covers the full range of interventions - pharmaceuticals, biologicals, biotechnologies, procedures, therapies and practices - for the full range of health and health care delivery - prevention, detection, diagnosis, prognosis, treatment, care.
NIHR Research Programmes

• There are three NIHR research programmes likely to be relevant to molecular pathology
  – Invention for Innovation (i4i)
  – Efficiency Mechanism Evaluation (EME)
  – Health Technology Assessment (HTA)

• All 3 operate in both commissioned and researcher-led mode
Efficacy and Mechanism Evaluation (EME) Programme

- Jointly funded by NIHR and MRC and managed by NIHR, the EME Programme sits between funders of basic science and early clinical research and the more applied NIHR programmes.
- Actively supports the translational pull through of promising interventions*, with significant potential to benefit patients and the NHS in the medium to longer term, from early clinical studies into later phase evaluation.
- Funds science driven clinical efficacy studies to test interventions and provides the opportunity to explore disease or treatment mechanisms, which may in turn lead to improvements in health and patient care.
- Supports and encourages academics and clinicians to work with commercial organisations, in particular SMEs.
- Has committed almost £90 million to internationally competitive research from across the UK during the last 5 years.

*the term intervention is used in the broadest sense and includes any method use to promote health, prevent and treat disease and improve rehabilitation or long-term care.
NIHR Invention for Innovation (i4i)

• Designed to translate healthcare technologies into patient benefit for the NHS with end user pull

• Beyond basic research moving technologies towards investor readiness

• i4i aims to advance the research and development of innovative healthcare technologies and their translation into the clinical environment for the benefit of patients by:
  • guiding the progression of innovative medical product prototypes, and
  • providing business advice to the medical technology professionals it funds.

• Funding for collaborative projects involving academics, clinicians and companies
NIHR Invention for Innovation (i4i)

Next Generation Mobile Diagnostics for HIV
BRCs/BRUs leveraged funding

- **DH/NIHR awards**
- **Total external funding**

<table>
<thead>
<tr>
<th>Year</th>
<th>DH/NIHR</th>
<th>Total External</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007/08</td>
<td>£67</td>
<td>£381</td>
</tr>
<tr>
<td>2008/09</td>
<td>£149</td>
<td>£361</td>
</tr>
<tr>
<td>2009/10</td>
<td>£150</td>
<td>£467</td>
</tr>
<tr>
<td>2010/11</td>
<td>£142</td>
<td>£497</td>
</tr>
<tr>
<td>2011/12</td>
<td>£157</td>
<td>£545</td>
</tr>
<tr>
<td>2012/13</td>
<td>£172</td>
<td>£683</td>
</tr>
</tbody>
</table>

*National Institute for Health Research*
Blood test 'detects sepsis in hours'

By Helen Briggs
BBC News

A rapid blood test to diagnose blood poisoning, or sepsis, at the hospital bedside could potentially save thousands of lives, say researchers.

Early studies at King's College London suggest the condition can be diagnosed in two hours using a simple blood test.

Current diagnostic methods take up to two days, which may delay treatment with life-saving antibiotics.

The condition - caused when the body's immune system overreacts to infection - causes 37,000 UK deaths each year.

In the study, published in the journal PLOS ONE, researchers identified a biomarker for diagnosing sepsis rapidly in blood samples.
The first multi-gene DNA sequencing test that can help predict cancer patients' responses to treatment has been launched in the National Health Service (NHS), thanks to a partnership between scientists at the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC), a collaboration between Oxford University Hospitals NHS Trust and Oxford University.
Researchers identify cardiomyopathy gene

16 February 2012

Researchers at Royal Brompton Hospital and Imperial College London have used high-speed DNA sequencing technology to provide detailed genetic analysis of 300 heart patients. The study findings, published in the New England Journal of Medicine, are hailed as ‘the beginning of the end’ for diagnosing inherited dilated cardiomyopathy (DCM).

DCM is one of the leading causes of heart failure, affecting more than 30,000 people in the UK. The condition often develops due to a genetic cause and leads to scarring of the heart wall and damage to the muscle. This causes the heart to become weakened and enlarged, preventing it from pumping efficiently.

The study, which is an international collaboration between teams at Royal Brompton, the National Heart & Lung Institute at Imperial College London, Harvard Medical School in the United States and University of Trieste in Italy, identified a mutation in the Titin gene as being related to the most common genetic cause of DCM. The mutation appears in one in four of all patients with the condition.

The UK-based team members, who carried out their work at the National Institute of Health Research’s NIHR biomedical research unit (BRU), says the findings mean that 50 per cent of all patients can be effectively screened and diagnosed for DCM and family members can be tested to show if they are also affected.
NIHR BioResource

7 NIHR BRCs and one NIHR BRU:
Cambridge
Imperial
Guy’s and St Thomas’
South London and Maudsley
Oxford
University College London Hospital
Newcastle
Leicester Cardiovascular (BRU)

Healthy volunteers and patients provided samples (of blood or saliva) and agreed to be recalled by genotype and phenotype to participate in experimental research studies.

Four themes:
Rare Diseases
Cardiovascular & Metabolic Disease
Infectious, Immunological & Inflammatory Disease
Neuroscience

Launch: March 2014
Diagnostic Evidence Cooperatives

**Leeds Teaching Hospitals NHS Trust**
Liver diseases, Musculoskeletal diseases, Renal diseases.

**Newcastle upon Tyne NHS Foundation Trust**
Cancer, Cardiovascular disease and stroke, Genetics, Infection, Liver disease, Musculoskeletal disease, Respiratory, Transplantation.

**Oxford Health NHS Foundation Trust**
Primary care IVDs: Horizon scanning and rapid reviews to identify new and emerging IVDs, Identifying unmet needs for IVDs, Integrating primary care with laboratory services, Patient, carer and clinician factors in implementing IVDs, improving evidence for primary care IVDs.

**Imperial College Healthcare NHS Trust**
Cancer, Cardiovascular diseases, Gut health, Infectious diseases, Metabolic medicine, Primary Care, Respiratory diseases.
Diagnostic Evidence Cooperatives

Invention

Evaluation

Aoption

Diffusion

Industry Engagement

IVD Developers
- Include: Industry, Academia, NHS

Stage 1: Selection, Modelling & Prioritisation

Stage 2: Analytical & Clinical Validity Assessment

Stage 3: Assess Existing & Propose Clinical Care Pathway

Stage 4: Qualify Analytical & Clinical Validity

Stage 5: Evaluate Clinical Utility

Stage 6: Evaluate Cost-effectiveness

Stage 7: Output Document/Report

NIHR DEC Infrastructure Funding

In-Vitro Diagnostic Development Pathway

DEC access to Clinical expertise and resources
- Research sites, Biobank samples & data, Databases

DEC Methodological expertise and resources
- Pathway & Economic Modelling, Evidence Synthesis, Clinical Informatics

Potential Stakeholders:
- Patient Groups & Public
- NIHR Infrastructure
- DH Academic Health Science Centres (AHSCs)
- Trade Associations
- IVD Developers
- NIHR Horizon Scanning Centre
- NICE Scientific Advice

Potential Funders:
- RESEARCH COUNCILS – EPSRC (Stages 1,2,3), MRC (Stages 2,4,5)
- Innovate UK – Biomedical Catalyst, Smart Awards
- NHS England - SBRI Healthcare – Specific Themed Calls
- NIHR I4I Product Development Awards
- NIHR I4I Challenge Awards (Stages 3, 5)
- NIHR HTA (Stages 4,5,6)
- NIHR Research for Patient Benefit (RfPB)
- NIHR/MRC EME (Stages 3,4.5)
- EU RELATED FUNDING (HORIZON 2020, FP7, ...)

Contributors to Discussion(s):
- Patient Groups & Public
- NIHR Diagnostics Assessment Programme
- NIHR Infrastructure
- Medicines & Healthcare products Regulatory Agency (MHRA)
- Notified Bodies
- NHS Providers of Pathology Services
- Clinical Pathology Accreditation (UK) (CPA)
- NHS commissioners
- NIHR Horizon Scanning Centre
- NICE Diagnostic Assessment Programme

Recipient of Output:
- Patient Groups & Public
- NIHR Diagnostics Assessment Programme
- NIHR Infrastructure
- Medicines & Healthcare products Regulatory Agency (MHRA)
- Notified Bodies
- NHS Providers of Pathology Services
- Clinical Pathology Accreditation (UK) (CPA)
- NHS commissioners
- NIHR Horizon Scanning Centre
- NICE Diagnostic Assessment Programme

Healthcare System Impact

Economic Benefit

Patient Benefit
NIHR Clinical Research Infrastructure

NOCRI supports industry through:

- Establishing collaborations
- Managing relationships
- Introductions
- Sign-posting

NIHR Office for Clinical Research Infrastructure (NOCRI)

NOCRI@nihr.ac.uk
www.NIHR.ac.uk/NOCRI
AHSNs, AHSCs and the research and innovation landscape

NIHR Infrastructure
CRN, HTC, DECs

NIHR Infrastructure
BRC, BRU, CRF

NIHR Infrastructure
CLAHRC

MRC Programmes

INVENTION

EVALUATION

ADOPTION

DIFFUSION

AHSC

AHSN

NHS Patient Care
National Institute for Health Research

1 October 2014

Nathan Moore
Infrastructure Manager, Research & Development Directorate, Department of Health
MRC EPSRC Nodes Call

1 October 2014

Dr Penny Wilson
Innovation Platform Leader, Stratified Medicine
Innovate UK Status

• The original DTI Innovation Unit and advisory “Technology Strategy Board” was set up in 2004
• It was spun out of government as a “non-departmental public body” in July 2007, relocated to Swindon and staffed with people from business
• Since then its budget has increased from £250m to £440m a year
• Engaged with over 3700 companies across many application areas
• Works across government, companies and the third sector

Over 2000 CR&D projects launched
4000 business partnerships and almost all the UK’s universities
Together with partners and business, over £2bn invested in UK innovation
Technology Strategy Board
Driving Innovation

Joining up the Toolset
...every step of the way
Stratified Medicine Innovation Platform

• Launched October 2010

• Aims to realise the potential of stratified medicine in the UK

• With partners will invest up to £200m (£50m from the TSB, £28.4m committed to date)

• Human dimension of infectious disease programme integrated into SMIP in July 2012

• Works in partnership across government and with the private and third sector to maximise UK potential for economic growth and patient benefit
SMIP UK Roadmap Key Themes

• Incentivising adoption
• Increasing awareness
• Patient recruitment – consents and ethics
• Clinical trials
• Data – collection, management and use
• Regulation and standards
• Intellectual property
• Bio-banks and biomarkers
• Increasing the impact of R&D investment

Public dialogue: innovateuk.org/stratified-medicine-final-report
Fourteen infectious disease and SMIP competitions to date

• DIIA Series 1. Feasibility, Fast track, POC for STIs and HAIs
• DIIA Series 2. Sepsis 1, Sepsis 2, Assessing the impact of near-patient testing
• DIIA Series 3. TB POC diagnostics, *Endemic animal disease competition*
• SMIP Round 1. Tumour Profiling & Data handling, Inflammatory biomarkers, Business models
• SMIP Round 2. Adverse Effects and Non responders (2 Phase SBRI)
• SMIP Round 3. Advancing in-vivo imaging for stratified medicine
• SMIP Round 4. Improving cell and tissue analysis for stratified medicine
• SMIP Round 5. Patient stratification and neurodegenerative diseases (Diagnosis and care management, Data integration and new business models)
  Full stage closes October 2014
• SMIP Round 6. KTP. Modelling across the development pipeline
  To open 2014
• SMIP Round 7. SBRI planned for 2015
A Precision Medicine Catapult

Penny Wilson
Innovation Platform Leader, Stratified Medicine
penny.wilson@innovateuk.gov.uk
What is a Catapult centre?

- A **business-focused** technology and innovation centre
- **Bridge the gap** between businesses, academia, research and government
- Makes world-leading technical capability available to businesses to solve their technical challenges

- Provides:
  - Technology infrastructure
  - Expertise
  - Connections
Technology Readiness Levels

1. Basic Principles Observed
2. Demonstration in a laboratory environment
3. Prototype demonstration in operational development

Universities
Research Centres, RTOs

Industry (Large & SMEs)
Test&D, CRO

Technology Strategy Board Integrated Programmes
We plan to address 2 of the barriers to PM

- Commercialising new tests is slow and costly, with the returns not justifying the risks
- Performing precision medicine clinical studies (i.e. combining diagnostics and therapies) is complicated
• How can we improve the generation of evidence
• How can we facilitate the generation of evidence with industry
• What studies are absolutely essential before introduction into clinical practice

2014 UK Diagnostics Forum
Changing the Landscape of Adoption of Diagnostics
Our proposed solution

• Lower the costs and risks of bringing new PM tests to market by
  • Setting up a test development and validation lab
  • Offering rapid and easy access to clinical settings to show these tests work in the real world

• Make PM clinical studies easier and faster by
  • Creating a PM-focused clinical trial system of 30-40 hospitals and a PM pathology lab service.
Development lab

- Rapid prototyping, development and validation of new tests, algorithms and diagnostic instruments
- *In vitro* diagnostic focused

---

**Help SMEs**
- Understand and capture the commercial opportunity
- Produce clinically reliable and robust tests and diagnostic platforms
- Test products in real clinical settings
- Accelerate approval and reimbursement of PM products
The lab will offer

- **Business and clinical expertise**
  - Dedicated team with a network of clinical and health system experts

- **Technical expertise and infrastructure to produce clinically reliable and robust tests and platforms**
  - Analytical chemists, test developers, and medical engineers
  - Hospital diagnostic test platforms
  - Prototyping facilities

- **Access to clinical settings**
  - Path labs, medical clinics (via MRC nodes, DECs or directly)

- **Regulatory and health technology assessment expertise**
  - Regulatory and HECON experts working closely with key agencies to understand and deliver data requirements
PM test-bed

- Dedicated infrastructure to deliver PM clinical trials quickly
  - A network of 30-40 hospitals
  - Covering 15-20 million population

- A centralised PM pathology lab service
- Rapid regulatory approval
- Easy sample and clinical data access
  - Through routine consenting
- Fast enrolment of as many patients as possible
  - Using dedicated enrolment coordinators
Disease focus

- Our target diseases are ones likely to have a real world impact within 10 years
  - Cancers (particularly the common ones: lung, breast, colorectal, prostate)
  - Infection
  - Inflammatory conditions like rheumatoid arthritis.
Projects will follow a stage-gated approach

<table>
<thead>
<tr>
<th>Stage</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Screening</td>
</tr>
<tr>
<td>1</td>
<td>Opportunity assessment</td>
</tr>
<tr>
<td>2</td>
<td>Optimisation</td>
</tr>
<tr>
<td>3</td>
<td>Lab validation</td>
</tr>
<tr>
<td>4</td>
<td>Clinical validation</td>
</tr>
<tr>
<td>5</td>
<td>Clinical utility</td>
</tr>
</tbody>
</table>

Projects can start and leave at any stage
Mission

The Catapult’s mission is to grow the precision medicine industry in the UK to substantial levels by:

• **Taking PM products into testing in clinical settings**, de-risking them for further investment;

• Being a **source of clinical expertise** and access to NHS clinical partners;

• **Providing technical expertise** and infrastructure to ensure products are robust and clinically useful;

• **Providing regulatory expertise** to ensure that products can get to the clinic safely, in the shortest amount of time;

• **Creating opportunities** for collaboration, both nationally and globally; and

• Being a **source of business expertise** and knowledge of routes to grants, investment finance and markets, so that commercially viable products are progressed and investable
Catapult Locations

- **Offshore Renewable Energy**
  - Glasgow

- **High Value Manufacturing**
  - AFRC – Strathclyde
  - CPI – Wilton / Sedgefield
  - AMRC & NAMRC – Rotherham
  - MTC – Ansty
  - WMG – Coventry
  - NCC – Bristol

- **Future Cities**
  - London

- **Connected Digital Economy**
  - London

- **Cell Therapy**
  - London

- **Satellite Applications**
  - Harwell

- **Transport Systems**
  - Milton Keynes
Continua ‘ecosystem’

- **SENSORS**
  - Home sensing & control
  - Blood pressure
  - Glucose meter
  - Pulse oximeter
  - Baby monitors
  - Spirometers
  - Medication tracking
  - Fitness equipment
  - Consumer electronics

- **CONNECTIVITY**
  - ZigBee
  - Bluetooth
  - MICS / MEDS
  - Ethernet

- **AGGREGATION COMPUTATION**
  - PC
  - Personal Health System
  - Cell Phone
  - Set Top Box

- **SERVICES**
  - Personal Health Record Service
  - Diet or Fitness Service
  - Healthcare Provider Service
  - Monitoring Service
  - Disease Management Service

**Service User Domain**

**Service Provider Domain**

**Service Commissioner Domain**

Adapted from “Continua Alliance Overview” © Continua Alliance 2007
Join us at Innovate UK 2014
5 - 6 November, Old Billingsgate, London

Many thanks!
MRC EPSRC Molecular Pathology Nodes Call

Jonathan Pearce (MRC), Stephen Oakeshott (MRC) and Victoria Marlow (EPSRC)
Agenda

- Background
- What is a node
- Call parameters
- EoI stage
- Only a start
What is molecular pathology and why a joint call

- Molecular pathology seeks to understand the origins and mechanisms of disease at the level of macromolecules (e.g. DNA, RNA and protein) and apply this knowledge for patient benefit
  - It is open to all disease areas, types of technology, clinical speciality/sub-speciality that can help meet these goals

- The application of molecular pathology understanding requires:
  - biomarkers characteristic of clinically important disease strata; and
  - technologies able to robustly and reproducibly discover and measure these

- It therefore depends upon the fusion of biomedical, clinical, engineering and physical sciences
For MRC the call builds on our investment in stratified medicine

- £60m initiative to develop disease-specific research consortia:
  - defining strata and characteristic biomarkers
  - testing stratification hypotheses
  - exploring underpinning mechanisms

- Portfolio of 9 consortia, c. 14 by year end

- Brings together 30 academic and 41 commercial partners in open innovation collaborations

- Each consortia is a stratified medicine discovery engine able to originate and test new stratification hypotheses
EPSRC Involvement

- EPSRC is the main UK government agency for funding research and training in engineering and the physical sciences.

  - Build critical mass around UK research strengths in engineering and physical sciences that underpin healthcare.

  - Maximise industrial involvement and increase translation to products / practices.
The importance of EPS research to Health and Life Sciences

Independent review group chaired by Patrick Maxwell to explore the relationship between EPS and HLS.

**Conclusion** - EPS research has played a major role in advancing health and life sciences.

**Recommendations**
- proposals to encourage interdisciplinary working
- the role for challenge-driven research
- the need for doctoral training in interdisciplinary research
- incorporating EPS into the UK strategy for life sciences
- regular reviews of activity at the interface between disciplines

http://www.epsrc.ac.uk/newsevents/news /healthandlifesciencesbooklet.aspx
EPSRC Background Investments

- The EPSRC supports a £64M underpinning portfolio in analytical science
- Which focuses on the development of novel techniques or the novel application of existing techniques, for the analysis of chemical or biological systems and entities
- Partnering on this call is an opportunity to build on this investment and encourage the application of analytical techniques into a healthcare application
Agenda

- Background
- What is a node
- Call parameters
- EoI Stage
- Only a start
Capturing the opportunity

- We are both keen that our existing investments have robust pathways and capabilities to enable them to reach patients and provide health and economic benefits.

- Review highlighted benefit of establishing joint research/clinical service ‘nodes’ aligned with industry.
Initial focus on discovery and validation of novel molecular pathology approaches

- We anticipate nodes will initially be positioned at discovery/early development boundary working on
  - Discovery and validation of biomarkers associated with disease strata
  - Development of novel sensing and analytical technologies for new diagnostic tools
  - Application of mathematical and statistical methodologies for the extraction of information from complex datasets.

- Longer term, we expect nodes to traverse the path to adoption/delivery, as tests under development mature
Nodes as virtuous circles - Population use stimulating and supporting research

- Closing the circle by complementing and extending current service could stimulate new research by providing real world population level data combining health records with molecular pathology fingerprints.
- Skimming of existing tissue flows could support discovery and validation.
- Use of Diagnostic and Research data bins.
Pooling of capabilities

- Each node should either include or link to:
  - Leading biomedical, clinical, engineering and physical sciences communities
  - Innovative clinical practice and pathology/genetic services
  - Industry

- While nodes will be expected to have a single co-ordinating core, they may need to extend their reach to other institutions to access required resources / capabilities
We anticipate that applicants will have differing balances of existing strengths and that funding may be used to develop one or more areas.
Nodes Network

• Together the nodes will be expected to cooperate as a network, for the benefit of the UK by, for example, sharing best practice and assisting in the evaluation and diffusion of next generation tests.

• The nodes and network will be required to complement partner investments including Innovate UK’s Precision Medicine Catapult and NIHR’s Diagnostic Evidence Centres and related initiatives including...
The network might play a role akin to the UKGTN for non-rare, non-genetic tests

<table>
<thead>
<tr>
<th>Modality</th>
<th>Developer</th>
<th>Type</th>
<th>Regulatory Approval</th>
<th>Evaluation</th>
<th>Adoption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>All</td>
<td>All</td>
<td>Yes but efficacy not required</td>
<td>NICE (TAP)</td>
<td>Mandated</td>
</tr>
<tr>
<td>Commercial</td>
<td>Commercial</td>
<td>All</td>
<td>Yes but efficacy not required</td>
<td>NICE (DAP)</td>
<td>Not Mandated</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>Hospital</td>
<td>Rare Genetic</td>
<td>No</td>
<td>UKGTN</td>
<td>Not Mandated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-Rare/Non-Genetic</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Possible scope of Network support
Agenda

- Background
- What is a node
- Call parameters
- EoI Stage
- Only a start
Funds available

- £17.5m (MRC £15m, EPSRC £2.5m) to support up to eight molecular pathology nodes
  - Will support up to eight awards, with diverse research focus and structure, of three to four years duration
MRC Support for Translation and Industry Engagement

Confidence in Concept

Biomedical Catalyst

Basic medical research  Prototype discovery and design  Pre-clinical development  Early clinical trials  Late clinical trials

MRC Industry Collaborative Awards

EME

DPFS
Diagnostic proposals - DPFS

- Over the last two years, 17% of proposals to the DPFS scheme have sought to develop non-imaging diagnostics

- Only 9% of funded awards have been in this area

- Diagnostic proposals fail in four primary ways:
  - The underpinning science may be weak or out of remit;
  - The applicant team may lack critical expertise, leading to a flawed proposal;
  - The team may lack access to key resources, particularly samples and assays;
  - The statistical justification for the work may be lacking.
Diagnostic proposals – common issues

- Unsuccessful diagnostic proposals can broadly be categorised into three camps:
  - Science-led, following up on discovery science;
  - Technology led, driven by desire to validate exciting technology;
  - Clinically led, driven by need.

- Typical weaknesses are:
  - Lack of statistical justification is a common weakness;
  - Clinical expertise can be lacking in science and technology led proposals;
  - The target biomarker may be weakly validated;
  - Clinically driven proposals may lack translatability, being focussed on early discovery.
Molecular pathology nodes

- By bringing together broad expertise into a core facility, the proposed molecular pathology nodes could:
  - Provide an environment where technical, scientific and clinical experts can work together from an early stage;
  - Directly provide support to generate early proof-of-concept data following initial discovery research;
  - Support subsequent proposals to DPFS by providing infrastructure, expertise and access to clinically annotated and high quality samples.
EPSRC in the translation pathway

MRC (including UK Regenerative Medicine Platform, RCUK LifeLong Health and WellBeing)

EPSRC, BBSRC

Innovate UK, including Health KTN, Biomedical Catalyst, Cell Therapy & Precision Medicine Catapult, Innovation Platforms (Stratified Medicine, Assisted Living)

National Centre for the Replacement Refinement and Reduction of Animals In Research (NC3Rs)

Wellcome Trust, Cancer Research UK

DH, including NIHR HTCs, NHS England and AHSNs
EPSRC Support

- Responsive mode
  - Remit query service
    http://www.epsrc.ac.uk/funding/howtoapply/basics/remit/remitqueries/

- Targeted calls for proposals
  - Bridging the Gaps between the EPS and AMR
    http://www.epsrc.ac.uk/funding/calls/bridgingthegapsepsamr/
  - Transforming Approaches to Improving Hearing Aid Technology
    http://www.epsrc.ac.uk/funding/calls/improvinghearingaidtechnology/

- Fellowships – Early and Established Career Stages
  - Diagnostics
    http://www.epsrc.ac.uk/skills/fellows/healthcaretechnologies/priorityareas/diagnostics/
  - Analytical Science
  - Chemical Biology and Biological Chemistry
    http://www.epsrc.ac.uk/skills/fellows/physicalsciences/
Funds available

- £17.5m (MRC £15m, EPSRC £2.5m) to support up to eight molecular pathology nodes
  - Will support up to eight awards, with diverse research focus and structure, of three to four years duration
## Timetable

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workshop registration deadline</td>
<td>15 September 2014</td>
</tr>
<tr>
<td>Call workshop</td>
<td>1 October 2014</td>
</tr>
<tr>
<td>EoI deadline</td>
<td>4pm on 10 November 2014</td>
</tr>
<tr>
<td>EoI Panel meeting</td>
<td>5 December 2014</td>
</tr>
<tr>
<td>Proposal call open</td>
<td>23 December 2014</td>
</tr>
<tr>
<td>Proposal deadline</td>
<td>4pm on 10 February 2015</td>
</tr>
<tr>
<td>Funding decisions</td>
<td>late March 2015</td>
</tr>
</tbody>
</table>
Expert Panel Review

• EoIs and proposals will be reviewed by an expert panel, whose membership will be drawn from the UK and international research, clinical, service and industry sectors, including representation from both the MRC and EPSRC communities

• Academic and industry co-chairs, similar model to that used for the joint MRC/Innovate UK Biomedical Catalyst
  - Professor Patrick Maxwell, Regius Professor of Physics at the University of Cambridge
  - Dr John Jeans, Medical technology advisor to the Prime Minister
Agenda

- Background
- What is a node
- Call parameters
- EoI Stage
- Only a start
Vision, Positioning and Objectives

- **Vision**: What is the scientific/clinical opportunity you are seeking to capture?

- **Positioning**: How are you going to position the node at its start and, if appropriate, over the course of the award to capture this opportunity?

- **Objectives**: What will the node have delivered by the end of the award?

- **Value Add**: What will the new collaborations, infrastructure and research enabled by node support allow you to create above and beyond existing activities?
Positioning

- In this call, we are keen to explore different strategic models.
- Focus might be on:
  - a technology
  - a disease
  - a mechanism common to many diseases; and/or
  - a Pathology/genetics sub-speciality (e.g. histopathology, chemical pathology, etc)
- Positioning need not be fixed. A node might have an initial focus but plan to exploit its capabilities in new areas.
- Across the portfolio of nodes we would like to see a balanced coverage of existing and emergent opportunities.
## Areas of current and emerging molecular diagnostics

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>Current</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious diseases</td>
<td>Genomic Immunohistochemistry</td>
<td>Coagulopathies</td>
</tr>
<tr>
<td>Oncology</td>
<td></td>
<td>Psychoses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Autoimmune</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Technology</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Genomic</td>
<td>mRNA</td>
<td>Metabolome</td>
</tr>
<tr>
<td>Immunochemistry</td>
<td>Proteome</td>
<td>Digital pathology etc</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tests</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Single biomarker</td>
<td>Panels of markers from same class</td>
<td>Signatures of multiple biomarkers from different classes</td>
</tr>
</tbody>
</table>

Require New Methodologies
Attendance by Disease Area
Attendance by Technological Approach
Node Leadership

- Molecular pathology is the molecular understanding of disease, as such much of clinical research has a contribution to make

- We therefore expect that node leadership may be drawn from both within and beyond the speciality of Pathology
Skills and Training - academic pathology is in decline

Clinical academic pathology staffing levels since 2005 (FTE)

Academic grades 2013 (% Total FTE)

CAGR 2005-13

Pathology

All Specialities

-4%

1%
Innovative proposals tackling skills shortages are welcomed

• Such proposals might include:
  
  • Research intensive masters level courses, modules and/or taster fellowships of up to a year, to provide hands on experience
  • Opportunities for local specialists to develop their skill sets, perhaps through buying out clinical time
  • Intermediate to senior research focused posts (clinical and non-clinical) – commitment from HEI partners to these posts would be particularly welcome
  
• Worth also considering needs in statistics, bioinformatics and health-economics

• Not PhDs at this time, as we build up capacity, but strategic alignment of doctoral training funding by universities welcomed
Agenda

- Background
- What is a node
- Call parameters
- EoI Stage
- Only a start
Only a start

- The nodes call and related programmes will not fully address the review’s recommendations

- This first phase along with the Catapult, DECs, etc enables us to develop a coordinated and partnered programme linking and supporting the research, clinical, service and industry sectors

- If consistently and clearly presented by all partners, this could provide a compelling base for a combined cross-funder bid in the next CSR with the goal of

Making the UK an optimal environment for the discovery, development and adoption of innovative molecular pathology tests, to capture of the health and economic benefits of stratification