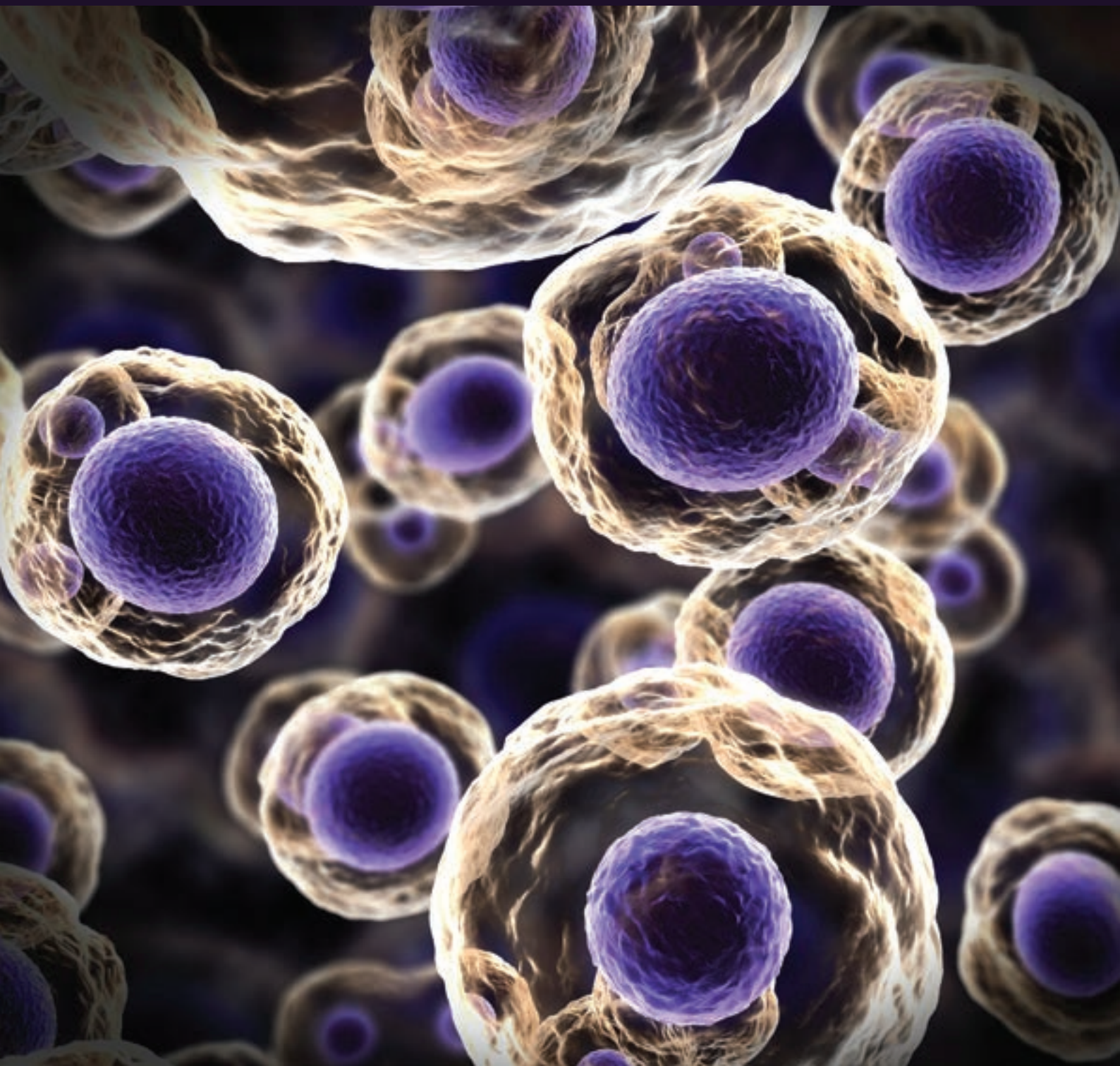
Life Sciences Industrial Strategy

– A report to the Government from the life sciences sector



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This Life Sciences Industrial Strategy has been developed in consultation with the Life Sciences Industrial Strategy Board. The Board has had broad representation from across the sector, reflecting the diverse nature of the life sciences industry and the ecosystem in the UK. I thank them for their valuable input and their commitment to this exciting work.

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Regius Professor of Medicine, University of Oxford
Chairman, Office for the Strategic Coordination of Health Research

Foreword – Professor Sir John Bell

The life sciences industry represents one of the dominant economic sectors in the UK. 'Health life sciences' refers to the application of biology and technology to health improvement, including biopharmaceuticals, medical technology, genomics, diagnostics and digital health. It has the advantage of very high productivity compared to other sectors, and generates a wide range of products including drugs, medical technology, diagnostics and digital tools, as well as products for consumer health. It is also widely distributed across the whole of the UK and brings significant jobs and growth to virtually every region. I was asked by the Government to bring industry together and produce a report that lays out the sector's vision of how the UK might exploit its existing strength to increase the pace of economic growth in this sector. The Life Sciences Industrial Strategy Board has worked hard at creating the vision that lies behind this strategy. There has been extraordinary engagement across all components of the sector, from those involved in small and mid-sized companies, through to those in the pharmaceutical, medtech and diagnostics sectors. The charity sector also has much to offer and provides very significant leverage on Government funding and they too have been engaged in developing the vision. Importantly, the NHS has also been engaged throughout this strategy's development and far from being a challenge to the NHS's founding values of universal care, free at the point of use, this agenda is central to ensuring and improving it for future generations and complements many of the objectives set out in the NHS's Five-Year Forward Review. Furthermore, many of the steps outlined in this Strategy are opportunities uniquely available to the NHS and could not be realised in many insurance-based healthcare systems.

The strategy places an emphasis on putting the UK in a world-leading position to take advantage of the health technology trends of the next 20 years through the establishment of the Health Advanced Research Programme.

The strategy also seeks to address a series of challenges under five key themes:

- Science: Continued support for the science base, maintaining strength and international competitiveness.
- Growth: An environment that encourages companies to start and grow, building on strengths across the UK, including expansion of manufacturing in the sector.
- NHS: NHS and industry collaboration, facilitating better care for patients through better adoption of innovative treatments and technologies.
- Data: Making the best use of data and digital tools to support research and better patient care.
- Skills: Ensuring that the sector has access to a pool of talented people to support its aims through a strong skills strategy.

The issues of pricing were explicitly not included in the scope of the report.

It is the view of industry that this strategy needs to be seen over at least a five year period, not as a moment in time when a sector deal is agreed. To retain the UK's competitive edge in this sector, there is a requirement for sustained effort over a longer period of time, and the proposals here and in the sector deal are designed to be thought about in that longer-term context, with both industry and Government having responsibilities and commitments over a longer time frame. This strategy should be viewed in the context of the Government's wider industrial strategy agenda, and where proposals may complement those coming forward from other sectors (through, for example, the review of Artificial Intelligence), they should be developed with common interests in mind.

Importantly, to deliver the potential for economic growth through the projects and programmes outlined in this strategy, there will be a need for oversight of this programme over the next five years. Governance that sits on top of the strategy needs to define accountability for the relevant programmes and regularly review delivery from both industry and Government against the objectives of the strategy. With that in place, the strategy will emerge as a dynamic set of actions that will ensure the most desirable outcomes for the economy, industry and the NHS.

This strategy provides a unique opportunity for the country and I hope it can be delivered effectively in the coming years.

John Bell GBE, FRS, FMedSci
Regius Professor of Medicine, University of Oxford
Chairman, Office for the Strategic Coordination of Health Research

Summary of recommendations

Section		Core Recommendation	Reinforcing Actions	Strategic Goal
HARP		Create the Health Advanced Research Programme (HARP).	• Establish a coalition of funders to create the Health Advanced Research Programme to undertake large research infrastructure projects and high risk 'moonshot programmes', that will help create entirely new industries in healthcare. • Continued support for genomics in medicine including advancing proposals by the CMO for increasing genomic testing and screening. • Creating a platform for developing effective diagnostics for early, asymptomatic chronic disease. • Digitalisation and AI to transform pathology and imaging. • Support projects around healthy ageing.	Create 2-3 entirely new industries over the next 10 years.
Reinforcing the UK science offer	Discovery Science	Sustain and increase funding for basic science to match our international competition.	• The UK should aim to be in the upper quartile of OECD R&D spending. • Encourage discovery science to co-locate. NIHR should continue to be supported with funding increases in line with Research Council Funding. • Government should ensure the environment remains supportive of charitable contributions through enhancing the Charity Research Support Fund. • Capitalise on UKRI to increase interdisciplinary research, work more effectively with industry and support high-risk science.	The UK should attract 2000 new discovery scientists from around the globe.
	Translational Science	Further improve UK clinical trial capabilities.	• Document the number of novel trial designs used as well as the quantity of 'change of practice' trials in the UK compared to elsewhere. • The UK should work with industry and regulators to establish a working group to evaluate the use of digital health care data and health systems; to evaluate the safety and efficacy of new interventions; and to help ICH modernise its GCP regulations. • Government should improve the UK's clinical trial capabilities so that the UK can best compete globally in our support for industry and academic studies at all phases. • Design a translational fund to support the pre-commercial creation of clinically-useable molecules and devices to intervene and treat disease, which can then be explored in preclinical and early clinical studies. • Use Government and charitable funding to attract up to 100 world-class scientists to the UK, with support for both their recruitment and their science over the next ten years.	To support a 50% increase in the number of clinical trials over the next 5 years and a growing proportion of change of practice and trials with novel methodology over the next 5 years.

Section		Core Recommendation	Reinforcing Actions	Strategic Goal
Growth and Infrastructure	Fiscal support	Ensure the tax environment supports growth.	• Support the aims of the HMT review into patient capital. • UK Government should ensure the UK's tax environment is internationally competitive in supporting long-term and deeper investment. • Address market failures through Social Impact Bonds and measures to encourage AMR research. • Consider how UK-based public markets can be used more effectively in the sector. • Review the eligible costs recognised by the SME R&D Tax Credit and large company RDEC schemes, and consider raising further the RDTC employee limit.	Create four UK companies valued at >£20 billion market cap in the next ten years.
	Clusters and 'place'	Support the growth of Life Sciences clusters.	• Government, local partners and industry should work together to ensure the right infrastructure is in place to support the growth of life sciences clusters and networks. • UK's existing clusters should work together and with government to promote a 'single front door' to the UK for research collaboration, partnership and investment.	
	Manufacturing	Attract substantial investment to manufacture and export high value life science products of the future.	• Accept in full the recommendations of the Advanced Therapies Manufacturing Action Plan and apply its principles to other life science manufacturing sectors. • There should be a programme in partnership with industry to develop cutting-edge manufacturing technologies that will address scale-up challenges and drive up productivity. • UK Government should optimise the fiscal environment for manufacturing investment to drive investment in industrial buildings, equipment and infrastructure for manufacturing and late-stage R&D. • Consider nationally available financial incentives – grants and loans, or capital allowances combined with regional incentives – to support capital investment in scale-up, and prepare for manufacturing and related export activity. Industry suggests incentives need to amount to 10-15% of the total capital commitment of a project to be internationally competitive. • Make support and incentives for manufacturing investment and exporting available to business through a single front door, provide a senior national account manager accountable for delivery and simplify the customer journey.	Attract ten large (£50-250m capital investment) and 10 smaller (£10-50m capital investments) in life science manufacturing facilities in the next five years.

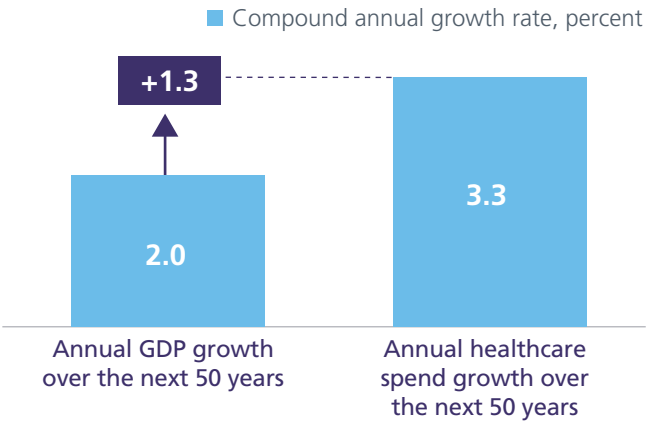
Section		Core Recommendation	Reinforcing Actions	Strategic Goal
NHS Collaboration		The Accelerated Access Review should be adopted with national routes to market streamlined and clarified, including for digital products.	• Utilise and broaden the Accelerated Access Review to encourage UK investment in clinical and real-world studies. Deliver a conditional reimbursement approval, for implementation as soon as licensing and value milestones are delivered so that patients can benefit sooner. • Create a forum for early engagement between industry, NHS and arms-length bodies (e.g. NICE, MHRA) to agree commercial access agreements. • The Government should use the recommendations from the AAR to streamline the processes and methods of assessment for all new products, simplifying and accelerating access and using a single clear decision point. Ensure this streamlined access framework is part of a holistic medicines policy with a leading role for NICE and including a new voluntary agreement as a successor to the current agreement. • Value assessments should be evolved in the long-term with improved patient outcome measures, affordability and cost management data extending beyond one year timeframes. • NICE's funding model for technology evaluation should be set up in a way that does not stifle SME engagement.	In the next five years, the NHS should engage in fifty collaborative programmes in late-stage clinical trials, real world data collection, or in the evaluation of diagnostics or devices. The UK should be in the top quartile of comparator countries, both for the speed of adoption and the overall uptake of innovative, cost-effective products, to the benefit of all UK patients by the end of 2023. In the absence of a more robust metric, the Government's Annual Life Science Competitiveness Indicators report should be used to measure this metric.
Data		Establish two to five Digital Innovation Hubs providing data across regions of three to five million people.	• Building on the standards set out by the National Data Guardian and Care Quality Commission, the health and care system should set out a vision and a plan to deliver a national approach with the capability to rapidly and effectively establish studies for the generation of real world data, which can be appropriately accessed by researchers. • ePrescribing should be mandatory for hospitals. • NHS Digital and NHS England should set out clear and consistent national approaches to data and interoperability standards and requirements for data access agreements. • Access to currently available national datasets should be accelerated by streamlining legal and ethical approvals. • There should be a forum for researchers across academia, charities and industry to engage with all national health data programmes.	Establish 2-5 data hubs.

Section		Core Recommendation	Reinforcing Actions	Strategic Goal
Data (continued)		Establish two to five Digital Innovation Hubs providing data across regions of three to five million people. **(continued)**	• A new regulatory, Health Technology Assessment and commercial framework should be established to capture for the UK the value in algorithms generated using NHS data. A working group should be established to take this forward. • Two to five digital innovation hubs providing data across regions of three to five million people should be set up as part of a national approach and building towards full population coverage, to rapidly enable researchers to engage with a meaningful dataset. These should operate in line with the NDG's recommendations on patient data, and include longitudinal data covering primary, secondary and social care to allow evaluation of innovative tools to establish their impact on care pathways and cost within the healthcare system. These regional hubs should also have the capability to accelerate and streamline CTA and HRA approvals, together with local sign-off and data access agreements, operating within the national framework, to improve the speed of trial initiation. One or more of these should focus on medtech. The UK could host 4-6 centres of excellence that provide support for specific medtech themes, focussing on research capability in a single medtech domain such as orthopaedics, cardiac, digital health or molecular diagnostics. • National registries of therapy-area-specific data across the whole of the NHS in England should be created and aligned with the relevant charity.	Establish 2-5 data hubs. **(continued)**
Skills	Movement of skilled people		• A migration system should be established that allows recruitment and retention of highly skilled workers from the EU and beyond, and does not impede intra-company transfers.	Establish a migration system that allows us to recruit the best international talent.
	Skills Action Plan	Develop and deliver a reinforced skills action plan across the NHS, commercial and third sectors based on a gap analysis of key skills for science.	• Develop and deliver a reinforced skills action plan across the NHS, commercial and academic sectors based on a gap analysis of key skills for science. • Create an apprenticeship scheme that focuses on data sciences, as well as skills across the life sciences sector, and trains an entirely new cadre of technologists, healthcare workers and scientists at the cutting-edge of digital health. • The Government should establish Institutes of Technology that would provide opportunity for technical training, particularly in digital and advanced manufacturing areas. • There should be support for entrepreneur training at all levels, incentivising varied careers and migration of academic scientists into industry and back to academia to increase influx of talented scientists and entrepreneurs in the public and private sectors. • A fund should be established supporting convergent science activities including cross-disciplinary sabbaticals, joint appointments, funding for cross-sectoral partnerships and exchanges across industry and the NHS, including for management trainees. • High quality STEM education should be provided for all, and the government should evaluate and implement additional steps to increase the number of students studying maths to level 3 and beyond.	

Introduction

As the UK plans its future outside the European Union, identifying and supporting specific sectors of the economy to grow and expand quickly becomes a clear priority. Life sciences are a major component of the current economic base of the UK with the sector generating £64 billion of turnover, and employing more than 233,000 scientists and staff.[1] In the coming decades, healthcare spending will outgrow the economy in OECD countries by 3.3% versus 2% CAGR, creating a sustainability challenge for healthcare systems and new opportunities for life sciences industry growth. This is driven by macro-economic forces such as an ageing population, a growing middle-class and the growing burden of chronic diseases that will accompany the significant change in demography. The global life sciences industry is expected to reach >$2 trillion in gross value by 2023 (approximately $1.6 trillion today). Given its importance to the innovation economy in the UK and its potential for growth there are few, if any, sectors more important to support as part of the industrial strategy. The importance of life sciences was recognised in the 2011 'Strategy for UK Life Sciences', and since then considerable progress has been made in areas of genomics, science funding and programmes such as the biomedical catalyst and catapults. In recent months we have seen important indications from government that they are committed to the life sciences with the announcement of £197 million of Industrial Strategy Challenge Fund (ISCF) support for Leading Edge Healthcare, the publications of the CMO's Genomic report and the Government Response to Dame Fiona Caldicott's review of Data Security Consent and Opt-outs, and the announcements on funding for implementation of the Accelerated Access Review (AAR).

Projected OECD GDP vs. healthcare spend



SOURCE: OECD GDP long-term forecasts 2009-60; OECD public spending on health and long-term care: a new set of projections – cost containment scenario used

The enormous gains in health outcomes and life expectancy achieved over the last 30 years can continue but it is likely that this will depend on both existing innovation platforms for drug and device discovery, and also a host of new scientific platforms for improving health. These will include digital tools, robotics, artificial intelligence based on machine learning and totally new therapeutic approaches to disease such as gene therapy, nucleic acid based therapies or cell therapy. The UK is powerfully positioned to lead in the discovery and evaluation of these new approaches. It is clear that the single most important changes in healthcare will emerge with the increasing digitisation of a wide range of information. Everything from patient records, X-rays, pathology, images, genomics, healthcare management tools, and the input from a wide range of digital monitoring devices will soon be available to healthcare providers digitally and will fundamentally change the way we think about human disease and how best to manage it. New innovations are also likely to transform the way health systems operate. The longstanding public health ambition of creating a healthcare system focussed on early detection or prevention may now be possible as a result of innovative new technologies.

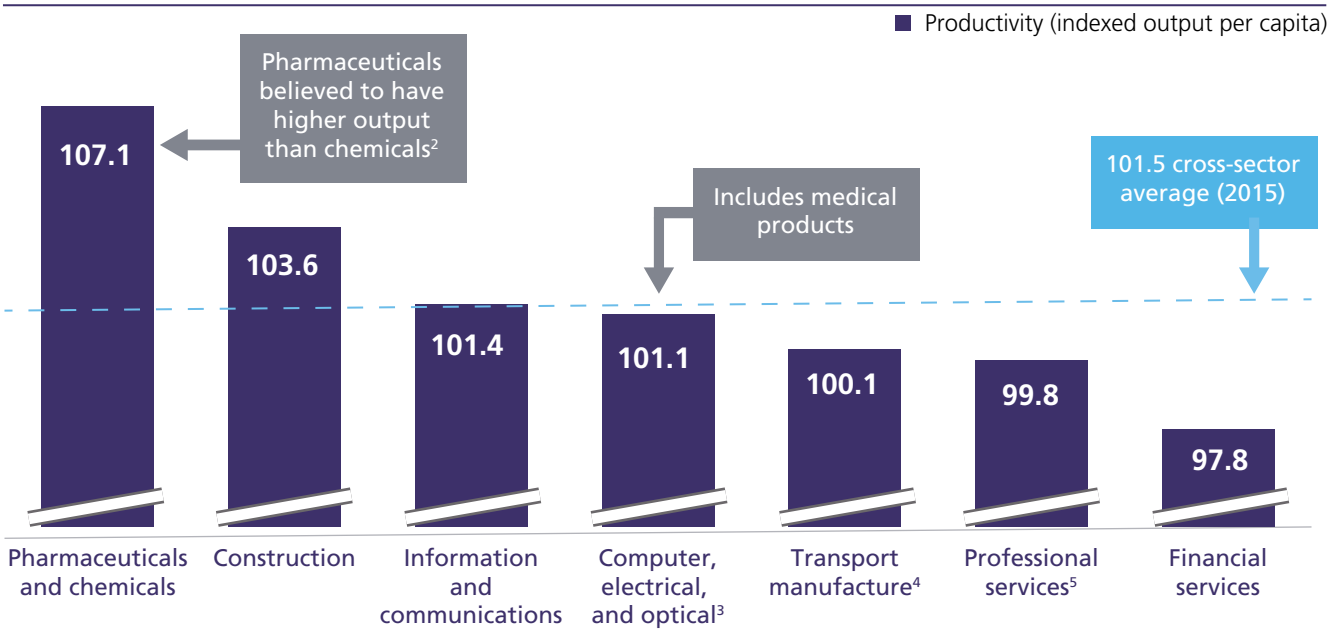
1 HM government, 2016, Strength and Opportunity 2016: The landscape of the medical technology and biopharmaceutical sectors in the UK. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/607193/strength-and-opportunity-2016-bioscience-technology-accessible.pdf

Transformation of the NHS to keep up with the changing pattern of disease and demography is a crucial objective over the next twenty years and, if appropriately applied, the same innovation that drives global economic growth could also be used to both improve outcomes in the NHS and, ultimately, to reduce cost.

This sector brings with it opportunities to increase economic growth and to produce benefits for patients treated in the NHS. A potential added benefit might be to help with the task of improving the efficiency of the NHS. If the NHS is to be a partner of the life sciences sector then it is appropriate that economic gains made through the life sciences strategy and the resulting efficiency benefits in the NHS should be recognised and directly used to support additional Government investment back into the sector. This would create a virtuous cycle whereby the success of the UK's life sciences sector yields sustainable, increased investment in medicines and technologies which benefit patients.

In addition to new industry sub-sectors, we must also continue to excel in those sectors that have dramatically improved patient outcomes. Pharmaceuticals, for example, have a higher output than most other sectors of the economy. On indexed output per hour, pharmaceuticals exceed the output of other major sectors such as communications, computing, electrical and optical, transport, manufacturing, professional services, and financial services:

UK productivity by sector – selected examples
Indexed output per hour, 2015[1]



1 Index of 100 represents 2013 UK average (i.e., comparator is UK output per hour averaged across all industries in 2013)
2 The Economist intelligence Unit (2015)
3 Includes medical devices
4 Includes automobiles and other transport equipment
5 Includes scientific R&D

Source: ONS (2016)

Furthermore, in a country where productivity is a major challenge, public sector life sciences discovery activity, although still underfunded on a per capita basis is dramatically more productive compared to other countries such as the USA or Germany. In 2015, for example, UK public life science R&D spend was $76 per capita compared to $109 in Germany and $159 in the US[2]; yet produced 185 life science publications per million people; compared to 66 in Germany and 121 in the US.[3]

2 NIH; UK Government; AMRC; Förderatlas DFG; Federal Statistical Office (includes charity, government and EU funding [for Germany and UK]).
3 2015 filtered by country and region and by life sciences e.g., ((Boston AND United States) AND ("2015/01/01"[Date – Publication]: "2015/12/31"[Date – Publication])). Weighting is by H index of journal Source: Pubmed, Elsevier Scopus.

With all of this in mind, we have created an industrial strategy which capitalises on our strong science base and which addresses the issue of scaling small companies to create more mature enterprises. We have attempted to shape the opportunity to capitalise on manufacturing advances and have worked closely with the NHS to propose a new collaborative environment where industry and the health system work together, underpinned by the rich datasets that the NHS can now provide. A combination of a strong science base, a vibrant commercial sector in health and a comprehensive, engaged, data-rich healthcare system could provide an ideal environment for the UK to lead in many of these emerging areas of life sciences and to create globally successful new industries.

Vision:
Build our life science industry into a global hub
that makes the UK the home of clinical research and medical innovation

A globally-unique and internationally competitive life sciences ecosystem supported by collaboration across industry, the NHS, academia and research funders to delivering health and wealth

Health Advanced Research Programme: Bringing together a coalition of funders to anticipate a future vision of healthcare and create new industries in the UK based on 'grand challenges', such as healthy ageing, diagnosis-led healthcare, and AI

SCIENCE	GROWTH	NHS	DIGITAL
			
Building on strengths in discovery research and supporting translation of our world-class science base	Enabling SME growth, manufacturing and supporting infrastructure across the regions of the UK	Building on the Accelerated Access Review, enabling the NHS to embrace cost-effective innovations for patients	Supporting collaboration on real world evidence, enabling innovators and the NHS to research new technologies

SKILLS

Ensuring the UK has the talent and skills to underpin future life sciences success

REGULATION

Securing patient safety and delivering the best ecosystem for life sciences

GLOBAL BRITAIN

Working with the best global partners and driving new opportunities for trade and investment

A joint programme of delivery between industry, NHS and Government to monitor and oversee implementation will be agreed through a Life Sciences Sector Deal

We have also proposed a programme to deliver solutions to future healthcare challenges, known as HARP – the Health Advanced Research Programme – through which the NHS and UK-based industries can work together to create new and more efficient ways of delivering world-leading and sustainable healthcare. These are exciting opportunities, but will require a coordinated effort between patients, the healthcare system, funding agencies and industry. It will also require scale and significant commitment to bold and potentially risky science. Enhancing the UK's capabilities for discovery and development of new medicines, creating new diagnostics and medtech capabilities, and building companies that develop whole new areas of medical innovation using data analytics, artificial intelligence and engineering will allow the UK economy to benefit from the next exciting era of health-related innovation and will also provide the tools for transforming our healthcare system. The emerging picture is that many of these fields are converging to create exciting prospects for the life sciences sector. Both pharma and medtech will be profoundly influenced by data and digital advances, and disciplines such as AI will impact life sciences widely. To lead globally in these fields we will need more integration and convergence across the piece and we will need the explicit support of the healthcare system.

If managed carefully, EU exit may be used as a catalyst to take steps to speed the growth of the life sciences sector in the UK. Healthcare is a global business and the UK should seek to expand and develop its global markets as well as being a destination for inward investment that wishes to take advantage of world class science and infrastructure – ultimately for the benefit of all patients.

It is important to remember that this sector is amongst the most competitive globally and many countries have recognised the opportunity associated with life sciences investment. Standing still is therefore not an option, the UK must deliver a whole new set of opportunities if it is to keep its existing companies and grow new ones. The future of regulation of life sciences products needs careful thought, as does the need to supply the sector with the international talent that it depends upon. Care must be taken to ensure continued reliable access to the global talent pool that has allowed this sector to be so successful to date. The country's strength in clinical trials puts it in an enviable position, but the UK commercial environment needs improving, with the NHS working more effectively with industry. To assure the future of the UK life sciences sector, it is necessary to improve the relationship between the healthcare system and industry, and for these partners to work more coherently together to deliver better patient outcomes and create economic growth.

This Strategy is a blueprint for investment by Government and the private sector to strengthen and enhance our capabilities in life sciences to drive economic growth more rapidly and develop new technologies for patients. It both reinforces existing strengths and creates opportunities for the NHS to work with industry to transform healthcare; it also creates new global businesses, based on NHS data and innovations developed here. Successfully implemented, this strategy should ensure that the UK remains one of the great global leaders in life sciences research, creating opportunities for inward investment, building new, significant companies that make and sell products internationally, and train and employ a high-value workforce in all areas along the value chain from fundamental discovery through to manufacturing and commercialisation.

By making the UK a global partner for discovery and development of the full range of health-related products, this strategy will attract global investment into the UK that will benefit not only the economy but will also directly support NHS activity, improving the quality of patient care. It will also attract advanced manufacturing in the longer term and will provide a fertile environment for life sciences companies to grow. At its heart lies the NHS, which holds the key to a unique offer to industry that can help secure the UK's position as a leading life sciences cluster. Because competition is fierce, it is a holistic strategy and all aspects need to be delivered.

The Government's Industrial Strategy Green Paper named the life sciences as a key strategic sector in the UK that could come forward and develop a sector deal. This strategy document should start the conversation between industry and government as to what both parties can invest, in order to achieve the ambitious vision set out and reap the benefits in the UK of improved health and a strong economy.

Governance and Implementation

1) Although there are elements of this strategy which are clearly not appropriate for a Sector Deal, such as fiscal recommendations, several key recommendations can form the basis for constructive discussions on an early agreement between the Sector and Government. The development of the Life Sciences Industrial Strategy has brought together a number of players across a diverse sector, and once a deal has been agreed this should evolve into appropriate governance structures to monitor the Deal's implementation.

2) Although it is not possible in advance of that process to say exactly how implementation and governance will work, there are some key principles it will be important to follow:

   a. Clear, identifiable leadership of a self-defined sector: this should include input from small and large companies, pharma, biotech, medtech, diagnostics and digital. The NHS and charities should be engaged. The sector should be configured in a way that is representative of its diversity, including organisations that go beyond its participants (such as key research institutions, devolved administrations, local authorities and other key partners).

   b. Implementation Planning: as a public commitment between Government and Industry, a Sector Deal will include an agreed implementation plan, setting out how the Deal will be delivered on both sides, with clear milestones and timescales for doing so.

   c. Oversight of delivery by senior, accountable leaders: each element of a Deal will need a senior Government and sector lead, who has genuine accountability, can ensure delivery and can take action as needed to address risks / challenges. A right-sized oversight board representing the key elements of the package will provide strategic oversight. The oversight board will be expected to report regularly on progress (at least annually) and escalate any delivery issues with the relevant Government or sector participants.

   d. Success metrics: the implementation plan will need to include a clear set of stretching but realistic success metrics for each element of the Deal to measure progress.

The Health Advanced Research Programme (HARP)

While considering the role of the science base in the UK in supporting the Life Sciences Industrial Strategy, it is clear that the strength of both basic and clinical science in the UK is a major feature of the environment that both attracts and retains industrial activity in the UK. Both publicly funded research supported by Government and charities, and industrial research in small and large companies, operates at the cutting-edge, leading innovation. Many of the recommendations of this strategy will add further platforms on which to expand and diversify this activity. The availability of a stronger digital environment, reinforcing and expanding the skills base, enhancing the available risk capital for emerging companies, and creating a rich, collaborative research environment with the NHS, all provide new opportunities for expanding and developing the science base. To take advantage of these new opportunities, however, it will be necessary for funders to find mechanisms to support a greater number of higher risk/higher reward projects and also to support larger scale science programmes that the UK has already shown that it can execute extremely well. The core research activities of conventional response-mode funding are solid in the life sciences, but there is increasingly a need to look for mechanisms to support both larger scale science projects and programmes that are higher risk.

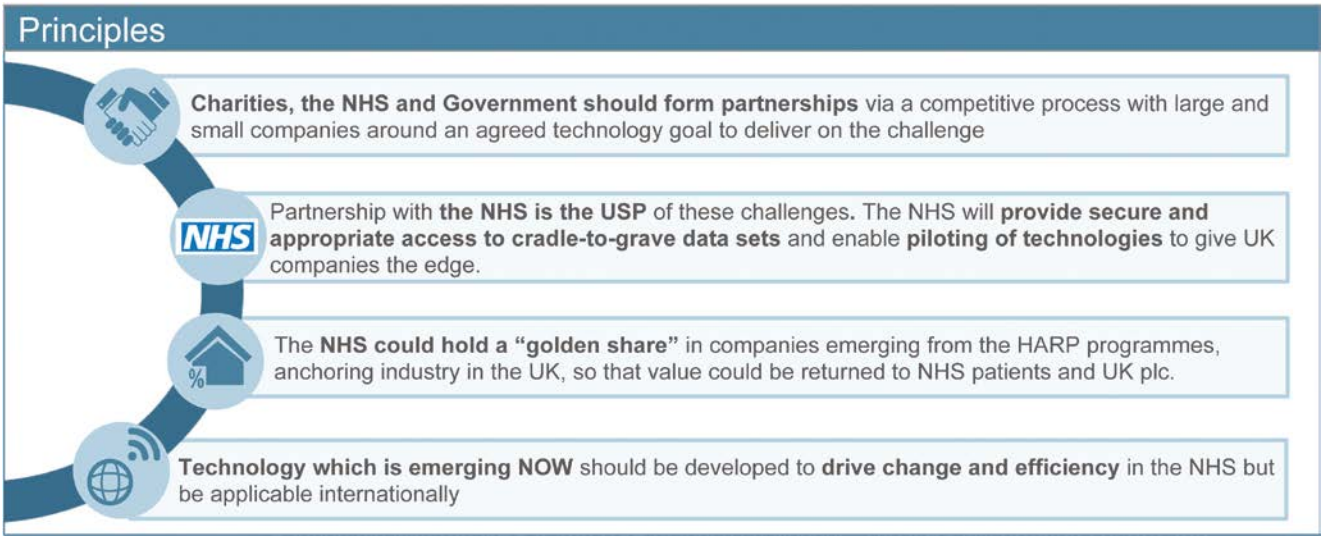
The strategy for life sciences recognises the need to consider and fund projects that will impact on the direction of healthcare delivery over the next twenty years. Some should be large-scale infrastructure projects that have historically put the UK in globally leading positions in areas such as precision medicine and genomics. UK Biobank and Genomics England (GeL) are two existing examples of such programmes, but there is a need to consider other such possibilities. In addition, it is clear that DARPA-like projects[4] in the UK could be aimed at encouraging industry to take on bold, far-sighted ambitions in the life sciences to potentially create whole new industries based in the UK. The intention should be to create commercial success by leading and developing new industrial sectors underpinned by novel technology and higher risk science. These programmes will need new decision-making processes. UK Research and Innovation (UKRI) is already making significant progress in funding new types of science, as are the major charities that have an ambition to pursue such new scientific opportunities. We have labelled this broad class of scientific opportunities as the Health Advanced Research Programme (HARP) and provide a few early examples of what these programmes might look like.

There are several features of these HARP programmes that are essential for the programme to be successful:

- These programmes need to be well resourced, sufficient to undertake the necessary R&D but also to effectively commercialise products globally. Scale is important. We expect each of these programmes will require several hundred million pounds in investment.
- These programmes will need multiple partners and funders. Charities will be central to many of these, as will support from Government and UKRI. In addition these projects will require the NHS to be a partner particularly by providing unique and perhaps exclusive access to large data sets necessary for most of these programmes and by providing a healthcare context to pilot new approaches to medicine (e.g. very early diagnosis of disease). Finally industry is at the heart of these initiatives and a competitive process to select partners, ideally UK companies, will be necessary.

4 The Defense Advanced Research Projects Agency is an agency of the U.S. Department of Defense responsible for the development of emerging technologies for use by the military. DARPA highlights that their success depends on the vibrant ecosystem of innovation within which the Agency operates.

- Most of these programmes will require NHS involvement for success. In projects where data is the key infrastructure, the UK needs to ensure that some of the benefits are returned to the healthcare system, including access to technology. In some cases this could be achieved with a 'golden share' held by the Department of Health or NHS England to ensure that the company would continue to be based in the UK and would provide ongoing benefits to the health system. Governance and decision-making will need to include the NHS, as well as major charities and UKRI. The governance structure should allow flexibility in the way projects are run, and for differing configurations of partner organisations to be involved.



The UK has experience with such programmes in a pre-competitive space. In the fields of precision medicine and genomics applied to patients, the UK has already embarked on two globally leading initiatives, UK Biobank and Genomics England. These projects have positioned the UK as the country that has defined the future of these fields. UK Biobank has already achieved very substantial industry engagement and is proving a magnet for both diagnostic and pharma companies. Genomics England is at an earlier stage of evolution but has already set the global standard for healthcare genomic data in rare disease and now, increasingly, in cancer. As parts of the scientific infrastructure these are excellent examples for future large-scale HARP projects.

HARP Opportunities

a) Genomics in medicine

The UK has already attained a uniquely powerful position in the field of genomics applied to healthcare. Not only has it sponsored some of the fundamental science that underpins this field, such as the sequencing of the human genome, but it has also been the first to apply at scale genomics to well-characterised patient populations. This has been a significant inflection point for the entire field, creating a wealth of opportunities to apply genomic science to healthcare and has also allowed the NHS to be the leading healthcare system globally to be providing large-scale genomics in routine care. The ambition for genomics in the Strategy must be to maintain the UK's globally leading position and to invest alongside industry to ensure that these genomic datasets are used to improve the discovery and targeting of therapies and to ensure that patients obtain more precise and useful diagnostic information in a range of disorders. Collaboration to achieve these goals should be supported by a National Genomics Board, as recommended by Dame Sally Davies.

The Strategy can significantly contribute to sustaining the UK as the global genomics leader – building on the momentum of GeL and UK Biobank and supporting Dame Sally Davies' 'Generation Genome' vision, in four ways:

- By ensuring, in collaboration with industry, that there are sufficient funds to allow the whole genome sequencing of the 500,000 people that make up UK Biobank and support for the informatics infrastructure to both hold the data and make it available to underpin the whole field of precision medicine. There has been readiness from industry to commit up to £150 million as their contribution to this aspect of the life sciences genomic strategy, though there is likely to be more resource needed to complete the sequencing and to establish the required informatics capability to store the genomics and healthcare data. This programme should be aligned with the GeL programme to gain further scale and competitiveness and for expertise to be shared.
- Capturing the data generated by a commissioned whole genome sequencing service in NHS England. This will rapidly accumulate large numbers of relevant variants and produce the richest dataset for rare diseases in the world. This data should be part of a national genomics dataset linking whole genome sequence to phenotype.
- A key objective must now be to complete the pathway in the NHS for routine whole genome sequencing of cancer samples with appropriate patient consent. This will require the completion of the tissue-handling pathway initiated by GeL, a 2-4 week turnaround in returning data, and the systematic application of genomic data in the management of patients with all forms of solid and liquid tumours. There has been considerable progress with this programme in recent months and excellent genome-wide data is being generated now, revealing that actionable variation in tumour DNA from whole genomes is present in the majority of tumours sequenced, far exceeding the return seen with panels or exomes. This is likely to be a major breakthrough in the treatment of cancer and will have profound implications for precision medicines across oncology.
- In support of the UK's emerging commercial capabilities in DNA sequencing and in recognition of the global reach of genomic technologies in healthcare, a programme in high-throughput microbiological sequencing addressing the issues of rapid diagnosis and antibiotic resistance, both in the UK and in the developing world.

Together these programmes need to be aligned, expertise shared and data stored centrally to create a unique, secure and appropriately consented dataset of more than a million whole genomes alongside rich clinical datasets. This will keep the UK at the cutting edge of genomics in healthcare and should form a crucial platform for building a range of genomics companies that specialise in sequencing data analysis or clinical decision support in the UK.

b) Creating a platform for developing effective diagnostics for early, asymptomatic chronic disease

In identifying the changes that are likely to occur in healthcare over the next twenty years, it is clear that there will be much opportunity to migrate the whole diagnostic paradigm much earlier in the course of most chronic diseases. We recognise that, for most chronic disorders, the disease process often starts decades before it presents symptomatically. This is true with diabetes and metabolic disease, cardiovascular disease, dementia and mental health, as well as cancer. Being able to identify individuals at the earliest stage of their disease will completely change the therapeutic paradigm for these disorders, but will also fundamentally entirely transform the way that healthcare is delivered. Such early diagnostics form one of the most important contributors towards the long sought after goal of moving towards a healthcare system that is more focused on sustaining health, rather than treating late-stage patients with symptomatic disease.

With the NHS, the UK is uniquely motivated to become the exemplar site for the development of these new diagnostic and screening methodologies. It is impossible to embark on large-scale studies of early diagnosis without the programme working in partnership with a healthcare system, as it will be necessary from the start to adapt the way patients with these disorders are managed such that optimal outcomes can be achieved. This would be difficult, if not impossible, to do in a conventional, insurance-based healthcare system and, indeed, the NHS is optimally positioned to take advantage of this emerging data as it migrates more resource into a disease prevention or public health paradigm.

The ambition should be to establish a platform that will allow such early phase diagnostics to be tested and evaluated using a wide range of different technologies, including protein biomarker testing, genetic and epigenetic testing, physiological testing using sensor technology, cognitive function testing and big data analysis of large-scale healthcare records.

The UK has had success with UK Biobank and other cohorts such as the Million Women Study and could expand these cohorts with a new, very large sample of individuals with biological materials stored, follow up available digitally, alongside the opportunity to collect multiple samples, as well as concentrate collections in high risk populations where the conversion rate from normal to disease is likely to be high. For example, in cancer, those with genetic liabilities to cancers (polyposis coli, BRCA1/2 mutations), disorders such as Barrett's oesophagus, ulcerative colitis or heavy exposure such as long-term heavy smokers with high risk of lung cancer, could all be collected as individual cohorts within a broader cohort to allow a wide range of new technologies to be applied for the identification of very early disease. This is likely to attract very substantial flows of commercial investment. Such a cohort would make the UK the leading centre in the world for evaluation of early diagnostic technology and would bring substantial new inward investment.

c) Digitisation and Artificial Intelligence to transform pathology and imaging

Data in the healthcare system provides crucial opportunities to fundamentally change the way health services are provided and developing digital tools, such as AI, are going to form an increasingly important segment of the life sciences sector. An area repeatedly highlighted as being ripe for innovation is pathology where modern tools should allow digital images to replace the manual approach based on microscopy. Systematic digitisation of pathology images could be readily established providing substantial efficiencies in the pathology service within the NHS, allowing the system to become increasingly virtual and reducing the need for every hospital to have the full on-site set of pathologists. Importantly however, this also creates the opportunity to create AI-based algorithms that could provide grading of tumours and prognostic insights that are not currently available through conventional methodology. Again, this opportunity requires a partnership with the NHS to provide a steady flow of well-characterised samples in combination with good longitudinal data, as these two characteristics will inevitably allow the creation of the most competitive algorithms both in the immediate future and over time. No other system has the scale to provide such important data that, when captured, could produce a globally dominant commercial offering in this diagnostic space.

AI is likely to be used widely in healthcare and it should be the ambition for the UK to develop and test integrated AI systems that provide real-time data better than human monitoring and prediction of a wide range of patient outcomes in conditions such as mental health, cancer and inflammatory disease.

d) Healthy Ageing

It is clear that one of the major challenges with healthcare systems over the next twenty years will be to better manage the healthy ageing of a large part of the population. As we move to a setting where almost 30% of the population will be over the age of 65, a wide range of engineering, digital monitoring and technology-based solutions will be required to maintain mobility, allow people to stay at home, and provide much more effective out-of-hospital care. This is the basis for an entirely new industry that could effectively use the NHS and care systems as test beds for products. A more systematic effort to create commercial products could reduce cost and improve outcomes for this population, be it through digital

monitoring of disease or mobility, aids for maintaining a safe environment in the home, engineering solutions for mobility, 'smart homes' devices to enhance functionality in the home environment, or aids for people with musculoskeletal disorders. Therefore, there is a significant commercial opportunity; this is primarily an opportunity for digital and engineering medtech companies and could be embedded in the NHS to provide commercial evaluation capabilities.

If it is acknowledged that healthy ageing is a crucial goal and has significant opportunities associated with it commercially, we should consider our ability to build new business based on an understanding of the general processes associated with ageing. It may prove possible to intervene, not on organ-specific disease but in the general underpinning mechanisms of ageing. The UK has underperformed in developing research programmes in this area of biology but opportunities clearly exist and it is worth consideration whether programmes targeting the fundamental process of ageing such as stem cell senescence, DNA repair, telomere shortening, caloric or nutritional restriction or IRS signalling could produce whole new pharmaceutical or healthcare companies that could address this market.

Although these are a set of examples of potential HARP initiatives, the process of selecting appropriate challenges should be left to the key partners, all of whom may contribute financially. Creating an appropriate structure where partners can contribute resources to create the necessary commercial entities in the UK that will go on to dominate these fields is an essential next step of the Strategy. Different approaches to collaboration may be required for different projects.

Establish a coalition of funders to create the Health Advanced Research Programme to undertake large research infrastructure projects and high risk 'moonshot programmes', that will help create entirely new industries in healthcare.

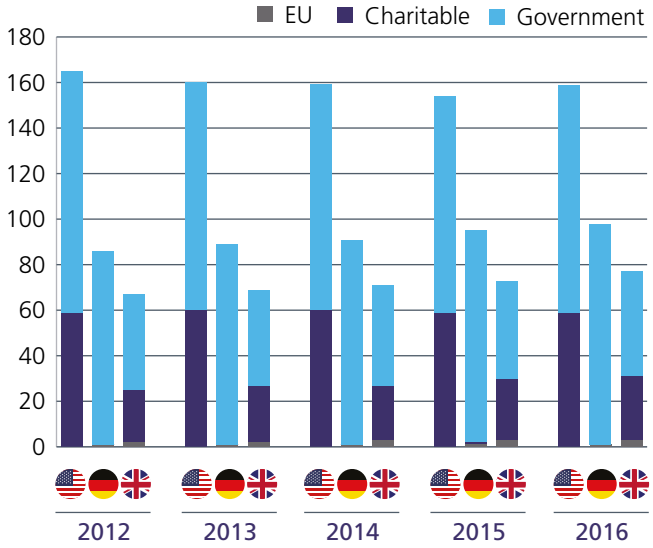
Strategic goal: Create 2 to 3 entirely new industries over the next ten years.

A. Reinforcing the UK Science Offer

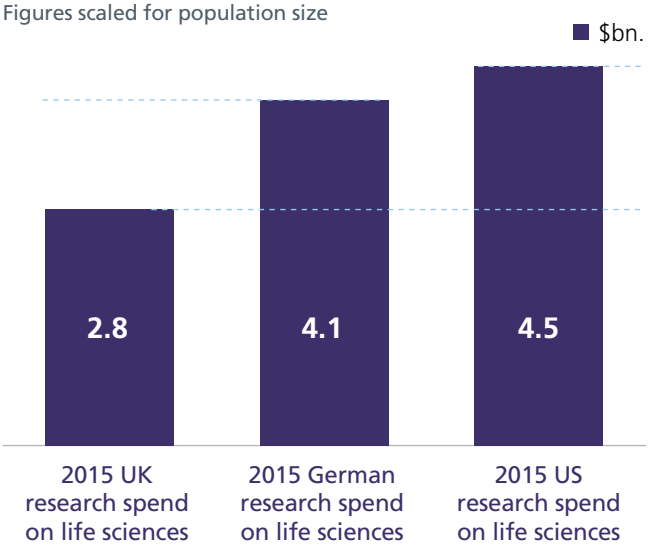
a) Expanding Public Support for the Science Base

The UK has a powerful life sciences research base that has underpinned the successful growth of this sector, supported by 3 out of the world's top 10 leading universities. Despite the fact that the UK falls well behind other countries in investment in the biomedical sciences, both by the public and by the charitable sectors, we dramatically outperform our key competitors on a per capita basis. In a country where improving productivity remains a major opportunity for the economy, this is a sector where research productivity is twice as great as that in the US and almost three times greater than in Germany. This feeds through to a significantly larger number of jobs per public spend and the highest gross value added per public spend globally.

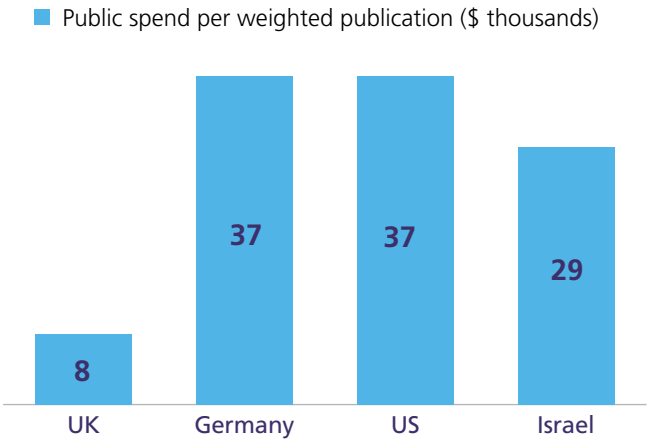
Science Funding



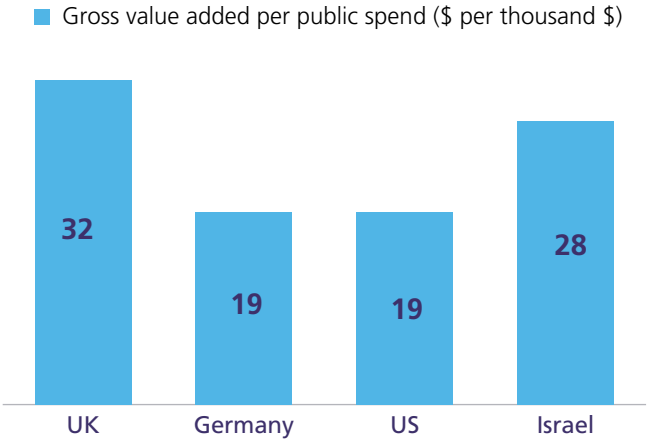
UK investment need to match US/DE



UK science productivity



GVA per spend

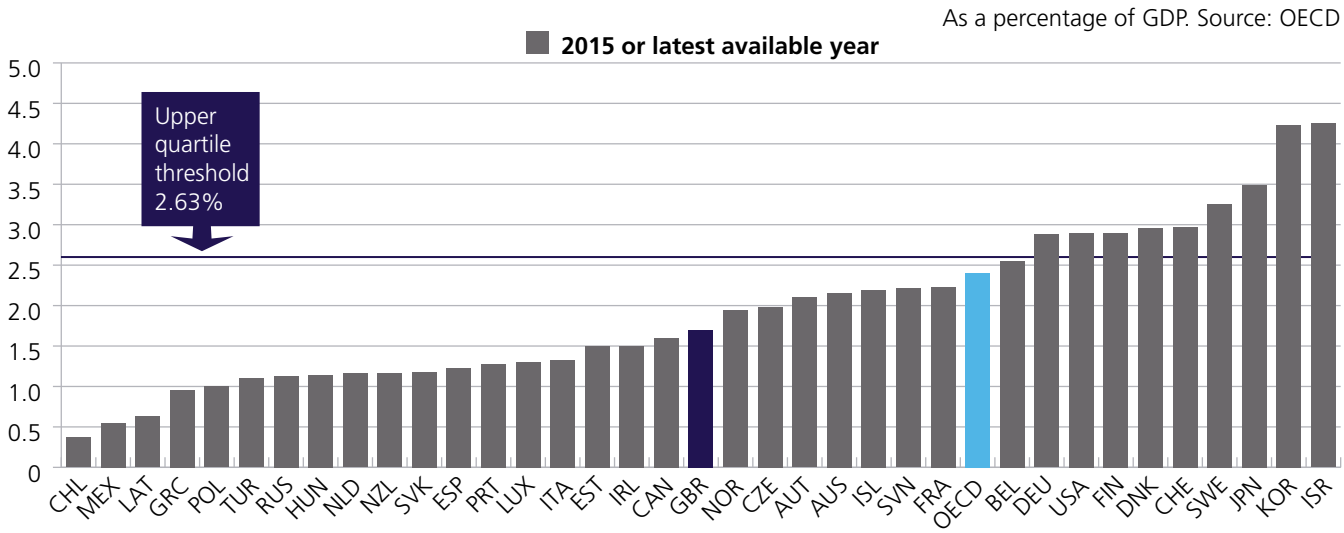


Source (all graphs): Internally commissioned research

The UK Government is a key source of funding of both basic biomedical science and translational science research, with £2bn of life sciences research funded by Government through a number of mechanisms, including the Medical Research Council (£928m in 15/16) and National Institute for Health Research (~£1bn. p.a.).[5] The Biotechnology and Biological Sciences Research Council, Economic and Social Research Council and the Engineering and Physical Sciences Research Council also provide substantial funding in life sciences. This is bolstered by significant industry (~£5.7bn p.a.), European and medical research charities' investment (£1.6bn p.a.) from bodies such as Cancer Research UK, British Heart Foundation and the Wellcome Trust.[6] In relation to pre-competitive research, the UK should also seek to continue to be involved in Europe's Innovative Medicines Initiative (IMI) – a public / private funding initiative aiming to speed up the development of better and safer medicines for patients. It is an important interface for academic industry collaboration.

The economic case for public investment in biomedical and health research is strong. For every additional £1 of public research expenditure, private sector R&D output rises by 20p per year in perpetuity.[7] Investment from the public sector into science has been growing slowly since 2009, albeit the sector has been saved from significant budget reductions during recent years. Investment has delivered a cutting-edge landscape in the UK, including expansions of Biobank; the 100,000 genomes project; the Francis Crick Institute; and over £5.7bn of industry investment into UK life sciences. In November 2016, a substantial new commitment to raise science spending in the UK was made by the Chancellor in the Autumn Statement. This was both welcome and necessary if the country is to continue to compete in biomedical and other science-based industries in the coming years. Even with this very substantial new funding, to reach an additional £2 billion per annum for the whole science base by 2021, there will be a need to continue to grow the science budget to remain internationally competitive.

OECD member states gross domestic expenditure on R&D



Even with the new funding, the UK falls well behind competitors in R&D spend as a proportion of GDP. To maintain momentum and drive economic growth, particularly in life sciences, it is essential that the UK grows support for R&D to achieve a level which is in the top quartile of OECD countries. This would be approximately 2.6% of GDP over the next 5 years.

5 Association of Medical Research Charities, 2017. *Medical Research Charities: our impact at a glance.* Available at: http://www.amrc.org.uk/sites/default/files/doc_lib/2016Infographic.pdf

6 Ibid., Industry spend on R&D in pharmaceuticals, devices, and scientific research; Source: OECD; charity data from AMRC

7 Haskel, J., Hughes, A. & Bascavusoglu-Moreau, E., 2014. *The Economic Significance of the UK Science Base; Campaign for science and engineering report. UK-IRC.*

In achieving the best outcome with significant new R&D resource, it will also be essential to modify both the approach for creating the science strategy and the decision-making that allocates research funding – UKRI is well positioned to make these fundamental changes.

> The UK should aim to be in the upper quartile of OECD R&D spending over the next 5 years. Currently R&D spending is 1.6% of GDP but needs to be increased to 2.6% to enter into this top quartile.

The UK life sciences ecosystem: a snapshot

Much of the new inward investment from international pharmaceutical companies is from those who wish their discovery science to be in close adjacency to the most successful basic science programmes in biomedicine around the world. The co-location of pharmaceutical discovery sciences adjacent to the best universities (AstraZeneca in Cambridge, Novo Nordisk in Oxford) highlights the importance of sustaining their competitive position. On this basis, there should be ample opportunity to capitalise on the science base in the UK to attract such discovery and development programmes here.

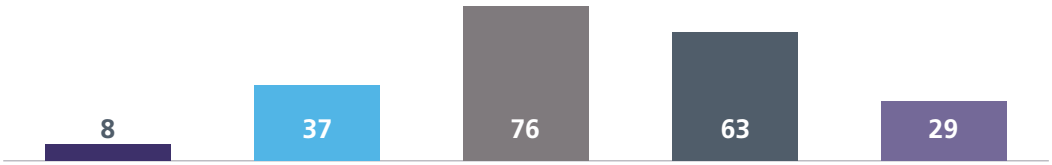
Importantly, many of the programmes supporting academic basic science are also responsible for some of the country's most successful company start-ups. For example, the Laboratory of Molecular Biology in Cambridge has spun out a number of important technologies, companies and products in the sector in recent years (e.g. humanised monoclonal antibodies such as Humira). Sustaining strength in the basic sciences and linking this to the creation of small companies is therefore a crucial component of this life sciences strategy.

The key UK attribute driving success in life sciences is the great strength in university-based research. Strong research-based universities underpin most of the public sector research success in the UK, as they do in the USA and in Scandinavia. National research systems based around institutes rather than universities, as seen in Germany, France and China, do not achieve the same productivity in life sciences as seen in university-focussed systems.

Public spend per weighted publication

$ thousands

Low = strength
High = weakness



Weighted publications per patent

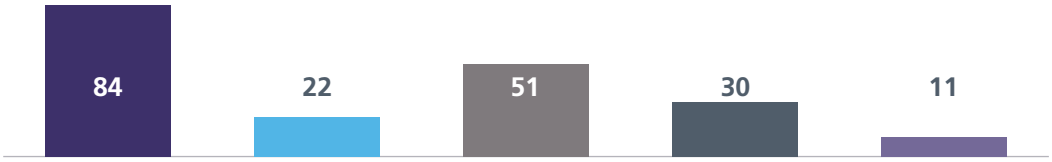
Number

Low = strength
High = weakness

Jobs per public spend

Number per million $

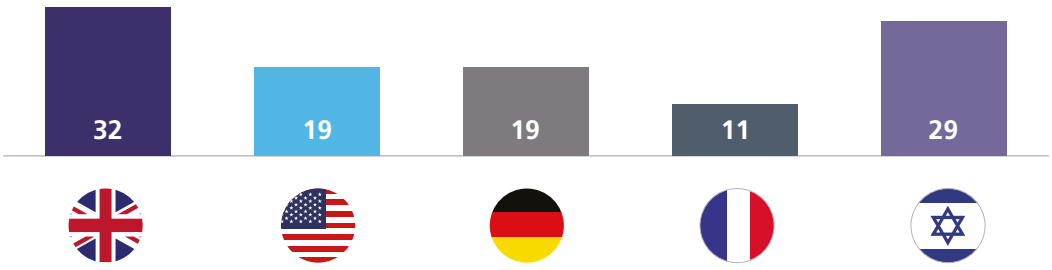
High = strength
Low = weakness



Gross value added per public spend

$ per thousand $

High = strength
Low = weakness



The UK has three of the top ten universities globally, according to the Times Higher Education League tables for 16/17, and also places six institutions in the top 20 for pre-clinical and clinical subjects.[8] Importantly, our universities also provide key partners for NHS hospitals and together create strong Academic Health Science Centres and Networks that allow the NHS to participate in cutting-edge clinical research. They also provide ideal venues for convergent science activity. It is therefore crucial that Government funding streams continue to ensure the success of university-based research that is likely to remain the cornerstone of the public sector contribution to life sciences.

One of the most important developments in the biomedical science base in the UK has been the creation of a funding stream through the National Institute for Health Research (NIHR) based in the Department of Health. Created in 2006 after the Cooksey report, *A review of UK health research funding,* this research funding agency has focused entirely on creating a strong environment for translational research within the UK and the NHS. Similar programmes in the Devolved Administrations have further enhanced UK capabilities in translation, which involves the application of science to patient populations and the delivery of clinical trials. The success of this programme is reflected by a comparison of the number of journal articles resulting from individual funder agencies in the six leading major international clinical medical journals, where the NIHR is second globally as a funder of these papers and, combined with MRC, the UK Government-funded science base is the most successful in the world in absolute, not per capita terms, even exceeding the US National Institutes of Health (NIH) across clinical, applied and translational studies.[9]

In relation to pre-competitive research, the UK should also seek to continue to be involved in Europe's Innovative Medicines Initiative.

The UK should sustain and increase the funding for basic science, to match our international competitors, particularly in university settings, encouraging discovery science to co-locate. NIHR should continue to be supported, with funding increases in line with Research Council funding.

The life sciences are unique compared to other scientific endeavours in the UK in that they have a large and powerful charitable support base contributing £1.6bn in funding, brought together under the umbrella of the Association of Medical Research Charities (AMRC). The Wellcome Trust has been a major driver of the UK's competitive international position, being pivotal in enabling world-leading centres such as the Sanger Institute and the Wellcome Trust Centre for Human Genetics. Similarly, disease-specific charities are a crucial part of the science base, including CRUK as the world's largest cancer charity that underpins most UK cancer research, as well as the British Heart Foundation, Diabetes UK and Arthritis Research UK and Rheumatism UK. On a *per capita* basis, however, the UK still brings in less charitable support than the USA where charitable funding is 2x per capita more than in the UK.[10]

The impact of the charity sector has also been partly underpinned by the Government's Charity Research Support Fund (CRSF) which helps academic institutions pay the overhead costs required for charity-funded research. This contribution has fallen significantly in real terms in recent years making it difficult for research institutions doing charity-funded research to cover their costs. Since 2010, the CRSF has been fixed at £198 million per year in England; a real-terms decrease of £38.7 million over 6 years. In the same period, charity

8 Times Higher Education, 2017. *World University Rankings 2016-2017.* Available at: https://www.timeshighereducation.com/world-university-rankings/2017/world-ranking. Times Higher Education World University Rankings Overall & by subject: clinical, pre-clinical and health 2016-17 https://www.timeshighereducation.com/world-university-rankings/2017/subject-ranking/clinical-pre-clinical-health#!/page/0/length/25/sort_by/rank/sort_order/asc/cols/stats

9 Journals: The Lancet, NEJM, JAMA, BMJ, PLoS Medicine and BMC medicine. MRC (61) and NIHR (87) bring a total of 148 publications. Adding charity funders (Wellcome Trust, CRUK and BHF) this rises to 225. NIH published 130 in total.

10 US Charity Spend is $59 per capita, compared to $28 per capita in the UK. US charity spend is based on spend in the US and explicitly excludes money raised in the US and spent overseas; UK charity data taken from AMRC annual reports and includes R&D

funding has increased from £1.14bn to £1.6bn. This CSRF support is a crucial component of the funding structure that supports medical science and needs to be sustained and ideally returned to its previous level to help maintain the diversity of funding sources and the breadth and depth of the science base. The decline in funding of indirect costs for charity research is coupled to an increasing tendency for Research Councils to construct approaches that avoid paying indirect Full Economic Costs (FEC). Together, these are having a significant impact on the viability of research in universities and have led to the institutions raising industrial overhead costs to fill the gap. This is unhelpful.

Government should ensure the environment remains supportive of charitable contributions to the science base through enhancing the Charity Research Support Fund.

It will be crucial that the UK utilises the new structure under UKRI to modernise its approach to science funding in the public sector, acknowledging the importance of convergent research activities in the Life Sciences that require support from different scientific disciplines across computing science, statistics, and engineering disciplines. Such convergence is exemplified in the field of Synthetic Biology that offers great potential for growth through an engineering approach to biology. The UK is building a successful hub in this area that could be accelerated, with connected support to join academic expertise with business opportunities. The importance of the physical sciences to life sciences has never been greater and it is also essential to support the emerging field of data science, particularly with support to enhance bioinformatics and clinical data analytics. It is promising therefore that Government is investing £103m in the Rosalind Franklin Institute to create a centre of excellence bringing together physical and life sciences.

UKRI could consider how UK research council funding has made little contribution into some high-risk areas of science including gene editing technology, immuno-oncology and high throughput genomics, when funding agencies such as Wellcome Trust and NIHR have played an important role. It is the role of UKRI to consider how this might change. In future, new funding streams should look for mechanisms to create opportunities for more risk taking and research that will make significant breakthroughs in the field.

Capitalise on UKRI to increase interdisciplinary research, work more effectively with industry and support high-risk science.

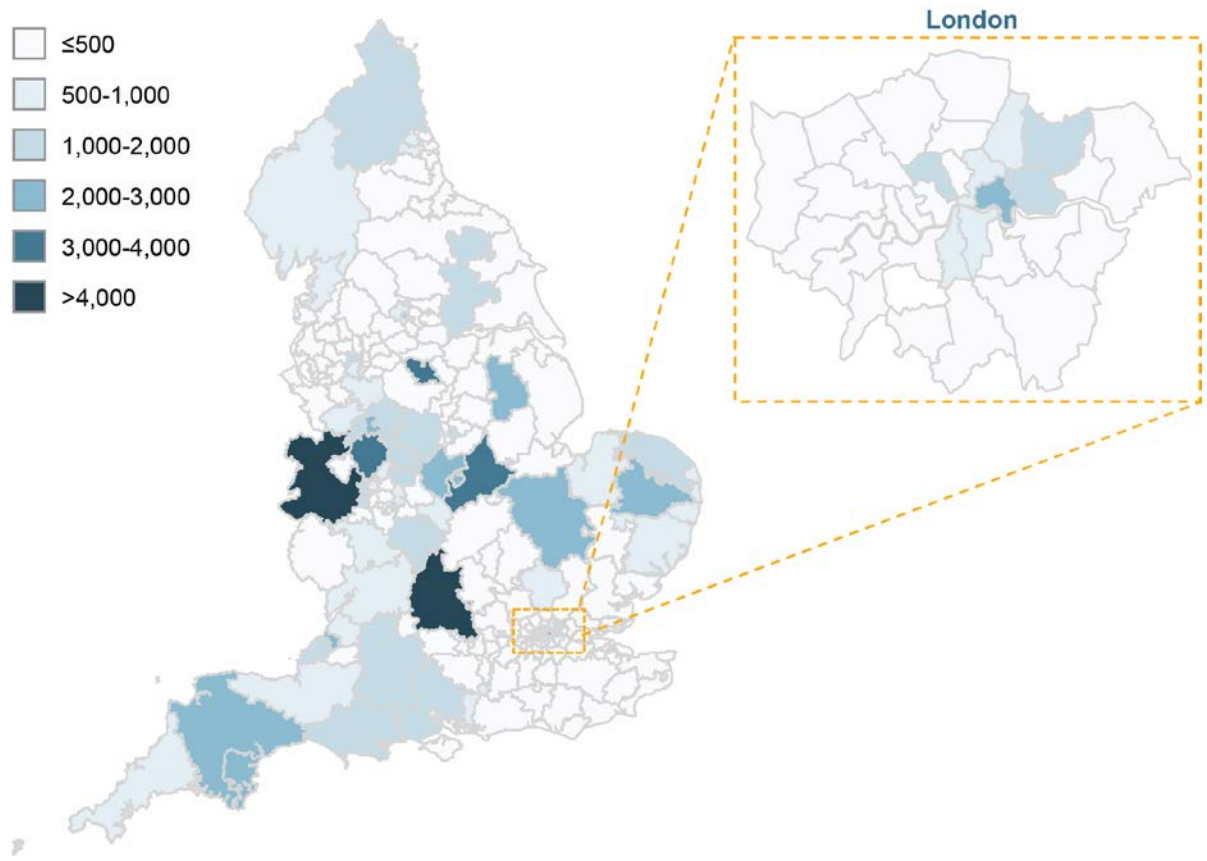
Strategic goal: The UK should attract 2000 new discovery scientists from global pharmaceutical companies to the UK over the course of the next five years, and create 10,000 new jobs in emerging new companies and disciplines in life sciences.

b) Further improve the speed and efficiency of UK clinical trial capabilities

The UK's globally leading position in translational medicine is crucially important to the industrial strategy as it provides an important interface for industry in facilitating the development and demonstration of utility of a wide range of commercial products from global as well as smaller, UK-based organisations. The UK has clinical trial activity across all stages in the EU and is on par with comparator hubs for phase II trials. In 2016/17, over 660,000 patients were recruited through the NIHR Clinical Research Networks to research studies and clinical trials in the NHS, and CRN commercial studies have risen from 317 in 2010/11 to 1008 in 2016/17. Around 35,000 patients were enrolled on commercial trials in 2016/17.

There still remains considerable room for improvement in translational science to enhance the UK's capability to attract more clinical trials from industry – a major source of inward investment in the life sciences space. The UK should focus particularly on novel trial designs and 'change of practice trials' to ensure it remains at the cutting edge of translational research.

Number of participants in clinical trials in each Clinical Commissioning Group area, 2015–16



Source: NIHR research activity league table 2015/16

i) Large-scale trials

The position of the UK in delivering large-scale clinical trials with industry has improved enormously over the past ten years. This is because the country is well supplied with strong clinical trialists and the creation of clinical trial networks by the NIHR has greatly enhanced the functional capability to deliver large-scale trials quickly and efficiently, enabling a considerable increase in trial activity in the NHS over the past ten years. Barriers, however, do still remain, including administrative burden, 'on-costs' (unfunded consequences of trials) and poor digital evidence collection infrastructure.

Despite this, the country is well positioned to deliver a host of new innovations in large-scale clinical trials, including the use of digital tools to enhance the quality of data collected and to speed up recruitment.

Trial activity is patchy across the UK: Shropshire and Oxfordshire CCGs have over 10 times the number of clinical trial participants than some other CCGs. As we increasingly move towards precision medicine, the NHS needs to get better at running more complex trials (which may use novel trial designs) in diseases with smaller patient cohorts and at recruiting patients in more targeted ways (e.g. using genomics).

As the UK seeks to do more complex and innovative trials, MHRA needs to continue engaging with sponsors to assist with innovative protocol designs and should facilitate efficient approval of complex trials and amendments to such trials, for example, to add new arms. The UK should attempt to lead the innovation in clinical trial methodology, such as basket trials, and should also attempt to embed routine genomic analysis to make trials more targeted, smaller and more likely to deliver high efficacy.

Document the number of novel trial designs used as well as the quantity of 'change of practice' trials in the UK compared to elsewhere.

Internally commissioned research indicates that, while the best in Europe, the UK "lacks the infrastructure for partnerships with industry to conduct tailored or large clinical trials compared to e.g. US, Singapore".

Improvements could be made in several important areas. Although efforts have been made to streamline ethical approval for clinical trials through the creation of the Health Research Authority[11] (HRA), this office still does not operate with the efficiency that is necessary. Steps are in place to improve the delivery of national ethics approval and to reduce bureaucracy and red tape in this arena. A small additional investment would greatly advance this activity.

Trial protocols that have been agreed nationally can be seriously delayed at hospital trust level as a result of trust governance procedures interfering with the rapid adoption of trial protocols. This is a recalcitrant problem that needs urgent resolution and a concordat should be established defining best practice against which trusts would be audited. This would prevent the pattern in some trusts of slowing down or obstructing the implementation of trials by micromanaging the approvals process. This concordat should also be placed in the NHS contract. Standardised cost structures should be agreed and would form part of the concordat. Failure to maintain high standards against such a concordat should lead to loss of funding from NIHR or exclusion of individual hospital trusts from large-scale trial protocols. Additionally, the CQC may wish to consider incorporating research office performance in their review of trusts' operations.

Regulatory Studies in a Healthcare Setting

There should be an ambition to develop the regulatory environment and digital capability to enable the evidence generated in healthcare systems to improve the speed and efficiency of regulatory studies. Few things could have such a major impact on the cost effectiveness of trials ultimately feeding through to better data and potentially much less expensive drugs. Current regulation of trials is based on standards agreed by ICH in 1995, well before hospitals became digitised. Automated capture of efficacy and safety signals within a healthcare system are likely to be as robust as the current methodology and the impact on the cost of studies will be very significant, allowing bigger or more studies to occur, thereby improving confidence in the result. In addition, longer-term follow up and automated pharmacovigilance should be easier, allowing healthcare records to inform long-term outcomes and safety. This will require regulators, health systems and industry, as well as academic trialists, to work together in updating ICH-GCP regulations. A review of ICH-GCP is already underway[12] but the NHS could be uniquely positioned to lead the pilots in this area.

The UK should work with industry and regulators to establish a working group to evaluate the use of digital health care data and health systems to evaluate the safety and efficacy of new interventions and to help ICH modernize its GCP regulations.

11 Data shows that progress has been made in speeding up clinical trial approval. For commercial trials the time from final Research Ethics Committee decisions to full HRA Approval is now (as of March 2017) at a median of less than 10 days, with the total time from application to HRA Approval of 80 elapsed calendar days (i.e. including time for applicants to respond). National Institute for Health and Research (NIHR), *Performance in initiating and delivering research – trend analysis.* Available at: https://www.nihr.ac.uk/research-and-impact/nhs-research-performance/performance-in-initiating-and-delivering-research/performance-in-initiating-and-delivering-research-trend-analysis.htm

12 Cf. .ICH, 2017. *ICH Reflection on 'GCP Renovation': Modernization of ICH E8 and Subsequent renovation of ICH E6.* Available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/GCP_Renovation/ICH_Reflection_paper_GCP_Renovation_Jan_2017_Final.pdf

There are considerable opportunities for the NIHR and NHS clinical trial infrastructure to distinguish itself from other clinical trial environments by moving rapidly to take advantage of the increasingly mature digital capabilities in the NHS. Digital recruitment has already begun using Clinical Practice Research Datalink (CPRD), which has developed a unique, integrated clinical trials platform to support real world clinical studies right across the drug development pathway. CPRD was established in the government's Plan for Growth strategy in 2012 and is jointly funded by NIHR and MHRA – 19 of the top 20 global pharmaceutical companies have used their data services. Digital tools also provide unique opportunities for measuring outcomes and generating much richer datasets, as well as via the longitudinal nature of the data, to demonstrate utility of healthcare interventions. These assets, along with the implementation of digital tools to provide the environment for paperless trials will all greatly enhance the quality of information obtained by commercial partners when operating in the NHS and will greatly speed up both the recruitment and the implementation of clinical trials, including the use of electronic data capture and informed consent, thus significantly reducing cost. This may require some trade-off between trials infrastructure for nursing and for digital, but the increase in activity it is likely to generate should bring the resource necessary to sustain the current level of personnel, but also improve the digital environment.

An important constraint on clinical trial activity is the extra patient cost that can limit the involvement of Trusts in trial protocols. Funds should be found to cover these costs in order to eliminate this impediment to trial participation. NHS England, Department of Health and Public Health England have commenced a joint project to review issues relating to Excess Treatment Costs and formulate strategies to address these.

ii) Early development studies

Early in the development of new therapeutics or devices, trials focus upon a detailed investigation of a relatively small number of individuals. Speed is crucially important at this stage of development and the UK should, through appropriate networks, be optimally positioned to progress such studies rapidly and efficiently. It is important that these early-phase programmes are also supported by outstanding clinical science as they should provide an opportunity to explore the precise biological effects on pathways and disease. There are examples of strong networks that have been able to create rapid and effective exploratory development programmes in particular disease areas, such as NIHR Clinical Research Network, NIHR Translational Research Collaborations, the NIHR Clinical Research Facilities network and the Experimental Cancer Medicine Centres network. The Birmingham Trials Acceleration Programme is an excellent example of an early phase programme and demonstrates that it is possible to create rapid access to patients and underpinning science and to use these to establish powerful industry partnerships.

It is therefore recommended that funding agencies look again at how such early-phase networks can be identified and supported, enhancing the ability of the UK to provide useful early-stage data to the life sciences industry. A set of early clinical trial networks capable of rapid patient recruitment backed by strong science capability would be a great attraction to industry. The DH and NIHR should consider how these can be best established, building on existing good practise, enabling better networking across the country and ensuring regions deliver a joined-up offer.

UK Haemato-oncology Trials Acceleration Programme
Birmingham Health Partners and Bloodwise

The haemato-oncology Trials Acceleration Programme (TAP) represents a novel national trials infrastructure which was established by the charity Bloodwise in 2012 in response to the dramatic increase in the number of potential new drugs for the treatment of blood cancer.

Based on a 'hub and spoke' model, a central trials acceleration hub hosted by Birmingham Health Partners facilitates trial set up and delivery within a national network of 13 major leukaemia centres, each with dedicated research nurse funding and collectively covering a catchment region of 20 million. This integrated delivery structure has significantly reduced trial set up time from 30 to 9 months at the same time as accelerating patient recruitment. By recruiting 260 patients ahead of schedule and collecting more than 2000 samples for next generation sequencing it has also identified a novel molecular signature of clinical outcome. In total the TAP has facilitated recruitment of 950 patients across a portfolio of 19 early phase trials and resulted in industry partners bringing around £150 million of potentially life-saving new treatments to patients across the UK.

The TAP model is now being applied in other diseases including arthritis and stem cell transplantation. By accelerating the set up and delivery of complex clinical trials of novel agents with integrated genomics, this novel infrastructure has the potential to further establish the UK as a globally unique environment for the rapid delivery of practice informing studies, in turn driving inward investment by the global pharmaceutical sector.

The UK Government should improve the UK's clinical trial capabilities so that the UK can best compete globally in our support for industry and academic studies at all phases.

Strategic goal: To support a 50% increase in the number of clinical trials over the next 5 years and a growing proportion of change of practice and trials with novel methodology over the next 5 years.

c) Create capacity for generating pre-commercial molecules against good therapeutic targets

While the UK has considerably enhanced abilities to compete in both discovery and translational research programmes – spending more per capita on translation than the US – analysis indicates that the UK still fails to extract the most value (for example IP[13]) from our discovery research in comparison to international hubs.

An important gap in the pipeline from basic scientific discoveries through to clinical application is the ability of the UK public sector research base to obtain both therapeutics and devices that can be safely evaluated at the earliest stages in humans.[14] Testing such targeted products in a translational setting, would produce insights that would de-risk the creation of small companies and also enhance the early translational capabilities of clinicians and investigators.

The translational capabilities of public sector biomedical research organisations have never been fully evolved simply because it is difficult to do early translational studies without appropriate therapeutic molecules or devices. These are not made available by companies and hence there is little for academic centres to work on

13 The UK does not produce as many patents per quality publication as Germany and the US. Between 2011-2016 the UK published 80 papers per patent, compared to just 7 papers in Germany and 11 in the US.
14 Tkach K., 2016. *Mind the Gap*. Biocentury Publications

to acquire these early development skills. The loss of investigators with expertise in clinical pharmacology is, for example, a consequence of the lack of molecules available to be investigated in this setting.

Therapeutic Molecules – US programmes

The challenge of creating therapeutic molecules is overcome in the USA by several programmes at the National Institutes of Health. The Vascular Interventions/Innovations and Therapeutic Advances (VITA) and the Small Business Technology Transfer (STTR) schemes provide grants to academics that allow them to further develop their understanding of fundamental pathways and targets by resourcing the creation of antibodies, cell-based therapies, viral vectors or small molecule drugs by Contract Research Organisations (CRO). The USA has been much more successful in promoting these capabilities in academia through programmes such as Harrington and SPARK. The creation of an equivalent programme would allow the development of expertise in this early translational space to evolve amongst investigators in the UK.

In addition, this step of creating new molecules has proved very important in the USA by de-risking therapeutic programmes so that, when companies are created, this can occur with much better understanding of the role of targets and pathways in disease pathogenesis with substantially de-risked, clinically-useable molecules and will better prepare investigators to establish viable companies.

Outside of programmes supported by Cancer Research UK, few if any academic groups are capable of the drug discovery necessary to create clinically-useable molecules but these can be readily produced for academics by the Contract Research Organisation (CRO) industry. The cost of creating novel therapeutic molecules in CROs and undertaking the necessary pre-clinical and absorption, distribution, metabolism, and excretion evaluation of these molecules would be approximately £3-5 million per grant.[15] There should also be opportunities to produce medtech innovations and test them in humans. £50 million would support 10-15 programmes. This could be delivered across NIHR and the Medicines Discovery Catapult in Manchester, with the support of industry experts to ensure appropriate drug-like molecules or antibodies are created with this funding. Creating a fund that provides academic groups with this commercial support, advice and guidance would therefore address this shortfall in the UK landscape. Providing support and experience of commercial processes and decision-making could better support the development of more robust companies.

By creating an opportunity for investigators to undertake these early-stage investigations with molecules made by CROs, an important step will be taken to ensure that biotechnology companies are not started too early as, historically, they have been in the UK. By ensuring that there is more clinical data, a major step will be taken in reducing the risk and enhancing the chances of success of biotechnology companies.

This approach would build on the successful US models[16] and complements existing UK Research Council and Innovate UK funding to:

- Support and accelerate the creation of more robust UK life science companies, reducing the need for early company formation or private investment by 'de-risking' drug asset creation and allowing academic groups to develop more commercially relevant evidence of a product before having to spin out.
- Give academics the chance to use and benefit from industrial insights, processes and decision-making to develop their discoveries further along the translational pathway. This would allow them to gain experience in exploratory development and clinical pharmacology, both areas of strategic importance in UK biomedicine.

15 Paul, S., M., et al, 2010. *How to improve R&D productivity: the pharmaceutical industry's grand challenge.* Nature Reviews Drug Discovery, Macmillan Publishers Limited

16 NIH funding programmes such as:, The Harrington Project for Discovery and Development and SPARK run out of Stanford University

- Better link funding for academics (i.e. supported by Research Councils) with commercially focused resources and expertise (i.e. supported by Innovate UK).

This strategy suggests that the fund is initially focussed on molecules, before including biomarkers and devices at a later stage.

Design a translational fund to support the pre-commercial creation of clinically-useable molecules and devices to intervene and treat disease, which can then be explored in preclinical and early clinical studies.

d) Ensure the supply of global talent

The most important features of a successful basic science base in the UK are appropriate funding levels for the activity, but also access to highly-skilled scientists to work in the sector. The potential disruption associated with Brexit could lead to some loss of talent from the sector; as such, creating an opportunity to bring very high-level talent into the country over the next five years is important. Industry has highlighted that it is important to have an immigration policy that ensures that non-UK staff can remain in the country, enables intra company transfers, and responds to employer need. Reducing barriers to recruiting non-UK nationals can be facilitated through simplifying the Tier 2 visa process, reduction in the time for which a role needs to be advertised to meet the Resident Labour Market Test, speeding up the visa approval process, removing restrictions on salary offered and moderating the heavy fee burden for consideration of applicants and their dependents.

It is also recommended, that the funding agencies, in partnership with major charities, create a high-level recruitment fund that would pay the real cost of bringing successful scientists from abroad to work in major UK university institutions. International scientists will expect globally comparable salary scales, even with the depreciation in the value of sterling, increasing the cost of recruiting such individuals by 15-20%; in addition, funds need to be provided for these scientists to launch programmes immediately and to ensure that other aspects of their recruitment are covered, including support for spousal employment, schooling, housing, etc. Such programmes of international recruitment have been put in place in other jurisdictions such as Canada. It is recommended that a similar scheme for high-level recruitment is put in place to support the basic science base in the UK with recruitment of highly-talented individuals over the next ten years.[17]

Government funding, combined with charitable funding, should create a programme to attract up to 100 world-class scientists to the UK with substantial financial packages and support for both their recruitment and their science over the next ten years.

17 The recently announced Rutherford Fund addresses this issue.

B. Growth & Infrastructure – making the UK the best place for life sciences businesses to grow

One of the most important objectives of this Strategy must be to achieve higher and more sustained growth levels for the sector. This will require new approaches to upscaling small and mid-sized enterprises in the sector and a different approach to establishing and expanding a manufacturing base in the UK. As in other countries, much of this new growth is likely to emerge from clusters where strong scientific activity is adjacent to small and emerging companies and which are attractive places for large companies to also co-locate. These clusters provide a unique mix of talent, finance and infrastructure that make them the driving force for economic growth in all high-tech sectors. Three subjects – scaling SMEs, manufacturing and clusters – are therefore the focus of the growth section of this strategy.

a) Fiscal support for SME growth and retention

Scaling life sciences companies in the UK to become companies that have achieved regulatory approval of products and are capable of both making and selling these locally and abroad has historically been a challenge. Despite the UK having a history of great companies emerging from UK science, including Celltech, Solexa, Aztec, Kudos and Cambridge Antibody Technology, we have not had success growing these companies and they have been acquired before they have reached their potential. New approaches are needed for scaling small and mid-sized companies and to establish and expand the UK manufacturing base.

An analysis of this problem reveals several important factors responsible for this failure. The first is a misalignment of the available types of risk capital, compared to the realities of 10-15 years for discovery and development of novel drugs and innovative, higher-risk medical device or diagnostic products.

- The UK has relied heavily on angel investment and venture capital (VC) support for its SME sector. VC funds typically seek to exit their investment within the life of their funds. To realise their profits within 5-7 years after investing leaves little time for companies to grow and scale. Most UK VC companies lack the deep pools of risk capital seen in their American equivalents[18] which, in turn, appears to condition UK life sciences companies' ambition and approaches to raising private and market finance.
- This issue will be further compounded for industry if the European Investment Fund is not replaced or continued in an alternative manner to avoid the potential loss of the (20-30%) core funding source of UK VC funds.
- Patient capital funds have a completely different investment strategy and as a result look to optimize their returns over the full development life of companies. These vehicles have a very different approach to investments and are essential for the scaling of life sciences companies. More of these are emerging and include Woodford Patient Capital fund, OSI, and Syncona. It is from these that scaled companies are likely to emerge.
- UK pension funds do not normally invest in the tech sector, including life sciences in the UK, due to relatively high levels of risk, poor knowledge of the sector in the investing community and poor returns on investments made in the 1990s.
- Owners and private wealth including family wealth can be sustained in patient capital funds but UK incentives to support this type of investment, such as Entrepreneurs' Relief and inheritance tax, need to be modified to encourage such investment and sustained organic growth.

18 US PE and VC funding in life sciences is 20x that of UK (Internally commissioned research)

- The EIS and SEIS schemes have been very successful in encouraging entrepreneurs to operate in this sector, and have generated over £20bn of equity investment across all sectors since they were introduced. While they were extended in 2015[19] to offer greater support to innovative businesses, they are still modest by international standards in terms of their current funding limits and holding periods – the US QSBS scheme has no limit to funds raised and shares must be held for over 5 years.

On average, UK firms raise 2.4 rounds of VC funding prior to IPO in comparison to 3.8 rounds for US firms,[20] and 1.9 rounds compared to 2.5 in the USA when exiting by trade sale. The fraction of UK healthcare exits by IPO (11%), is less than half of that in the USA (24%) or in Europe (27%). Furthermore, the wider capital markets in the UK are not operating as effectively (or efficiently) as they could for this sector, limiting the growth of SMEs into robust companies with management time to develop it and more than one product.

Patient Capital

The lack of long-term capital – or "patient capital" – has recently been recognised and, as a result, new funds have emerged with the capability of supporting companies for a longer term through the scale-up phase.[21] However, even with these funds, the UK continues to lag the US on a per capita basis, by billions of pounds of capital necessary to grow solid and sustainable companies.[22]

Basic research	• **Government funding**, e.g. Research Councils, HEFCE etc. • **Charitable funding**, e.g. Cancer Research UK, Wellcome Trust etc.	• **Government funding**, e.g. NIH grants, Direct subsidies etc. • **Philanthropic donations**, e.g. CF Association etc.
Translational research	• **Biomedical catalyst**, majority of funding in aliquots under £500,000, few over £1m. • **NIHR translational collaborations**, including dementia and rare diseases • **NIHR Biomedical Research Centres & Clinical Research Centres**	• **Public funding**, e.g. NIH's SBIR/STTR grants • **Targeted interests**, e.g., NIAID $11.2m for AIDS, DOD and CDC-backed projects

Start-ups	• **Catapults**, including cell and gene therapy, high value manufacturing, etc.
	• **British Business Bank interventions** e.g. Enterprise Capital Fund, Venture Capital Catalyst
		• **Mix of private and public funding**,
		  • SBIR grants
		  • Pharma investment and acquisition
		  • VC funds target NIH grant holders

Small and medium enterprises	• **VC funding**, e.g. Woodford, Abingworth, Syncona, Schroder • **Patient Capital e.g.** IP group, Woodford, Syncona	• **Large Amounts of Private funding**, including VC funding deployed from Boston and San Francisco, substantial industry investment bringing R&D in house

19 HM Revenue & Customs, 2015. *Income Tax: amendments to tax-advantaged venture capital schemes.* Available at: https://www.gov.uk/government/publications/income-tax-amendments-to-tax-advantaged-venture-capital-schemes/income-tax-amendments-to-tax-advantaged-venture-capital-schemes

20 British Business Banks Analysis; International Comparison of venture capital exits for Patient Capital Review, August 2017.

21 Notable amongst these are Woodford Patient Capital Trust, Malin PLC, Syncona and Oxford Science Innovation. These join the IP Group and Invesco as being long-term risk capital providers for the sector.

22 Closing the US-UK funding gap per capita would require a further $17bn, – UK lacks late-stage VC funding for life science companies. 28% of UK funding is late stage vs. 58% of California funding. Late-stage VC funding is 8x greater in California than the UK. 4x more VC funding overall is available in California than in the UK. (Internally commissioned research)

Other countries have taken different approaches that have better supported the growth of mid-sized companies. In the USA, the deep pools of risk capital in major venture capital firms and the public markets have produced a range of new companies that have brought multiple innovative new products to patients and become substantial engines for economic growth. For example, Gilead, Celgene, Vertex, Biogen, and Genentech were biotech companies that emerged as a new generation of companies with highly innovative products but in all cases this journey took more than 20 years.

Continental Europe has had considerable success creating biopharmaceutical companies of scale. The stability necessary for long-term growth, and protection against these companies being bought, is often related to a substantial shareholding held by foundations or by families. Such ownership structures allow them to grow over time. Novo Nordisk, UCB, Altana, Roche, Boehringer Ingelheim, Serono and Servier have all had family or foundation-based share ownership providing long-term stability. In many cases, the ability to pass shares between generations without tax exposure has provided a mechanism for these companies to survive long-term.

In this context, it is also worth encouraging the greater use of different share classes as used extensively by both family-based companies and new technology giants[23] in the USA to allow business founders to retain ownership through voting shares held by a limited number of investors to ensure that long-term strategies can be adopted successfully.

Recent evaluation by UBS of the performance of family or founder-owned companies demonstrates that those retaining founder ownership control have significantly better performance than conventional public companies.[24] Similarly, for companies offering both voting and non-voting shares in this sector there is evidence that non-voting shares do not trade at significant discount to voting shares. Introducing some of these important fiscal and cultural changes about the way we think of growing companies is essential for the growth of this sector in the coming years in the UK.

The UK has had a series of companies that had the potential to transition to large biopharmaceutical companies, had the necessary patient investment or family-based ownership been in place. Cambridge Antibody Technology, when sold to AstraZeneca, had a host of potential products and could have become a new, independent UK pharma company, had it managed the last stage of scaling that involved late-stage development, registration, manufacturing and commercialization of one or more products. Similar examples have included Celltech, Aztec, Kudos and Solexa. The current candidates for becoming mature companies in the UK have all benefitted from long-term patient capital rather than venture capital. Adaptimmune and Immunocore have had fifteen years of investment, the last twelve years without venture capital, while Oxford Nanopore, at the forefront of the race to develop new sequencing technology, has had twelve years of patient capital support from investors.

The SME sector of UK life sciences needs to migrate increasingly to new sources of long-term capital. It is essential to create incentives for longer-term investment that will help new biopharmaceutical and medtech companies to emerge with products and sales and to be based in the UK. This strategy welcomes HM Treasury's patient capital review launched by the Chancellor in the 2016 Autumn Statement and the input being led by Sir Damon Buffini.

This review will hopefully provide an in-depth assessment of the options for increasing the risk capital available to encourage the scaling of companies. Early-stage start-up capital is largely available in the UK but scale-up capital is short and life sciences have a particular problem given that it often requires up to 12-15 years to generate successful products. We anticipate that the Buffini advisory group will show how

23 5/7/2017. *Voting Rights: Second Class*. Financial Times. Available at: https://www.ft.com/content/e4a6456e-6185-11e7-8814-0ac7eb84e5f1

24 UBS, 2015. *Why do Family-Controlled Public Companies Outperform ? The Value of Disciplined Governance.* Available at: https://finanzascuantitativas.files.wordpress.com/2015/08/ubs-why-do-family-controlled-public-companies-outperform.pdf

best to encourage greater investment in the technology-based sectors, how to optimise the tax benefits for those who invest and approaches to increasing equity pools focussed on longer term opportunities. The life sciences sector will respond to the recently opened consultation.

Support the HMT review into UK patient capital needs

In industry's view, at present there is a need to consider mechanisms to build long-term capital pools through tax relief, such as:

- **Entrepreneurs' Relief:** extend the qualifying period beyond one year and reduce the 5% ownership threshold so that interest is extended and more founders or key employees with smaller holdings can benefit.
- Extend the funding limit for **EIS and SEIS relief schemes** to £15million or potentially £25million for knowledge-rich companies to support stronger investment to accelerate growth and increase the minimum holding period to create a stronger incentive for holding equity for over five years.
- Using the **ISA structure**, to increase the flow of funds from retail investors into the tech economy, particularly into long term patient capital funds (this will require support from the FCA).
- Improve **Inheritance tax relief** to encourage and sustain longer-term share ownership either in life sciences companies or in designated patient capital funds.
- The reduction in the **Business Property Relief** rate from 100% to 50%, for instance for investment in listed companies, should be reviewed with a view to encouraging such investments. This could equalise investment with unlisted companies and increase the listed share rate, encouraging such businesses to seek capital from public markets.

Consideration also needs to be given to how access to the European Investment Bank or the European Investment Fund can be maintained or replaced with another source of anchor capital. These provide significant core funding for UK venture capital and are an essential part of the investment capital landscape.

UK Government should ensure the UK's tax environment is internationally competitive on an on-going basis in supporting longer-term and deeper investment.

Fiscal interventions to address market failure

1) Social Impact Bonds

It is important to think of ways to generate risk capital to support commercial enterprise that both generates a profit and has important social impact. A mechanism is available to do this in the form of social impact bonds (SIB). SIBs are contracts with the public sector, which commits to pay for improved social outcomes. Investment is raised from socially-motivated investors, who then receive payments from government if the social outcomes improve. Investors assume the business risk. The use of SIBs in preventing chronic health issues is spreading. SIBs to tackle cardiac conditions (Canada), Type 2 diabetes (Israel) and asthma (USA) are already in operation. SIBs are also being discussed to raise risk capital to fund experimentation with novel approaches to tackling health issues in developing countries, such as malnutrition, cleaning dirty water, detection of cervical cancer, and so on. Although their use in medical research has not been evidenced today, they are a versatile way of attracting risk capital which could fund such applications, and consideration needs to be given to how the life sciences industry might be incentivised to invest in SIBs.

2) Antimicrobial resistance (AMR)

Anti-microbial resistance presents a major challenge for healthcare systems and the UK government has made major contributions in identifying the problem and encouraging research in the area. This is an area

where investor support has been hard to find, particularly to support SMEs in early clinical development. It is important to consider how support might be provided to deal with this market failure, either through Government pull funding or direct investment.

Address market failures through Social Impact Bonds and measures to encourage AMR research.

Improve efficiency of UK public markets for life sciences companies

A further problem in the life sciences sector that prohibits the growth to produce multiple mid-sized or large companies in the sector is that the public capital markets do not work effectively for this sector. A comparison of companies on the London Stock Exchange compared to the NASDAQ exchange reveals that there is very limited trading in the sector generally on the LSE or AIM and particularly for emerging mid-sized companies. This is in contrast to the level of trading activity seen on NASDAQ. Listing rules appear to be more conservative and costly in London than in the US and the sector is not followed by a significant number of analysts or commentators, further limiting the interest in the sector from investors. Conservatism amongst UK investors appears widespread and also underpins the challenges in raising long-term capital funds. In particular, pension funds that invest in this sector actively in the US are not participants in this sector in the UK, and influencing and educating gatekeepers for these funds to consider this sector should be a priority. The clarification by the US Department of Labour's 'Prudent Person Rule' in 1979 allowed pension funds to invest in higher-risk assets, creating a flood of new risk capital into the sector. The recent Oxford Science Innovation fund, for example, raised its entire second round outside the UK without apparent difficulty. It is not at all clear why international investors should view the sector and the UK so positively while UK-based institutions remain conservative.

Consider how UK-based public equity markets can be used more effectively in the sector.

The SME R&D tax credit scheme is seen to be highly effective for this sector, offering generous relief for a defined set of eligible costs. This scheme provides additional tax relief which, together with standard relief, is in total worth about £46 for every £100 of qualifying expenditure. Alternatively, companies not in profit can claim a payable credit worth about £33 for every £100 of qualifying expenditure.

While the SME scheme is available for companies with fewer than 500 employees, the relief available for larger companies under the R&D Expenditure Credit (RDEC) is significantly less generous. This scheme provides a payable credit worth about £9 for every £100 of qualifying expenditure after tax, and is available to companies whether in profit or not. This risks a cliff-edge at the point that companies are attempting to complete large-scale, pivotal trials, build commercial teams, establish manufacturing and organise their regulatory approvals. It may also disincentivise employment growth.

In addition, as scientific and technological practices change and other countries extend their own tax support accordingly, the UK risks falling behind, notably in respect of some key eligible costs. For example, data acquisition costs are currently ineligible for R&D tax relief as these are neither computer software nor consumables. Big data and its analysis is a key 'feedstock' for research in the sector and is central to the future of life sciences R&D. These costs should therefore be eligible expenditure.

Review the eligible costs available through the SME R&D Tax Credit and large company RDEC schemes, and consider raising further the RDTC employee limit.

Scale-Up

The UK has had numerous opportunities to scale up and create new companies with excellent products in the life sciences sector, providing the opportunity for them to grow into new commercial champions. These companies have often been sold at a stage where they had promising products but were confronting the challenge of completing pivotal trials, gaining full regulatory approval, creating and deploying a commercial team globally, and solving the problem of manufacturing. These hurdles represent a significant obstacle to company growth, particularly in the context of the very substantial investment that would have been required to get these companies to the point where they were in a position to take on these final challenges.

Recognising that the UK has had many successful companies that have been ready for this final stage of scale-up but unable to take that step indicates that the life sciences strategy should recommend further action to address the obstacles these companies faced that prevented them from becoming successful, mature UK companies.

It is clear that scale-up challenges for companies are particularly difficult, given that investors are likely to have already invested between £100-500 million up to this point and will be asked to invest perhaps an equivalent amount again to get over this final set of hurdles.[25] The limits of the public capital markets in the UK in life sciences provides another challenge and makes it more difficult to obtain the funding necessary from this source. It seems clear that unless there is some solution provided which helps companies over this last set of obstacles, we will continue to fail to produce mature companies.

Although direct loans as available for the airline industry appear to be constrained because of state aid rules, it may be necessary to find other approaches which should include enabling or leveraging larger capital pools with the specific purpose of investing in this aspect of the sector. Alternatively, other fiscal interventions may be appropriate including manufacturing support, local growth support and extension of R&D tax credits.

We look forward to contributing to the consultation on patient capital and the subsequent response from the Treasury.

Taken together, measures proposed in this strategy on funding and fiscal changes aim to make the UK the very best place to do life sciences research, attract investment and for companies to start and grow. Although this report does not incorporate a full business case for this type of investment, the positive impact of such interventions on the growth of the world's most successful life sciences clusters (ie Silicon Valley and Boston) is clear. The associated economic benefits of such a high-value sector thriving in the UK would be significant.

Strategic goal: The UK creates four UK companies valued at >£20 billion market cap in the next ten years.

b) The role of clusters, infrastructure and 'place' in growing life sciences

Evidence shows that geographical clustering of companies in a sector alongside elements of their supply chain can bring additional benefits, where there is connectedness, dependency and complementarity, as well as knowledge transfer and shared spaces or services.[26]

The UK has an internationally recognised life sciences cluster in the South East of England, the Golden Triangle, comprising Oxford, Cambridge and London and the area between them. It houses four of the world's top twenty universities (three in the top ten), four of the top ten medical sciences faculties in the world and some of the world's largest research institutes – the Sanger Centre, the Francis Crick Institute and Harwell. Further it

25 Paul, S., M., et al, 2010. *How to improve R&D productivity: the pharmaceutical industry's grand challenge*. Nature Reviews Drug Discovery, Macmillan Publishers Limited

26 Porter, M., E., 1990. *The Competitive Advantage of Nations.* Harvard Business Publishing

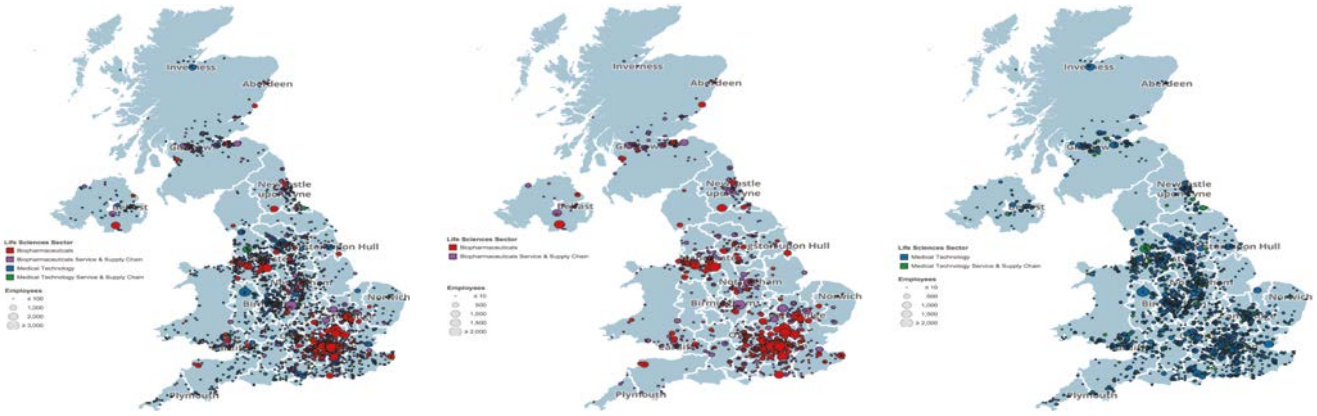
contains substantial science infrastructure and a very large number of small and mid-sized companies in the life sciences space.

The Thames Valley alone has over 500 life sciences companies and Cambridge has over 200 biotech companies and the largest array of science infrastructure in the cluster.[27]

By most measures, the Golden Triangle is the third largest technology cluster in the world, after Silicon Valley and Boston, and is a clear driver for economic growth in the life sciences sector.

Importantly, life sciences commercial activity is very broadly spread across the whole of the UK, with a strong presence in the North West of England, with companies such as AstraZeneca, and across Scotland in the Edinburgh-Glasgow corridor with companies such as Thermo-Fisher. Small and mid-sized medtech companies form a powerful cluster in the Midlands and, in the North, there is a combination of both large medtech companies such as Smith & Nephew, FUJIFILM, as well as a host of small companies in innovative digital and medtech sectors. Leeds supports 200 medtech companies and, with Sheffield, has a strong presence in orthopaedic medtech. Reckitt Benckiser, based in Slough, has its major production facility for over-the-counter products in Hull, as do Smith & Nephew, and both are major UK exporters. Unilever has a manufacturing base in Manchester and Walgreen Boots is based in Nottingham. South Wales has an excellent medtech cluster and is home to multiple CROs and Northern Ireland excels in diagnostics. Life sciences is already a truly UK-wide endeavour.

UK Life Sciences Employment 2016 (map)

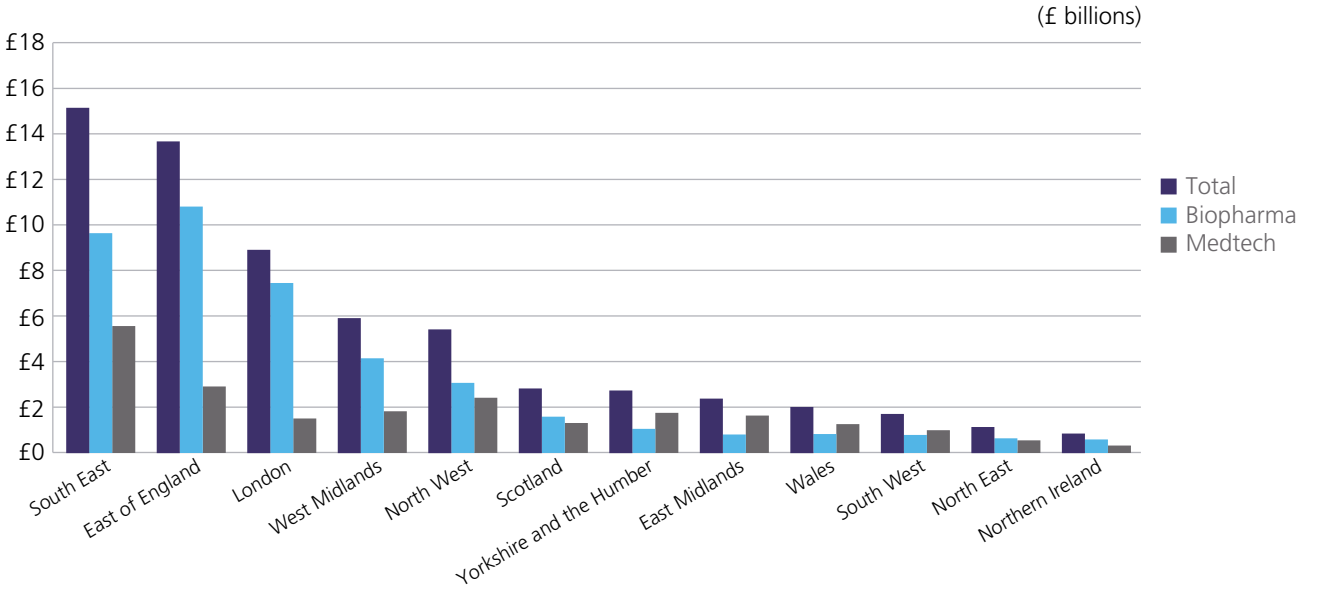


All life sciences | Biopharma | Medtech

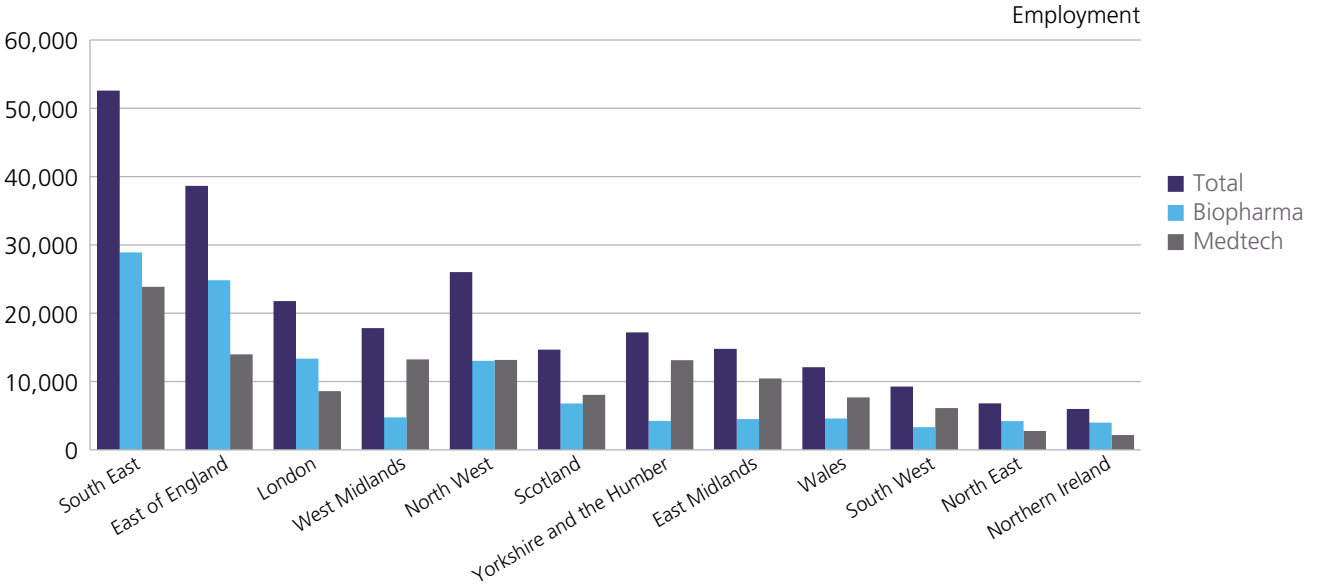
Source: Strength and Opportunity 2016

27 Oxlep, 2016. *Oxfordshire Sector Profile: Life Sciences.* Available at: http://www.oxfordshirelep.com/sites/default/files/Life%20Sciences.pdf;
Oxfordshire Sector Profile: Life Sciences, OxLEP http://www.oxfordshirelep.com/sites/default/files/Life%20Sciences.pdf;
Cambridge Cluster Maps http://www.camclustermap.com/#?&coll=%7B%22company-type%22%3A%22cambridge_based%22%2C%22sector%22%3A%5B%22life_science_and_healthcare%22%5D%7D

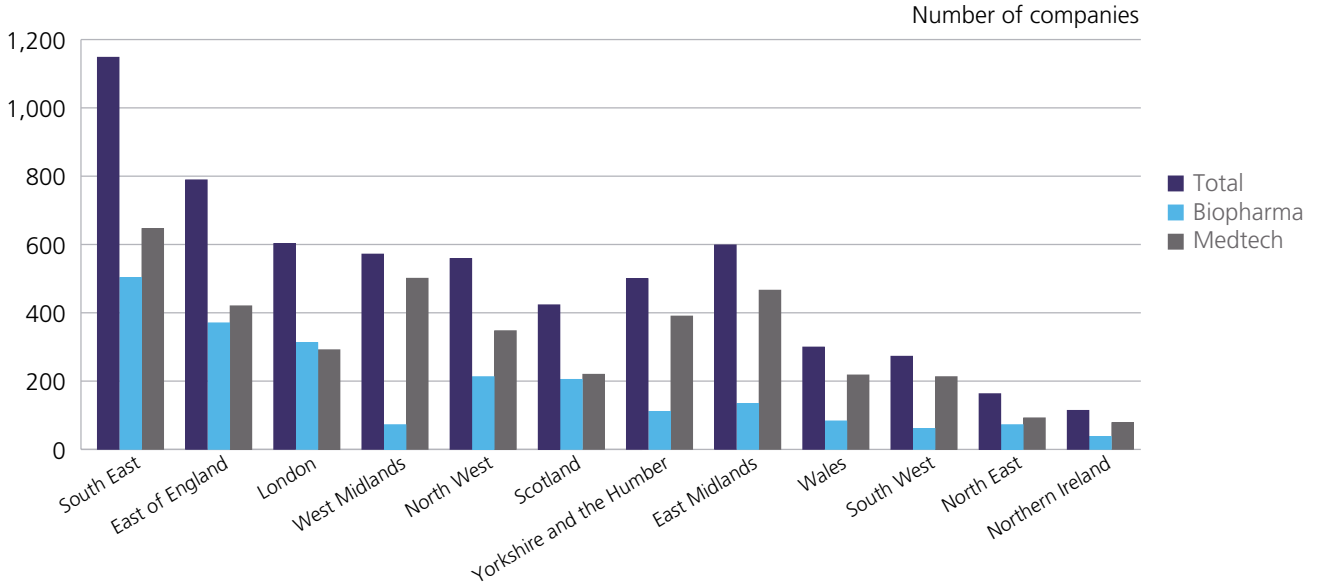
Life Sciences turnover by region



Life Sciences employment by region



Life Sciences companies by region



Source: Strength and Opportunity 2016

Infrastructure

Life sciences clusters are nearly always located around a university or other research institute and in the UK include elements of NHS infrastructure. However, evidence and experience suggests that governments cannot seed technology clusters[28] and their success is usually driven by the underpinning assets of universities and companies, and also by the cultural features of networking and recycling of entrepreneurs and capital.

Nevertheless, governments have a role in helping to identify emerging clusters and technologies and supporting their growth through funding for science and research and vital infrastructure.

An important component of the infrastructure that underpins new growth in life sciences is the incubator and there is evidence to suggest that companies based in incubators have a better survival rate and attract more investment than those that are not.[29] The specific requirements of life sciences start-ups can often only be met by specialist providers. Life sciences incubators typically provide laboratory and office space to start-ups to enable and support new enterprises in carrying out research, translation and building their businesses; facilities may be offered on short leases or on a day-to-day basis. Additionally incubators can facilitate knowledge transfer, mentoring and networking which are crucial to research-intensive industries. The BioCity 'UK Life Science Start-Up' 2015 report showed that of the 300-plus life sciences start-ups formed between 2010-2015, 57% are based in bio-incubators. The average investment in those companies located in a bio-incubator was three times more than for those outside a bio-incubator, with around 87% of all funds raised going into these companies. MedCity's 2016 report 'Planning for Growth – Demand for healthcare R&D space in London' showed that demand outstripped supply for mixed biology laboratory and office space; however, incubators can struggle to be economically viable particularly where real estate costs are high.

Government, local partners and industry should work together to ensure the right infrastructure is in place to support the growth of life sciences clusters. This includes transport into and across clusters (such as the Oxford-Cambridge rail link announced in autumn 2016, Heathrow expansion & HS2/3); housing and schools to attract skilled and talented people, as well as incubators and science parks to nurture and grow start-ups and SMEs. These need to be underpinned by fast broadband and flexible planning. This strategy welcomes measures in relation to upgrading infrastructure in the government's Industrial Strategy Green Paper, and the commitment in Autumn Budget 2016 and Spring Statement 2017 to additional capital to fund high-value economic infrastructure through the National Productivity Investment Fund.

Government, local partners and industry should work together to ensure the right infrastructure is in place to support the growth of life sciences clusters and networks.

28 Lord Sainsbury, 1999. *Biotechnology Clusters: Report of a Team led by Lord Sainsbury*, Minister for Science. Available at: http://www.iowabiotech.com/econ_dev_reports/uk_biotech_rpt.htm, Minister for Science, 1999

29 Biocity 'UK Life Science Start Up' (2015); MedCity 'Planning for Growth – Demand for healthcare R&D space in London (2016) Crocker, G., 2015. *Biocity UK Life Science Start-up Report.* BioCity. Available at: https://www.biocity.co.uk/knowledge/life-science-start-up-report; MedCity, 2016. *Planning for Growth – Demand for healthcare R&D Space in London*. Available at: http://www.medcityhq.com/wp-content/uploads/2016/05/MedCity-Planning-for-Growth-Demand-for-Healthcare-RnD-Space-in-London-March-2016-1.pdf

Identifying and selling regional strengths

Successful clusters are typically backed by a cluster organisation such as MassBio in Boston, MedCity in London, Oxford and Cambridge, and the Northern Health Science Alliance in the North of England. These organisations promote and market the clusters as well as providing brokering and signposting for investment and collaboration. Some also provide funding opportunities, business support and incubator, laboratory and office space. Research by the Centre for Cities published in 2014 suggested that the brand identity of key clusters in the UK is weak, impacting investment, talent, and demand, and that cluster networks are failing to connect people within and outside the cluster systematically.[30] The UK needs to be better and more coherent in selling this UK offer to the rest of the world.

UK's existing clusters should also work together to promote a 'single front door' to the UK for research collaboration, partnership and investment, joining up the multiple cluster organisations, trade bodies, and academic consortiums, to identify where the UK has internationally competitive excellence, generating and funnelling global interest and attracting inward investment to the right places.

Regions should make the most of existing opportunities locally to grow clusters and build resilience by working in partnership across local Government, LEPs (in England), universities and research institutes, NHS, AHSNs, local businesses and support organisations, to identify and coalesce the local vision for life sciences. Science & Innovation Audits, Local Growth Funds and Growth Hubs (in England), Enterprise Zones and local rates and planning flexibilities can all be utilised to support a vision for life sciences. Commercially successful companies can play a key role in nurturing the small companies in their geographies – stakeholder feedback suggests that the leadership and management skills required to take a company from science, research and financing to development, manufacturing scale-up and commercialisation are in short supply in the UK.

Regions and clusters can also benefit from a number of other recommendations within this strategy including Digital Innovation Hubs, specialist medtech hubs, the translational fund and support for clinical trials.[31]

UK's existing clusters should work together and with government to promote a 'single front door' to the UK for research collaboration, partnership and investment.

First for Pharma – North East England

The growth of the North East pharmaceutical and chemicals manufacturing sector is a strong example of successful Government industrial policy and investment from the late 1960s and early 1970s. Today, there are 17 major pharmaceutical manufacturers in the region plus a larger number of SMEs, contract development and manufacturing companies. The region exports £2.7 billion of pharmaceutical and other chemical products to the EU alone, comparable to the £2.9 billion of cars and other transport products. A recent survey of manufacturing site directors indicates that they are expecting to recruit an additional 7% of their current workforce in 2017 but at the same time many raised concerns over two aspects of Brexit a) the future of the UK's excellent manufacturing regulation systems which currently help support investment decisions and b) the need for tariff-free or low-tariff trade because many companies import raw materials and export products with very high added value.

Source: http://firstforpharma.co.uk

30 Centre for Cities & McKinsey & Company, 2014 *Industrial revolutions: capturing the growth potential*. Available at: http://www.centreforcities.org/wp-content/uploads/2014/07/FINAL_Centre-for-cities-report2014.pdf;
'Industrial Revolutions: capturing the growth potential' http://www.centreforcities.org/wp-content/uploads/2014/07/FINAL_Centre-for-cities-report2014.pdf

31 See sub-sections in 'Reinforcing the UK Science Offer' and 'NHS Collaboration'

Scotland, Wales, Northern Ireland

Scotland

Scotland is one of the largest life sciences clusters in Europe, employing over 14,000 people across 423 organisations, with a combined turnover of £2.8 bn.[32] The Strategy complements the health components of the key themes set out in Scotland's own broader strategy, The Life Science Strategy for Scotland: 2025 Vision, of innovation; sustainable production; creating a strong business environment; and internationalisation:

- **Innovation and commercialisation:** Through the Health Advanced Research Programme (HARP), this strategy hopes to work with NHS Scotland, Scottish Universities and Scottish Industry to identify the opportunities in healthcare twenty years from now and build an industrial and academic base to take advantage of these advances.
- **Sustainable production and creating a strong business environment:** The strategy intends to build on already strong foundations in life science innovation, with Edinburgh, Strathclyde and Dundee all featuring in the top 10 UK universities generating life sciences spin-outs. By optimising the tax environment, this strategy will further the development of such spin-outs and foster scaling of these firms.
- **Internationalisation:** The strategy will also seek to enhance international investment. Scotland already attracts major investment from foreign firms, for example US Pharmaceutical, Eli Lilly, has established its first venture fund within the UK in Scotland. The Strategy has the potential to attract further such investment into Scotland, by improving translational science and supporting pioneering pivotal trials in the healthcare system.

Northern Ireland

Northern Ireland's Strategy sector already turns over £800m and employs almost 5,800 people in 113 companies.[33] The Strategy seeks to further enhance NI's capabilities, through complementing NI's own Life & Health Science Strategy Action Plan 2016-20, particularly in its ambition to become a 'Living Lab': The Strategy hopes to build on NI's key strengths in the following areas: diagnostics development, enhanced clinical trials and health analytics.

- **Diagnostics development:** NI has two of the largest diagnostic companies, and NI has developed world leading methods (multiplex testing) for more accurate prevention. The Strategy seeks to encourage further such research and development, and work more effectively with UKRI to support industry doing high-risk convergent science.
- **Enhance clinical trials:** NI success in oncology research has been helped significantly by The Northern Ireland Cancer Trials Centre (NICTC). The Strategy seeks to bolster NI's clinical trial capabilities by using Government funding to attract more world-class scientists to the UK and design a translational fund to support the pre-commercial creation of clinically-usable molecules / devices. Additionally, the Strategy recognises the integrated nature of the NI health system, as the only fully integrated health and social care system in the UK. This system, combined with Ireland's Integrated Care Partnerships (ICPs), will help attract scientists for research and trials.

32 *Based on the 2016 'Strength and Opportunity' report on the health LSs sector. Figures are not comparable with those published by Scottish Enterprise which includes companies operating in the broader LSs sector;* HM government, 2016, *Strength and Opportunity 2016: The landscape of the medical technology and biopharmaceutical sectors in the UK.*
Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/607193/strength-and-opportunity-2016-bioscience-technology-accessible.pdf

33 Based on the 2016 'Strength and Opportunity' report on the health LSs sector. Figures are not comparable with those published by the Northern Ireland Science Industry Panel in Life & Health Sciences Northern Ireland, which includes companies operating in the broader LSs sector. Ibid.

- **Health Analytics:** A focus of the LSIS strategy is to foster skills in health analytics, which will help develop NI's already strong capabilities in this area in bodies such as the Administrative Data Research Centre, and companies such as Kainos and Exploristics. NI's fully integrated health and social care system, operational now for over 40 years, has created a truly unique dataset in the UK. Underpinned by Electronic Care Records, with every citizen having a unique patient identifier, NI has a cradle to grave record for more than 500,000 people – a distinctive selling point to industry.

Wales

Wales's life sciences sector is both fast-growing and innovative, employing nearly 12,000 people in 299 companies with a £2bn annual turnover.[34] Moreover, it has seen on average 5% annual growth in recent years.[35] Recognising this potential, the Welsh Government has established the Life Sciences Hub Wales, the Wales Life Science Investment Fund, Life Sciences Bridging Fund and the Life Sciences National Research Network to ensure the continuing expansion of the sector. The life sciences sector in Wales continues to grow and is expected to add £1bn GVA by 2022. Wales also has strengths in data systems for research, for example with the Secure Anonymised Data Linkage (SAIL) Databank. This holds a wide range of deidentified health and care datasets, from primary care to ONS and outpatient data, which can be linked and accessed via a remote gateway for approved research projects.

The Strategy seeks to support Wales's growing LS sector particularly around developing manufacturing and supporting growth and infrastructure:

- **Encouraging manufacturing:** Wales is developing as a hub of advanced manufacturing and is attracting advanced therapy companies, such as stem cell regenerative therapy firm ReNeuron, which is building one of the most advanced commercial cell therapy manufacturing facilities in the UK in Pencoed, South Wales. The Strategy will further encourage similar investments, through recommendations to support life sciences manufacturing throughout the UK.
- **Supporting growth and infrastructure:** Wales has developed medtech clusters of excellence in in vitro diagnostics, single-use technology and wound care. This strategy seeks to support the growth of these Welsh clusters by optimising fiscal incentives to support long-term investment.

34 Based on the *2016 'Strength and Opportunity'* report on the health LSs sector.
35 Life Sciences Hub, 2017. Available at: https://www.lifescienceshubwales.com

c) Expanding Life Sciences Manufacturing

Closing the export gap

Life science manufacturing makes a significant contribution to the UK economy. In 2016, UK life science exports were £30.7bn, accounting for 11.4% of all manufactured goods.[36] Pharmaceuticals and in vitro diagnostics from the medtech sector are the largest components of life science exports (84%) and the value of these exports increased by 17% in 2015 (to £25.1bn) and a further 3.1% in 2016 (to £25.8bn). Exports of medical devices increased from £4.5bn in 2015 to £4.9bn in 2016.[37] Overall, the UK runs a small life sciences trade surplus – revised balance of trade (excludes imports of illegal drugs) shrank from £1.6bn in 2015 to £0.1bn in 2016, but we are likely to move to a trade deficit unless action is taken by Government and by industry.

On productivity, the average GVA per employee in life sciences manufacturing was £105k in 2015, above aerospace (£84k) and more than double that across the economy (£49k).[38] The UK pharmaceutical manufacturing sector productivity level is 40% higher than German and Italy, 50% higher than Spain and almost twice the level achieved in France.[39] However, the average value of UK exports between 2011 and 2015 underperformed both in absolute terms and when expressed as a percentage of GDP.[40] This strategy therefore needs to attract manufacturing investments which will ramp up output and exports.

International competition

Our key competitors – Germany, US, Switzerland, Ireland and Singapore – have all prioritised life sciences manufacturing. Ireland has landed manufacturing investments from 9 out of 10 top pharmaceutical companies and 13 of 15 top medtech companies. It has become a European manufacturing base for many US companies,[41] achieved through establishing an autonomous Industrial Development Agency with ambitious FDI targets, supported by very strong fiscal and financial offers. Several major global companies now have more employees in Ireland than in the UK. Singapore established its Economic Development Board and, like Ireland, provided it with autonomy to implement specific economic development programmes, backed up again by attractive fiscal and financial incentives; today more than 30 of the world's leading biopharmaceutical companies have HQs in Singapore. The US is the global leader in the life sciences industry, is an early adopter of new classes of medicines with a large market, has good access to risk capital plus state and federal level support for research and innovation, and state or city level financial incentives for manufacturing investments. All of these have ensured the US has a substantial level of life sciences manufacturing. Both Germany and Switzerland have major pharmaceutical and chemicals industries, well-developed supply chains, coupled with low tax (Switzerland) and strong innovation support (Germany). Financial incentives are made available at local and regional level.

Turning our scientific discoveries into manufacturing growth

Over the last 10-15 years, the UK has been unable to capture significant new manufacturing investments – specifically, despite the discovery of monoclonal antibodies in the UK, we have failed to capitalise on this by securing commercial-scale manufacturing of these high-value products. Recent industry analysis has concluded that the US dominated at the early stage. Raising money from venture capital for manufacturing

36 ONS "UK Trade in Goods by Classification of Product by Activity: Quarter 4 2016"
37 Ibid
38 Office for National Statistics, 2015. *Annual Business Survey, UK non-financial business economy.* Available at: https://www.ons.gov.uk/businessindustryandtrade/business/businessservices/bulletins/uknonfinancialbusinesseconomy/previousReleases
39 PwC, 2017. *The economic contribution of UK Life Sciences industry*. Available at: http://www.abpi.org.uk/our-work/library/industry/Documents/The_economic_contribution_of_the_UK_Life_Sciences_industry.pdf
40 Total exports- UK $36bn, US $80bn and Germany $90bn and exports as a % GDP- UK 1.6%, US 3.1% and Germany 3.7%) OECD GDP, World Bank (Singapore), ONS UNCTAD STAT Data Centre codes 541 Medicinal and pharmaceutical products, 542 Medicaments including veterinary medicaments, 774 Electro-diagnostic apparatus for medical science etc, 872 Instruments and appliances
41 This includes Pfizer, Lilley, J&J and Medtronic-Covidien

in the UK was impossible; there was no real contract manufacturing sector and major pharmaceutical companies in the UK, who might have led investment, were relatively slow adopters of this new technology (GSK, AZ). The second wave of manufacturing investments has largely gone to Ireland, Singapore, Germany and the US, which together have attracted the bulk of $125 billion investment on new plant and equipment for the manufacture of biologics and other novel medicines in the last six years.[42]

The UK therefore needs to focus on not missing the next wave of manufacturing opportunities in the sector and this strategy sets out policies to ensure the UK captures internationally-mobile investment in order to close the export gap, boost productivity and contribute to a balanced economy through high-value jobs distributed across the country.

Attract substantial investment to manufacture and export high-value life science products of the future.

Life sciences manufacturing – areas for action

Technologies are changing

Many of today's medicines are manufactured through established platforms – primary manufacture involves on average around 8 chemical steps to make the active pharmaceutical ingredient (API). Manufacture of the final drug product involves a complex supply chain (multiple sites and countries) and often takes 18-24 months. Established platforms are generally inflexible, and new processes and approaches are urgently needed to allow for more agility, to incorporate an increasing role for automation and digitisation, to adapt to new therapeutic and product modalities, and to adapt to the requirements for more personalised or 'near patient' manufacturing. ReMediES and ADDoPT are two life science manufacturing projects addressing these challenges.

ADDOPT
ADVANCED DIGITAL DESIGN OF PHARMACEUTICAL THERAPEUTICS

Advanced Digital Design of Pharmaceutical Therapeutics.

ADDoPT https://www.addopt.org/ is a four year, £20.4m UK government-industry-academia collaboration designed to secure the UK's position at the forefront of pharmaceutical product design and manufacture. The initiative builds upon UK academic excellence and government infrastructure investments in big data analytics and simulation, as well as process modelling, optimization and control.

Digital Design for the pharmaceutical sector offers the prospect of more sophisticated definition, design and control of optimised pharmaceutical manufacturing processes, using both data analysis and first principle models in order to deliver new, higher quality medicines to patients, faster and more cost effectively.

The Digital Design philosophy combines fundamental research insight, and qualitative and quantitative mechanistic modelling to provide links between materials, manufacturing processes and the performance of the product for the patient. The ADDoPT investment is now a core component of the UK innovation ecosystem that will catalyze the digital transformation of the pharmaceutical sector in the UK.

42 CMOs and CROs Have Different Trajectories; CMOs may be gaining as strategic partners to large bio/pharma companies, but they have a much harder path to navigate. Miller J., *Stuck in Neutral: The CMO industry's value proposition is limiting its market penetration,* Pharmaceutical Technology Volume, 41:53, pg 72-73

REMEDIES is a £23 m project which brings together industrial stakeholders, academics, regulators and healthcare professionals, alongside teams from global pharmaceutical companies, major contract manufacturing organisations, equipment manufacturers and international logistics specialists, to scrutinise the many different elements of the medicines end-to-end supply chain. The project is co-funded by its industry partners and the UK Government's Advanced Manufacturing Supply Chain Initiative (AMSCI).

Key Objectives:

- Improve medicines supply (product availability, speed) by addressing end-to-end supply chain inefficiencies (inventory, waste)
- Develop production processes and supply chain delivery models that offer more responsive and cost efficient supply
- Develop and deploy smart packaging technologies that enable product tracking, compliance monitoring and patient engagement

Partner organisations:

New, and in some cases, disruptive technology platforms are emerging, presenting opportunities to the UK due to:

- Step-change in the way we make established medicines through process innovation (e.g. continuous processing, digital manufacturing).
- Synthetic biology, which will be important for the manufacturing of advanced therapeutics.
- Advanced therapeutics, including antibody drug conjugates (ADCs), oligonucleotides, viral vectors, microbiome and therapeutic vaccines, and cell and gene therapies.

Manufacturing decisions have to be taken much earlier: today's medicines are moving through development phases at a speed never seen before thanks to regulatory innovation including conditional licensing, incentives and mechanisms such as early access schemes in Europe and breakthrough status in the USA.[43] The intended manufacturing process needs to be set very early in the product development timeline because it will form an important part of the regulatory package submitted to gain approval to market a product. The decision on where and how to invest in manufacturing, either to pursue direct manufacturing or to choose and use a contract manufacturing partner, is made in parallel with the clinical development pathway.

Technology and regulatory changes are an opportunity for the UK because we are good at knowledge-driven process development. We also know that the location of late-stage development, scaling and early commercial manufacturing tends to be very sticky. Companies increasingly choose to site high-tech manufacturing close to development and scale-up as enablers. The UK already does a good job of capturing life sciences discovery and clinical development activity, as well as downstream commercial activity (such as European Headquarters), but there is a lot of leakage at the point of manufacture to lower cost, lower tax, or higher incentive locations.

43 Medicine Manufacturing Industry Partnership, 2017.Manufacturing Vision for UK Pharma: Future proofing the UK through an aligned technology and innovation road map. Available at: http://www.abpi.org.uk/our-work/library/industry/Documents/Manufacturing_Vision_for_UK_Pharma.pdf

This strategy is meant to address this leakage, create sticky activity and jobs around the country, and encourage a growing and more diverse (and resilient) life science product manufacturing and export base. The work of the Advanced Therapies Manufacturing Taskforce[44] has developed a clear set of actions to drive up investments in commercial manufacture of cell and gene therapies. The action plan is already having impact: an increasing number of global companies – both SME and large companies – are now looking at the opportunity to manufacture their cell or gene therapies at commercial scale in the UK. It is important therefore that the action plan should be fully delivered. It also forms a useful blueprint that can be scaled up for the broader life sciences manufacturing sector.

Accept in full the recommendations of the Advanced Therapies Manufacturing Action Plan and apply its principles to other life-science manufacturing sectors.

This programme should include technologies that deliver a step-change in the way we make established medicines through process innovation, advanced therapeutics such as cell and gene therapies, oligonucleotides, viral vectors and therapeutic vaccines. Establishing these in partnership with industry will incentivise re-investments in existing manufacturing plant and a greater share of investments into new manufacturing.

There should be a programme in partnership with industry to develop cutting-edge manufacturing technologies that will address scale-up challenges and drive up productivity.

Fiscal environment for manufacturing

Attracting more manufacturing to the UK depends on a conducive and internationally-competitive fiscal environment.

There are two stages of manufacturing considered as part of this strategy.

1) Pilot manufacturing: Emerging companies or new technologies to have access to sufficient capacity at Good Manufacturing Practice ("GMP") standard to produce the necessary material for pivotal studies and potentially supplies for the initial launch of new products.

2) Scale-up or Scale-out to provide sufficient product to exploit regional and global markets, which requires the creation of significant manufacturing capacity that can be built and evolving the skills developed in the proof-of-concept facilities. These are the facilities that will make a real difference to exports and balance of trade.

Together with the skills base, the fiscal environment is key to attracting companies seeking to develop, launch and manufacture products

The UK's current Corporation Tax rate is the lowest in the G20, but the UK only has a mid-table ranking in terms of Capital Allowances (CA) for investment in equipment, making it relatively less attractive to invest in pilot and full-scale manufacturing facilities in comparison to other countries. In relation to industrial buildings, including manufacturing facilities, the UK removed its investment allowance entirely in 2011. Competitor G20 countries typically offer capital allowances for investment in buildings of between 2-10%.

On capital equipment, France and Canada offer CA rates of 28 and 50% respectively, in comparison to an annual rate of 18% on a reducing balance basis in the UK.

44 Medicine Manufacturing Industry Partnership, 2016. *Advanced Therapies Manufacturing Action Plan: Retaining and attracting advanced therapies manufacture in the UK*. Available at: http://www.abpi.org.uk/our-work/mmip/documents/advanced-therapies-manufacturing-

Research and Development Tax Environment – Comparative Analysis

Country	Corporation Tax Rate	R&D Tax Incentives[i]	Patent Box[ii]
United Kingdom	19%	• Under RDTC, SMEs are entitled to an enhanced deduction of 230% of qualifying expenditure, or a cash payment of up to 33.35% of qualifying expenditure if in loss position. • Under RDEC, large companies are entitled to a taxable cash payment equal to 11% of qualifying expenditure. • Companies are entitled to a capital allowance of 100% of eligible R&D capital expenditure in the year of expenditure	10%
United States	15%-35% + local rate between 4.6%-12%	• The 'Traditional Research Tax Credit' equals 20% of qualifying expenses, exceeding a "base amount". • The 'Alternative Simplified Credit' is equal to 14% of qualifying expenses over 50% of the average qualifying expenses over the previous three years.	No Patent Box
Germany	15% + local rate between 14%-17%	• No R&D Tax Credits available.	No Patent Box
France	33.33%-35%	• Companies benefit from an R&D credit equal to 30% of the first EUR100m of qualified R&D expenditure (50% in overseas territories) and 5% after that. • SMEs are entitled to an 'Innovation Tax Credit' amounting to 20% of qualifying expenses for certain projects.	17%
Ireland	12.5%	• All R&D expenses are deductible in the year the expenses are incurred. • All qualifying research expenses (including capital expenditure) benefit from a 25% volume-based credit. • A 25% credit is also available for expenditure incurred in the construction or refurbishment of facilities used for R&D purposes.	6.25%
Belgium	33.99%	• Companies can choose between a one-time 13.5% additional deduction of all R&D investments or a 20.5% additional depreciation deduction. These can be converted into refundable tax credits (significantly lower than the deduction). • Other tax incentives are available for employing research staff.	6.8%

i This information refers to R&D Tax Credits relating to resources as opposed to capital costs.

ii Patent box regimes came under scrutiny in the OECD's Base Erosion and Profit Shifting (BEPS) Action Plan published in 2013. Since 2016, countries including the UK signed up to the new OECD rules and have implemented the 'nexus approach' whereby the portion of intellectual property income eligible for a reduced corporation tax rate is linked to the company's R&D spend. For more information visit the HMRC and the OECD websites.

Source: Deloitte, 2017 Survey of Global Investment and Innovation Incentives, March 2017.

The life sciences sector recommends that UK Government optimises the fiscal environment for manufacturing investment to drive investment in industrial buildings, equipment and infrastructure for manufacturing and late-stage R&D.

- Maintain the international competitiveness of allowances and wider support such as the Patent Box in terms of rate and extending the scope to a wider range of IP.
- Improve the UK's Capital Allowances regime, to support investment in industrial buildings and capital equipment
- Extend the current R&D Capital allowance to offer a payable credit

Finance

The UK is operating in an internationally-competitive environment to attract inward investment and to capture and retain domestic investment in manufacturing.

Building commercial-scale manufacturing capacity is highly capital-intensive and requires significant upfront investment, often several years ahead of a commercial product launch – these investment decisions need to be taken in parallel to a product's clinical development and regulatory pathway. Companies need to invest in land and shell buildings, high-quality utilities and significant capital equipment kit-out costs, in addition to the skills of the workforce to operate the plant.

Key international competitors, such as Singapore and Ireland, have worked harder to attract inward investments. They have targeted multinational companies and deployed highly effective account management with a strong 'offer' including fiscal incentives, financial incentives and flexible support to help companies get the skills required. Both countries have also focused on ease of access to major markets, with Ireland positioning themselves as a gateway to the EU and the US, while Singapore has been seen as a gateway to Asia.

In competitor countries, financial incentives in the form of grants, loans or 'in kind' support are available to support capital and revenue investment at a rate of between 10% and 15% of the total commitment. These countries make these incentives available to attract and anchor manufacturing and hence exports in the host location. This is well-established behaviour and the scale of the recurring economic benefit for the host location means that both SMEs and multinational organisations expect to be able to access incentives wherever they look to invest.

The UK should set a target of attracting ten large (£50-250m) and ten smaller (£10-50m) commercial-scale manufacturing facilities in the next five years. At an intervention rate of 10-15%, the low-impact scenarios (10 -£10m and 10-£50m investments) would need £60-90m public sector finance and the high-impact scenario (10-£250m and 10-£50m investments) would need £300-450m. The larger financial incentives are more likely to be made available through loans rather than grants. For SMEs, access to market rate loans may be more attractive whereas for larger companies who have an easier time raising private sector money, loans may only be attractive if offered at below-market rates. Although this might appear costly, it has the potential to capture high-value jobs across the country and generate new business for supply chain companies. It also has a long tail of benefit for the UK trade balance and will substantially influence the ability to close the export gap.

Consider nationally available financial incentives – grants and loans, or capital allowances combined with regional incentives – to support capital investment in scale-up, and prepare for manufacturing and related export activity. Industry suggests incentives need to amount to 10-15% of the total capital commitment of a project to be internationally competitive.

For early stage GMP manufacturing capacity required for clinical trials and commercial product launch, SMEs and even larger companies may be amenable to using shared facilities or platforms to de-risk their commitment, such as the 'hotel facility' on offer through the Cell and Gene Therapy Catapult manufacturing centre. Similar facilities should be considered for medicines manufacture supported by the Industrial Strategy Challenge Fund. The package of public funding announced to support innovative manufacturing should aim to anchor manufacturing of such products in the UK.

Currently, the UK has limited capacity to compete on grants or loans especially for single company or 'on demand' access. A Regional Growth Fund (RGF) ran in previous years and was used creatively to attract or retain high-value R&D and manufacturing investment in the English regions. This has been phased out except for exceptional cases where applications are accepted at the national and not regional level. RGF has helped support manufacturing investments by companies including UCB, Oxford Biomedica, Depuy Synthes, Actavis, Novartis, and Aesica.

Company Account Management

In addition to offering fiscal and financial incentives, both domestic and international companies should be supported to make the decision to invest in manufacturing in the UK. Competitor countries offer a 'one stop shop', and the UK should seek to emulate this support. The incentives and support that are currently on offer through Innovate UK, NIHR or local growth funds are highly varied in scope and may be available from a variety of national and local sources. It is a landscape that both domestic and global industry representatives have highlighted is challenging to navigate, understand and access. The Department for International Trade Life Sciences Organisation (DIT LSO) offers free and confidential support for inward investors to make the case to invest in the UK. Once a company has shortlisted the UK, DIT LSO also brokers access to subnational partners and support levers. This could include site selection, skills, supply chain, or regulatory and export support. This same level of support should be made available to scale-up domestic companies, by expanding the remit and resource of the DIT LSO.

Offering UK support through the perspective of the company (customer) journey is important. To be internationally competitive, companies need a senior national-level account manager fully accountable for delivery. The majority of support and incentives need to be available "on demand", and sufficiently mobile within the UK even if the offer needs to be drawn from multiple sources. Reviewing the incentives landscape and simplifying the customer journey could boost the UK's chances to win high-value, internationally-mobile investment in life sciences manufacturing.

Make support and incentives for manufacturing investment and exporting available to business through a single front door, provide a senior national account manager accountable for delivery and simplify the customer journey.

Strategic goal: The UK attracts ten large (£50-250m capital investment) and 10 smaller (£10-50m capital investments) in life science manufacturing facilities in the next five years.

C. NHS collaboration

a) Collaboration between the NHS and industry for the benefit of UK patients

Any credible life sciences strategy in the UK must have the NHS as an active participant. Not only is it a monopoly purchaser of commercial health-related products, but it is also potentially an enormous asset for those attempting to discover and develop new, innovative products and to properly test their utility in a healthcare system. Adoption by the system of innovation is key to improving outcomes for patients. This Strategy, however, should not only recognise the importance of the NHS to successful economic growth in the life sciences, but it needs to recognise the importance of active NHS engagement with commercial innovators in ways that could enable significant transformation in the way healthcare is delivered in the UK.

The shared objective of industry and Government should be to deliver outstanding patient outcomes. To achieve this and to create an innovation-led health system, innovative products that generate patient benefits should be adopted at a rate that places the UK in the top quartile of comparator countries. The NHS has made positive initial steps towards being more transparent by focussing on patient care and some outcomes (through initiatives such as the Clinical Commissioning Groups and Independent Advisory Groups; MyNHS; and the Care Quality Commission), and the NHS should continue to pursue an ambitious agenda in this area using independently-assessed publically available outcome metrics at a national and regional level. Historically, measures of uptake have always been disabled by the lack of comprehensive digitalised prescription data across the NHS. Government and industry should work together to try to fix this problem and agree an updated measurement along the lines of the annual Life Science Competitiveness Indicators report, which is the current standardised agreed metric. This would inevitably lead to better levels of uptake of innovative healthcare products that transform care and outcomes.

Medtronic – partnership working to generate efficiencies

Medtronic Integrated Health Solutions have been successfully partnering with NHS Hospital Trusts to manage and modernise their catheterisation laboratory, or cath lab, facilities and processes. These partnerships are an intended move away from the traditional, transactional, supplier-customer relationship, to shared risk-and-reward models that deliver value under long-term service agreements through a fee-per-procedure approach. Medtronic collaborates with Hospital Trusts over a 7 to 10-year period to re-equip, at no cost to the Trust (around £1m per lab), and then manage their cath labs, providing the latest medical technology, capital equipment and infrastructure, optimising operational efficiencies and clinical outcomes, running daily operations and developing local care pathways for patients who need access to cardiac care.

After several years of partnership with leading hospitals in England, key achievements include increased throughput with +15% in activity, 100% uptime, a doubling of on-time starts and a halving of wasted stock. Overall, these cath lab solutions can release +£1m of efficiency savings at a Trust level, which can be reinvested to improve patient access, and enable the clinical staff to spend more time on patient-facing activities.

Industry is willing to collaborate with the NHS to enable service transformation and support the continued improvement in patient outcomes. Building on the AAR and recognising the challenges that the current fiscal situation presents, this might include:

- Risk-sharing in development of tools and therapies using NHS infrastructure to run evaluative studies and delivering benefit sharing from proven technologies

- Partnering with medtech and diagnostics companies to reshape clinical pathways and improve efficiency
- Collecting real-world data and linking this in a closed system to assess clinical and cost-effectiveness.
- Modernisation of clinical trials including digitisation and regulatory innovation.

The arguments for more interaction between industry and the NHS in the evaluation of products are clear. UK patients and clinicians would benefit from innovative product use in the clinical trial setting knowing that, should the value be proven, the medicine would rapidly become more widely available, helping drive the spread of these innovations at pace and scale. The NHS would benefit from clinical trial revenues, early clinical experience and setting a global trend by using best standards of care, supporting improved planning and budgeting. Industry would benefit from improved predictability and early conditional reimbursement of a new innovation in the country where trial and early clinician and patient use has taken place.

The NHS has many potential assets that could be valuably applied in collaboration with industry to improve our understanding of how well therapies work in the real world, which patient populations are most likely to respond to therapeutic interventions and how innovations can be used to change whole pathways of care, ideally reducing cost and improving outcomes. There are some interesting examples of how this has already occurred. The Genomics England project is an excellent example of how the NHS worked together with a commercial technology provider (Illumina) and Genomics England to create a whole new pathway of state-of-the-art genomic technologies to better diagnose patients with rare disease and define genomic variants associated with cancer.

This is a good demonstration of NHS service transformation emerging from a collaboration with industry and one that could be replicated in many other domains as the NHS develops its ability to take a more collaborative approach with industrial partners. In order to progress a more collaborative environment between industry and the NHS, it is important that the NHS is equipped to agree partnership deals. This role could fall to the commercial team in NHS England, as suggested by the Accelerated Access Review, or be executed locally by Trusts – as is the case with the Oxford University / Drayson Technologies partnership.

Utilise and broaden the Accelerated Access Review to encourage UK investment in clinical and real-world studies. Deliver a conditional reimbursement approval, for implementation as soon as licensing and value milestones are delivered so that patients can benefit sooner.

Create a forum for early engagement between industry, NHS and arm's-length bodies (e.g. NICE, MHRA) to agree commercial access agreements.

There are significantly more potential opportunities for the NHS to engage in many aspects of the innovation agenda by driving the growth of successful life sciences companies in the UK, which will, in turn, help to transform the service itself. A clear innovation strategy is needed to extract this potential and although this agenda has been successful in some settings, it could go faster and be broader to increase the pace of transformation and efficiency improvements. A new philosophy of collaboration and trust must be an underpinning principle of the Life Sciences Industrial Strategy and should be achievable if the unified goal is to provide the best and most innovative health care to patients.

The above reflects a positive and productive relationship between the NHS, other arm's-length bodies and the life sciences industry. In order to facilitate transformation, the NHS has to act increasingly as a partner and collaborator with industry so that they can together devise ways of managing early adoption of innovation, through clinical trials or otherwise, and thereby invest in patient outcomes and increase the overall efficiency of the healthcare system.

Strategic goal: In the next five years, the NHS should engage in fifty collaborative programmes in late-stage clinical trials, real-world data collection, or in the evaluation of diagnostics or devices to enable UK patients to benefit from early access to innovation and drive improved patient outcomes. These could be shared-risk programmes that produce a reward to the NHS and a sustainable return for industry to support R&D and encourage innovation.

b) Adoption, access and diffusion

Evidence demonstrates that access to and diffusion of products in the NHS is often slower than in some comparable countries.[45] This environment risks creating a negative impression in boardrooms around the world with trials being diverted to geographies deemed more likely to use products. Partnership with industry through this strategy and a subsequent sector deal will be challenging unless there are clear signals that innovation will be encouraged and rewarded, and the challenge of adoption of new innovation at pace and scale is resolved.

There are several barriers to adoption and diffusion and many of these have been addressed in the recommendations of the AAR. We welcome the recently announced £86 million joint funding by BEIS and DH to support the implementation of the AAR. The implementation of this report will do much to create confidence in industry and should significantly reduce delay in the uptake of innovative products.

In the AAR, the opportunity to improve routes to market by identifying, evaluating, pricing and adopting innovations in the UK was clearly specified in its recommendations. This strategy endorses those recommendations in the AAR that propose:

- development of an enhanced horizon scanning process to enable thorough and joint planning between industry, NHS and government, and thereby more predictable NHS expenditure on technology.
- a transformative designation for those innovations with the potential for greatest impact.
- an Accelerated Access Pathway for strategically-important, transformative products.
- a single set of clear, national and local routes to get medical technologies, diagnostics, pharmaceuticals and digital products to patients.
- evolution of the process for assessing emerging technologies so that it is fit for the future.
- a range of incentives should support the local uptake and spread of innovation, enabling collaboration, and creating greater capacity and capability for change.
- broadening of conditional and adaptive approval pathways.

Industry has also highlighted a range of recommendations overlapping with and supplementing the AAR as potential priorities for implementation. They include:

- parallel processing of MHRA and independent NICE assessments.
- a single appraisal process and commercial discussion with NICE, NHS England and companies for each product, including flexible, confidential reimbursement and contractual arrangements.
- use of more flexible criteria to assess value in a structured decision-making process.
- enhanced ability of the NHS to collaborate locally to reshape and evaluate clinical pathways.
- system alignment to support consistent adoption and sustainability.
- robust monitoring of the implementation of these recommendations via NICE.

45 Department of Health, Department for Business, Energy & Industrial Strategy & Office for Life Sciences, 2017. *Life Science Sector Data.* Available at: https://www.gov.uk/government/publications/life-science-sector-data-2017

Industry urges further extending the recommendations of the AAR to evolve and simplify the access system for all products. This strategy proposes that all new medicines and selected high-potential medical devices and diagnostics should be appraised through a single, value-led, NICE-managed process, with an integrated opportunity for incorporating a commercial access agreement where necessary, providing access to a range of flexible funding and reimbursement vehicles. A resource impact assessment and clinical pathway change analysis should form part of the appraisal process, with an NHS adoption plan being published, alongside positive final guidance on the clinical pathway change required for the successful implementation of the treatment. Multiple criteria should inform the value assessment including a QALY-based, cost-effectiveness assessment, burden of illness, unmet need and therapeutic breakthrough impact. Final appraisal guidance should be published within 90 days of marketing authorisation or date of product release into the UK market, and should be subject to active, benchmarked uptake assessment. The industry strongly supports the NHS constitution's position on making medicines and treatments that have been approved by NICE available for use by NHS healthcare providers.

The key consideration in reframing access is the streamlining of the processes and methods of assessment to create a single access decision point for each new innovation. Importantly, the role NICE has previously undertaken defining the value of medicines should also be extended to devices, diagnostics and digital tools, and a wider range of of instruments than the QALY would be necessary to provide this value assessment. This process of evaluating non-pharmaceutical products has begun but needs to be accelerated and expanded. Speed and simplicity of this early pathway is essential and, in keeping with the AAR, a parallel evaluation by NICE and the MHRA would provide rapid access to Health Technology Assessment evaluations and regulatory approval, creating opportunities for rapid adoption and diffusion in the system.

Challenges around affordability for the NHS are recognised by industry, increasing the need to provide stable and predictable evaluations and outcomes for all parties. Industry suggests that a new long-term, voluntary framework agreement on medicines policy should be agreed with ABPI to take over from the current agreement by the beginning of 2019. As an overarching principle, the next voluntary agreement should balance patient access to new medicines, value for money for the NHS and the need to incentivise industry to invest in research and development for the next generation of innovative products.

The Government should use the recommendations from the AAR to streamline the processes and methods of assessment for all new products, simplifying and accelerating access and using a single clear decision point. Ensure this streamlined access framework is part of a holistic medicines policy with a leading role for NICE and including a new voluntary agreement as a successor to the current agreement.

A single access decision point should be capable of dealing with:

- High value / complex medicines with a single integrated access and commercial discussion.
- Routine, rapid access route for medicines not requiring commercial and access discussions.
- Flexible and confidential reimbursement and contractual arrangements.

The need to manage affordability within the NHS is clear, but this needs to be underpinned by a NICE-led framework without creating further barriers to access and adoption. This issue can be dealt with through improving the value which the NHS can offer industry, supported by robust horizon scanning, earlier budget planning and coordinated working between NICE, the NHS and industry as well as patient access schemes and specific commercial agreements. The availability of the commercial team in NHS England will assist this process substantially, as will their ability to explore a wide range of commercial arrangements, including volume-based pricing, outcomes-based pricing, indication-specific pricing and by methods which leverage

assets in the NHS other than price e.g. time, data, access. These alternative routes to reimbursement should be viewed as exceptions, but nevertheless important ones in dealing with the products that provide pressure on NHS budgets.

Although constraints in funding innovative products provides one mechanism for limiting expenditure in a financially-pressed healthcare system, it would prove more sustainable if efforts were made to increasingly use innovation to improve efficiency more widely in healthcare to meet the rapidly growing demand in the healthcare system.

There are many risks of not pursuing the access, adoption and diffusion agenda more effectively. The UK has become a challenging market to operate in and the risk is that this will ultimately lead to less clinical development taking place in the UK. In areas such as rare disease, where it is unethical to commence clinical studies unless there is a willingness to maintain therapy with effective products, there is a need for the NHS and industry to work harder together to achieve agreements on access. In cancer, the standard of care is essential before new medicines can be evaluated properly, and the UK is already beginning to lose out because it does not consistently offer a gold standard of care, sometimes making it challenging as a site for evaluation of new cancer medicines. Getting the balance right in encouraging rapid and efficient access to innovative medicines within a tight financial envelope will require flexibility and creativity on both sides, but if this can be achieved, the UK can grow its reputation as a destination for late-stage trials and as an excellent environment for the life sciences industry. Industry firmly believes in a value-based access and adoption system with a NICE-led system for value assessment. However, additional commercial access arrangements to deal with the issue of affordability, led by a commercial team in NHS England in collaboration with NICE could provide an integrated decision-making framework for the future.

SMEs producing innovative products can find it challenging to engage with the NHS. Efforts must be made to improve uptake of innovative products by the NHS, building on the promising early start being made by Academic Health Science Networks. It is clear that NHS procurement approaches and systems for setting reimbursement tariffs, together with the sheer number of purchasing or commissioning organisations within the NHS, can, make it very difficult for SMEs to find a route to market. This should be reconsidered if the NHS is to be a good customer for the sector.

Finally, consideration needs to be given to the issue of diffusion and widespread adoption within the NHS. This has historically been a limitation within the NHS and affects the commercial desirability of the UK market. Patients throughout the NHS should benefit from innovation equally, however innovations that have demonstrated value often take time to be diffused appropriately across the healthcare system. A structure to drive and measure diffusion is clearly urgently needed and NICE could provide the most appropriate vehicle to monitor uptake and adoption throughout the system. Firstly, there should be a shared estimate of UK uptake based on the work that NICE already does for each appraisal. This should be signed off by a joint NICE/NHSE/industry group and published shortly after each appraisal is completed. This would be supplemented by audited reports from healthcare providers on the level of uptake of innovations deemed by NICE to be sufficiently important that they need universal uptake. Failure to deliver such uptake of value-proven innovations needs to be declared publicly and measured by trust boards, CCGs and, then, potentially be included in the CQC regulatory framework. Improvement in the adoption rates and levels of important, cost-effective new innovations must ultimately be good both for the NHS and for patients. Independent monitoring of adoption and diffusion could be coupled with independent evaluation of patient outcomes, providing clear evidence of the impact of innovation within the system.

These issues of access, adoption and diffusion are sufficiently important to the life sciences industry and the recommendations made here and in the AAR should be taken forward by a subgroup of the Ministerial Industry Strategy Group supported by the OLS and incorporating existing work being undertaken by NICE, NHS England and industry.

Additionally, NICE are currently creating a new funding model for technology evaluation. When creating this funding model, NICE should consider how it covers the costs of appraisals of drugs, medical devices and diagnostics, in a way which does not stifle innovation or prevent SME engagement. There are two areas where this is particularly important: 1) there are proposals for charging a fee per technology appraisal, and NICE should carefully consider what represents a reasonable cost for their services; 2) SMEs should be given a special fee structure (as in the FDA and EMA), to facilitate uptake of their products.

Value assessments should be evolved in the long-term with improved patient outcome measures, affordability and cost management data extending beyond one year timeframes.

NICE's funding model for technology evaluation should be set up in a way that does not stifle SME engagement.

Strategic goal: The UK should be in the top quartile in comparator countries, both for the speed of adoption and the overall uptake of innovative, cost effective products, to the benefit of all UK patients by the end of 2023. In the absence of a more robust metric, the Government's annual Life Science Competitiveness Indicators report should be used to measure this metric.

c) Data

Progress in healthcare outcomes is substantially dependent on the development of pharmaceutical, medtech and digital products, evaluated by testing their impact on patients, whether in clinical trials or in the real world. The importance of such healthcare data in enabling evaluation of innovative technologies in the real world and delivering wide-ranging improvements to health and care, research and services has been widely recognised.[46]

Crucial to realising the potential for healthcare data to improve care is ensuring that the use of such data is acceptable and in the interest of patients and clinicians. A critical first step is the need to implement the recommendations of the National Data Guardian (NDG), which set out new safeguards for health and care data. The proposals in this strategy are designed in a way which is compliant with the NDG's recommendations.[47] Similarly all proposals should meet the relevant high data security standards as set out by the NDG and the recommendations of CQC.[48] Many more people support than oppose health data being used by commercial organisations undertaking health research,[49] but it is also clear that strong patient and clinician engagement and involvement, alongside clear permissions and controls, are vital to the success of any health data initiative. This should take place as part of a wider national conversation with the public enabling a true understanding of data usage in as much detail as they wish, including clear information on who can access data and for what purposes. This conversation should also provide full information on how health data is vital to improving health, care and services through research.[50]

46 The Healthcare Data Institute, 2015. *Unlocking the full potential of data analytic for the benefit of all.* Available at: http://healthcaredatainstitute.com/2015/11/25/white-paper-unlocking-the-full-potential-of-data-analytics-for-the-benefit-of-all/;

47 National Data Guardian, 2016. *Review of data security, consent and opt-outs.* Available at: https://www.gov.uk/government/publications/review-of-data-security-consent-and-opt-outs; all proposals to utilise deidentified / ICO code of practice anonymised data where possible, and any use of personal confidential data to have a clear legal basis e.g. via direct consent / s251 / CAG approvals

48 The Care Quality Commission, 2016. *Report into how data is safely and securely managed in the NHS.* Available at: http://www.cqc.org.uk/publications/themed-work/safe-data-safe-care

49 Ipsos MORI, 2016. *The One-Way Mirror; Public attitudes to commercial access to health data.* Available at: https://wellcome.ac.uk/sites/default/files/public-attitudes-to-commercial-access-to-health-data-wellcome-mar16.pdf

50 https://understandingpatientdata.org.uk/what-are-best-words-use-when-talking-about-data

One of the most important resources held by the UK health system is the data generated by the 65 million people[51] covered within it. The development of platforms to enable deidentified health data to be appropriately used to research and develop technologies would be of great benefit to patients in the system, to those managing the NHS and to researchers attempting to develop new therapies or improve NHS care. The ability to demonstrate the true value of products on an ongoing basis should allow a reduction in the cost and time to bring new treatments to patients, with the same data enabling healthcare systems to procure more effectively by, for example, rewarding outcomes or targeting treatments to those groups where they will work best.[52]

A data ecosystem that enables the NHS to understand the value of products and improve care pathways should build towards the full population of 65m, with longitudinal data across health and care, in order to be globally competitive[53] and to provide the highest quality research and care. This level of coverage would enable research requiring large population sizes (e.g. in rare diseases), evaluation of the true value of innovations across the whole of the UK, and increased quality for all research; for example, with more representative safety data or an increase in the predictive power of algorithms to identify disease risk.

The contribution of patients to research already enables the UK to hold several world-leading national data sources. Amongst others, CPRD holds data on 22 million patient lives,[54] UK BioBank holds wide-ranging data on 500,000 participants and GeL will soon have sequenced 100,000 genomes. NHS Digital collects many datasets and data flows from other organisations, such as the Office of National Statistics, which are currently used or have the potential for use in life sciences.[55] However, these sources, whilst they may be linked in some cases, do not all currently provide deep, near real-time data for research across multiple care settings as standard.

51 Office for National Statistics, *Population estimates.* Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates

52 2016. *Accelerated Access Review: Final Report – Review of innovative medicines and medical technologies.* Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/565072/AAR_final.pdf

53 Cf. other global systems ~5m population: Finland Linked National Health Registers, Sweden Quality Registries, Iceland Patient Registries; OLS research and EMA / IMI AdaptSmart briefing; systems across larger populations but not across all settings: FDA Sentinel, EMIF, EHR4CR.

54 Including 5 million currently contributing / registered

55 NHS Digital, *Data Collections.* Available at: http://content.digital.nhs.uk/datacollections

Uses of health data for research[56]

The **DECIPHER**[57] project links deidentified genetic and clinical patient data to aid the diagnosis and treatment of rare disease patients; its use is now a standard part of clinical practice in many countries. By matching patients with similar genetic and clinical changes, the project is improving genetic diagnoses, leading to better disease management and support for patients and their families, as well as providing the basis for research into developing new therapies.[58]

The **SABRE**[59] study is using GP and hospital data[60] to generate insights into diabetes and cardiovascular disease, particularly in the understanding of how ethnicity can affect the risk of diabetes. For patients, this has already enabled better targeting of prevention measures and early diagnosis initiatives to specific groups, for example by identifying that 50% of those with South Asian, African and African-Caribbean heritage develop diabetes by age 80.[61]

The **Salford Lung Study** is a world-first phase III digitally enhanced Randomised Controlled Trial (RCT) in COPD and asthma, utilising Salford's existing integrated electronic medical record infrastructure.[62] The use of patient records in this context has allowed patients in the trial to be monitored during 'normal' clinical practice, enabling evaluation of the real-world value and benefits of the medicine at a much earlier stage. The use of patient data as a basis of such trials will allow patients to access new medicines faster, and the health system to better understand their real value.

The Personalised Health and Care 2020 strategy, alongside the work of NHS Digital, NHS England and others, outlines a national ambition for a digitised health and care system, including collection of key datasets for research. Furthermore, there are a number of regions in the UK with particularly mature digital healthcare, for example the 16 acute and 7 mental health Global Digital Exemplar trusts.[63] Some regions have developed or are developing shared digital records with linked health and social care information, such as the Cheshire Care Record,[64] with the majority of areas having plans to put these in place. The Salford Lung Study has brought ~£60m to the local economy and involved training of over 3000 people.[65] As such, linking and unlocking the potential of existing data sources to enable this and other kinds of real-world research as standard would position the UK as a global leader in the area. Nationally, projects such as UK Biobank, which holds data with patient consent, have navigated the digital environment to access several crucial national datasets held by different agencies including ONS, NHS Digital and primary care system providers. The most significant obstacles for them have been regulatory, with regulation over access being different with each dataset.

56 Understanding patient data, 2017. *Case Studies*. Available at: https://understandingpatientdata.org.uk/case-studies
57 https://decipher.sanger.ac.uk/
58 Understanding patient data, 2017. *Treating rare genetic diseases*. Available at: https://understandingpatientdata.org.uk/case-study/treating-rare-genetic-diseases
59 http://www.sabrestudy.org/?cat=10
60 From NHS Digital
61 Understanding patient data, 2017. *Investigating trends in diabetes*. Available at: https://understandingpatientdata.org.uk/case-study/investigating-trends-diabetes
62 GSK, 2017. *Relvar Ellipta significantly improved asthma control in Salford Lung Study patients compared with their usual care*. Available at: http://gsk.com/en-gb/media/press-releases/relvar-ellipta-significantly-improved-asthma-control-in-salford-lung-study-patients-compared-with-their-usual-care/
63 NHS England, date. *Global Digital Exemplars.* Available at: https://www.england.nhs.uk/digitaltechnology/info-revolution/exemplars/; NHS Digital Maturity Index
64 https://www.cheshirecarerecord.co.uk/what-is-the-cheshire-care-record/
65 Internally commissioned research, NW eHealth, GSK data

The global healthcare analytics market was worth up to £3.3bn in 2014 and is forecast to grow at c.22% to 2018. The UK market is estimated to grow at c.24% CAGR to £365m by 2018 – at a faster rate than the global market, if issues such as dataset availability and linkage, and ensuring data access with the necessary controls and permissions are addressed.[66] The lack of comprehensive electronic prescribing, including indications across all hospitals for example, already impedes the ability of the NHS to know what has been prescribed and this will prevent novel pricing strategies such as indication-specific pricing or volume / outcomes based pricing being applied. Similarly, there is insufficient linkage between hospital and primary care IT systems, making real-world data collection difficult. NHS England and NHS Digital should move to address this rapidly.

Building on the standards set out by the NDG and CQC, the health and care system should set out a vision and a plan to deliver a national approach with the capability to rapidly and effectively establish studies for the generation of real-world data, which can be appropriately accessed by researchers.

ePrescribing should be mandatory for hospitals.

In order for the national ambition to be realised, systems across care settings and regions should be fully interoperable, with comparable data and access requirements. The strategy of the National Information Board and work of NHS Digital, including the National Data Services Platform, should move to define standards and mechanisms to enable easy linkage and comparison of data from different sources. Currently, data access agreements and requirements can vary between trusts and sources. A set of national-level requirements for data access, building on the recommendations of the National Data Guardian, could provide the common principles that data access agreements should include, at e.g. the trust level. This would provide the assurance for patients, trusts and innovators that could facilitate appropriate, consistent and timely data access to both protect patient privacy and enable research. Without clear guidance at a national level for both interoperability and data access, enabling appropriate and controlled access for research to representative and joined-up datasets, the full potential for UK data to improve health and care will not be realised.

NHS Digital and NHS England should set out clear and consistent national approaches to data and interoperability standards and requirements for data access agreements.

Currently, arranging linkage and access to national-level datasets used for research can require multiple applications and access agreements with unclear timelines. This can cause delays to data access enabling both research and direct care; as an example, delays in Hospital Episode Statistics linkage to clinical data for a rare disease specialist centre, requiring further amendments to Confidentiality Advisory Group (CAG) and HRA approvals,[67] led to an 18 month delay in a project for direct care supporting better disease detection and referrals.[68] Whilst NHS Digital have reduced time to completion through the Data Access Request Service to an average of 60 days,[69] there should be transparent, clear and faster response times across all data providers including when linking multiple datasets.

66 Monitor Deloitte, 2015. *Digital Health in the UK: An industry study for the Office of Life Sciences.* Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/461479/BIS-15-544-digital-health-in-the-uk-an-industry-study-for-the-Office-of-Life-Sciences.pdf

67 Which were not addressed in parallel

68 IMS case study; multiple similar experiences received by OLS from stakeholders

69 NHS Digital data, Feb 2017

Appropriate and secure access to currently available national datasets should be accelerated by streamlining legal and ethical approvals.

Existing programmes to digitise the health and care system and encourage better data use have the potential to create a system that delivers for research, patients and clinicians. However, although for example there is a Research Advisory Group for NHS Digital, there is no present requirement for input and consultation across the broader life sciences sector (including charities and academia) into all these programmes. Life sciences input should be used to expand the focus of health data programmes to provide a service for all those who would use health data to deliver treatments of value and improved care, including the research community beyond the NHS.

There should be a forum for researchers across academia, charities and the commercial sector to engage with all national health data programmes.

Algorithm development will be a key part of future research and development in the life sciences sector. Currently algorithms making medical claims are regulated as medical devices. Neither the current or planned regulations provide a framework to account for machine learning algorithms that update with new data. One approach to this may be in the development of 'sandbox' access to deidentified or synthetic data from providers such as NHS Digital, where innovators could safely develop algorithms and trial new regulatory approaches for all product types.

In addition to this, existing data access agreements in the UK for algorithm development have currently been completed at a local level with mainly large companies and may not share the rewards fairly, given the essential nature of NHS patient data to developing algorithms. There is an opportunity for defining a clear framework to better realise the true value for the NHS of the data at a national level, as currently agreements made locally may not share the benefit with other regions.

A new regulatory, Health Technology Assessment and commercial framework should be established to capture for the UK the value in algorithms generated using NHS data. A working group should be established to take this forward.

Digital Innovation Hubs

Whilst the potential of the UK's health data is clear, there is significant regional variation in digital maturity and the readiness of systems for real-world evidence (RWE) studies.[70] An early opportunity that has therefore emerged for the UK is the creation of regional systems of 'data hubs', called 'Digital Innovation Hubs' (DIH), that would contain comprehensive and secure data in primary, secondary and tertiary care as well as social care and community data for a population of between 3-5 million people. If such hubs operate to clear national data and interoperability standards as defined by e.g. NHS Digital, this should allow federation and development towards the long-term ambition of national coverage, would enable studies to be run across multiple hubs and de-identified data to be appropriately and securely linked to information from national datasets such as genomics or NHS Digital's Data Services Platform.

Any such hub would need to assure the public that they operate within data standards and requirements for security, privacy, ethical approval, and that national opt-outs are respected, as per the recommendations of the National Data Guardian.

70 NHS England, date. *Global Digital Exemplars.* Available at: https://www.england.nhs.uk/digitaltechnology/info-revolution/exemplars/ NHS Digital Maturity Index

Regional approaches have had demonstrable success in obtaining trust and data sharing agreements,[71] perhaps due to closer proximity and input to the data use, allowing a greater understanding of the benefits for direct care and from research. A regional approach, building upon areas of strength, would also allow faster development of the capability needed for research through access to longitudinal patient Electronic Patient Records (EPR) data, capturing both outcomes and costs[72] across a whole healthcare economy. This functionality would provide an ideal environment for innovators to test the impact of their innovations on care pathways and establish value evidence in a way that might be harder to do in other healthcare systems. DIHs should have the ability to conduct real-world studies and interventional trials rapidly and as standard; such a "plug and play" system could be of enormous utility for testing the impact of innovation on pathways and costs.

These innovation hubs should include both data architecture and additional elements of the ecosystem that would allow regional healthcare providers and researchers to work seamlessly together with pre-agreed approaches to costings and ethical and governance approvals. They should be embedded in well-established research-orientated environments capable of facilitating all study types, including digitally enhanced clinical trials.

A selection of 2-5 regions, corresponding to AHSN footprints capable of establishing such DIHs, should be made, utilising: evidence of EPR infrastructure, which has received significant investment and is maturing quickly; alignment with global digital exemplar sites; potential for data linkage along the care pathway; attractiveness to industry and collaborative partners; a track record of working effectively with industry; analytical expertise applied at scale to large data sets; methodological expertise in trial design; coherent geography covering 3-5 million people that aligns with patient flows; and a strong environment for clinical academic research, for example co-location / partnership with existing NIHR / CRN infrastructure. As these hubs develop, there will need to be support for study design, data management and project management, and each may evolve to support several hundred individuals in these roles. Ultimately, the goal should be to have coverage across the whole of the UK.

With populations ranging from 1.8 – 5.4 million,[73] Northern Ireland, Scotland and Wales are of a similar size to the DIHs proposed here, and all already have ongoing or planned initiatives to curate health data for research.[74] These systems all have the potential to deliver in the same way as DIHs and, if they can demonstrate this, should be considered for a DIH 'designation', with researchers being directed to them for the appropriate studies.

Medtech Centres of Excellence

Academic centres and NHS regional partnerships should also provide support for specific medtech themes, focusing on research capability in a single medtech domain such as orthopaedics, cardiac, digital health, or molecular diagnostics. This would align regional capabilities with a single medtech focus, allowing them to compete globally. The UK needs to grow centres that are globally-leading in specific medtech or diagnostic domains. This is likely to happen only where there is academic focus and engagement from the healthcare system for evaluation. There are relatively few examples of this currently in the UK. Leeds is a global centre for orthopaedic device R&D and manufacturing and is one such example that could be built upon. Ideally, the UK could host four to six such centres of excellence dedicated to a single medtech theme. NIHR should lead an exercise to identify such focussed centres and these should be evolved to make them magnets for global inward investment from major medtech partners.

71 see recent experience in Bradford; CHC citizen juries; Surrey

72 This could include linkage to NHS Digital patient level costed data flows when available, and imaging information such as the National Diagnostic Imaging Dataset

73 Office for National Statistics, *Population estimates.* Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates

74 For example, Innovative Healthcare Delivery Programme Scotland, SAIL, NI EHCR and honest broker service

Two to five Digital Innovation Hubs providing data across regions of three to five million people should be set up as part of a national approach and building towards full population coverage, to rapidly enable researchers to engage with a meaningful dataset.

These should operate in line with the NDG's recommendations on patient data, and include longitudinal data covering primary, secondary and social care to allow evaluation of innovative tools to establish their impact on care pathways and cost within the healthcare system.

These regional hubs should also have the capability to accelerate and streamline CTA and HRA approvals, together with local sign-off and data access agreements, operating within the national framework, to improve the speed of trial initiation. One or more of these should focus on medtech.

The UK could host 4-6 centres of excellence that provide support for specific medtech themes, focusing on research capability in a single medtech domain such as orthopaedics, cardiac, digital health, or molecular diagnostics.

Strategic goal: Establish 2-5 data hubs.

National Registries

For certain therapy areas, there is a strong case for establishing of further national data registries, following NDG recommendations and ideally building upon existing datasets or automated collections.[75] For example, there are systems in mental health that are well placed to enable registries.[76] For rare or orphan diseases, a registry approach could work with regional hubs to enable the required population sizes for research.[77] Patient trust would be enhanced if these are co-ordinated by the relevant patient charities, who should also have an active role in their governance and direction. These registries could also be well-positioned to identify patients appropriate for recruitment into clinical trials.

National registries of therapy-area-specific data across the whole of the NHS in England should be created and aligned with the relevant charity.

This data work programme should be carried forward in light of the National Data Guardian's recommendations on patient data and the associated government response.

75 For example, NHS Digital deliver over 50% of the current clinical audits, including the national diabetes clinical audit with 90% of GP data linked to HES and ONS data. Systems such as these may be well placed to be expanded for the life sciences.
76 South London and Maudsley NHS Foundation Trust, 2016. D-CRIS. Available at: http://www.slam.nhs.uk/research/d-cris
77 Public Health England, 2017. National Congenital Anomaly and Rare Disease Registration Service (NCARDRS). Available at: Cf. https://www.gov.uk/guidance/the-national-congenital-anomaly-and-rare-disease-registration-service-ncardrs.

D. Skills

The ultimate success of the Life Sciences Industrial Strategy is closely tied to the ability to train and recruit the best possible workforce, equipped with a breadth of critical skills. As a highly diverse sector, life sciences is dependent on a skills base that covers the major areas of biomedical science, but also areas such as engineering, computer science, data analytics, chemistry, physics and mathematics. There is an additional need for technical support in all these disciplines, as well as clinical and high-value manufacturing expertise. Finally, there is an additional urgent requirement to train and attract more entrepreneurs and individuals with commercial experience that can help grow our life sciences sector.

a) Movement of skilled people

Highly skilled workers are at the heart of almost of every aspect of this Life Sciences Strategy. In the current setting, the UK is highly dependent on a steady influx of international scientists and forecasts suggest that science sectors will cumulatively require 180000 to 260000 people by 2025.[78] Around 26% of academic staff in UK universities are non-UK nationals. Within STEM fields, 13% are from outside the EU and 17% from within.[79] This talent underpins the science base in universities, the growth of high-tech companies in the sector, the effectiveness of the NHS in delivering healthcare and the large companies contributing to life sciences within the UK.

Outside the EU, it will be essential that this flow of talented individuals is sustained and supported. Not only should the UK life sciences environment be a magnet for the most talented scientists from across Europe, but the UK should also attempt to attract the best scientists from around the world and to ensure we have a migration system that allows us to recruit skilled workers. We hope the migration review by the independent Migration Advisory Committee announced by the Home Office in July will support our view that international talent is essential for the sector.

A migration system should be established that allows rapid recruitment and retention of highly skilled workers from the EU and beyond, and does not impede intra-company transfers.

b) Skills Action Plan

In order for the skills base to be developed in line with the needs of the sector, the life sciences sector should come together to develop and deliver a reinforced skills action plan across the NHS, commercial and academic sectors, based on a gap analysis which identifies the key skill areas for future focus.

This is expected to include clinical pharmacology, clinical trials, manufacturing, data science, clinical science, engineering and biosciences.

Underpinning the advancement of the sector is also a need for people with regulatory skills, across industry, the health service and academia as well as regulators, not only to do the core work of medicines development, regulation and delivery to patients but to be resourced to develop standards for emerging technologies and methodologies.

78 Science Industry Partnership, 2015. *Skills Strategy 2025.* Available at: http://www.scienceindustrypartnership.com/media/529053/5202fd_sip_skills_strategy_2015_final_low.pdf

79 ABPI, 2016. *UK EU Life Sciences Transition Programme Report: Maintaining and growing the UK's world leading Life Sciences sector in the context of leaving the EU.* Available at: http://www.abpi.org.uk/our-work/library/industry/Documents/UK-EU-Steering-Group-Report.pdf

Develop and deliver a reinforced skills action plan across the NHS, commercial and academic sectors based on a gap analysis of key skills for science.

Data, Digital and Apprenticeships

The widespread, effective application of digital tools across the whole of the life sciences industry is occurring very quickly, as it is within the NHS, for example through the Global Digital Exemplar trusts which are aiming to be world leaders in the delivery of exceptional care with digital technology. The NHS.UK digital app library is enabling digital self-care and an environment for developers to build transformative digital health tools.[80] However, there exists an acute shortage of well-trained individuals capable of moving this agenda forward at speed.

A wide range of different skill sets is needed if this is to be successful. The ABPI *Bridging the Skills Gap* report highlights that "informatics, computational, mathematical and statistics areas" are a major concern for the industry and that data-mining is a high priority area. Individuals with digital qualifications would be immediately attractive to most healthcare providers around the UK, but equally of interest to those establishing better capabilities for digitally-enabled clinical trials, big data-based drug discovery and real-time tracking of patient populations

There is an opportunity to create apprenticeships to train people in informatics and data science, in addition to apprenticeship development from levels 2-8 across the sector.

Apprenticeships at levels 6, 7 and 8 will have an increasing role in addressing industry requirements for highly-skilled employees. There is a need to allow the sector to use the levy to deliver an apprenticeship programme that meets their needs. Included in this would be the development of appropriate university degree and postgraduate training; the possibility of reallocation of funds to support apprenticeships in supply chain enterprises or SMEs; making best use of sector Apprenticeship Training Agencies to support collaboration; and a user-friendly register of apprenticeship standards.

Create an apprenticeship scheme that focuses on data sciences, as well as skills across the life sciences sector, and train an entirely new cadre of technologists, healthcare workers and scientists at the cutting-edge of digital health.

Similarly, the UK needs more individuals trained in advanced manufacturing particularly as it aspires to capture significant amounts of this activity in the future associated with new types of therapeutics. Again a focus on these skills in the apprenticeship programme would be helpful.

80 NHS. *Digital Apps Library.* Available at: https://apps.beta.nhs.uk/

Institutes of technology

In the Government's Industrial Strategy Green Paper, support for higher level technical education through new Institutes of Technology has been recommended. Government announced £170m of capital funding to support higher-level technical education in STEM subjects through new Institutes of Technology and has committed to building a proper technical education system to sit alongside the academic track. We would support these developments with a particular focus for life sciences on skills training in the digital domain and also for high-value manufacturing.

These institutes should be linked to existing facilities to ensure that they interface with ongoing research and areas of UK scientific strength.

The Government should establish Institutes of Technology that would provide opportunity for technical training, particularly in digital and advanced manufacturing areas.

Entrepreneurship

If the UK is able to substantially close the gap in risk capital available for new and emerging companies in the life sciences, it will be essential that we have the capacity to support these businesses with high quality entrepreneurs. In global clusters that have a wealth of such individuals, many have emerged from the experience of being involved in successful or unsuccessful companies and bring that experience to new SMEs. In addition, however, there is a crucial role for universities and business schools to provide a high level of management and entrepreneurship training at degree and PhD level.

There should be support for entrepreneur training at all levels, incentivising varied careers and migration of academic scientists into industry and back to academia to increase influx of talented scientists and entrepreneurs in the public and private sectors.

Accelerating Convergence

It is clear from the scientific successes in biomedicine over the past three decades and from the opportunities that exist now that the interface between life sciences and disciplines such as computer science, mathematics, statistics, engineering and chemistry, provides an enormous opportunity for further innovation.

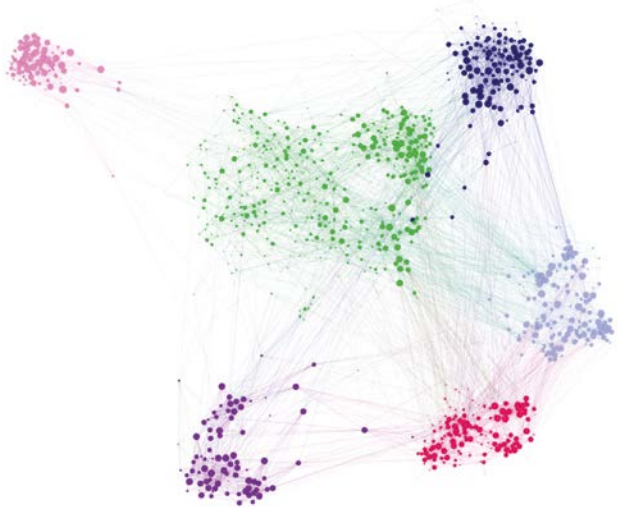
Convergence is occurring globally in life sciences, especially between diagnostics, personalised medicine and data science.

Companies headquartered in the UK, Silicon Valley or Massachusetts

All sectors map of companies 2006–16

Top segments[1]

- Company
- Connections between two companies based on a keyword match algorithm



	Companies	Funding[4]
Total amount	1,075	$29bn
Segment name	**Share of total**	**Share of total**
Data science and computing	41%	34%
Personalised medicines	16%	23%
Next-generation pharma products	14%	19%
Diagnostics	12%	12%
Engineering and life sciences	9%	9%
Automation	8%	3%

1 By number of companies (percentage of total companies)
2 Keyword match algorithm groups companies into the segment with the closest match. If a company falls between segments, the engine will pick the segment best suited
3 Node size determined by the number of connections to other nodes, so some nodes may be too small to see
4 Funding does not include exit deals such as IPO, M&As or buyouts

SOURCE: Pitchbook database for companies dating from 2006 to 2016; Gephi and SILA for analysis and location map creation

These convergent technologies can best be enhanced by the UK expanding its capabilities in training individuals across disciplines and sectors. The investment in the Rosalind Franklin Institute (RFI) will be an important step in creating this capability in the UK. The RFI will bring together researchers from UK academia (in physical sciences, engineering, computational and life sciences) and commercial R&D staff from leading pharmaceutical / life science companies and global manufacturers.

Opportunities for all research trainees, including the medical profession, to also develop skills in data sciences and other physical sciences will be an important component of enhancing convergent research. Medical training itself needs to consider how practitioners can operate in an increasingly quantitative environment and ensure that these core skills are embedded into the curriculum. Engineering and chemistry are also crucial scientific domains that have already had an enormous impact on capabilities within the life sciences and efforts need to be made to expand biomedical engineering and biological chemistry within the UK.

A UK strength has historically been the training of individuals in clinical pharmacology. Although this specialty has almost disappeared there remains a need for training in therapeutics, particularly with a wealth of new types of advanced therapies appearing. Understanding how these can best be evaluated and used clinically will need both specialist expertise and individuals trained to understand how best to use new modalities of therapy such as gene and cell therapy, nucleic acid based therapies or viral vector based interventions. The new convergent training program established by the British Pharmacological Society and the Faculty of Pharmaceutical Medicine could provide the mechanism for such training schemes.

A fund should be established supporting convergent science activities including cross-disciplinary sabbaticals, joint appointments, funding for cross-sectoral partnerships and exchanges across industry and the NHS, including for management trainees.

I. The flow of multidisciplinary students at Masters and PhD level should be increased by providing incentives through the Higher Education Funding Council for England.

II. Universities and research funders should embed core competencies at degree and PhD level, for example data, statistical and analytical skills, commercial acumen and translational skills, and management and entrepreneurship training (which could be delivered in partnership with business schools). They should support exposure to, and collaboration with, strategically important disciplines including computer and data science, engineering, chemistry, physics, mathematics and material science.

Further strengthening STEM education

As set out in the Industrial Strategy Green Paper nearly half of businesses report a shortage of STEM graduates as being a key factor in being unable to recruit appropriate staff.[81] The number of STEM undergraduates has been increasing over the last few years, and efforts need to continue be made to attract and teach young students in a range of science and engineering subjects.

All students should study a balance of biology, chemistry and physics, with rich practical experiences, up to the age of 16 and continue maths beyond 16. Teacher expertise should be enhanced through subject-specific continuing professional development and industrial placements, and more evidence should be gathered on the most effective strategies to address STEM teacher shortages. Students should also receive high-quality and independent careers advice conveying the range of opportunities in STEM-related careers. Industry can be valuable partners in showcasing careers opportunities, for example, Science Industry Partnership (SIP) members invest in the SIP Ambassador programme to highlight careers in science-based industries in schools.

Maths education is increasingly important in a data-rich environment and many young people do not pursue maths beyond 16. Government should ensure that all schools are aware that these decisions may limit future prospects for their students and should in the longer term attempt to increase the number of students studying maths at A level and through other level 3 maths qualifications (such as Core Maths). Additionally, level 3 maths should be particularly encouraged to those students studying science subjects beyond 16 to enable them to gain confidence in quantitative skills.

High quality STEM education should be provided for all, and the government should evaluate and implement additional steps to increase the number of students studying maths to level 3 and beyond.

81 Engineering UK's report Engineering UK 2016: The State of Engineering states that 46% of businesses reported a shortage of STEM graduates as being a key factor in being unable to recruit appropriate staff.

E. Regulation

The Medicines and Healthcare Regulatory Agency (MHRA) regulates medicines and medical devices for the UK. Their processes aim to protect public health by ensuring that products for UK patients meet appropriate standards of safety, quality and efficacy via the approach to testing products through clinical trials. The MHRA has a strong global reputation for innovation and leadership in the field of regulation, having been instrumental in shaping the European regulatory systems, and is seen by global industry as a "jewel in the crown" of the UK life sciences ecosystem.

The future of regulation in the life sciences will need to be considered in light of the UK leaving the European Union. As the process of determining the UK's future relationship with the European Medicines Agency, and how our existing regulators work within a global system is worked out, the focus should be on alignment in order to deliver the best decision-making for patient safety.

Any future arrangement should also take into account the impact of system design on the UK life sciences ecosystem – including retaining sufficient high-quality regulatory capability in the UK, and ideally the MHRA's innovative leadership in the field. Given the UK market size at around 3% of global pharmaceutical sales, a wholly free-standing system would likely be high cost – both in terms of efficiency and attractiveness to companies who typically apply to the largest markets first. Industry's view is that the UK and MHRA should therefore seek to continue to work closely with the EMA to deliver the best regulatory service for patients across the EU and UK. The best approach may differ across the various elements of regulation:

- For those activities where greater patient numbers will improve the evidence for decision-making such as pharmacovigilance and clinical trials, the UK and EU should look to continue to work together. Similarly, given recent agreements across FDA and EMA for mutual recognition of manufacturing inspections, the UK should continue to share expertise and collaborate with the EMA system as in the past, and seek to share in these mutual recognition agreements.
- Medical device assessment currently works across a wider-than-EU footprint with the CE-mark system being used by competent authorities from Turkey and Israel to Norway. It would therefore seem reasonable for the UK to seek to continue to operate within this wider framework. This is beneficial for medtech in terms of providing treatments and exporting products across Europe.
- For medicines licensing, continued involvement of the MHRA in the review of dossiers and joint scientific deliberations would enable patients across the UK and EU to benefit from the UK's high-quality regulatory expertise. The UK could make a 'sovereign decision' based on the shared information, should it not wish to seek to be part of the EU voting system.

There has been much discussion about the opportunity of the UK to develop an innovative regulatory approach to emerging technologies outside of the EU. This would follow on from the MHRA role in supporting the innovation of various elements of the EMA system such as the adaptive licensing system. It will be important for any future regulatory system to regulate emergent and convergent technologies such as cell and gene therapies and algorithms, as well as digital medicines. While this innovative strand in the MHRA approach might be theoretically desirable from a UK life sciences ecosystem point of view, it would only be additive if it did not jeopardise the UK's participation in the EU systems and processes. Relatively speaking, the UK market is too small even with the fastest and most innovative regulatory system in the world, to stand alone from a larger decision-making bloc.

Other aspects of regulation are also important to consider. There are significant risks that the direction of regulation in the area of data sharing will become more onerous in Europe from next year with the implementation of the General Data Protection Regulation (GDPR). Outside the EU we should attempt to maintain the current balanced approach to data sharing regulations if we are to enjoy the benefits for healthcare that are anticipated in that area. This will add to the attractiveness of an integrated digital environment in the UK because of the predictability and consistency of data sharing regulations. Similarly, stem cell research has also benefitted in the UK from a more science-friendly regulatory regime than that which is applied in other European countries and we should ensure we retain this approach.

Summary of submissions received

Professor Sir John Bell has led the development of a new Life Sciences Industrial Strategy in conjunction with the members of the Life Sciences Industrial Strategy Board. In addition to the input from Board members, a wide range of organisations have contributed evidence and views, the themes of which are summarised below, reflecting the chapters of this strategy:

Reinforcing the UK science offer

Many submissions reflected the need to sustain and increase Government funding for life sciences research. There was a repeated desire to see investment in an innovation landscape that facilitates the research, development, commercialisation and manufacturing of medicines and life sciences products in the UK.

Some organisations recommended that regulators should transform the speed and execution of clinical trials and regulatory approval.

Some submissions referred to a shift to a model of earlier detection and diagnosis of disease and an increase in personalised medicine, which needs innovative trial design.

Growth and infrastructure – making the UK the best place for Life Science businesses to grow

Many submissions proposed improvements to the fiscal environment in order to encourage and support investment, and anchor infrastructure in the UK.

It was also recommended that investments in new infrastructure to maximise the opportunities offered by advanced technologies and the digital space, should be accompanied by equal efforts to improve the availability of new treatments, technologies and services to UK patients.

NHS

Many contributors raised the need for the life sciences industry to work closely and collaboratively with the NHS, to deliver better cost-effective treatments to patients at scale and transform the patient access environment.

The proposals received highlighted issues of adoption and ensuring uptake of life sciences products in the health system at an accelerated rate. The use of data to accelerate research, and improve NHS productivity and patient care was a recurring theme.

A number of workshops were held with senior-level technical representatives from across industry (biopharma, med tech and digital health including AI analytics), the NHS, charities and academia. The output from these highlighted the potential of the UK to be world leading in the use of health data for research, and outlined an approach where regions working to clear national standards could build towards this ambition.

Skills

With regards to the movement of skilled people following EU exit, it was widely suggested that there should be an immigration system which allows talented and skilled students, researchers and workers to enter and remain in the UK in order to maintain global competitiveness.

A number of submissions indicated that an effective skills strategy needs to enhance the focus on STEM subjects in schools and universities.

Regulation

The section of this strategy that discusses the UK regulatory environment is reflective of extensive engagement with industry on the subject, and the content of submissions received.

Devolved administrations

In addition to the input from the Life Sciences Industrial Strategy Board members and a wide range of other organisations, during the development of the strategy there was active engagement with Scotland, Wales and Northern Ireland. Our discussions and workshops with the administrations' respective life sciences industries echoed the themes of the strategy above, notwithstanding differences in their health systems. As such, this strategy provides a framework for the improvement of the life sciences sector for the whole of UK.

Glossary

Accelerated Access Review (AAR) – the Accelerated Access Review aims to speed up access to innovative drugs, devices and diagnostics for NHS patients.

Basket Trials – cancer treatment method based on the mutations which divide their growth, rather than cancer location.

HARP (Health Advanced Research Programme) – the strategy for life sciences recognises the need to consider and fund projects that will impact on the direction of healthcare delivery over the next twenty years. The programme aims to encourage industry to take on bold, far-sighted ambitions in the life sciences to potentially create whole new industries based in the UK.

Humanised monoclonal antibodies – antibodies from non-human species whose protein sequences are modified, increasing their similarity variants produced naturally in humans.

IRS signalling – Insulin Receptor Substrate signalling.

Million Women Study – A national study of women's health, involving more than one million UK women aged 50 and over. It is a collaborative project between Cancer Research UK and the National Health Service, with additional funding from the Medical Research Council and the Health and Safety Executive, which aims to answer many outstanding questions about the factors affecting women's health in this age group.

Pharmacovigilance – defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem (WHO).

Stem Cell Senescence – senescence is the process by which cells cease to divide, thought to be associated with ageing.

Telomere shortening – involved in all aspects of the ageing process on a cellular level.

Test beds – specific programmes where products are combined and tested together; two are on diabetes and dementia in Bristol and Surrey.

Translational Science – an interdisciplinary branch of the biomedical field supported by three main pillars: benchside, bedside and community. It is the combination of disciplines, resources, expertise, and techniques within these pillars.

Acronym	Expansion
AAR	Accelerated Access Review
ABPI	Association of the British Pharmaceutical Industry
ADC	Antibody Drug Conjugates
ADME	Absorption, Distribution, Metabolism, and Excretion
AHSN	Academic Health Science Networks
AMR	Antimicrobial Resistance
AMRC	Association of Medical Research Charities
API	Active Pharmaceutical Ingredient
BEIS	Business, Energy and Industrial Strategy
CA	Capital Allowances
CAG	Confidentiality Advisory Group
CAGR	Compound Annual Growth Rate
CCG	Clinical Commissioning Group
CMO	Chief Medical Officer
CPRD	Clinical Practice Research Datalink
CQC	Care Quality Commission
CRN	Clinical Research Network
CRO	Contract Research Organisation
CRSF	Charity Research Support Fund
CRUK	Cancer Research UK
CTA	Clinical Trial Authorisation
DH	Department of Health
DIH	Digital Innovation Hubs
DIT LSO	Department for International Trade Life Sciences Organisation
EIS	Enterprise Investment Scheme
EMA	European Medicines Agency
FCA	Financial Conduct Authority
FDA	US Food and Drug Administration
FEC	Full Economic Costs
GDPR	General Data Protection Regulation
GMP	Good Manufacturing Practice
GVA	Gross Value Added
HMT	HM Treasury
HRA	Health Research Authority
HTA	Health Technology Assessment

HTA	Human Tissue Authority
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICH-GCP	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Good Clinical Practise
ICP	Integrated Care Partnerships
IMI	Innovative Medicines Initiative
IP	Intellectual Property
IPO	Intellectual Property Office
LEP	Local Enterprise Partnership
LSE	London Stock Exchange
MHRA	Medicines and Healthcare Products Regulatory Agency
MRC	Medical Research Council
NDG	National Data Guardian
NICE	National Institute for Health and Care Excellence
NICTC	Northern Ireland Cancer Trials Centre
NIHR	National Institute of Health Research
OECD	The Organisation for Economic Co-operation and Development
ONS	Office for National Statistics
QALY	Quality Adjusted Life Year
R&D	Research & Development
RDEC	Research and Development Expenditure Credit
RDTC	Research and Development Tax Credit
RFI	Rosalind Franklin Institute
SEIS	Seed Enterprise Investment Scheme
SIB	Social Impact Bond
SME	Small and Medium-sized Enterprise
STEM	Science, Technology, Engineering and Maths
STTR	Small Business Technology Transfer
TAP	Trials Acceleration Programme
VC	Venture Capital
VITA	Vascular Interventions/Innovations and Therapeutic Advances