Just what the doctor ordered? Is the Life Sciences Industrial Strategy the right prescription for Britain's life sciences sector?

An analysis of the UK Life Sciences Industrial Strategy and Sector Deal in the context of the UK's withdrawal from the European Union. Commissioned by IQVIA.

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Editorial

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IQVIA is a human data sciences company formed through the 2016 merger of IMS Health and Quintiles. IQVIA offers a broad range of solutions that harness advances in clinical research, healthcare information, technology, analytics, and human ingenuity to improve patient outcomes. They are the UK's 4th largest life sciences employer, with a team of 3,800 spread across the UK, generating £650 million in revenue. IQVIA conducts 30 per cent of all commercial clinical trials in the NHS. Their London office employs over 250 Real-World Evidence and artificial intelligence scientists and is a global hub for their Real-World Evidence and Healthcare Analytics, with over 1 billion non-identified patient transactions per year globally. With their knowledge and expertise, they are well placed to support the UK Government and pharmaceutical industry in maintaining the position of life sciences as the 'jewel in the crown' of the UK economy.

Stephen Dorrell
Chair, Public Policy Projects.

Foreword

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Globalisation is not a choice; it is a fact which needs to shape our thinking about life sciences with much greater urgency than we have yet recognised. This was true before the UK voted to leave the EU; our decision to introduce new barriers in our trading relationship with the EU27 simply reinforces a national imperative where we already needed to raise our game.

The challenges are clear. The research community are global citizens; their focus is human knowledge and they make progress by sharing and debating their insights with their scientific peers – with little regard to who issued their passports. The companies which fund their research, and enable patients to benefit from their discoveries, trade across frontiers because their products are of benefit to all human beings, and because limited patent life means that they need rapid access to the global market place to generate the resources which will fund the next generation of research.

To attach a national label to a life science enterprise is to completely miss the point.

> ***Life sciences are truly a keystone in the arch, and this report examines the steps necessary to safeguard their contribution in a world where the competitive forces are gathering and hostile.***

The question for national policymakers is how to attract those enterprises to trade in their countries to realise the benefits they can bring. In Tokyo, Brussels, and Washington, not to mention Rio, Beijing and New Delhi, some of the brightest minds are challenging themselves to maximise their share of this life-enhancing activity. There should be no doubt about its strategic importance. The UK life science sector contributes £30 billion to our GDP, but its significance is much greater. Its global competitiveness underwrites the science base of UK universities and participation in its front-line research underwrites the clinical quality of UK healthcare.

In our 2016 report entitled 'Finding a cure: Getting the best Brexit deal for Britain's Life Sciences', published by Public Policy Projects and commissioned by IQVIA (formerly IMS Health and Quintiles), we identified the implications of Brexit for UK life sciences and called on the Government to ensure efforts were equally focussed on the needs and interests of UK life sciences as they have been on the financial sector.

In August 2017 the Life Sciences Industrial Strategy (LSIS) was published in partnership with both the Department of Health and Social Care and the Department for Business, Energy and Industrial Strategy. The LSIS "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"[1] and sets the objective that, by 2023, the UK should be in the top quartile of comparator countries for the speed of adoption and overall uptake of innovative, cost-effective science.

Both departments recognised that the future of the sector will be significantly impacted by EU withdrawal and therefore that policy must provide solutions to the challenges that Brexit will bring.

This report asks whether the LSIS and Sector Deal are sufficient to meet the challenges raised by Brexit; it identifies the areas where the answer is "no" and calls on the Government to place these issues at the centre of the deal it seeks during negotiations with EU partners.

The report is challenging and timely and addresses issues which will reshape our lives in unwelcome ways if they are not addressed as a matter of extreme urgency. Most fundamentally, the smooth exchange of knowledge and trade between countries is vital to ensure the safety of UK patients as they seek the quality health and care services they expect and deserve.

Recommendations

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1. The UK should continue to have a 'deep and special relationship' with the EU and related bodies in the life-sciences sector, including securing associate membership of the European Medicines Agency and alignment with the Clinical Trials Regulation and the General Data Protection Regulation.

2. It is vital for the UK to secure a unique trading relationship with the EU, securing the trade and free movement of medicines, biological samples, and investigative medicines and diagnostics.

3. The UK Government should commit to making non-identified patient level data more readily available for appropriate commercial research and that the National Data Opt-Out is successfully implemented to optimise the UK's rich health data eco-system, as part a of wider goal to make the UK the global leader in life sciences, clinical trials and real-world evidence studies.

4. The UK should position itself as a destination for inward pharmaceutical investment, taking advantage of its world-class science and unique patient health data ecosystem and infrastructure.

5. The UK Government should consult on and introduce clinical research performance metrics aligned with global standards to improve clinical trial success rates and predictability. It should also introduce new measures to support the engagement of patients for clinical trial participation, including promoting clinical trials as a routine part of patient care and allowing UK doctors to directly contact patients, the so-called 'right to write' provision.

6. The UK should maintain access arrangements for the best talent from across the global scientific community.

7. The UK Government should continue to underwrite funding in research and science, by raising government spending in research to 2.4 per cent of GDP by 2027 and maintain ongoing engagement with the successor to the EU's research funding programme, Horizon 2020.

8. The Life Sciences Industrial Strategy Implementation Committee should deliver an accelerated national plan for Digital Innovation Hubs with a key focus on interoperability.

9. Collaboration and engagement with industry needs to be improved across the NHS and research landscape with an empowered clinical leadership to drive forward the pace of projects being initiated.

Introduction

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Following the EU referendum, the President of the UK's Academy of Medical Sciences, Professor Sir Robert Lechler, discussed the impact of the result:

> *"This represents the biggest challenge to the UK's research sector in living memory."* [2]

While UK participation in EU projects and compliance with EU law will not end abruptly, addressing the UK's future direction of travel is vital. In addition to the ongoing Brexit negotiations, focus has been placed, through the LSIS and Sector Deal, on the policies and financial support that can be put in place to support UK industries in the global market place.

The LSIS covers five broad themes: the UK's science base; growth and infrastructure; collaboration between the NHS and industry; the digitalisation of healthcare; and ensuring access to the skills needed to support a flourishing life sciences industry.

Set against the backdrop of the UK's decision to leave the EU, the publication of the LSIS and the accompanying Sector Deal come at a pivotal time for the sector. As the Sector Deal illustrates, the potential of patient data alongside the advance of digital technologies provides a real opportunity to harness the role of the NHS as a full partner within the life sciences sector. This will achieve maximum patient benefit and drive the success of the life sciences sector. The question is whether this is enough to mitigate the risks that Brexit brings.

In her Mansion House speech in March 2018, the Prime Minister recognised the importance of maintaining the beneficial relationships between the UK and EU industries:

> *"We will want to make sure our regulators continue to work together; as they do with regulators internationally. This will be essential for everything from getting new drugs to patients quickly to maintaining financial stability. We start from the place where our regulators already have deep and long-standing relationships. So, the task is maintaining that trust; not building it in the first place.*
>
> *"We will also want to explore with the EU, the terms on which the UK could remain part of EU agencies such as those that are critical for the chemicals, medicines, and aerospace industries: the European Medicines Agency, the European Chemicals Agency, and the European Aviation Safety Agency. We would, of course, accept that this would mean abiding by the rules of those agencies and making an appropriate financial contribution."*[3]

One important example where this ambition is focused is in retaining some form of working membership of the European Medicines Agency (EMA), which would mean investment in the development of new medicines continuing in the UK. Membership, or at least establishing a new form of 'associate' membership, of the EMA could ensure that the UK retains its global top-three position as an early-launch reference country because it would keep the existing market authorisation process, avoiding incremental time and uncertainty.

While the EU has announced the reallocation of the Medicines and Healthcare Products Regulatory Agency's (MHRA) activities to other European agencies[4], it should be recognised that the MHRA has effectively assessed more new medicines than any other member state. Continuing a close relationship with the MHRA would therefore be of benefit to the EMA, enabling the EMA to access the MHRA's considerable expertise and skill.

However, as identified in *'Finding a cure'* 2016, the UK's withdrawal from the EU raises a series of challenges for the future of the life sciences sector. The perception of the UK's attractiveness was immediately impacted by Brexit, and in its 2018 survey of global pharmaceutical industry board level executives, IQVIA established that the industry remains concerned about the UK's ability to maintain its global strength both as a clinical research location and as a primary drug launch country.[5]

Following the publication of the LSIS and the first Life Sciences Sector Deal, is there more that the UK can do to maximise the opportunities of Brexit?

Life Sciences Industrial Strategy

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In January 2017 the Government published its Industrial Strategy Green Paper,[6] which set an 'open door' challenge to industry to make proposals to transform and upgrade their sector through 'Sector Deals'. For life sciences, Sir John Bell was commissioned to develop a new strategy to make the UK the best place to invest in life sciences. Sir John's report, published in August 2017[7] and referred to as the Life Sciences Industrial Strategy (LSIS), provides recommendations to the Government on the long-term success of the life sciences sector. It was written in collaboration with industry, academia, charity, and research organisations and is organised into seven themes: Health Advanced Research Programme (HARP) proposal; reinforcing the UK science offer; growth and infrastructure; NHS collaboration; data; skills; and regulation.

Core recommendations and strategic goals of the LSIS: Enhancing the UK as a global life sciences leader

Figure: 1

Focus	Core recommendations	Strategic goals
Science base	Establish the HARP to undertake large research infrastructure projects and high-risk "moonshot programmes"	Over the next decade, create two to three entirely new industries in fields such as genomics, diagnostics, digital health technology, artificial intelligence or healthy ageing
	Increase funding for basic science to ensure the UK is in the upper quartile of OECD R&D investment	Attract 2,000 new discovery scientists from around the world
	Enhance UK clinical trial capabilities	Over the next five years, increase the number of clinical trials by 50 per cent and raise the proportion of change-of-practice studies and trials with novel methodologies
Growth and infrastructure	Ensure the tax environment supports growth	Over the next decade, create four UK-based companies with a market capitalisation of >£20 billion
	Boost investment in manufacture and export of high-value health technologies	Over the next five years, attract 10 large (£50 million to £250 million capital investment) and 10 smaller (£10 million to £50 million capital investment) life sciences manufacturing facilities
NHS collaboration	Adopt the Accelerated Access Review's recommendations to create streamlined national market access routes for health technologies	Over the next five years, the NHS should undertake 50 collaborative programmes in late-stage clinical trials, real-world data collection or the evaluation of medical devices or diagnostics
		By 2023, the UK should be in the top quartile of comparator countries for speed of adoption and overall uptake of innovative, cost-effective products
Data	Establish digital innovation hubs that each provide data across regions of 3 million to 5 million people	Set up two to five digital innovation hubs to ensure access and integrate data from across the UK from local integrated care records and national datasets, realising the benefits of the UK's unique and rich patient-level data ecosystem
Skills	Develop a Skills Action Plan	Build a migration system that facilitates recruitment of the best talent from around the world

The Sector Deal for life sciences

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The Sector Deal for life sciences was published as part of the Industrial Strategy White Paper – *'Building a Britain fit for the future'*[8] in December 2017. This sector deal is the first in a series of deals that the Government intends to agree with the sector to realise the vision set out in the LSIS. It was warmly welcomed by the sector and has already formed the background for implementation:

> *"We believe the UK to be a unique bioscience centre of excellence and this investment presents a major opportunity for us to work in collaboration with the UK government to build on the forward thinking and ambitious Industrial Strategy white paper being published by the government today." Louise Houson, Managing Director, UK and Ireland, MSD*[9]

The LSIS 'business environment' workstream identifies the launch and roll-out of sector deals – partnerships between government and the private sector – as a key policy. It announced the first sector deals within the life sciences, construction, artificial intelligence and automotive sectors. The sector deals are designed to build upon the successful model of collaborative working between the Government and industry, as exemplified by existing partnerships such as the Office for Life Sciences.

The deal includes:

Reinforcing the UK science offer: The Government will increase total R&D funding to £12.5 billion by 2021/22. Significant commercial investments in UK science facilities have been announced, including: a major investment by MSD in a state-of-the-art UK discovery centre in London anticipated to accommodate 950 staff; Novo Nordisk's establishment of a £115 million diabetes research centre in Oxford; and QIAGEN's plans to partner with Health Innovation Manchester to develop a new genomics and diagnostic campus as well as expanding its existing operations in Manchester. The deal also includes significant investments by GlaxoSmithKline (GSK) and AstraZeneca in initiatives to harness advances in UK genomics research in the development of medicines.

Health Advanced Research Programme (HARP): The deal provides substantial concrete commitments for HARP – a collaborative programme between industries, charities and the NHS focused on ambitious long-term UK-based projects – including investment of up to £210 million into an early-diagnostics and precision medicine challenge. Four areas are identified as potential areas of focus for HARP include: Genomics in medicine; Creating a platform for developing effective diagnostics for early, asymptomatic chronic disease; Digitisation and Artificial Intelligence to transform pathology and imaging; Healthy Ageing – the commercial opportunity for supporting better health in later life. HARP is envisioned to support innovation and translate opportunities into commercial success for the benefit of patients as well as industry.

Medicines manufacturing: The Government has committed £162 million for developing medicines manufacturing infrastructure, including two national manufacturing centres and three advanced therapy treatment centres to be co-located in UK hospitals. The deal highlights the recent announcement by Seqirus (Appendix 1) of its £40 million investment in a new high-tech 'fill and finish' facility in Liverpool, illustrating industry's increased recognition of the UK's prominence in advanced therapy manufacturing.

Scale-up of UK businesses: Measures to improve access to finance to enable scaling-up of UK businesses have been announced, such as the establishment of a new £2.5 billion Investment Fund incubated in the British Business Bank. The Sector Deal aims to support those companies developing innovative products or therapies to increase their manufacturing or production activity and build commercial value.

Clinical trials environment: The deal outlines proposals to promote inward investment in UK clinical trials through the streamlining of clinical trial approval processes, and further investment in NHS research infrastructure. Major collaborations between industry and academia were announced, including a collaboration between Janssen Pharmaceutica NV and the University of Oxford to develop novel clinical trial methodologies.

Access to data: NHS England, NHS Digital and Health Data Research UK will lead the delivery of a programme for establishing three to five regional digital innovation hubs, with the aim of improving access to patient datasets for research purposes.

NHS collaboration: The deal recognises the importance of the NHS to the UK life sciences landscape, and of the opportunities for improving care pathways and patient services through improved collaborations between NHS and industry. It highlights particularly successful collaborations such as the new 15-year partnership between Johnson & Johnson Managed Services and Guy's and St Thomas' NHS Foundation Trust to deliver an Orthopaedics Centre of Excellence at Guy's Hospital.

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Infrastructure and Clusters: The deal includes investment in life sciences 'clusters', including housing and infrastructure projects in the Oxford-Milton Keynes-Cambridge corridor and a £350 million investment programme in Leeds City Region's leading MedTech hub. Major commercial developments in key clusters were announced, such as BBI Group's new global headquarters in Crumlin, South Wales.

Skills base: The deal highlights the need to ensure a highly skilled workforce through measures to support high-skilled immigration as well as support for industry's investment in the UK's domestic skills base.

A post-Brexit UK – leading the world in real-world evidence

The LSIS notes that "one of the most important resources held by the UK health system is the data generated by the 65 million people covered within it."[10] Developing new integrated platforms to facilitate the use of non-identified patient-level data in the research and development of new health technologies will accelerate clinical trial recruitment. This in turn will reduce clinical research costs and help to increase the number of real-world evidence studies, securing not only greater benefits for patients and reducing risk for NHS commissioners but also generating income and creating efficiencies for the NHS. This will ultimately position the UK as a dynamic destination for innovative research.

The strategy suggests that "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."[11] Targeting treatments to patients where they will work best is the crux of the promise of the benefits of personalised medicine. The combination of the 100,000 Genome Project and the UK's rich data ecosystem would uniquely position the UK on the global research map.

The report suggests that a new regulatory Health Technology Assessment (HTA), and commercial framework should be established "to capture for the UK the value in algorithms generated using NHS data"[12] and that a working group should be set up to take this work forward. The strategy suggests this will address the historic tendency for agreements to be made locally and not shared with other regions, resulting in the standard lack of best practice in data sharing across the country. It is crucial to understand what is meant by and achievable through the application of de-identified real-world data (RWD) - and the types of data that are collected as RWD.

Definition of real-world data and sub-types

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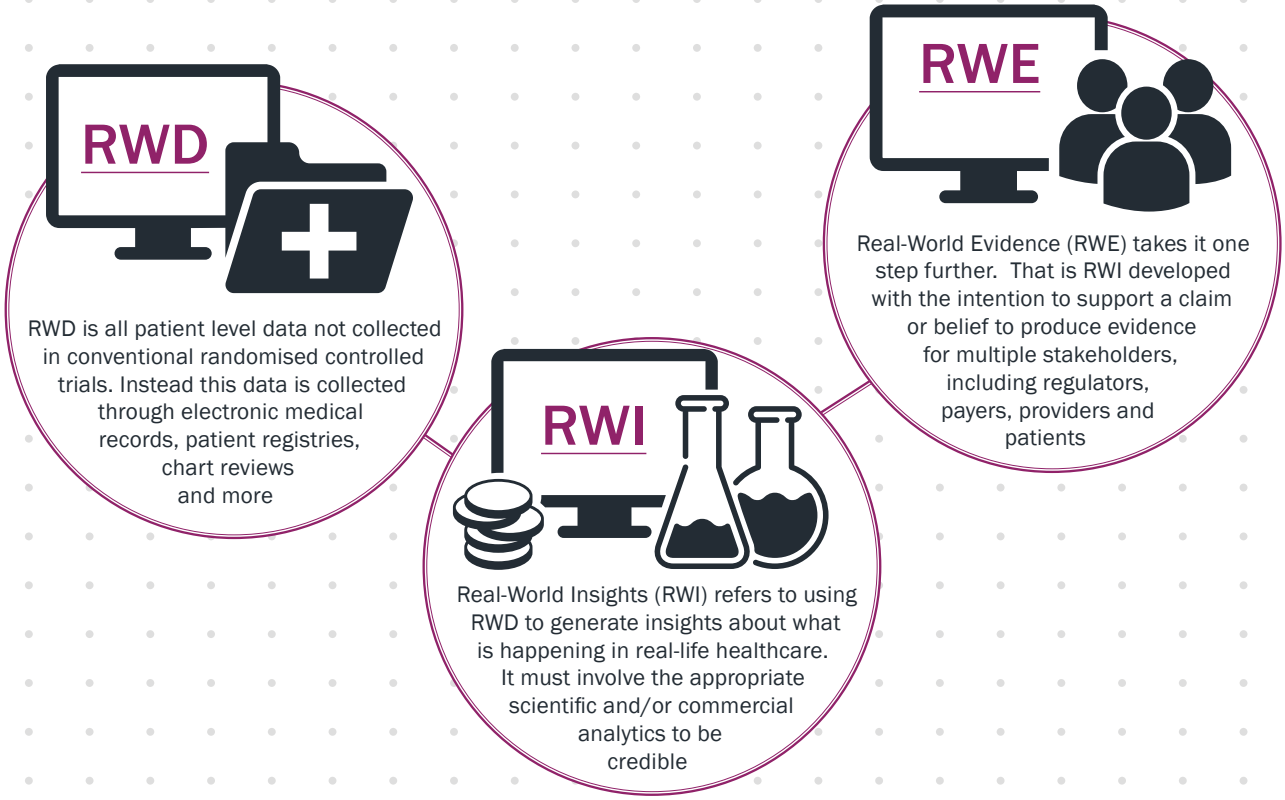
Figure: 2



It is increasingly recognised that RWD will become a key part of the decisions that affect UK patients' access to medicines. For example, the recently reformed English Cancer Drugs Fund (CDF) includes the requirement to collect two years of RWD on those cancer drugs approved for funding by the CDF.

"The use of real-world data is vital to support quality improvement of service but also in building the services and therapies of the future on a solid foundation of evidence and clinical outcomes." Professor Andrew Morris, Director, Biomedical Research Institute, University of Dundee[14]

The UK is a global leader in the development of implementation of RWD due to: the pioneering HTA process which has influenced global decision-making through its methodological innovation in assessing new and increasingly complex medicines and devices; our unique free at the point of care, single payer healthcare system with many existing healthcare databases and disease registries; and the strong links already in existence between the pharmaceutical industry and academia, enabling access to the required skills for the collection, analysis and use of RWD.

Real world evidence supply and demand landscape

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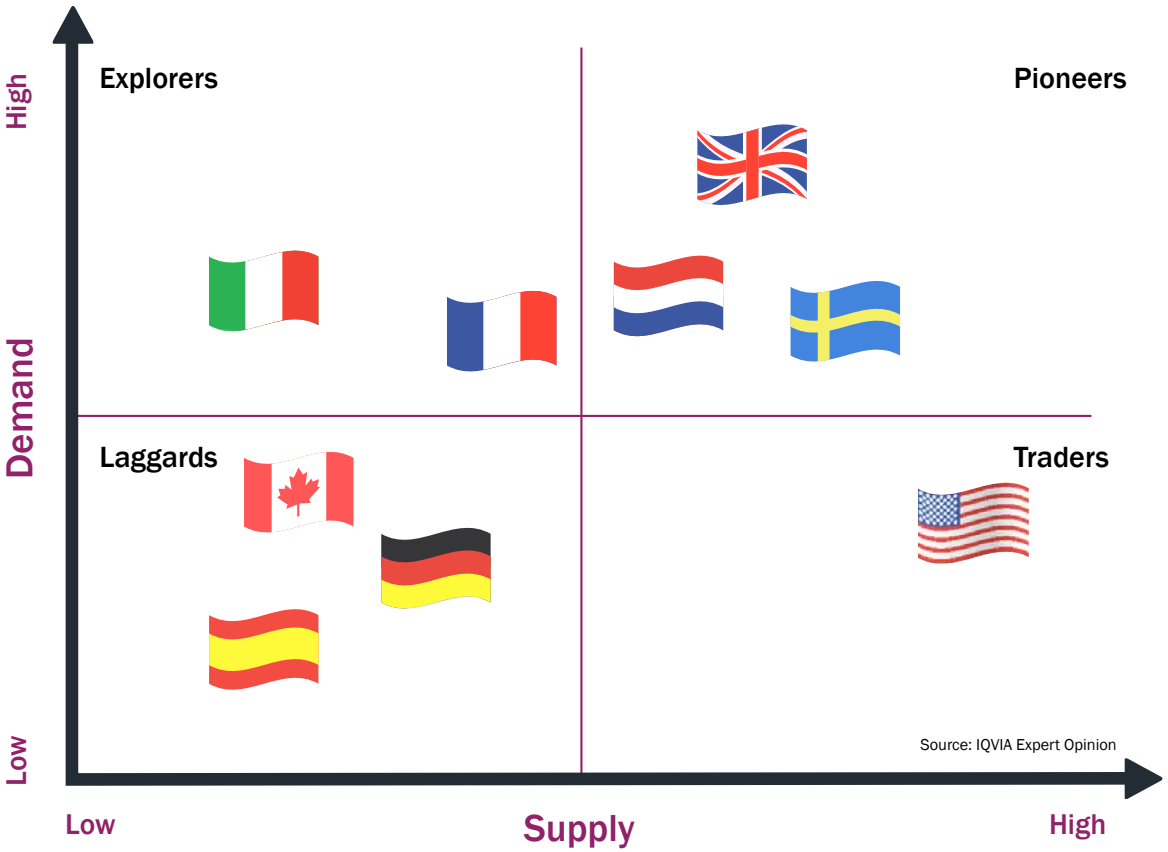
Figure: 3



It is vital to build on our existing global leadership in RWD to spread the use of this relatively new science into practice across global research and evaluation systems.

Encouraging the use of real-world studies has significant potential to support investment in innovation and the use of skills present within the NHS, UK academia, and the pharmaceutical industry in the UK. As the LSIS aims to achieve, it encourages a real working partnership approach from pharmaceutical industry, academic researchers, and clinicians.

Potential applications of real-world insights across the healthcare system

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RWD has a wide range of applications, with tangible benefits to patients

Figure: 4

	Pharma Needs	Pharma Benefits	Patient Benefits
R&D	Disease insights: Prevalence, diagnosis, treatment patterns, and unmet needs	Better targeted R&D investments, and study design for clinical trials	Earlier identification of undiagnosed patients
Medical Affairs and Safety	Insight on how drugs are being used, patient safety, and drug effectiveness	More sophisticated recommendations on who gets drug, and how they are taken	Fewer patient adverse, and improved patient responses to drugs
Health Economics & Outcomes Research	Inform assumptions on disease, treatment, and burden of disease	More evidence based models for drug funding applications, identifies patient and societal preferences	Quicker, more positive funding decisions, quickening access to effective drugs
Commercial	Insight about how patients are diagnosed, monitored, and treated		Earlier access to drugs for the most appropriate patients

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UK life sciences benefit from a strong research environment:

- Four of the world's top six universities for research in and study of clinical, pre-clinical and health topics (Cambridge, Imperial College, Oxford, and UCL) are based in the UK.
- Companies benefit from sophisticated regulatory and intellectual property (IP) protection systems – developed through our membership of the EU and which will be vital to maintain alignment upon withdrawal from the EU.
- Biotech company clusters and partnerships are found across the country (e.g. MedCity in the South East, NHSA in the North of England and IBioIC in Scotland), making up the largest biotech pipeline in Europe.[15]
- The UK is a leader in global public health issues such as dementia and antimicrobial resistance, and new technologies such as genomics.

A strong RWD and RWE capacity has the potential to make the UK attractive to the international pharmaceutical industry – differentiating and boosting our life sciences industry post-Brexit, with the resultant benefit to the overall economy, as well as the clear benefit to patient outcomes.

As part of the development of Digital Innovation Hubs, the LSIS points out that 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. This would have the capability to rapidly and effectively establish studies for the generation of RWD, which can be appropriately accessed by researchers.

However, to place the UK at the forefront of the RWD industry and secure the benefits to the sector would require a supportive regulatory and assessment environment that maximises potential uses of RWD. Regulators are increasingly using RWD, and this should be further encouraged, at the same time as far greater efforts to ensure both health technology assessors and payers recognise the value of RWD that is internationally relevant.

A recent example of this progress can be seen in the NICE Highly Specialised Technology Appraisal for Strensiq (asfotase alfa). Originally, NICE backed the therapy in February 2017 as an option for treating the bone manifestations of hypophosphatasia in babies with perinatal-onset and infantile-onset disease, but not in people those with juvenile-onset disease.

As a result of an appeal, an amendment to the final guidelines in July 2017 recommended Strensiq for all eligible patients with paediatric-onset hypophosphatasia, following an improved deal that includes a five-year managed access agreement. This not only reduced the cost of the drug and the financial risk to the NHS but during this time, extra information on the therapy's use is being collected to help shape future guidelines on its use.[16] The research findings will have an international impact.

Data in the healthcare system provides crucial opportunities to fundamentally change the way health services are provided and digital tools, such as artificial intelligence, are going to form an increasingly important segment of the life sciences sector. It is crucial that work is undertaken to ensure RWD gathered in a post-Brexit UK environment can be applied in international markets. This is a fundamental issue for RWD as the UK may develop a separate research, assessment and regulatory infrastructure.

The potential of RWD is already evident in work undertaken by a partnership between the NHS Cancer Vanguard, IQVIA, and Merck&Co. In 2016, the medicines optimisation team at the NHS Cancer Vanguard selected IQVIA as a winner in the Pharma Challenge - an invitation for life sciences companies to be true partners in service innovation and redesigning care.

IQVIA, working with The Christie NHS Foundation Trust, The Royal Marsden NHS Foundation Trust, and University College London Hospitals NHS Foundation Trust partnered with Merck and used non-identified RWD and patient app technology to shine a light on variations in drug usage, treatment costs, pathway variations and outcomes in metastatic colorectal cancer. The programme took just 9 months to complete.

Covering a population of 10.7 million people, the project analysed medicine usage data to better understand the experience of cancer patients during treatment, establish the variance that existed in oncology drugs used to treat the most common cancers, and the drivers of this variation. By collecting relevant data, it has helped to shape an evidence-based and patient-centric approach to service redesign and medicines resource optimisation. One novel aspect of the study involved asking patients to record their symptoms – such as mobility, and energy levels – using innovative digital technology.

In total the project collected 111,000 data points over a 35-week project. One patient entered symptoms on 188 days over a 200-day period. The research found a sevenfold

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variance in the proportional use of biological therapy versus chemotherapy between the peer comparators. This allowed the different NHS trusts to compare their total service to patients and see where they could improve and learn from each other.

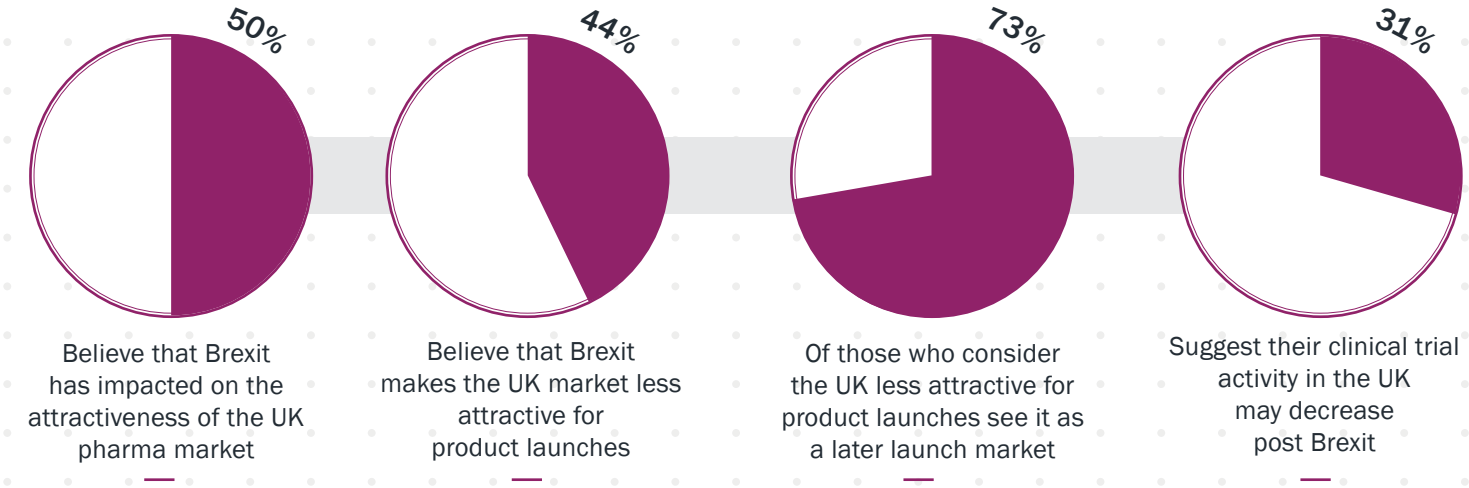
The clinical team at The Christie NHS Foundation Trust is now looking to develop this work as a randomised clinical trial, to see how their treatment processes can be enhanced using innovative technologies to remotely track symptoms over time. The programme has now been extended to improve equity of access in breast cancer referrals across Greater Manchester. This partnership is a clear embodiment of the LSIS vision – collaboration in action, using data and digital tools to support research and improve patient care.

The UK as a location for life sciences – a global market view

In 2016 'Finding a cure' noted the immediate impression of the Brexit vote on the life sciences sector. Overnight the UK became a less attractive place to do science and as a net recipient of funding for health and biosciences, withdrawal from the EU and its funding programmes would have significant financial impacts on the level of research conducted within the UK. Between February and March 2018 an IQVIA survey of global pharmaceutical industry board level executives revealed ongoing uncertainty that the LSIS will be sufficient to address the historic challenges of access to new medicines in the NHS and the impact of Brexit negotiations on the UK life sciences marketplace.

IQVIA Survey – Which way UK? Gauging the attractiveness of the UK market to the global pharmaceutical industry

Figure: 5



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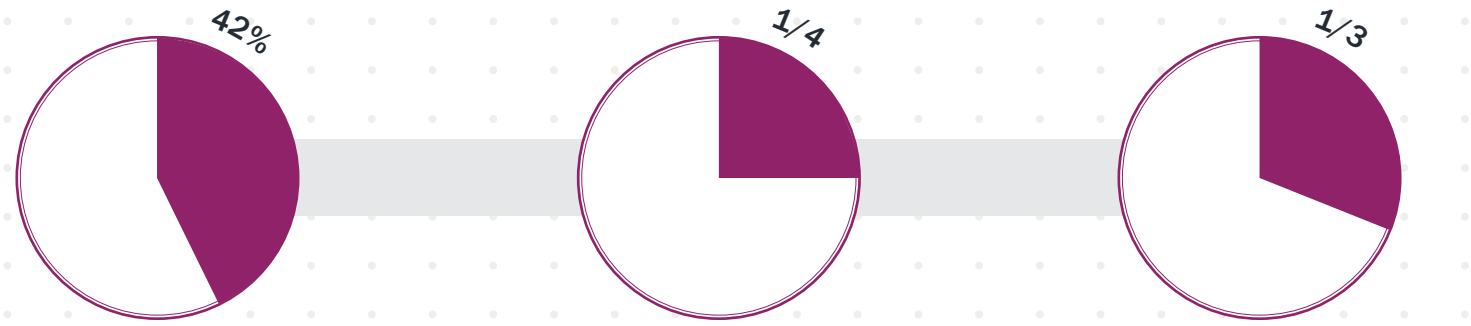
Opinion is divided regarding the extent to which the UK remains attractive for their organisation.



42 per cent still feel the UK is attractive but over a quarter now fairly or strongly disagree

Over a quarter do not yet feel the LSIS and Sector Deal have improved the attractiveness of the UK to their organisation and a fifth neither agree nor disagree

Just over a third do not expect the UK to remain a prime clinical trial country and fifteen per cent neither agree nor disagree.

A total of 127 responses were included in the results

Notwithstanding the impact of Brexit on the UK market's attractiveness, the life sciences sector has faced a number of challenges from the initiation of clinical research to the difficulty of ensuring patients can access the most effective treatments and care, to improve health outcomes and wellbeing across the UK.

In the last twenty years numerous reviews have been undertaken to understand why the adoption of innovation that has been proved as effective can often be so slow within the NHS. Patients in France and Germany are now five times more likely to get a new medicine than those living in Britain[17] and Government analysis shows that, on average, for every 100 patients in comparable countries who get access to a new medicine in its first year of launch, just 18 patients in the UK receive the same.[18] With 7,000 new medicines in the global pipeline,[19] this should be a growing and urgent priority to improve and accelerate assessment processes and drive uptake of new treatments once they have been approved.

The NHS spends over £1.2 billion on research and development funding via the National Institute for Health Research (NIHR), and only a small percentage of that goes on activity designed to spread innovation,[20]

> *"Essentially, the NHS has a short-term approach to adopting innovation with an ultimate ambition to release cash from the system. But the real opportunities to create efficiencies come from long-term transformational projects, with appropriate funding to support them."*[21]

Funding life sciences research for a global industry

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UK life sciences have access to a wealth of funding initiatives in Europe, including Horizon 2020 and the European Investment Fund. In fact, as of 2011, the UK was the beneficiary of 16 per cent of the funding from one such initiative, compared with the UK's contribution to the EU of 11.5 per cent.[22]

To mitigate the risk to funding in the immediate term, the Government quickly committed to underwriting funding from EU's Horizon 2020 projects secured while the UK is in the EU. Through the LSIS and Sector Deal, the Government has agreed £2.3 billion of investment into research and development (as part of the National Productivity Investment Plan) and committed to raising spending to 2.4 per cent of GDP by 2027 and 3 per cent over the longer term. In addition to this, it has reinstated the Biomedical Catalyst and launched a set of Challenge Funds to further support UK businesses and research. This has given some confidence to the sector that the UK Government will continue to support life sciences as the UK leaves the EU.

However, UK access to EU funding beyond Horizon 2020 is still unknown. To ensure the UK remains a dynamic market for innovation, significant investment will need to be maintained. Currently, pharmaceutical companies invest 16 per cent of their European R&D spend in the UK, while realising only 9 per cent market share by sales.[23] The UK is a highly active participant in Horizon 2020. It ranks second in the EU in the number of participants with signed Horizon 2020 contracts, with 8,749 so far.[24] This includes 362 participants from the University of Cambridge, 345 participants from the University of Oxford and, in Scotland, 206 from the University of Edinburgh. The UK also has 2,349 Marie Skłodowska-Curie Actions (MSCA) fellows supported by Horizon 2020.[25] The UK's continued involvement in successor programmes is critical to the industrial priorities of the UK and the EU.

Horizon 2020 supports a range of public-private partnerships, which the UK is involved in. For example, the Innovative Medicines Initiative (IMI), the world's largest medical research public-private partnership, brings together the pharmaceutical industry with academia, small and medium enterprises (SMEs) and other stakeholders, to accelerate the discovery and development of new medicines.

While the UK aims to achieve a unique free-trade deal with the EU, it important to consider other scenarios. In terms of potential models to adopt post-Brexit, non-EU countries such as Norway and Turkey have been considered as they currently participate in Horizon 2020 as associate countries and Israel is a net beneficiary. This could provide a route for the UK to maintain access to the fund and its soon-to-be successor Framework 9.

As a non-EU (associate) member state, strict criteria need to be met, such as free movement of people – currently a key red line in Brexit negotiations. Associated non-member states are expected to contribute to funds based on GDP and population, which was a major source of disagreement during the referendum campaign and by many of its supporters.

A central element of the campaign was to secure the UK's financial independence from the EU – rather than face a situation where the UK must pay more than its current contribution to EU programmes to reap its benefits. The UK may have to accept differing levels of involvement since it will no longer be a net contributor.

While Switzerland has access to the European Free Trade Association, it was temporarily reduced to the status of partial associate by the EU due to its referendum vote limiting mass immigration.[26] If the UK implements similar restrictions – in line with many of the arguments for Brexit – there is a significant likelihood that a similar response to UK efforts to access the Single Market will be meted out by the EU.

To continue to operate at an equivalent level of international collaboration, it is likely that there will need to be a significant increase in funding provided by the UK Government. Introducing a separate system of funding for research projects and clinical research may reduce the scale of investment and cross-border collaboration. Those seeking funding may experience greater levels of bureaucracy, particularly if applying to states and funding streams separately. This will potentially impact on the UK's ability to operate at the forefront of research and innovation.

While EU national governments are likely to want to maintain access to the UK's world-leading academic and research environment, there remain significant barriers to the UK's participation in EU projects, not least those funded outside Framework 9.

The Government's paper, *Collaboration on Science and Innovation: A Future Partnership*,[27] refers to associated country and third-country access to Horizon 2020 with the funding obligations that such participation entails. The paper notes that even the 16 associated countries lack a formal vote over the Horizon 2020 work programme and mentions the *"degree of influence"* that committee attendance offers them.[28]

As the sector undergoes the major upheaval in the funding environment, the commitment to increase UK spending to 2.4 per cent of gross domestic product by 2027 is relatively modest. This is in comparison to the 3 per cent EU-wide target set in 2000. It is markedly lower than the 2015 R&D level in Israel, South Korea, Japan, Sweden, Austria, Denmark, Finland, Germany, Belgium and the United States which range from 2.4 to 4.2 per cent.[29]

The LSIS report suggests that "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."[30]

At the publication of the LSIS, the Government announced £160 million of funding for new initiatives: £146 million for five major projects in the field of advanced therapies, advanced medicines, and vaccines development and manufacturing, and a further £14 million for 11 medical technology research centres to promote collaboration between the NHS and industry. It remains to be seen if the Government will be willing to commit the resources required to implement the report's full range of proposals.

The HARP announced in the LSIS will aim to undertake large research infrastructure projects and 'moonshot programmes' and create two to three entirely new industries within the field over the next decade. There are therefore exciting opportunities, yet the context for those involved in these projects is the significant challenges that will continue to exist, because of the UK withdrawal from the EU and the new relationships with its institutions.

Improving the research infrastructure – promoting collaboration

'Finding a cure' recognised that the benefits the UK and the life sciences sector derives from Europe-wide co-operation go far beyond purely financial benefit. As set out in the Prime Minister's Lancaster House speech in January 2017, "A global Britain must also be a country that looks to the future. That means being one of the best places in the world for science and innovation."[31]

The Government is clear that the UK will continue to be involved in major scientific work in Europe and across the world and that it intends to seek an ambitious science and innovation agreement with the EU that will support and promote science and innovation across Europe both now and in the future. Collaboration is particularly important in some fields, for example precision medicine and rare disease, as it provides access to large and diverse patient groups (including both rare disease and rare variants of common disease) for medical research and clinical trials.

The UK has a strong history of collaborating with European partners through the EU, pan-European and other multilateral and bilateral initiatives. The UK is a top five collaboration partner for each of the other 27 member states,[32] and contributed almost 20 per cent of the total research work carried out within EU health programmes between 2007 and 2016.[33] The UK has participated extensively in the IMI – over 90 per cent of IMI projects have involved at least one UK institution.[34]

The UK also has a key role in European Reference Networks (ERNs), which support European cooperation and knowledge sharing in the field of rare diseases, leading a quarter of the 24 networks and participating in nearly all, thereby pooling knowledge and sharing research expertise. At present, ERNs are only open to EU member states and EEA members.

While the UK Government seeks to explore with the EU 'ways to facilitate multilateral collaboration between the UK and EU member states',[35] and looks to key non-EU partners, including the US as the UK's top research partner, the LSIS and Sector Deal attempt to boost the collaboration within internal partners – particularly the NHS and industry:

> *"We are trying to shift the nature of the interaction between the industry and the Department of Health from being essentially confrontational to one where they can work constructively together"*[36] *Sir John Bell, Co-Chair, LSIS Implementation Committee.*

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As noted earlier in the report, there are significant challenges to the NHS in terms of fulfilling its research potential – not least the financial constraints it has faced in the past decade. These constraints have become evident in restrictions on the use of treatments for conditions such as hepatitis C. In 2014 NICE approved the use of Sovaldi (sofosbuvir) as an effective treatment for hepatitis C, curing up to 90 per cent of patients. Yet, as a 12-week course would cost £35,000, NHS England requested a delay in the statutory 90-day NICE implementation target to reduce the impact on its already strained budget.

In March 2016, NHS England acted further to manage the impact of NICE's recommendation by announcing its commitment to treat 10,000 patients through 22 new 'operational delivery networks', but that these centres would have a 'run rate', a maximum number of patients they would be allowed to treat each month in the financial year 2016–17.[37]

NHS England made clear that if this number was exceeded, "the dispensing provider will bear the financial cost of treatment".[38] At the same time, the World Health Organisation (WHO) issued hepatitis C treatment guidelines that included recommendations for the new class of medicines – direct-acting antivirals (DAAs) to treat all HCV genotypes.[39] In April 2015, WHO included several of the new DAAs in the WHO Model List of Essential Medicines including Sovaldi. In May 2016, the WHO World Health Assembly adopted its first-ever viral hepatitis strategy, with a goal of eliminating hepatitis B and C as public health threats by 2030.[40]

The NHS struggles to adopt innovation and spread best practice and so may benefit from greater interaction with an industry that seeks out innovation and a partnership designed to spread best practice. Despite the UK being the third highest country for introducing new medicines, we have the lowest uptake of medicines in the EU; 5 at year 1, pre-NICE and year 5-post-NICE decision. The UK already had a well-deserved reputation as a challenging access market with low and slow uptake of innovation even before the uncertainty created by Brexit.

As seen in Figure 6 the UK pharmaceutical market is forecast to grow in volume terms at a Compound Annual Growth Rate (CAGR) of -0.43 per cent during the period 2017–2022, a level that is particularly low in comparison with other EU countries. This reflects both pressures in the retail sector due to the combined effects of NHS cost containment and medicines optimisation measures, while hospitals are seeing the impact of financial pressures on access to inpatient care, with increasing waiting times for routine procedures.

Germany is under similar pressure as hospitals face financial difficulties and staff are under economic pressure to discharge patients quickly, but with overcapacity issues in the secondary care sector. At the same time Hungary, Sweden, Norway, and Poland are expected to experience high growth – in part due to positive reimbursement and rebate agreements.

Forecast volume Compound Annual Growth Rate by country 2017–2022

Figure: 6

	UK	Germany	France	Spain	Italy	Hungary	Sweden	Norway	Poland
CAGR (%)	-0.43	0.86	-0.42	0.91	0.34	2.06	2.63	2.18	1.91

Compound Annual Growth Rate (CAGR) is used to refer to the mean annual growth rate of an investment or market over a certain period of time. It can be explained as a measure of growth based on the assumption that the investment or market grows in terms of value on a steady rate, compounded annually.

In Figure 7, IQVIA analysis shows that there is still much uncertainty about the nature and impact of any new UK-EU relationship. In the analysis there are a number of possible changes that may impact on pharmaceutical sales within the five-year forecast period. These include measures to accelerate access to new medicines, the UK macroeconomic outlook, delays to new product launches and post-Brexit trade agreements. Accordingly the analysis modelled three forecast scenarios: updside, base case and downside. At this point in the negotiations the five-year CAGRs in the base case, upside and no-Brexit (i.e. the Brexit-related events are not applied to the baseline forecast) scenarios do not significantly diverge, suggesting that the impact of Brexit on pharmaceutical sales will be limited over the next five years in these settings. The downside scenario expects that the five-year CAGR would be 0.4 per cent lower than the base case forecast.

The MHRA has reaffirmed the UK's desire for a transition period to allow for a smooth withdrawal and set out the MHRA's expectations for a close working relationship with Europe to ensure continued access to the best and most innovative medicines. Thus, in the base case forecast, the expectation is that the UK's MHRA will align itself with the EMA and have mutual recognition procedures for drug registration after the UK leaves the EU. In the downside scenario the UK regulatory pathway would diverge post-Brexit. This, together with the UK's

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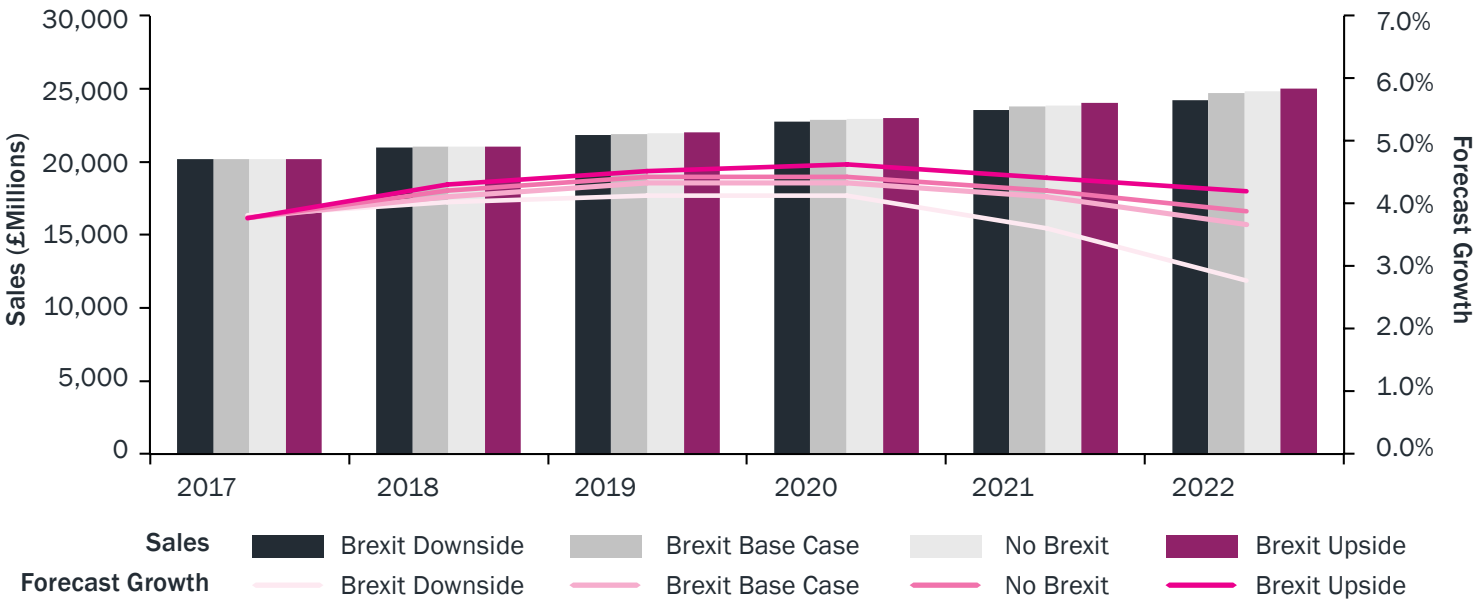
tough pricing and market access, would lead to the country becoming less commercially attractive for the pharmaceutical industry and delay entry of new product launches.

There are various possible scenarios for a post-Brexit trade relationship with the EU. In an upside scenario the free movement of pharmaceuticals will be maintained, and EU exhaustion of rights will continue to apply, i.e. parallel trade will continue. Therefore, a new trade agreement is expected to have negligible impact; the impact of this event is therefore excluded in this scenario.

In the base case forecast, there could be a change in parallel trade dynamics within the EU but there could also be opportunities outside the EU; nevertheless, under a possible downside scenario, there is a risk that under a new agreement additional trade barriers and tariffs could restrict, and increase the cost, of pharmaceutical trade.

UK total market sales and forecast growth 2017–2022*

Figure: 7



Compound Annual Growth Rate (CAGR) is used to refer to the mean annual growth rate of an investment or market over a certain period of time. It can be explained as a measure of growth based on the assumption that the investment or market grows in terms of value on a steady rate, compounded annually.

*At ex-manufacturer price levels, excluding rebates and discounts

In Figure 7, IQVIA market analysis shows that the LSIS could go some way towards alleviating some of these issues, though it cannot address the difficulty of parallel trade issues. Parallel Trade also provides an element of price competition for branded medicines, which supports the NHS to negotiate cheaper prices. As the House of Commons Health and Social Care Select Committee notes, it is estimated to have saved the NHS €986.2million between 2004 and 2009.[41] Some medicines are currently only available in the UK through parallel trade and shifting the manufacture of these products to the UK could take time, meaning that the future supply could be affected by Brexit.

The Committee recommends the Government clarify in its response to the report whether the UK can participate in the WTO Pharmaceutical Tariff Elimination Agreement and that it should seek clarity on when the agreement will be updated.

If the agreement is not updated before the UK leaves the EU, the Committee also recommends that the cost of tariff barriers to trade for the products affected be developed and that Government seek to maintain parallel trade in medicines with EU Member States in the ongoing negotiations. As the Committee also notes, it will be important for Government to consider its contingency planning in this area and that it assesses the impact of loss of parallel trade to the UK, including the NHS, which it should make publicly available.

While it cannot address the areas of negotiation and ongoing relationships with the EU, the LSIS look at ways to improve collaboration within the UK. It calls on the NHS to engage in 50 collaborative programmes with industry over the next five

years, such as late-stage clinical trials, RWD collection, or the evaluation of diagnostics and devices. These could take the form of shared-risk programmes that produce a reward to the NHS along with a sustainable return to industry. This should go some way to mitigating the impact of Brexit. Collaboration in innovation is already taking place between industry and the NHS. As noted earlier, the NHS Cancer Vanguard working with industry partners is the scale of partnership that cannot be replicated in other systems. In a post-Brexit market, the benefit of such partnership working will make the UK an attractive location for clinical and RWD research. Sir Robert Lechler notes progress that has been made in developing the LSIS and Sector Deal:

> *"We're already beginning to see more risk sharing between commercial partners and NHS adopters. The report mentions Medtronic, which has successfully persuaded several NHS hospital trusts to start using novel devices. They will share the risk, in the sense that if this doesn't save money in the long run they'll share the cost. That's quite a radical approach and it'd be good to see more of that."*[42]

Another example is GSK's work with GPs in Greater Manchester to run the innovative four-year Salford Lung Study, in what has been the world's first drug trial under 'real world' conditions.[43] In a global first GSK obtained permission to test Relvar Ellipta (fluticasone furoate/vilanterol), a drug to treat asthma and chronic obstructive pulmonary disease, before it had received full regulatory approval. It did this by setting in place an electronic patient data-monitoring system that ensured any adverse reactions were immediately communicated to physicians. Patrick Vallance, President for Research and Development at GSK, noted the global interest and impact the study has had, with both the US Food and Drug Administration (FDA) and US National Academy of Sciences "paying a lot of attention to it…as they look at how you set up systems to be able to generate so-called real-world evidence".[44]

Following on from the more specific proposals in NHS England's Twelve actions to improve clinical research and wider consultation by NHS England,[45] the ambition to support greater collaboration by creating a more significant infrastructure for research and innovation – promoting data collation and access to data registries, clinical information and RWD – has the potential to place the UK at the forefront of life science research and development.

There are initial steps government can take as part of this consultation to improve the clinical trial process in the UK. These include standardising clinical trial contracts and the rates that are charged to provide greater industry certainty. Clarity and aligning performance metrics with global standards will help to improve trial success rate and predictability.

Introducing performance management of trials and greater efforts to support the identification of patients for clinical trial participation, including promoting clinical trials as a routine part of patient care, will improve recruitment to trials which is vital to the success of research in the UK. As part of these efforts, allowing doctors to directly contact patients who could benefit from participation in clinical trials, the so-called 'right to write' provision, would be a highly valuable step that does not exist and which delays access to clinical trials.

In terms of the LSIS, the HARP, the Industrial Strategy Challenge Fund programme and the establishment of UK Research and Innovation to bring together the seven Research Councils, Innovate UK and Research England will, if implemented fully and with sufficient funding, make a considerable difference to the UK research infrastructure. Health Data Research UK will maximise the use of biological, clinical, environmental and social data sources, addressing research challenges that require a depth and scale of data that cannot be achieved through individual research programmes and supporting the development of the RWD sector to operate at the forefront of global research. However, the role of Genomics England must be developed within this network to ensure the globally significant work undertaken in genomics in the UK is at the heart of HARP.

The Government's approach to delivering this programme will be laid out in future phases of the sector deal, but it is intended that HARP will invest in high-risk research, in a similar model to the US Defence Advanced Research Projects Agency.

The Government is developing measures to improve the UK's health data infrastructure by establishing several regional interoperable Digital Innovation Hubs which will support the use of data for research. They will create controlled environments for real-world clinical studies; the application of novel clinical trial methodology and the comprehensive evaluation of new innovations to speed up breakthroughs. NHS Digital is working with partners to set out clear and consistent national standards for data and interoperability and is working to build a remote access environment to promote access to data for analysis.

However, there remains a gap in understanding how these hubs will operate in practice. This extends to how their priorities will be developed to ensure recognition of the scope for RWD and a clear structure of accountability for delivery of

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outcomes on expanding the use of RWE in research projects and clinical studies. Significant work needs to be undertaken to embed these hubs on the ground, ensuring access to non-identified patient data for industry in a secure framework. These issues are best addressed by the NHS working closely with all stakeholders, for example, by including industry as partners in the development of the hubs.

Without a clear implementation plan within an accountable structure and with clear outcomes, the potential to drive innovation in RWD will not be maximised. Instead, the challenges that have beset the NHS in adopting digital technology and data sharing best practice will continue to limit the delivery of world-leading healthcare. Given the context of Brexit, the time for action is becoming more urgent.

Regulatory alignment and innovation in clinical trials

A central concern raised in *'Finding a cure'* and referred to in the LSIS and Sector deal is whether the UK will establish its own clinical trial system or remain aligned with the Europe-wide regulatory structure which the UK has helped to design and reform.

In the development of a medicine, medical device or medical digital technology, EU regulations govern processes, including the launch and adoption. A key element of this regulation is the Clinical Trials Directive, which will be superseded by the planned Clinical Trials Regulation (CTR). The new regulation is intended to reduce the bureaucracy of the previous directive, making trials more transparent, improving patient safety and encouraging researchers to work together. It is now expected to come into force in 2020, after the UK has officially left the EU. This will mean the CTR will not automatically become UK law via the EU (Withdrawal) Bill. It is therefore vitally important that the Government formally adopts the new regulations before the formal 'exit' day or commit to implementing an equivalent UK regulation once withdrawn from the EU. As set out in the Government's White Paper '*The future relationship between the United Kingdom and the European Union*', it must also ensure that it secures agreement from the EU to endorse this alignment. [46]

Aligning regulations in this way will enable UK patients to take part in pan-EU trials, and thus access potentially life-saving new treatments. However, if the UK is no longer aligned with EU regulation in this area, any UK involvement in such trials is likely to add increased bureaucracy and costs. This will ultimately impact on patients.

The risk is that the UK could be excluded from participating in these trials particularly at design stage. The MHRA and other UK bodies currently have significant influence in shaping European regulations, setting the European and even global standard. The agreement made between the UK and EU as to our regulatory relationship will therefore have a significant impact on the level of influence the MHRA and other bodies have, and thus their status in the global clinical trial network.

In addition, the new relationship will affect both the commercial attractiveness of the UK to the highly competitive global pharmaceutical industry and the speed at which British patients will be able to access innovative medicines. As shown earlier in IQVIA's Market Attractiveness Survey (Figure 5), there is real concern across the global pharmaceutical industry that the changes that will occur within the operation and regulation of clinical trials within the UK will act as a disincentive to companies in deciding where to establish a clinical trial. 39 per cent of respondents to the survey believe Brexit will make the UK a less attractive location to run clinical trials.

The Government recognises that clinical trials are a global business and remains committed to a deep and special relationship with the EU as the best way to promote improved patient outcomes.[47] The Government will therefore look to continue to work closely with the EMA and other international partners.

In her Mansion House Speech, in March 2018, the Prime Minister confirmed that the UK will leave the single market and the customs union.[48] However, it is clear that in the response from the main adviser to EU's chief Brexit negotiator, Stefaan de Rynck, the EU is yet to be convinced of the UK's desired outcome to withdraw from the EU but to maintain a form of customs union:

"If you are in a very integrated market but you don't have the joint enforcement structures then you can see the potential for all kinds of difficulties."[49]

The LSIS and Sector Deal do not talk at length about the impact of regulatory divergence although it notes there is some positive benefit that a UK-only regulatory structure could have for UK life sciences. For example, the General Data Protection Regulation (GDPR), implemented in May 2018, will make data collection and sharing more onerous in the EU.[50] The strategy recommends that, following Brexit, the UK should "attempt to maintain the current balanced approach to data sharing regulations"[51] with a view to creating an integrated digital environment that will attract manufacturers and benefit patients.

However, even companies that are based outside the EU but provide goods or services to individuals in the EU, or that monitor their behaviour, will be required to comply with the terms of the GDPR.[52]

The LSIS recommends different approaches for the various elements of regulation:

- For clinical trials, pharmacovigilance, and other activities in which larger patient populations improve the quality of evidence for decision-making, the UK and the EU should pursue continued collaboration. The UK should also seek continued participation in mutual recognition agreements, such as the FDA/EMA agreement about manufacturing inspections.

- For pharmaceutical licensing, continued participation of the MHRA in the EMA's dossier reviews and joint scientific deliberations would be beneficial to patients in both the UK and the EU. If the UK did not wish to be involved in the EU voting system, it could make its own 'sovereign decision' based on the shared information and deliberations.

- For medical devices, the LSIS considers it would be reasonable for the UK to seek to continue to use the CE marking system, which applies not just in the EU, but also in Israel, Norway, and Turkey.

The recent announcement that the MHRA will lose its involvement in evaluating medicines for the EMA from the date it formally leaves the EU in March 2019, is a considerable disappointment. Instead, rapporteurs from other EU states plus Norway and Iceland will take on full responsibility for the medicines due to be reviewed by the MHRA. However, the MHRA is maintaining its commitment to continuing a close working relationship with the EMA.

The LSIS is cautious on the need to talk about the UK pioneering an innovative regulatory approach to emerging technologies, such as biosimilars, cell and gene therapies, algorithms, and digital medicines. However, the UK should consider the potential for securing a lead through adopting such innovative approaches. The EU's positive approach to biosimilars has secured a major lead in treatment approvals, having approved 42 medicines since 2006, compared to the 10 treatments approved by the FDA since 2016.[53] Within the current EU regulatory system, the MHRA has been a leading advocate of reform (e.g. adaptive licensing). But as the LSIS report states, a post-Brexit UK would need to ensure that any pursuit of new approaches to regulation did not jeopardise its involvement in EU systems and processes.[54]

A supportive business environment

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The LSIS and Sector Deal recognised the need to improve the support that is available to ensure that innovation and scientific discovery within the UK is translating into commercialisation and uptake of medicines and devices in the UK. The Government recognises the strength of the UK, as a member of the EU, to commercial organisations wishing to develop their business and to access UK and EU markets.

For companies outside of the EU, the UK offers several comparative advantages over other EU countries, including the ease of hiring and retaining a workforce, the strength and diversity of the UK life sciences ecosystem, strong intellectual property, legal frameworks and excellent transport connections with Europe and the rest of the world.

However, the fundamental issue in the UK's withdrawal from the EU is the negotiation of a trade deal. Future trading relationships on goods and services between the EU and the UK will have a major impact on the strength of the industry – and the wider UK economy.

A big hurdle for the EU will be the UK's wish to establish a new trading relationship that maintains open access to the EU market. The Prime Minister has already stated her belief that none of the EU's existing trade agreements with third parties such as Norway and Switzerland are suitable models, because they require countries to pay into the EU budget but have no input on the rules.

In addition, a trade agreement such as that between the EU and Canada, or on World Trade Organisation (WTO) terms, would significantly reduce UK access to EU markets. These options "would mean customs and regulatory checks at the border that would damage the integrated supply chains that our industries depend on,"[55] the Prime Minster has said. Therefore, the Government will be looking to negotiate an entirely new trading arrangement with the EU.

There are several areas where trading arrangements will impact significantly on life sciences and the provision of healthcare within the UK. As noted in *'Finding a cure'*, the WTO exempts finished pharmaceuticals from tariffs, but in addition to this list not having been updated to products brought onto the market after the WTO agreement, active pharmaceutical ingredients are also not included.

A move away from single market access may have a detrimental impact on the life sciences supply chain. Any potential import/export duties and new border controls would add burdens on a pharmaceutical trade that simply do not exist under EU membership. This would affect pharmaceutical trade with countries with which the EU has trade agreements – which have given the UK greater access to over 50 international markets and led to significantly increased levels of trade. Furthermore, it may affect pharmaceutical manufacturing, if the process involves numerous stages, potentially with processes outside of the UK.

The difficulties in ensuring the ongoing free movement of products particularly investigative medicines for use in the clinical trial process remain a major concern across the healthcare system.[56] This is likely to have a considerable impact on the export of investigational medicinal products manufactured in the UK for use in trial sites located in the EU, and vice versa. Whatever the final agreement, there are likely to be cost implications associated with duplication of the administrative and regulatory procedures required to enable clinical studies conducted on a cross-border basis.

The Prime Minister has prioritised integrated supply chains and a trading arrangement that is as frictionless as possible with no tariffs or quotas and with mutual recognition of products:

> *"Reciprocal commitments to ensure fair and open competition, an independent arbitration mechanism, an ongoing dialogue, data protection arrangements and maintaining the links between our people. These are the foundations that underpin the ambition of this unique partnership."*[57]

However, there is still a gap between the Government's desired trading arrangements and the position of the EU – laid out clearly in the response to the Prime Minister's speech by the European Council on 7 March 2018. In his statement regarding the EU's draft negotiating guidelines, Donald Tusk, President of the European Council, commented:

> *We invite the UK to participate in EU programmes in the fields of research and innovation, as well as in education and culture. This is key to maintain mutually beneficial and enriching personal networks in these vital areas, and for our community of values to prosper also in future."*[58]

Pharmaceutical and device manufacturers and suppliers are having to consider that the UK's ideal arrangement will simply not be agreed by the EU. Instead, they could face new EU/UK border controls, which would prove disruptive and time-consuming in the short-term, and ultimately make the UK a less competitive player creating an expensive barrier to Europe's medicines supply chain. As European Council guidelines set out:

> *"Being outside the Customs Union and the Single Market will inevitably lead to frictions. Divergence in external tariffs and internal rules as well as absence of common institutions and a shared legal system, necessitates checks and controls to uphold the integrity of the EU Single Market as well as of the UK market. This unfortunately will have negative economic consequences."*[59]

The European Council recalls that the four freedoms of the Single Market are indivisible and that there can be no "cherry picking' through participation based on a sector-by-sector approach, which would undermine the integrity and proper functioning of the Single Market.[60]

Disruptions to the supply of medicines and other health technologies remains a central concern across healthcare bodies,[61] with the priority being to ensure that patients and the wider public are not negatively impacted should agreement not be reached within the negotiation timescales. The scale of trade between the UK and the EU is substantial, delivering medicines and medical devices to patients in the UK and the EU. For medicines, 45 million patient packs go to the EU from the UK every month, and 37 million patient packs go from the EU to the UK.[62]

It is a major concern for the parallel trade of active ingredients and even clinical samples, which are a fundamental part of the clinical research process, as well as the significant risk that exists in terms of stockpiling of medicines which could create public health risks for both UK and EU residents. This is a particular concern with regard to biologic and biosimilar products. Given that the manufacturing process is so long, any window of opportunity to stockpile ahead of a potential interruption of supply has now passed. Barriers to the trade of such material will have a highly detrimental impact on the sector, and more importantly to the care and treatment of UK patients. As the Health and Social Care Select Committee recommends,

> *"The Government should publish the external analysis of supply chain issues that has been commissioned and set out their contingency planning to ensure the safe supply of medicines, medical devices and substances of human origin after the UK leaves the EU."*[63]

That the LSIS and Sector Deal make little reference to the EU negotiations and the likely impact of future trading arrangements on the life sciences sector is unsurprising, but it is highly unlikely that the measures contained within the strategy can fully mitigate those consequences. Cooperation between the two markets on medicines regulation should remain a priority for the Government – for patients in the UK and across Europe.

> *"Making sure the supply of medicines is uninterrupted is essential to ensure patients in the UK and EU can get the medicines they need from day one of Brexit."*[64]

The LSIS and Sector Deal seek to boost the manufacturing of innovative medicines within the UK, with a Government commitment of £162 million to develop the manufacturing infrastructure and enable small and medium-sized businesses to produce advanced therapies. This includes the establishment of two new national centres – the Medicines Manufacturing Innovation Centre and Vaccines Development and Manufacturing Centre – alongside the existing national centres.

This investment in the infrastructure is intended to make the UK a uniquely attractive location for complex medicines manufacturing so that the UK can become a leading hub for advanced therapy manufacturing. The LSIS focuses on access to risk capital to allow the expansion of highly innovative companies and, importantly, the scaling of those companies by using more patient capital.

As more new medicines and products are developed, the need to have trading arrangements that minimise the bureaucratic barriers for UK businesses will become fundamental to successful product development cycles.

The life sciences sector relies heavily on IP protection: the system of patents and supplementary protection certificates protects the enormous investment in R&D and trademark rights safeguard commercial strategy. Much of UK IP law is either harmonised with, or directly derives from, European law. The UK is also a signatory to the European Patent Convention (EPC), an agreement independent of the EU. The EPC provides a one-stop pan-European patent application procedure which results in a 'European patent'.

The UK's relationship and governance by the Unitary Patent (UP) would be impacted by the withdrawal from the EU, particularly if the UK is denied access to Europe's Unified Patent Court (UPC). This could result in potentially lengthier and more costly patent disputes for companies. The Sector Deal makes broad reference to IP – recognising it as the base on which the sector survives and that a strong discovery base is associated with a growing capacity and future clinical development and manufacturing.

However, the system is based on a series of national patents which must be enforced or challenged on a country-by-country basis. The UP System, overseen by a UPC, has developed as a solution to this problem – with the resultant reduction in the bureaucracy and cost involved in enforcing patents across the EU.

Both the UP and UPC are created by a separate international treaty that is independent of the EPC and the EU Treaties, although signatories must submit to EU law in all proceedings before the UPC. The UK has now implemented the UPC Treaty, with the life sciences division of the Court to be based in London; however, it remains questionable whether the UK could participate in the UPC post-Brexit and the negotiations will need to address this.

The business environment is influenced by the operation of Supplementary Protection Certificates (SPCs), which provide crucial extended protection for certain patented medicines that have unusual barriers to marketing. As *'Finding a cure'* notes it is imperative for UK pharma that the SPC regulations are either transposed entirely into UK domestic law or remain in force as a feature of the UK's relationship with the Single Market.

Similarly, for EU trademarks held by UK pharma, there is little provision within the Sector Deal or current iterations of the negotiating positions of the UK or EU as to how to protect those trademarks held by UK pharma within the EU. Even if the UK Government were to convert EU trademarks into UK trademarks, they would no longer be enforceable on a pan-EU basis, and UK pharma companies could lose the right to decide when it first places trademark-bearing products on the UK/EU market.

These protections for pharma operating across UK and EU markets are key elements in ensuring the commercial viability of products and the willingness of companies to operate within the UK subject to its alignment with the EU.

The LSIS and Sector Deal are focussed on scaling up, improving the financial environment and access to investment. *'Finding a cure'* demonstrated how dependent the life sciences sector is on the EU's venture capital (VC) funding, with currently 25–40 per cent of total VC funds coming from within Europe, without which there will be significantly fewer biotech start-ups.[65]

In recent years, financing for UK life science companies reached its highest level for at least a decade:

> *"Fundraising from equity markets and venture capital soared in 2014... Money raised through stock market flotations rose more than eightfold in 2014 to £408 million — accounting for more than 40 per cent of the total raised in this way by UK biotech companies in the past 10 years."*[66]

By 2016 the amount of private equity investment in biotech and healthcare in the UK had risen to £665 million invested in 67 UK companies.[67]

It has been a complaint of entrepreneurs in life sciences that there has been a shortage of risk capital to help commercialise breakthroughs from the strong UK science base and reduce dependence on the country's larger pharma companies.[68]

At the launch of the UK Bioindustry Association's (BIA) report in January 2018, *'Pipeline Progressing: the UK's global bioscience cluster in 2017'*,[69] Steve Bates, BIA Chief Executive, acknowledged that the uncertainty and changing landscape of Brexit is a challenging context for raising finance. By 2016, the life sciences sector had 5,142 companies and generated approximately £63.5 billion in turnover – up by 6.2 per cent on the previous year. It supported 233,000 jobs with 98 per cent of med-tech firms in the UK being SMEs.[70]

Data collected from MedCity has revealed that investment into London's life sciences companies reached nearly £1 billion in 2017, with a total investment into the UK's life sciences sector reaching £2.8 billion in 2017 with 63 per cent in 'The Golden Triangle' of Cambridge, London, and Oxford.[71]

The BIA has also reported that UK biotech company Initial Public Offerings raised more than twice as much in 2017 (£234 million) than in 2016 (£105 million). Cell and gene therapy companies attracted some of the biggest deals of the year, with Orchard Therapeutics raising £85 million in series B funding; immunotherapy company, Autolus, raising £60 million; and Imperial College London spin-out, Cell Medica, closing a £60 million Series C round.[72] As the report was published, Sarah Haywood Price, CEO at MedCity, said: "The pace of innovation in the life sciences sector, from genomics to digital health and gene therapies, coupled with a fertile funding environment and supportive regulatory system, has helped fuel this record investment."[73]

Analysis by the British Business Bank in 2015 on the location of equity deals shows that cities such as Edinburgh, Manchester, Cambridge, Newcastle, Bristol, Liverpool, Brighton, and Glasgow have clusters of small businesses using equity finance, albeit on a smaller scale than in London.[74] Research by the Enterprise

Research Centre points to high-growth businesses being spread across the whole of the UK.[75] This demonstrates the potential to encourage more equity investment to support high growth firms in other UK areas.

A strong equity finance market is essential for ambitious smaller businesses looking to grow and it will be particularly important to compete effectively in a post-Brexit global market. Proposals in the Sector Deal to support business to scale-up are therefore opportune and will help to position the sector well to maximise investment opportunities. The Government announced a significant range of investment funds and financial incentives that will encourage small business to expand and work in partnership with government. The Government has committed £162 million from the first wave of the Industrial Strategy Challenge Fund to develop innovative medicines manufacturing infrastructure and to enable SMEs to manufacture advanced therapies.

The LSIS and Sector Deal point to the potential of the Accelerated Access Collaborative (AAC) – the vehicle for implementing the recommendations of the Accelerated Access Review[76] (AAR) – and the development of innovative commissioning routes as vital to the sector's performance – with the NHS as the sector's biggest customer in a single payer system.

The Sector Deal recognises the NHS as a key part of the business environment for the life sciences industry and that the response to the AAR marks an important commitment from the UK Government. This includes a streamlined approvals system and an £86 million investment to support small and medium-sized businesses and evidence collection to get the right products to patients.

Placing the responsibility for improving the NHS commercial capacity will represent a major task for the AAC. However, this does represent a shift to ensure that engagement between the NHS and the sector will be more closely aligned to the Department of Health and Social Care through the AAC.

While it is welcome to include the AAC in both the LSIS and Sector Deal, it is important to ensure that a proper plan is developed to ensure the stated objectives are achieved and there is clear accountability for its progress, as Sir Robert Lechler from the Academy of Medical Sciences acknowledges:

> *"I hope we will see some real action on implementing its recommendations, especially having a mechanism to identify novel and transformative new agents and therapies and then fast-tracking them into clinical use."*[77]

Access to talent, developing home-grown skills

Indivisible from the issue of any future trade deal is the wish of the UK Government to secure more control over immigration and the number of people from across the EU and beyond who, through UK membership of the EU, have had the right to settle in the UK.

It is without dispute that a major concern for many of those who voted to leave the EU, and indeed for some of those who did not, is the level of immigration into the UK as the EU has expanded. It is becoming clear that any restriction on freedom of movement will also restrict the parameters of any future trade deal and of UK membership of EU bodies.

UK life sciences have thrived by working across national boundaries within the EU. As a global industry, life sciences benefit more than other industry from freedom of movement for workers and the UK's withdrawal from the EU has already impacted on its access to the best talent in the workforce. There is evidence, even prior to Brexit, that the UK's increasingly restrictive immigration policy was having a negative impact on the ability to recruit the best scientific talent. Anecdotal reports indicate that the referendum result is already further damaging recruitment.[78] It is welcome to note that the House of Commons Science and Technology Committee is looking to develop proposals for an immigration system that supports science and innovation in the UK, and the need to attract and retain skills that support UK life sciences.[79]

Seventeen per cent of researchers and academics in higher education institutions are EU nationals and 72 per cent of UK-based researchers spent time at non-UK institutions between 1996 and 2012.[80] Half of researchers from Cancer Research UK's Beatson Institute are from other EU countries and a further 28 per cent are from non-EU countries.[81]

Researcher mobility is associated with better international networks, more research outputs, higher-quality outputs and, for most, better career outcomes.[82] A report by Rand Europe on the international mobility of researchers found that, in the UK, the proportion of researchers and doctoral candidates who are from outside the UK is increasing.[83]

The UK has led the EU in hosting researchers funded by the European Research Council as well as MSCA researchers. Over 2,200 researchers from across the world have come to the UK as part of MSCA.[84] In addition to funding exchanges, the EU facilitates mobility for researchers in the UK and across Europe through the European Research Area, which aims to address barriers to mobility and make Europe a more attractive research destination, acting as an open labour market for researchers.

The pharmaceutical and life sciences industries directly employ 220,000 people in the UK, approximately 7 per cent of whom are 'non-British' EU citizens.[85] Bringing freedom of labour movement to an end by exiting the Single Market could cause a short-term decline in productivity, with a longer-term question over the UK's attractiveness for investment due to the ability to attract and retain top talent.

The UK is seeking to agree a continued system for the mutual recognition of professional qualifications. It is investing £100 million in the Rutherford Fund[86] to attract highly skilled researchers to the UK. This provides fellowships for early-career and senior researchers, both from the developed world and from emerging research powerhouses such as India, China, Brazil and Mexico.[87]

The Sector Deal is clear on the importance of ensuring that a highly skilled workforce is available within the sector – both by building the skills base across the UK and enabling high-skilled immigration. Through the deal, the Government has committed to changing immigration rules to enable world-leading scientists and researchers endorsed under the Tier 1 (Exceptional Talent) route to apply for settlement after three years. The deal includes a commitment to reduce red tape in recruiting international researchers and members of established research teams, by relaxing the labour market test and allowing the UK's research councils and other select organisations to sponsor researchers.

There will be a further opportunity to take forward work in future phases of the Sector Deal to ensure the UK skills base continues to meet the needs of the sector. There is still significant work to be undertaken. This will understand how the UK can continue to support researcher mobility and collaboration with EU research projects as the discussions on freedom of movement become one of the focuses of the negotiations. The UK and the EU must ensure that their research communities can continue to access the high-level skills that support innovation in science and technology.

In addition, the Sector Deal looks to boost the development of apprenticeship standards in priority subjects such as bioinformatics, medical and chemoinformatics. Work on clinical trials and regulatory affairs standards for apprenticeships is also underway. These actions are part of the Government's aim to reach 20,000 apprenticeships in the science sector by 2020.

The Science Industry Partnership (SIP) is rolling out a regional approach to meeting the industry's skills need – and new Skills Advisory Panels with employers, colleges and government. While the Sector Deal commitments are welcome, this is another area where greater detail is required. This includes understanding the relationship between national industrial strategies and local strategies being developed through local government structures.

Industry must have clear involvement in the up-skilling of local populations to support apprenticeships and further qualifications. These are long-term ambitions and it is vital that the work that is taking place through research collaborations can be continued in the short to medium term.

There are several challenges to overcome in increasing the supply of apprentices in the life sciences industry, as identified in the SIP's Skills Strategy.[88] They are:

- Low numbers of life sciences companies taking on apprentices.
- The life sciences industry has traditionally recruited graduates for technician level jobs.
- The jobs are high level, often science based and can be quite specialist.

Science apprenticeship numbers have begun to rise, but they need to be significantly increased to meet the future demand for technical staff. There is high demand for 'big data' staff across all areas of the economy and for the life sciences it is a difficulty in finding people with the right mix of skills – combining scientific or healthcare knowledge with the computational, statistical data mining, and analytical competence needed.[89]

Projected Life Sciences Staffing Demand

Public Policy Projects

Figure: 8

In total up to 126,000 new staff will be needed between now and 2025 for life science industries:

32,000
In pharmaceuticals

92,400
Across medical tech & the evolving Biomedical Tech sectors

The growth of the advanced therapies sector in the UK will rely on commensurate growth in the available talent pool:

400 - 600
Additional skilled staff needed over next two years in advanced therapies

For the science industry to maintain its current qualifications profile, anticipated need is:

up to 37,000
Apprentices

78,000
Graduates

70,000
STEM technicians to meet replacement and new demand

Science Industry Partnership Skills Strategy 2016

The strategy further notes areas with some of the biggest skilled gaps in sciences industries include informatics, computational sciences and statistics. Over 90 per cent of respondents to a recent ABPI survey rating skills in these areas as a medium or high concern.[90]

Demand for informatics skills is expected to grow across all areas of the economy, increasing pressure on the shortages in this area. As the role and potential of artificial intelligence (AI) increases across science and healthcare, skills that support the development of, and work with, AI such as core maths and stats skills, as well as programming and coding ability, are expected to become increasingly valued.

Therefore, it is helpful that both the LSIS and the Sector Deal recognise the importance of the development of these skills for the future of the life sciences, as much as maintaining the partnership working and access to expertise from across the globe. Encouraging and supporting innovation in life sciences relies heavily on the development of new skills and expertise – across all levels of the industry. Working in partnership with industry to ensure the UK workforce can support innovation as well as current practice is essential for education and training to keep pace with the industry.

Conclusion

Public Policy Projects

If managed carefully, the UK's exit from the EU may be used as a catalyst to take steps to increase the growth rate of the UK life sciences sector. The pharmaceutical industry and life sciences sector is a global business and the UK should seek to expand and develop its global markets. It should market itself as a destination for inward investment to take advantage of world-class science and infrastructure – ultimately for the benefit of all patients. This paper has shown that while the LSIS and Sector Deal between the Government and the life sciences industry is welcome, it does not provide all the necessary answers to the risks the industry faces from the UK's withdrawal from the EU.

In terms of maintaining the significant investment that UK research and development has benefitted from as a member of the EU, there has been clear recognition by the Government of how important it is to maintain funding. In the short term, by underwriting participation of Horizon 2020, to major projects receiving funding through the LSIS and Sector Deal, to a longer-term commitment to raising government spending in research to 2.4 per cent of GDP by 2027. While this is commendable, it should be reiterated that this is relatively modest compared with many other countries. The UK's continued involvement in successor programmes is critical to the industrial priorities of the UK and the EU.

Whether the UK retains 'associate member' status, with its challenging freedom of movement demands, or is successful in negotiating a new model of partnership, it is likely that there will need to be a significant increase in funding provided by the Government to implement the report's full range of proposals.

The UK's ambitions to lead global life sciences would also benefit from a greater focus on capitalising on its unique non-identified patient data ecosystem and thereby expanding the use of RWD across the research, development and commissioning processes – after all the UK is already a global leader in this area. Although by its nature, it is difficult to translate findings to other contexts, there is greater potential to use insights gained across populations – as recognised in the Salford Lung Study. It is vital to build on existing global leadership in RWD to spread the use of this relatively new science into practice across global research and evaluation systems.

As Digital Innovation Hubs are developed, 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 RWD, which can be appropriately accessed by researchers. At the heart of the LSIS is the proposal to establish the HARP 'moonshot' programme of research projects, with a greater level of risk than traditional research projects. The aim is to encourage innovation that will translate to commercial success. However, proper funding aside, the programme must have clear structures of accountability to fulfil the commitment that the UK will be in the top quartile of innovation uptake.

The data recommendations require investment in terms of expertise and facilities, collaboration with life sciences data experts and a clear focus on interoperability, collection and sharing between NHS organisations, other health bodies and industry.

The HARP, the Industrial Strategy Challenge Fund programme and the establishment of UK Research and Innovation, if implemented fully and with sufficient funding, will make a considerable difference to the UK research infrastructure. However, the role of Genomics England must be developed within this network to ensure the globally significant work undertaken in genomics in the UK is at the heart of HARP. While partnership working with industry is a central theme within both the LSIS and Sector Deal, there are clear opportunities in the implementation of new structures to involve industry from the beginning. An example is in the operation of the digital innovation hubs, to support secure access to data across both the NHS and industry.

The clinical trials approval process could be simplified and streamlined by creating a single agency rather than responsibility spread between several bodies, as it is currently the case. This body should develop performance metrics, aligned with global standards, to help improve trial success rates and predictability and mainstream patient participation in clinical trials. The UK should continue to implement EU rules in this area after withdrawal.

The agreement that is made between the UK and EU as to the future regulatory relationship will have a significant impact on the level of influence the MHRA and other bodies have, and thus their status in the global clinical trial network.

It is welcome that the Government remains committed to a deep and special relationship with the EU as the best way to promote improved patient outcomes[91] and will look to continue to work closely with the EMA and other international partners.

The issue of regulatory alignment presents both opportunities and risks in terms of allowing the UK freedom to develop a new, and potentially, more commercially appealing system. However, the ongoing free movement of products (particularly investigative medicines) for use in the clinical trial processes remain a major concern across the healthcare system. Whatever the final agreement, there are likely to be cost implications associated with duplication of the administrative and regulatory procedures required to enable clinical studies to be conducted on a cross-border basis.

Future trading relationships on goods and services between the EU and the UK will have an even more significant impact on the strength of the industry, and the wider UK economy. A move away from single market access may have a detrimental impact on the life sciences supply chain, with any potential import/export duties and new border controls adding burdens on a pharmaceutical trade that simply do not exist under EU membership. It may affect pharmaceutical manufacturing, if the process involves numerous stages, potentially with processes outside of the UK.

Although the Government's ambition may be to develop a unique agreement with the EU that addresses some of these risks, there is clearly some way to go before the EU will consider such a deal. It is unsurprising that there remains deep concern as to the potential disruption to the supply of medicines and other health technologies. As noted earlier in the report, the scale of trade between the UK and the EU is substantial, with 49 million packs of medicines exported and 37 million packs imported between the UK and EU, ensuring the supply of medicines and medical devices to patients in the UK and the EU. Yet the LSIS and Sector Deal make little reference to the likely impact of future trading arrangements on the life sciences sector, nor the risk to public health in the UK and EU of medicines stockpiling and possible medicines shortages as we approach March 2019. Co-operation between the two markets on medicines regulation should therefore remain a priority for the Government – for patients in the UK and across Europe.

Instead, the LSIS and Sector Deal seek to boost business environment for life sciences announcing £162 million investment to develop the manufacturing infrastructure and enable small and medium-sized businesses to produce advanced therapies, as well as measures to allow the expansion of highly innovative companies and, importantly, the scaling of those companies using more patient capital. The focus on increasing the availability of venture capital funds to help commercialise breakthroughs from the research base and expand the operations of smaller companies is a further welcome workstream for the Sector Deal, particularly as the context of Brexit raises concerns for companies about the availability of financing.

Although the LSIS and Sector Deal both include the potential of the AAC as vital to the sector's performance and, indeed, place the AAC as responsible for improving the NHS commercial capacity, it will be important to ensure that a proper plan is developed to ensure the stated objectives achieved and there is clear accountability for its progress. It is therefore of some concern that the Collaborative has not announced any successful products or technologies since it was established in November 2017. There are only five products or technologies to be assessed, down from the 10 promised.

Issues such as trading arrangements and legal protections are not addressed in a significant way by the LSIS and the mitigations to promote innovation and production, will struggle in the absence of an agreed trade deal. From intellectual property law, to the operation of the system around patents and UK participation in the Unitary Patent Court, to the system governing Supplementary Protection Certificates, and EU trademarks held by UK pharma – the protections available to pharmaceutical companies operating in the UK and across the EU are vital to commercial viability, they should be maintained in line with EU regulations to retain existing protections to companies that operate across the UK and Europe.

Finally, being able to access the best talent from across the global scientific community is critical for the sector. The loss of access to the knowledge and skill of researchers and clinicians across the UK will have an impact. Yet as is widely recognised, the EU also benefits from access to the UK's knowledge, expertise and culture of research and innovation. Therefore, it must be a priority to develop the UK supply of researchers, academics, and clinicians to maintain the UK's access to such globally recognised expertise. The commitments to developing the workforce and the focus on apprenticeships in the LSIS and Sector Deal are welcome. But this must be followed by an implementation plan that ensures the ambition is delivered.

Science apprenticeship numbers need to be significantly increased to meet the future demand for technical staff in the sector. This must particularly focus on developing skills on 'big data', combining scientific or healthcare knowledge with the computational, statistical data mining and analytical competence needed.[92]

The LSIS and Sector Deal provide welcome support for the life sciences sector and for many areas these proposals are a good starting point to maintain and improve the position of UK life sciences. However, further measures will be needed to truly meet the ambitious vision set out in the LSIS.

As underlined in evidence from The Wellcome Trust to the House of Lords Science and Technology Inquiry into the LSIS, the strategy – through the intended multiple Sector Deal 'waves' – must be delivered as a full package otherwise it will lose its optimum impact:

> *"It will require action over a number of years. It is not just a single moment in time when a strategy is published, or a sector deal is agreed. It is going to require significant effort from all those parties. You cannot just deliver on a subset because the whole delivers much more than the sum of its parts."*[93]

The Government has stated that the Sector Deal published in 2017 is the first of a wave of deals that will see ongoing support for the sector[94] and measures to ensure the success of life sciences as the post-Brexit environment becomes clearer. Should the Government secure the ambitious deal with the EU, the LSIS and Sector Deal will succeed in delivering exactly what the doctor ordered, a world-leading life sciences sector in the UK.

Appendix

About Seqirus

In July 2015, bioCSL and the influenza vaccines of Novartis joined forces to create Seqirus, now the second largest influenza vaccine company in the world. Seqirus is a transcontinental partner in pandemic preparedness and a major contributor to the prevention and control of influenza globally. Seqirus' long established parent company, CSL Limited, has a rich heritage in influenza and their manufacturing facility in Melbourne, Australia, has been producing flu vaccine for nearly five decades. It has now joined with Seqirus Liverpool in the UK, a Centre of Excellence for egg-based influenza vaccine manufacturing.

Glossary

Public Policy Projects

Adaptive Licensing (of new medicines) is an alternative approach to the current established system of marketing authorisation. Adaptive licensing means 'drug candidates' that meet a serious unmet medical need can be initially approved for use in a restricted patient group, with their use then gradually expanded to broader patient populations as additional safety and efficacy data is generated. This allows licensing to align more closely with patient needs for timely access to new medicines, and for data to be gathered on an ongoing basis.

Advanced Therapies are new approaches to medicine that use stem cells, genes and tissues to develop therapies, gene-editing technologies (to repair or replace faulty genes) and nucleic acid (DNA and RNA) therapies. Many of these products use viral vectors to deliver to the target cell.

Non-identified patient level data – non-identified data has been subject to a process that removes the association between a set of identifiable data and the patient so that there is no reasonable basis to believe that the information can be used to identify an individual.

European Medicines Associate Membership is a model being proposed by the UK that would involve a financial contribution to the organisation's budget and a level of agreement to the regulations that govern the EMA. It is a model that is sought by the UK in terms of a future relationship with the European Chemicals Agency and the European Aviation Safety Agency. This is an area of ongoing negotiation between the UK and EU.

Horizon 2020 Associated Countries - Associated countries participate in Horizon 2020 under the same conditions as EU states. Thirteen counties (including Norway, Israel and Switzerland) have 'Associated Country' status and contribute to Framework Programme budgets proportionally to their GDP. This enables their researchers and organisations to apply for Horizon 2020 projects with the same status as those from EU states. Associated Country status is open to countries that are members of the European Free Trade Association (EFTA) and current EU candidate nations. The terms of their association differ slightly by country. They do not have a role in the negotiations that shape EU research funding.

Horizon 2020 Non-associated third countries Institutions and researchers from other countries can also apply and participate in EU Framework Programmes, under the 'openness' strategy, and in some circumstances receive direct funding. Depending on the exact scheme, third countries might have to provide matching funds.

Investigative Medicines or Investigative Medicinal Products are a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.

Marie Skłodowska-Curie Actions (MSCA) is a programme of grant funding for all stages of researchers' careers and encourage transnational, intersectoral and interdisciplinary mobility. The MSCA enable research-focused organisations (universities, research centres, and companies) to host foreign researchers and to create strategic partnerships with leading institutions worldwide. The programme is part of the Horizon 2020 scheme and is now the main EU programme for doctoral training, financing 25,000 PhDs between now and 2020.

'Moonshot' programmes – the term "moonshot" derives from the Apollo 11 spaceflight project, which landed the first human on the moon in 1969. Such projects or programmes are intended to be ambitious, exploratory and ground-breaking without any expectation of near-term profitability or benefit and also, perhaps, without a full investigation of potential risks and benefits.

Parallel trade (also known as parallel imports) refers to importing units of medicines (in practice usually patented products) from other countries at lower prices than are available in the UK. Products can be imported thanks to the legal position that once a manufacturer places a product on the market in the European Union, purchasers can sell that product on without the consent of the patent holder. The development of the European single market has facilitated the trade. The UK's decision to leave the European Union will therefore have implications for parallel trade, although the details will depend on the nature of the final deal.

Patient Capital is long-term investment that supports entrepreneurs and investors to make a return from the substantial growth of a business rather than through short-term profits from low-risk projects. Finance is typically provided through an entrepreneur's own long-term commitment to his or her business and/or equity investment from external investors, e.g. business angels, venture capital funds or the public markets. In addition, some forms of debt instruments (e.g. venture debt) may meet this definition, while some forms of equity investment may not (e.g. some approaches to leveraged investment). Patient capital supports entrepreneurs to bring disruptive innovation in products, processes and business models to market, where returns tend to be made over the longer term. As such, patient capital becomes crucial in sectors that require substantial investment by new firms before a financial return is made such as life sciences, digital and other technology development.

Personalised Medicine separates patients into different groups—with medical decisions, practices, interventions and/or products being tailored to the individual patient based on their predicted response or risk of disease. The term has risen in usage in recent years given the growth of new diagnostic and informatics approaches that provide understanding of the molecular basis of disease, particularly genomics. This provides a clear evidence base on which to stratify (group) related patients, tailoring treatment decisions to a patient's unique need.

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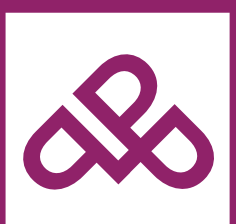

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