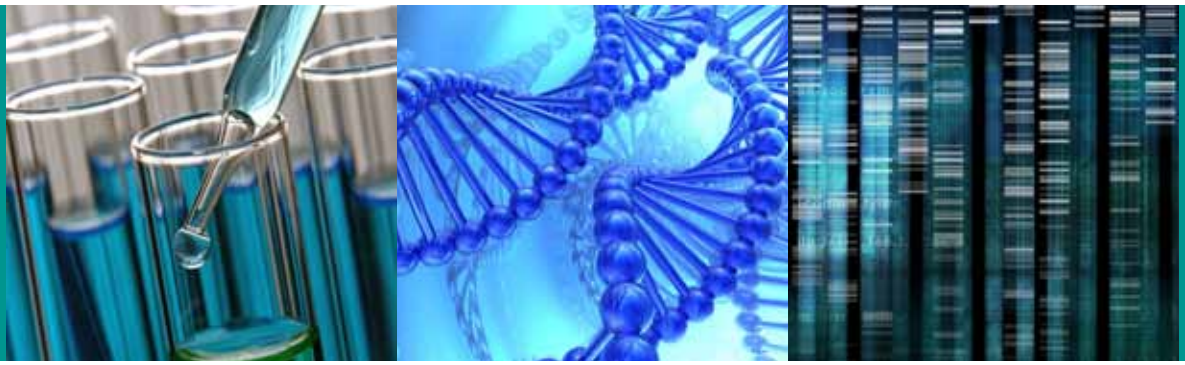
Technology Strategy Board
Driving Innovation



Stratified Medicine in the UK

Vision and Roadmap

Arthritis Research UK
DH Department of Health
CANCER RESEARCH UK
MRC Medical Research Council
NHS National Institute for Health and Clinical Excellence
The Scottish Government
NHS SCOTLAND

Stratified Medicine in the UK Vision and Roadmap

Summary

A consortium of government bodies and leading charities has joined forces to accelerate the development and uptake of stratified medicine in the UK. The Technology Strategy Board, Medical Research Council (MRC), Cancer Research UK (CRUK), Arthritis Research UK (ARUK), Department of Health (DH), Scottish Government Health Directorate (SGHD) and National Institute for Clinical Health and Excellence (NICE) have formed a partnership to take forward the Stratified Medicine Innovation Platform. Together they will invest around £200m over five years in the area of stratified medicine. Stratified medicine can be summarised as identifying the right therapy for the right patient at the right time in the right dose.

This publication sets out a shared vision for the UK to be the best place to develop, and have adopted, stratified medicine. It also outlines a technology roadmap that describes nine thematic areas which, if advanced successfully, will help accelerate the development and uptake of stratified medicine in the UK. The vision and roadmap grew out of a series of workshops attended by more than 100 people representing a broad range of stakeholders

Background

Even the best medicines are not equally effective in all patients. Disease processes and treatment choices can vary from person to person even though they may have similar symptoms. It is estimated that only 30-70% of patients respond positively to any particular drug. Recent advances in science, particularly in molecular biology and genomics, mean that it will become increasingly possible to identify the underlying molecular mechanisms of disease. Developing diagnostic tests that indicate the molecular cause of a disease enables the development of new treatments that can more precisely target the disease, as Herceptin does for certain forms of breast cancer. Predicting in advance which groups of patients will respond to a particular therapy and providing treatment accordingly is known as stratified medicine (or personalised medicine).

Across the world, healthcare models are facing greater challenges, both physically and financially, in providing for a growing, ageing population with an increasing burden of disease. The upward trend in spending means healthcare is becoming a more and more significant part of a nation's GDP, and the long-term sustainability of current models of provision is increasingly questioned. A stratified approach has the potential to address some of these issues and at the same time improve patient outcomes.

Costs are increasing too for the supply side. Pharmaceutical R&D productivity is decreasing, meaning higher costs for fewer new drugs. Data shows that, starting with 5,000-10,000 candidate molecules, it can take up to 15 years, and cost more than $800m, to get one new drug to market. The sustainability of this model of drug development is increasingly being questioned and many suggest that using molecular biology to select likely responders could lead to reduced development times, fewer failures, and lower costs. Diagnostics companies are an important part of the solution, but developing and commercialising robust tests can be expensive and difficult.

Stratified Medicine Innovation Platform

Global society faces many challenges. By applying technology and innovation we can help to meet these challenges and, at the same time, open up new opportunities for business. Innovation platforms focus on specific societal challenges where government is taking action through policy, regulation, procurement or fiscal measures. By improving co-ordination between the key players from industry, academia and government, innovation platforms can identify barriers to meeting the challenge, map possible routes to overcoming the barriers, and align activities to support innovative solutions. The aim is to deliver a step change in the ability of UK businesses to provide solutions for the global marketplace, boost UK economic performance, and provide higher-quality, better value healthcare services.

The Stratified Medicine Innovation Platform (SMIP) seeks to build on the UK's strength within global healthcare industries and put it at the centre of the next generation of medicine. It is a five-year programme to accelerate the development and uptake of stratified products and services. The innovation platform is a consortium of seven partner organisations all working towards a common vision. The partners are Technology Strategy Board, Medical Research Council (MRC), Cancer Research UK (CRUK), Arthritis Research UK (ARUK), Department of Health (DH), Scottish Government Health Directorate (SGHD) and National Institute for Health and Clinical Excellence (NICE). Each of these partners in the programme management group serves a different constituency but each has agreed to align activities towards a common goal with benefits for all stakeholders. Together they will invest around £200m in stratified medicine.

Achieving the rapid development and uptake of stratified medicine in the UK will be a difficult and complex task. It needs all components of the UK infrastructure to work together around a common plan and towards a common goal. The SMIP has started the process of building a shared vision for stratified medicine in the UK and a plan to achieve it. An early statement of a UK vision was refined and validated through widespread community engagement, including through workshops where more than a hundred people from more than 70 organisations helped to shape and refine the vision and plan.

This document presents a summary of the views heard from these sessions in the form of a UK Vision for Stratified Medicine in 2025, and a roadmap to achieve it. It attempts to capture some of the excellent stratification-related activity currently going on in the UK, but cannot claim to be comprehensive or an agreed consensus from all of the represented groups. The current version of the roadmap is a starting point. It will constantly evolve as new people contribute to it, and better understanding is developed. Those interested in engaging further with the SMIP are encouraged to join the special interest group on **_Connect** (**https://ktn.innovateuk.org/web/stratified-medicines-innovation-platform**).

A Shared Vision

The vision is for the UK to be the best place to develop, and have adopted, stratified medicine. This will benefit patients by improving outcomes, help physicians to select the most appropriate therapies, increase the cost-effectiveness of health service provision and help business to innovate more successfully.

This vision was developed over a series of workshops which explored what the UK landscape should look like in 2025. The key aspects of the vision are given in the box below:

A UK Vision for Stratified Medicine

- The UK should be the best place to develop, and have adopted, stratified medicine. This will benefit patients, provide cost-effective solutions for the NHS and other healthcare providers and create opportunities for business
- There should be an increased collaborative culture throughout the sector based around shared resources, and systems should be in place for effective data collection, sharing, governance and use across sectors (including NHS, business, academia, regulators and NICE)
- It should be quicker and less expensive to develop new drug-diagnostic combinations and have them licensed, and success should be reflected in increased UK economic growth
- It should be possible for all NHS patients to be involved in medical research if they wish, including through use of patient information and records, in order to inform the next generation of successful therapies
- There should be a smooth reimbursement process for stratified therapies and diagnostics, and an intellectual property (IP) framework that encourages innovation
- The UK health system should have established stratified care pathways, and evidence should be available to show that patient outcomes are improved where stratified medicine is used

A Shared Roadmap

A technology roadmap identifies the long-term objectives in an area and seeks to understand the possible routes to satisfy them. It can be used to guide the development of new products, processes or services, and to help shape the future direction of an emerging technology. Developing a roadmap has three major uses. It helps reach a consensus about a set of needs and identifies a range of possible solutions to satisfy them; it provides a mechanism to help forecast the required deployment of those solutions; and it provides a framework to help plan and coordinate technology and system developments.

The stratified medicine roadmap describes thematic areas which, if advanced successfully, will help accelerate the development and uptake of stratified medicine in the UK. The themes were identified at a series of workshops attended by a broad stakeholder community that included commercial companies developing therapeutics, diagnostics and data handling solutions; medical charities; and representatives from the healthcare sector including clinicians from across a number of therapeutic areas, pathologists, commissioners, managers and representatives of public sector bodies. In addition, there were academics representing research in all of the main topics around stratification of patients. The roadmap captures the range of views expressed by this broad group of stakeholders. It calls for activity in nine thematic areas.

The UK Stratified Medicine Roadmap: The Nine Themes

1. Incentivising adoption
2. Increasing awareness
3. Patient recruitment – consents and ethics
4. Clinical trials
5. Data – collection, management and use
6. Regulation and standards
7. Intellectual property
8. Bio-banks and biomarkers
9. Increasing the impact of R&D investment

The UK Stratified Medicine Roadmap contains a panel for each of these themes. Each panel describes how things are perceived to be now and articulates a vision of how they might be in 2025. Some of the barriers to achieving this vision are presented and activities that would accelerate the development of stratification are proposed. Some of the excellent work already in train is highlighted. Many topics are closely interlinked and some occur in more than one panel: for a stratified medicine system to work effectively in the UK, many of these issues will have to be progressed at the same time. The Stratified Medicine Innovation Platform on its own will not be able to achieve everything that needs to be done, but an attempt has been made to show what our own contributions might be. In order to save space in the following panels, acronyms are used. These are detailed in a glossary at the end of the document.

1. Incentivising adoption of SM in the NHS

Current Perceptions

Reimbursement mechanism for SM related Dx tests not always clear leading to unequal provision

Slow test adoption - commissioning structure a barrier

Infrastructure is not equally distributed and may be sub-scale in some locations

Differing requirements for in-house tests compared to industry developed tests

Current NHS genetics policy and services not designed for large-scale testing

Pathology budgets stretched and not linked to care pathways

Slow adoption of tests without Rx company support

Barriers

Budgets and processes in NHS not designed for diagnostic/drug combinations

Only few clinical decisions based on genetic tests

Uncertain markets for point of care testing vs. centralised testing

Dx companies can struggle to provide data for independent NICE assessment

Uncertain pathology capability in emerging techniques

Aggressive national pathology cost savings may discourage adoption of new techniques

No long-term strategic planning in NHS for SM services

Future State

A smooth integrated system: fair & beneficial to all stakeholders

Equitable access to the right tests for the right patients at the right time

Infrastructure available to all with equal access to treatments

Tests reimbursed at a level that is cost effective and incentivises new development

Patient/public engagement and acceptance

Informed commissioning (quality, cost, turnaround etc)

Enablers

Overall framework development by Human Genomics Strategy Group

Enhancing NHS informatics capability

Increasing evidence base leading to more widespread clinical acceptance of the value of genetic tests

Minimally-invasive biomarker tests

NICE diagnostics arm is an enabler for value assessment

National commissioning or funding for stratified medicine, both tests and treatments

Value assessment of Dx/Rx combinations to inform commissioning

Examples of current UK activity

NHS/DH initiative to improve cancer gene testing

HGSG review of commissioning, innovation and service delivery in all genetic medicine

Ability to use Cancer Drug Fund to buy associated complex diagnostics

Value-based pricing review of drug procurement in NHS

SMIP/CRUK SMP large-scale demonstrator programme in cancer

Pathology modernisation

Nicholson Review of Innovation in the NHS

OLS Senior Industry Group addressing business-NHS engagement

NIHR/NOCRI work to improve access for clinical trials

Trade Associations (ABPI, BIVDA, ABHI, etc.) work with NHS on new commissioning structures

Potential Role of SMIP

Help provide evidence to support policy development for commissioning and procurement

Help supply chain to develop new business models

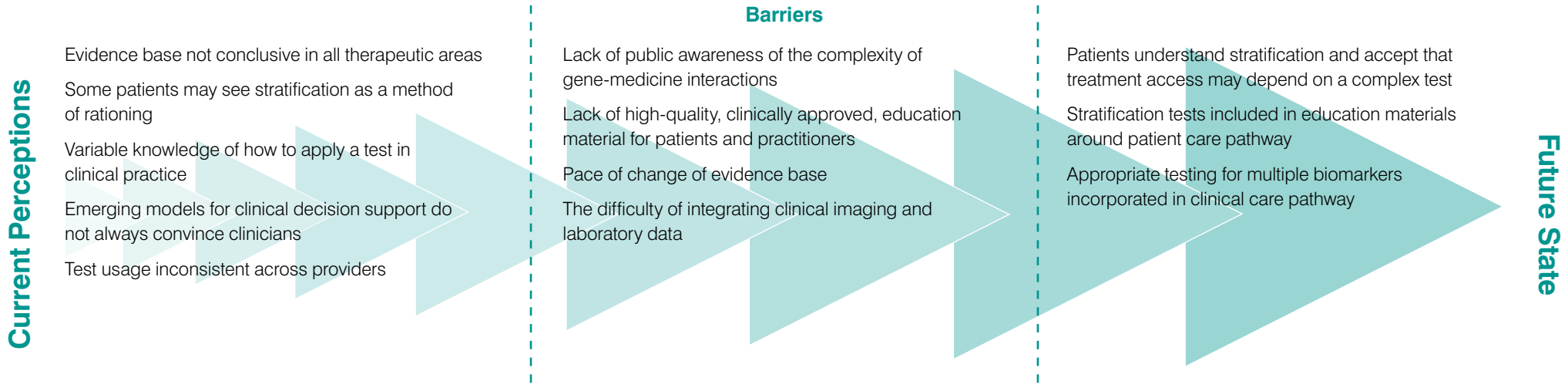
Support health economic assessment of diagnostic testing to inform NHS pricing

Support CRUK SMP and other demonstrators by funding associated technology development

Interim support for innovative molecular diagnostics in adoption phase

Help represent businesses in NHS policy/commissioning development

2. Increasing stakeholder awareness



Enablers

More awareness among front line staff of clinical utility and benefits

Agreement and sharing of genetic medicine health economic analyses

Tools for physicians to provide clear interpretation of complex test results

Physician-driven development of education materials for healthcare professionals involved in genetic medicine

Development of tests for use at point of prescription (pharmacy/GP) or patients able to test themselves

Centralised communication resource to suit a range of health professionals

Better engagement with patient support groups in disease specific areas

Patient access to global communication channels

Examples of current UK activity

Education working group of the HGSG

Various bodies already developing guidance materials

Appointment of NHS Chair in Pharmacogenetics

CRUK large-scale demonstrator in cancer

Potential Role of SMIP

Develop decision-making tools for physicians

Develop communication resource for education of health professionals

Involve patient support groups and Royal Colleges in SMIP programme development

Accelerate and communicate programmes that demonstrate validity of approach

Help extend approach into other therapeutic areas

3. Patient recruitment (consents & ethics)

Current Perceptions

- Identifying and recruiting appropriate patient cohorts can be time-consuming
- R&D approval process can be complex and time-consuming
- When patient consents are study or site-specific, data cannot be used for other purposes
- Sometimes local ethics and R&D approval process can inhibit larger national studies
- Problems with national programme for IT has held back novel data solutions

Barriers

- Data held in a range of databases and formats across healthcare providers
- Data quality may be low in data that has not been monitored and audited
- Inconsistent processes and standards for research consents
- Privacy concerns around data storage and use
- Excessive caution from some (unrepresentative) minority pressure groups

Future State

- A streamlined process for trials consent and patient recruitment, and trials are safe
- Consent for broad and unspecified future use, supported by appropriate regulation of personal data
- Single, and internationally valid, consent and ethics approval
- Primary care has important role in patient recruitment
- Use of data and samples for research based on 'opt-out' rather than 'opt-in'

Enablers

- Structure of NHS gives unique opportunity to deliver standardised research consent
- Novel IT solutions for capturing, communicating, storing and analysing data
- Public engagement about use of samples and genetic data for research
- Development of an overarching ethical framework
- Cost of storing massive data sets decreasing
- Patient groups support non-restrictive consents and effective R&D approvals
- Development and widespread use of generic consent forms
- Implementation of Academy of Medical Sciences recommendations on streamlining research regulation
- Connection of ethics committee with patient groups, starting with current disease areas of focus like cancer
- Policy communication, IT enablement & governance.
- Education and public awareness campaign demonstrating wider benefits to the community of participation in research
- Collaboration in clinical trials recognised in clinician performance assessment

Examples of current UK activity

- Academy of Medical Science report and recommendations
- Leading hospitals already running generic consent for all patient samples
- HGSG working on this area
- Plan for Growth actions on research approvals and recruitment to studies
- NIHR Translational Research Partnerships process for research consent in inflammatory disease
- Various data access and sharing initiatives (Generation Scotland, Cancer Registries, General Practice Research Database)
- Improved national and international data standards are enabling data sharing

Potential Role of SMIP

- Engage with patient groups on programme development and benefits of consent
- Support Government implementation of AMS recommendations
- Consulting with stakeholders on routine/generic consent

4. Clinical Trials

Current Perceptions

Localisation of commissioning and independence of providers leads to varied and complex implementation of national clinical trials

NIHR involve patients group

Networks such as NCRI encourage and enable national trials

Delays before patient recruitment starts is often the time-limiting step in studies

AMS report describes the situation well

Barriers

Uncertain impact of localisation agenda in healthcare and changes in commissioning

Relative higher prices for trial activities in UK versus BRIC countries

Future State

Reduced time and cost to conduct clinical trials

Reduced time to start complex genetic research projects

Reduced cost to recruit the appropriate subjects to enable stratified medicine

All patients are able to participate in clinical trials/population-based genomic research

Centralised solutions to access rare genetic types (e.g. web-based platform)

Exclusion of inappropriate patient populations on grounds of safety genotypes

Selection of appropriate patients for efficacy testing

Enablers

AMS report and recommendations

National initiatives to improve trials environment (CRUK, NOCRI, etc)

Public increasing their levels of participation in research

Faster ethics approval based on patient choice and critical health 'need'

Develop robust online (internet) recruitment

Develop standards within NHS for provision of patients into clinical trials

Better connection of infrastructure including IT systems and Biobanks

Examples of current UK activity

NIHR Clinical Research Networks, including cancer, could help in stratified medicine

NOCRI helping industry engagement with NIHR trials infrastructure

NIHR common frameworks and guidelines to reduce patient recruitment times

Potential Role of SMIP

Similar to role in patient recruitment

Help create critical mass to accelerate trials process

Communicate unmet needs (prioritisation)

Demonstration of a consistent database of patient accessible records.

Develop web-based recruitment tools

5. Data

Current Perceptions

Routine data collection and quality variable across the UK, better in Scotland

NHS Information Centre as central repository and access point for data but currently not meeting researcher requirements

Government data transparency drive (opengov)

No national programme for IT

Range of IT systems in use

Barriers

Morale issues following NPfIT failure

Most data has not been consented for access

Default position is to not make anonymised data available for research

Bespoke systems do not or cannot communicate without significant investment

Data protection issues seen as a barrier within trusts

Future State

Population-wide consented patient data available for analysis by researchers

Routine use of anonymised patient data sets by NHS & industry to improve patient outcomes

Increased use of routine data in post-marketing surveillance

Routine collection of health economic data around SM

Enablers

Massive data sets

Public support for research

IT capabilities improving

Encourage more open working between academia, NHS & industry

Cultural/policy encouragement to share data

Implement IT practices and routine generic consent for use of appropriately anonymised clinical data for research between institutions

Large-scale demonstrator programmes (regional or therapeutic-area focused)

Simplification of data protection rules around patient data

Build in and embed quality systems into NHS data handling

Examples of current UK activity

Generation Scotland

Individual routine consents

CRUK/Eastern Cancer Registry partnership & SMIP investment in data handling

Ongoing improvements to cancer registries

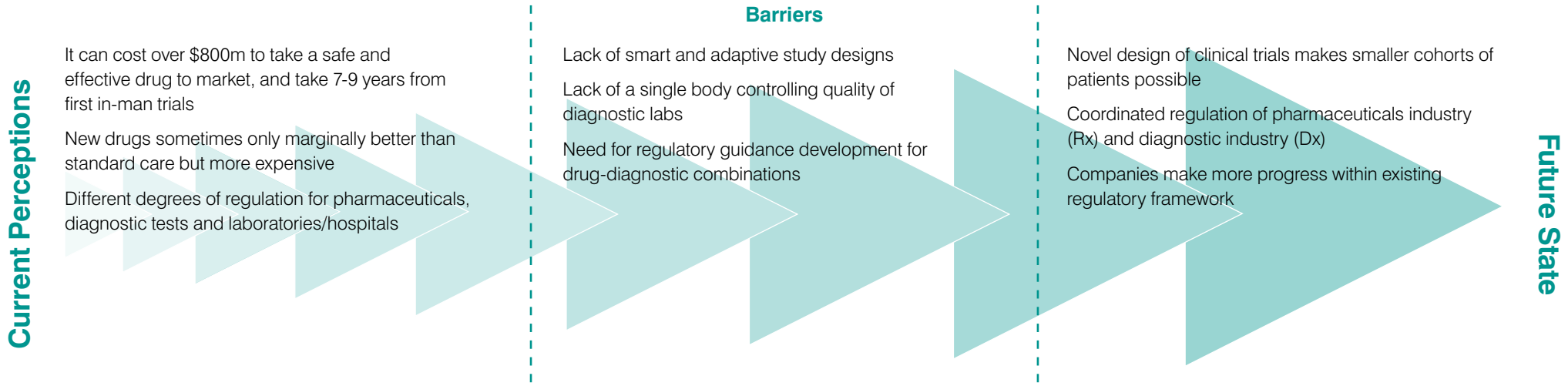
Establishment of Patient Reported Outcome Measures (PROMS) by Dept Health in England

Potential Role of SMIP

Develop tools to allow secure data mining of patient data across distributed data sources

Demonstrate that access to data repository by NHS & industry will improve patient outcomes and/or make UK a much better place to do research

6. Regulatory Framework and Development Pathway



Enablers

Regulatory guidance for co-development of diagnostics and treatment

DH and BIS encouraging EU Commission to improve regulatory framework

Facilitate co-development of drugs and diagnostics by alignment of the regulatory processes

Setting up of an expert committee (akin to the Committee for Advanced Therapies set up by the ATMP Regulation)

Examples of current UK activity

EU Commission on the revision of the IVD directive

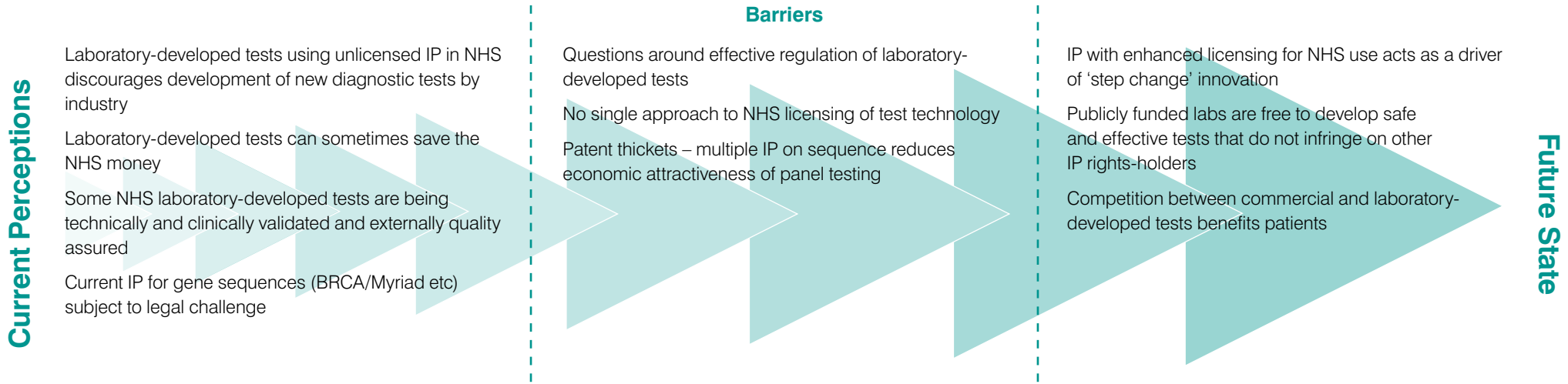
NHS QIPP agenda includes work on quality and standards

Potential Role of SMIP

Help in novel clinical study design

Encourage discussion with regulatory agencies

7. Intellectual Property



Enablers

Patent box tax incentive

Excellent technology platform & biomarker science base

Business models for developing & exploiting new & existing IP that provides fair return on investment whilst maintaining reasonable end user cost

Develop IP protection on the test, not the underlying gene sequence

Provide a strong home market (NHS) with value based pricing (product & service) and willingness to adopt new tests

A stronger domestic industry with global outlook, able to capitalise on excellent science base

Examples of current UK activity

EU In-Vitro Diagnostic consultation in process

OECD guidelines for licensing genetic inventions

HGC recommendations on IP and DNA diagnostics

Potential Role of SMIP

Provide support for diagnostic companies and co-development

Support SMEs in early IP filing

Commission health economics studies

Support development of new business models and pricing mechanisms

8. Bio-Banks and Early Biomarker Detection

Current Perceptions

- No central overarching database of biomarkers or biosignatures
- Many biosamples not clinically annotated
- Limited standardisation of tissue collection or consent
- Not everyone sees the value of centralised biobanks
- Stand-alone, incompatible tissue and data infrastructures
- UK Biobank has recruited 0.5m people

Barriers

- Localised clinical and research databases are hard to use for national level research
- Lack of technology platforms for use in clinical biomarker research
- Require policy framework for biomarker validation
- Many biomarkers do not have associated therapies

Future State

- UK-wide database of biobanks is used for stratification studies
- All tissue collected with consent for broad clinical research and data capture
- Routine, effective collaboration on biomarker ID
- A range of early biomarkers identified for future validation
- Coordination for Biomarker research via mandated central database
- In silico trials to ID biomarker

Enablers

- Accreditation system for biobanks
- Improve coordination of funding for biobanks
- Standardisation of procedures, including sample handling storage and consent process
- Ensuring biobanks store comprehensive clinical data
- Broad & enduring consent or implement opt-out rather than opt-in for data analysis in research
- Improved biomarker discovery and validation through new approaches
- Linking of databases and biobanks
- Improving IT to enable metadata approach across multiple systems
- Increase in pharma collaboration and pre-competitive activity

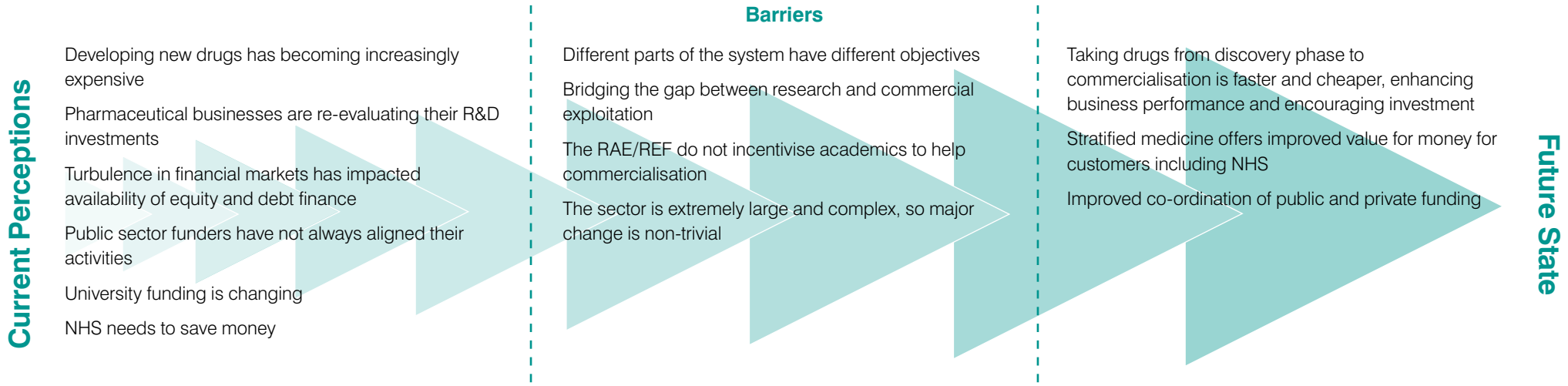
Examples of current UK activity

- UK Biobank programme standardising access procedures
- Generation Scotland
- Routine generic consent at sample-acquisition in major teaching hospitals
- NIHR/NOCRI Translational Research Partnerships

Potential Role of SMIP

- Help develop standards for biobanks
- Map existing UK databases and biobanks
- Support development of sample handling & preservation technologies
- Support development of biosignature analysis and data storage techniques
- Encourage widespread adoption of best practice
- Help connect existing infrastructure to create critical mass
- Enable access to infrastructure to accelerate development of new tests and therapies

9. Increasing and Leveraging UK R&D investment



Enablers

- Creating a coordinated UK programme
- Incentivise stakeholders to share pre-competitive data
- Stakeholder support for SM
- Full audit of UK capabilities /IT, biomarkers, Dx, Rx, clinical etc
- Better coordinated UK and EU funding streams
- Understand the value of cooperative investment
- Taking an international perspective

Examples of current UK activity

- ABPI work in this area
- OSCHR work in this area
- Nicholson Review of innovation in the NHS
- NorthWest exemplar
- Stratified Medicine Innovation Platform investments to date

Potential Role of SMIP

- Commission health economic studies
- Help develop new business models for stratified medicine
- Ensure coordination of partner activities
- Help create critical mass through a UK-wide programme
- Engage in international programmes

Stratified Medicine Innovation Platform Partners

The innovation platform seeks to make the UK the best place to develop, and have adopted, stratified medicine products and services. This is an extremely ambitious vision that will require activities across multiple technology areas, policy streams and government departments. Each of the Stratified Medicine Innovation Platform partners has a specific remit and can contribute significant resources and expertise from their core areas of capability. Together, the group covers a broad spectrum of interests. By aligning activities, many of the issues described above can be progressed.

The Technology Strategy Board aims to help businesses to develop innovative new products and services, while the Medical Research Council funds outstanding research in the science base and has a major initiative in stratified medicine. Cancer Research UK is the world's leading cancer charity dedicated to saving lives through research, and Arthritis Research UK has an interest in achieving better outcomes for patients in its disease area: both have stratified medicine at the centre of their strategies. The Department for Health and Scottish Government Health Directorate are government departments whose main role is to improve health and achieve better health, better care, and better value for all. The National Institute for Health and Clinical Excellence is tasked with assessing medical interventions, both therapies and diagnostics, and recommending their use based on value calculations.

The SMIP programme management group would greatly welcome input from other players. The Medicines and Healthcare products Regulatory Agency (MHRA) and the National Institute for Health Research (NIHR)/ NIHR Office for Clinical Research Infrastructure (NOCRI) have already started working closely with the innovation platform, and it is hoped that others would also like to participate. There will be areas where others are better placed to lead, and we can support their programmes.

How to engage with us

For the UK to achieve the vision set out in this document, significant advancements in technology and changes to systems and processes will be required. This cannot be achieved by any single organisation and will entail coordinated activity across the entire healthcare sector. This UK Stratified Medicine Vision and Roadmap can form the focal point for companies, public sector bodies and government to coordinate their efforts. The innovation platform partners have begun this coordinated activity and would welcome help and advice from others whose actions could help accelerate the journey towards the ultimate goal. A web-based community has been created to encourage engagement (**https://ktn.innovateuk.org/web/stratified-medicines-innovation-platform**). This will be supported by the innovation platform and will highlight future workshops, funding calls and ongoing discussions on specific stratified-medicine-related topics. We would also encourage others to use this forum to share information, raise awareness, identify partners and generate yet more momentum.

Glossary

ABHI	Association of British Healthcare Industries
ABPI	Association of British Pharmaceutical Industry
AMS	Academy of Medical Sciences
ATMP	Advanced Therapy Medicinal Products
BIS	UK Department for Business, Innovation & Skills
BIVDA	British In-vitro Diagnostic Association
BRIC	Brazil, Russia, India and China
CRUK	Cancer Research UK
CRUK SMP	Cancer Research UK Stratified Medicine Programme
DH	Department of Health
Dx	diagnostic
HGC	Human Genetics Commission
HGSG	Human Genome Strategy Group
IP	intellectual property
IT	information technology
IVD	in-vitro diagnostic
NCRI	National Cancer Research Institute
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NIHR	National Institute for Health Research
NOCRI	NIHR Office for Clinical Research Infrastructure
NPfIT	National Programme for IT
OECD	Organisation for Economic Co-operation and Development
OLS	Office of Life Sciences
OSCHR	Office for Strategic Co-ordination of Health Research
PROMs	patient reported outcome measures
QIPP	quality, innovation, productivity and prevention
R&D	research and development
RAE/REF	Research Assessment Exercise/Research Excellence Framework
Rx	therapeutic
SM	stratified medicine
SMIP	Stratified Medicine Innovation Platform

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