Scaling Up Scottish Life Sciences After Brexit

**IQVIA and Quest Diagnostics -
the companies behind Q² Solutions**

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IQVIA is a leading global provider of information, innovative technology solutions and contract research services, focused on using data and science to help healthcare clients find better solutions for their patients. IQVIA and Quest Diagnostics created the Q² Solutions joint venture in 2015, combining the best of each parent organisation's capabilities in clinical trials and laboratory services. Scotland is already a leading go-to destination for life sciences investment.

The life sciences industry is a large and critical part of the global healthcare system, and, according to the latest information available from the IQVIA Market Prognosis service, is estimated to have generated approximately $1.1 trillion in revenue in 2017. Revenue growth in the life sciences industry globally is expected to range from 3% to 6% between 2018 and 2022. (Source: IQVIA Annual Report 2017)

Formed through the merger of IMS Health and Quintiles, IQVIA is headquartered in the USA. It has more than 55,000 employees operating in more than 100 countries, including approximately 29,000 Research & Development Solutions employees, and almost all employees are full-time.

In Scotland, IQVIA has 700 Q² Solutions and 240 IQVIA staff, totalling 940 (see below for details about Q² Solutions). It continues to create jobs in Scotland, with 70 new/ incremental positions in the last year, many of them science positions, such as pathologists and laboratory personnel.

IQVIA offers a broad range of solutions that harness advances in healthcare information, technology, analytics and human ingenuity to drive healthcare forward. It enables companies to rethink approaches to clinical development and commercialisation and to innovate with confidence, as well as accelerate meaningful healthcare outcomes.

Its insights and execution capabilities help biotech, medical device and pharmaceutical companies, medical researchers, government agencies, payers and other healthcare stakeholders who tap into a deeper understanding of diseases, human behaviours and scientific advances, in an effort to advance toward cures.

As a human data sciences company, IQVIA has one of the largest and most comprehensive collections of healthcare information in the world, which includes more than 530 million comprehensive, longitudinal, non-identified patient records spanning sales, prescription and promotional data, medical claims, electronic medical records and social media. This scaled and growing dataset contains approximately 30 petabytes of proprietary data sourced from more than 120,000 data suppliers and covering over 900,000 data feeds globally. Using this data, IQVIA delivers information and insights about more than 85% of the world's pharmaceuticals, as measured by 2016 sales.

IQVIA's data is widely referenced in the industry and used by governments, payers, academia, the life sciences industry, the financial community and others. Most of this information is available on a subscription basis. Other reports and information are available publicly through our IQVIA Institute for Healthcare Informatics (the "IQVIA Institute").

IQVIA is the UK's fourth largest life sciences employer, with a team of 3,800 employees working across the UK and is the largest life sciences employer in Scotland. IQVIA conducts 30% of all commercial clinical trials in the NHS and operates a unique research model, partnering with three exemplar NHS 'Prime Sites' in Scotland, London and the Peninsular covering a population of around 13 million people. These Prime Sites are high-throughput research centres where IQVIA invest in training to increase efficiency, site performance and access to patients, and where it thus conducts most of its UK research. Within Scotland, there are 53 sites currently open to enrolment, across 36 different protocols; 29 additional sites scheduled to open in the next six months; and 219 patients have been recruited across Scotland (excluding glomerular filtration rate projects) in the previous 12 months. For all therapies, the breakdown is 30% oncology/haematology; 17% Alzheimer's disease & central nervous system; 15% renal; 11% respiratory; 10% cardio-vascular & diabetes; 7% gastroenterology; 6% mental health, and 4% others.

IQVIA and Q² Solutions are currently expanding their capabilities in genomics testing at its Scottish laboratory Q² Solutions, with the initial phase expected to be completed by the end of the year. This expansion positions Q² Solutions as one of the only laboratories to have next generation sequencing capabilities in three continents.

IQVIA is a global leader in real world evidence studies, with over 1 billion de-identified patient transactions globally per

year– the UK is a global hub for its Real-World Evidence and Healthcare Analytics programmes. This data helps pharmaceutical companies understand epidemiology (incidence, distribution and treatment) and consider the feasibility of clinical trials. With its institutional knowledge, therapy expertise and extensive data insights, IQVIA is well placed to support the UK and Scottish Governments and the global pharmaceutical industry in maintaining the position of life sciences as the 'jewel in the crown' of the UK economy.

Quest Diagnostics is the world's leading provider of diagnostic testing, information and services that patients and doctors need to make better healthcare decisions. Its services range from routine blood tests — such as total cholesterol, Pap testing and white blood cell count — to complex, gene-based and molecular testing. Healthcare organisations and clinicians benefit from state-of-the-art health information technologies that help improve patient care and practice management. It provides interoperable technologies that help healthcare organisations and physicians enter, share and access clinical information without costly IT implementation or significant workflow disruption. Quest Diagnostics helps biopharmaceutical, medical device and diagnostics customers improve human health through innovation that transforms science and data into actionable medical insights to improve patient health outcomes. Its laboratories operate 24 hours a day, 365 days a year, and touch the lives of patients more than 147 million times each year.

The company was founded in 1967 and became an independent corporation in 1996 under its current name, with its headquarters in Secaucus in New Jersey.

Its products and services involve:

- Diagnostics information services
- Clinical trials
- Healthcare IT
- Wellness & risk management
- Drug screening

In respect of its role as a major employer and business, Quest Diagnostics:

- Engages a workforce of about 45,000 employees dedicated to putting patients first every day
- Operates more than 2,200 patient service centres
- Has a medical and scientific staff of more than 650 MDs and PhDs
- Provides logistics capabilities that include approximately 3,700 courier vehicles and 23 aircraft which collectively make tens of thousands of stops daily.

This global reach, coupled with its extensive capabilities, led Quest Diagnostics to partner with IQVIA to launch Q^2 Solutions as a leading global clinical trials laboratory services organisation, combining the best of each parent organisation's clinical trials laboratory services capabilities. As a result, Q^2 Solutions is a quality-driven, responsive partner with strong global experience and deep scientific and medical expertise, as demonstrated in Livingston, where it carries out four million clinical trial tests a year.

Tony Brown
Vice President and General Manager, Global Central Labs
Q² Solutions

Foreword

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Q² Solutions is a global clinical trials testing laboratory company, which was formed in 2015 as a joint venture between IQVIA (then known as Quintiles) and Quest Diagnostics. Q² Solutions combines the unique strengths of each parent organisation's capabilities in clinical trials and laboratory services to provide greater innovation, quality and value for its customers.

We made the decision to base our clinical trials laboratory services in Scotland because of the rich life sciences ecosystem that exists here, and the services provided at the Q² Solutions Laboratory at the Alba Campus are integral to our global life sciences supply chain. The Scottish Government has been tremendously supportive of the life sciences sector; resulting in new investment in Scotland by biotech and pharmaceutical companies over the years and a commitment to increase the sector to an £8 billion in turnover by 2025.

Q² Solutions is Scotland's largest life sciences employer, employing 750 people from across the country, and with an increase in the permanent headcount of 12% since 2016. Our team at the Alba campus enables global pharmaceutical, biotech and diagnostic companies to conduct seamless clinical research from start to finish, including protocol design, study start up, distribution and clinical data management. The Q² Solutions Laboratory processes over four million biological samples annually, 900,000 custom sample collection kits and a wide range of biomarker support and potential next generation genome sequencing.

Q² Solutions continues to invest in new technologies to reflect current and future market trends and is presently expanding the scope of research activities at the Alba Campus to include next generation sequencing. This is a key part of our strategy to ensure that we can continue to comprehensively support the evolving research needs of the global life sciences industry from our flagship laboratory site in Scotland.

The UK life sciences ecosystem faces an unknown future due to the current uncertainties surrounding Brexit, however provided solutions can be discussed, agreed and implemented, we can overcome the current uncertainties. Q² Solutions commissioned this white paper to support a deeper appreciation of the value of life sciences to Scotland, to explore the potential implications of Brexit, with both its risks and its opportunities for the health and wealth of the people of Scotland, and to put forward our perspective on how the Scottish life sciences economy can further evolve and *thrive* in a post-Brexit world.

Through our continuous engagement with National Research Scotland (NRS) and the wider Scottish Government, Q² Solutions is *pleased* to support programmes such as the Scottish Government Economic Strategy and its plans for developing the Scottish life sciences sector. The infrastructure provided by NRS creates a strong base for our operations here in Livingston and we look forward to continued engagement in the months and years ahead.

The recommendations in this paper aim to provide a narrative for discussion of how some of the risks posed by Brexit might be mitigated by ensuring that the life sciences sector is kept front and centre in the Brexit negotiation process by the UK and Scottish Governments. The Scottish Government has worked hard to ensure that the voice of the Scottish life sciences industry is heard at a national level.

"Leaving the European Union will be a test for us all and the life sciences sector faces unique challenges. We need to overcome the potential risks to Scottish life sciences."

Tim Sheppard
SVP and General Manager
Northern Europe IQVIA

Foreword

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Scotland has a long history as a leading nation in medical science and IQVIA's continued investment in Scotland reflects this strong heritage. We are now the largest life sciences employer in Scotland. As a human data sciences company, IQVIA are committed to continued investment in Scotland and seek increased partnership with the Scottish government to continue our growth.

Since the 2016 merger of IMS Health and Quintiles to form the company 'IQVIA', IQVIA has offered a broad range of solutions that harness advances in clinical research, healthcare information, technology, analytics and human ingenuity to improve patient outcomes in Scotland. Our collaborative footprint with Q^2 Solutions, in which IQVIA has a 60% share, on the Alba Campus in Livingston ensures that IQVIA is well placed to support Scottish Government and the global pharma and biotech industry in maintaining the position of life sciences as the 'jewel in the crown' of the Scottish economy.

As IQVIA is the global leader in commercial clinical trials, it is significant for Scotland that IQVIA appointed Scotland and its research hospital network as one of our 20 global 'Prime Sites', where we focus resources to maximise clinical trial throughout. A subset of 'Prime Sites' are the investigator sites, where investigators (medical doctors) reside to perform clinical trials. Two hundred and nineteen patients were recruited to clinical trials across Scotland in the last 12 months. As well as the globally strategic Q^2 Solutions Laboratory, there are also over 200 global clinical project leaders and regulatory team leaders based in Livingston.

The Livingston Alba Campus is a hub for the Scottish life sciences sector, whose expert and highly-skilled staff deliver cutting edge science, generate innovative research solutions, and ensure that global life sciences have the laboratory support needed to ensure clinical trials are successfully completed. We believe that the recommendations in this White Paper, if implemented, will support our continued investment in Scotland and expand its strategic importance to the global life sciences industry.

"We believe that the recommendations in this White Paper will support our continued investment in Scotland and its importance to the life sciences industry." Tim Sheppard, Senior Vice President (SVP) and General Manager, Northern Europe IQVIA, 6 November 2018

The Scottish Government has been one of the most vocal in Europe about their life science sector expansion plans. As a company we welcome the opportunity to further engage with, and encourage, the growth of the life sciences supply chain in Scotland. Given the context of Brexit, there is uncertainty. In this context, the Scottish Government must take every opportunity to make sure the voice of Scottish life sciences is heard in the ongoing negotiations around the future of UK life sciences post-Brexit, to ensure the future of inward investment to the Scottish economy.

Greater industry-NHS collaboration is critical for patients in Scotland, and our plans to expand the number of clinical trials in the UK will only serve to help patients across the country. Collaboration is already strong, and, as this white paper demonstrates, it will be vital to build on this strength to help mitigate some of the impacts of Brexit in the months/years ahead.

Background to the paper

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The global market in life sciences imports, excluding the UK, was £307bn in 2016, and in the UK, turnover was approximately £63.5 billion. (Life Sciences Sector Report to Parliament following House of Commons debate in November 2017). Such significant figures explain the need to address the subject.

"Scotland is already a leading global life sciences cluster and in the past few years Scotland has seen many positive developments, with a number of international companies looking to expand their presence here." (2017 Life Sciences Strategy for Scotland - '2025 Vision')

Scotland is already a leading global hub for life sciences, employing over 37,000 people across some 700 organisations. Companies in this sector contribute in excess of £4.2bn turnover and about £2bn gross to the Scottish economy. Since 2010, company turnover has increased by 29%, gross value rose by 24% and total employment in companies by 13%. (Source: Ibid)

The life sciences sector in Scotland comprises a wide range of interrelated sub-sectors, including medical technologies (medtech), biotechnology companies, diagnostics, contract research organisations and other pharma services activities, pharmaceuticals, digital health, agritech, aquaculture and animal health. Biotech/medtech/diagnostics companies comprise nearly half of the sector in Scotland, and pharmaceuticals about 5%. This differs significantly from the composition of the sector in the rest of the UK. (Source: Life Sciences Scotland Industry Leadership Group, November 2017)

This progress originally developed in conjunction with companies already based in the UK, both British and non-British, but increasingly foreign companies are being directly attracted to Scotland and the reasons for this are set out later in this paper. It is now home to a range of multinationals and small and medium sized enterprises.

The stated aim of the Scottish Government is to increase the life sciences industry turnover to £8bn by 2025. (Source: Life Sciences Strategy for Scotland 2025 Vision in Scotland, 2017)

The Scottish Government has identified the life sciences sector as a priority sector of economic significance. Its support is demonstrated by the fact that 34% of Business Enterprise Research and Development spending in Scotland is attributable to life sciences.

This support from the Scottish Government can also be expected to benefit Scottish patients, for the ultimate rationale of the life sciences industry, and its justification, is to improve the care of patients.

Why Scotland

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The reasons that companies decide to invest in Scotland vary greatly, from government and economic inward investment offerings (including support from Scottish Enterprise Life Sciences and Scottish Development International) to expertise and existing contacts.

That such companies feel appreciated in Scotland is a significant factor. As the First Minister has stated *"Life sciences is an exciting and developing growth sector for Scotland's economy"* (Speech 10 August 2017). She subsequently expanded on this saying *"Scotland is long renowned for innovations in medicine and in life sciences. We are now leading pioneering research in precision medicine tailoring healthcare to fit an individual's genetics and lifestyle. Our clinical expertise, our expertise in genomics and our access to high quality healthcare data, perhaps the best and most joined-up healthcare data anywhere in the world, makes us a natural centre for this new approach to medicine."* (Speech, 16 May 2018)

The Scottish Government has made a clear effort to support the life science sector in Scotland.

Key issues for global life science companies thinking about establishing a base in Scotland include:

- A unified health service and access to health data, with key physicians
- The close relationships between Scottish institutions and their people
- World-class universities and a science-research base, with internationally acclaimed academic leaders
- Access to the European Union market
- Language.

That English is the everyday language in Scotland and is the "lingua franca" of today, not only in the western world but globally, fuelled by the internet, has been a factor in attracting investment by life science companies to Scotland. US life science companies in Scotland are numerous, including not only major companies but also small and medium-sized enterprises. For example, IQVIA and Quest Diagnostics whose joint enterprise, Q^2 Solutions, is based in Livingston, has over 900 employees and is the largest employer in Scotland for life sciences.

Scotland has a further advantage of having manageable and compact institutions. Companies have been very pleasantly surprised to find that, as one manager commented, *"everyone seems to know everyone"*. This wider reach is a very positive and attractive element of Scottish society. It enables companies to contact the right people in a straightforward manner when they want to learn about public policies and to explain their own views.

Its science base means that Scotland ranks worldwide among the top three for research productivity and impact (Source: Life Sciences in Scotland, 2017). It has more universities per head than any other part of the European Union, as well as higher education institutions. Its world-leading research centres attract some of the brightest international scientists.

NHS Scotland treats a population of c.5 million, via a unified healthcare system, and to some of the best integrated data in the world. These data include:

- The UK's national prescription/dispensing and hospital imaging datasets
- Primary care data connections being developed through the national SPIRE programme (Scottish Primary Care Information Resource)
- Multiple disease-related registries
- A network of tissue bank repositories.

Through NHS Research Scotland, the health service provides a single access point for industry, dedicated clinical research facilities and globally competitive approval and business start-up times. It works collaboratively across all health boards to provide a comprehensive and complete service. This national approach results in fast, efficient and reliable support to deliver high-quality clinical trials in Scotland.

NHS Research Scotland also plays a key role in supporting the delivery of high-quality clinical research in genetics, and managing participant recruitment to meet deadlines and targets, both for genetics studies led from Scotland, and studies led from other nations in which Scottish sites are participating.

Innovators within NHS Scotland are also encouraged to work with industry. Key physicians are to be found in NHS Scotland and in the medical departments of universities, adding quality to key clinical opinion leaders.

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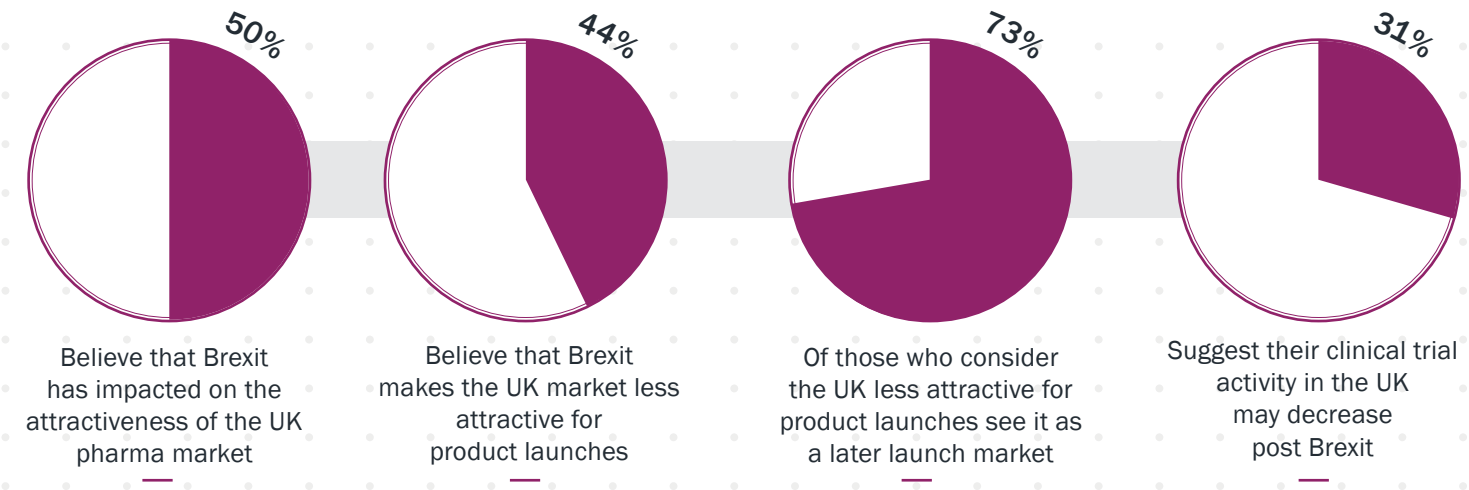
Another key issue for companies investing in Scotland has been access to the European Union market of over 500m people, even more if the European Economic Area is included, and the ability to access this market easily. However, an IQVIA survey of global pharmaceutical industry board level executives (as seen in Figure 1) between February and March 2018 revealed a high degree of uncertainty. Half of those surveyed believed that Brexit would have an impact on the attractiveness of the UK pharma market and 44% that it would make the UK market less attractive for policy launches. The future for clinical trials is also troubling, with 31% suggesting that clinical trial activity in the UK may decrease post-Brexit and just over a third not expecting the UK to remain a prime clinical trial country. (Source: *Just what the doctor ordered? Is the Life Sciences Industrial Strategy the right prescription for Britain's life sciences sector?* Public Policy Projects, July 2018)

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

Figure: 1



How exactly Scotland and the rest of the UK will manage leaving the European Union is therefore of huge and vital importance.

The chair of the Life Sciences Scotland Industry Leadership group stated in a public letter that the uncertainty arising from the UK Government's decision to leave the European Union *"is already having negative impacts on these life sciences companies in Scotland and the concern is that this is set to intensify."* (Dave Tudor, 10 November 2017)

He added that the main areas that life science companies felt needed to be addressed were:

*"**Regulation** – the sector is of the clear view that UK life sciences regulation should not diverge from EU regulation and should continue to see continued cooperation with the European Medicines Agency. We would strongly resist creating a new and untried Scottish life sciences regulator when there is a long established global regulatory system.*

***Trade & Supply** – Ease of movement of our goods and supplies needs to continue tariff free and there needs to be minimal customs procedures to allow quick and efficient distribution of our products across the EU. As a minimum there needs to be continued mutual recognition for testing and release between the UK/EU & EU MRA Partners to ensure security of supply to our patients. Companies also stress the importance of the US life sciences market and are supportive of a UK/US trade deal being initiated along with any UK/EU agreement.*

***Access to talent** – companies want experts and life sciences managers from the EU and overseas to be able to enter the UK at least as easily as at present; we would have concerns over any restrictions on highly-skilled talent entering Scotland.*

***Maintaining R&D** - the sector needs to continue to benefit from the excellent R&D relationships and collaborations. Securing science funding levels is imperative."*

Interestingly, and perhaps not surprisingly, these concerns are almost identical to those in the rest of the UK, so although the points below are in the wider UK context, they are every bit as applicable to Scotland. They can be obviated by a trade deal which, as set out in the recommendations above, ensures a frictionless movement of life science related supplies.

Recommendations

1. The life sciences sector should be kept front and centre of the Brexit negotiation process by the UK and Scottish Governments. The UK Government needs to listen to the views from all constituent countries and their parties if it wishes to secure a trade deal which benefits all.

2. Any trade deal with the EU should assure the current status quo of frictionless movement of life science-related supplies and human biological specimens so that the risk to patient access to medicines and clinical trials is minimal, which is vital to Scotland as well as the UK as a whole.

3. Assuming an agreement with the EU on broad principles, the next priority for the UK and its constituent countries is the need for a transitional period. In this, all parties are in general agreement. The European Union has suggested such a period up to December 2020, assuming that sufficient progress has been made in key areas, and this is the least that is needed. For the life science sector, a total period of at least five years would be preferable from the Article 50 application of March 2017.

4. Building upon the excellent legacy that it has created, the Scottish Government is ideally placed to increase its efforts to encourage the life science companies in Scotland to grow, thus generating more inward investment. The Scottish Government, through its ministers and life science agencies, also needs to continue their intensive work to secure investment from abroad. Indeed, many of these companies will come from the USA, where Scotland is already developing good links and has language advantages compared to other EU countries.

5. Future public policy towards life science development in Scotland should focus where it is strongest and where growth prospects are high. The life science focus in Scotland is already on biotech/medtech/diagnostics companies, which comprise nearly half of the life sciences sector in Scotland, with pharmaceuticals at about 5%.

6. As the EU's draft negotiating position appears to suggest that continued UK membership of the European Medicines Agency (EMA) membership may be rejected, the UK Government should seek a mutual recognition agreement (MRA) between the UK and the EMA. This would ensure the free movement of medicines – built on reciprocal Good Clinical Practice inspections, the waiving of batch testing of products on entry and sharing information on inspections and quality defects. Canada already has such an MRA with the EMA, entirely separate from its recent EU trade agreement, which creates a negotiating precedent for such an arrangement.

7. Provisions for clinical trials should be included in such a UK/EMA MRA or a new one created if necessary. This area is particularly important for Scotland, which is heavily involved in clinical trials. A 'no-deal' scenario would mean that clinical trial supplies (which include specimen collection kits) from the UK/EU would require an extra Qualified Person. This may cause unnecessary delays in getting an investigational medicinal product (any medicinal product which is being tested within a trial or any product, including placebo, used as a reference in a clinical trial) to trial sites, which might hold up trial commencement, so disadvantaging the UK, and critically might interrupt treatment for patients participating in those trials.

8. The Life Sciences Industrial Strategy of 2017, which sets out detailed proposals to maintain and expand the UK's life science industry, needs to be implemented in full, with a final deadline of 2023.

9. EU migrants make a significant contribution to life sciences, including research and development, manufacturing and distribution, so access to overseas highly-skilled talent is critical for the sector. There should be initiatives to attract the skill sets necessary for the life sciences sector in Scotland, as well as developing resources from within Scotland itself. Finally, the rights of EU nationals living and working in the UK should be protected and their status secured.

10. The uptake of digital technology in Scottish Healthcare needs to be addressed if, as the Health and Sport Committee in the Scottish Parliament found, the system has too many weaknesses. These weaknesses currently undermine one of the important attractions of Scotland, with its unified NHS system and high scientific reputation.

11. It is imperative for the life sciences industry that, post-Brexit, the Supplementary Patent Certificate (SPC) regulations either remain in force as a feature of the UK's relationship with the Single Market or are transposed entirely into UK domestic law. The Supplementary Patent Certificate (SPC) extends the duration of certain rights associated with a patent, normally by about five years, but the proposed Unified Patent system, which the UK has ratified, does not have provision for SPCs, although this is still under discussion.

12. The proposed new fund in the British Business Bank, seeded with £2.5 billion of public money announced by the Chancellor in November 2017, as well as the Scottish Investment Bank's fund of £2bn over ten years, are welcome, but will need to have their resources greatly increased in size to offset the loss of funding from the European Investment Bank. The latter is Europe's largest single source of venture capital, and accounts for more than one-third of investment in UK-based venture capital funds across all sectors.

Negotiating Brexit – Facing the future

On 23 June 2016, the United Kingdom experienced a moment of unexpected and seismic change. By a relatively small margin, the British electorate voted by approximately 52% to 48% in support of leaving the EU. The referendum result represents arguably the most epochal shift in UK foreign policy since the Suez Crisis of 1956. (Chatham House Paper, October 2016)

The Scottish Government should continue to support the requirements of the Scottish life science sector within the UK and EU, ensuring that it is kept front and centre of the negotiating process. Figure 2 highlights the challenges faced by the UK life sciences market. Even without Brexit, the UK's share of the global life sciences economy is predicted to shrink and with a no-deal scenario, the sector faces significant challenges in the years ahead.

Assuming an agreement with the EU on broad principles, the next priority for Scotland and the UK is the need for a transitional period. The European Union has suggested such a period up to December 2020, assuming that sufficient progress has been made in key areas, and this is the least that is needed. It took Greenland, with a population today of 57,000, three years to leave the European Union, and the main thing that was discussed was fish. The UK is a very different proposition and on a totally bigger scale, and it may well be that December 2020 is still too soon and that a total period of at least five years is needed from the Article 50 application of March 2017.

From a life sciences viewpoint, a transitional period will give breathing space within which to resolve several vitally important issues. The Life Science Industry Coalition stated:

"A transitional period beyond March 2019 is considered critical to ensure that companies, national competent authorities and the EMA can deliver any changes necessary as a result of Brexit, whilst ensuring that other regulatory licensing, maintenance and supervision activities and supply to patients are continued without disruption." (Position Paper, 2017)

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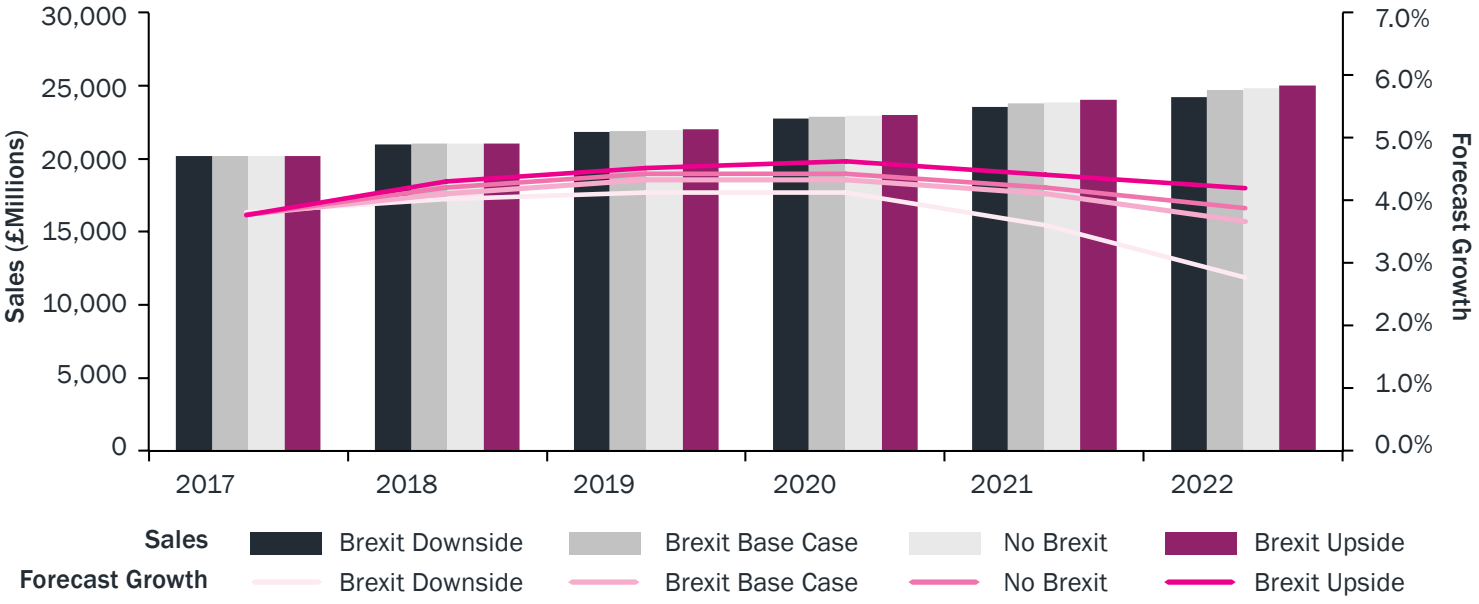
UK total market sales and forecast growth 2017–2022*

Figure: 2



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

The European Medicines Agency (EMA)

A) Medicines

The EMA plays a pivotal role in supporting medicine development for the benefit of patients. Its scientific committees provide independent recommendations on medicines for human and veterinary use, based on a comprehensive scientific evaluation of data. The agency's evaluations of marketing-authorisation applications submitted through the centralised procedure provide the basis for the authorisation of medicines in Europe. They also underpin important decisions about medicines marketed in Europe, passed to EMA through referral procedures. EMA coordinates inspections in connection with the assessment of marketing-authorisation applications or matters referred to its committees.

Many medicines are intended for a particular country, so do not go through the EMA process. The one exception is orphan drugs for rare diseases, which have to be submitted to the EMA.

The EMA is moving its headquarters from London to the Zuidan business district in Amsterdam, with the move to be completed by 29 March 2019. This move was widely understood and foreseen as a consequence of the UK leaving the EU. Of greater concern, and less expected, is that the EMA has announced that the UK will no longer be able to engage as (co)-rapporteur for new marketing authorisation applications for which the centralised procedure would finish after 30 March 2019. This will mean a loss to the EMA of experienced and qualified rapporteurs, a disproportionate number of whom came from the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK, with a serious loss of revenue for the latter. Crucially this will inevitably create delays in the licensing of, and access to, new medicines for UK patients.

Medicine manufacture involves complex supply chains, in which goods used in the research, development, production and packing are transported between facilities in different countries. There are currently no declarations on the movements of goods between EU member states. To indicate the scale of trade in finished products alone, a recent survey of member companies of the European

Federation of Pharmaceutical Industries and Associations showed that every month 45 million packets of medicines are supplied from the UK to the EU and 37 million medicines packets go from the EU to the UK. (Source: Life Sciences Coalition Position Paper, 2017)

Although there are no tariffs on medicines coming into the EU, a no-deal Brexit would mean that exports of new medicines to the EU post-March 2019 would face non-tariff barriers such as extensive batch testing requirements. This must be followed by regulatory approval, which can take up to 12 months. In addition, it is currently unclear if there are sufficient laboratories in the EU to cope with the huge increase in testing without further delays.

The time and costs required in the re-testing of medicines will drive up company costs, and substantial delays could have an adverse effect on essential medicines which have a limited shelf life and/or require cold storage.

The UK Government paper *How medicines, medical devices and clinical trials would be regulated if there's no Brexit deal (August 2018) includes the following points:*

"Most medicines on the UK market already have a UK Marketing Authorisation (MA), and this will be unaffected by our exit from the EU. However, most new medicines come to market via a licencing route overseen by the EMA. These are collectively known as Centrally Authorised Products (CAPs).

To ensure such medicines will continue to be authorised for use in the UK, all CAP MAs will automatically be converted into UK MAs on 29 March 2019....

After EU Exit, to market a product in the UK, an initial MA application will need to be submitted to the MHRA and will go through a national assessment. MHRA will take a streamlined approach to approving UKMA applications that places no greater burden on industry and ensures that patients can access new and innovative medicines at the same time as EU patients."

The EMA has offered its own guidance on the outlook for the negotiating process. In a EudraVigilance Operational Plan, the EMA indicated that it is working on the assumption that the UK will become a "third country" after March 2019 – indicating a likely hard exit from the EU.

Awareness of the very difficult situation in relation to the EMA and other EU agencies led the Prime Minister, in her Mansion House speech in March 2018, to call for the UK to become an "associate member" of the three agencies below, explaining that:

"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.

As the Health and Social Care Select Committee pointed out "the EU's draft negotiating position appears to suggest that continued UK EMA membership may be rejected." (March 2018).

If an MRA can be agreed, however, the benefits would be considerable. An MRA would cover:

- all legislation and guidance documents;
- post-authorisation pharmacovigilance data, particularly in relation to adverse drug reactions, as well as safety concerns arising from periodic safety update reports and post-authorisation obligations and commitments;
- applications for scientific advice, orphan designation, marketing authorisation or post-authorisation activities of significant public health interest;
- applications for the agreement of paediatric investigation plans;
- good clinical practice (GCP) inspections for specific products and GCP inspection reports available to EMA or the European Commission;
- information technology systems supporting regulatory processes.

Such an MRA would allow the EMA and the UK to:

- rely on each other's GCP inspections;
- waive batch testing of products on entry into their territories;
- share information on inspections and quality defects.

This is not a difficult aim. Canada already has this kind of MRA with the EMA, entirely separate from its recent EU trade agreement, so a stand-alone agreement has been shown to be possible. Indeed, MRAs have also been concluded by the EMA with Australia and New Zealand.

B) Clinical Trials

The regulation of clinical trials aims to ensure that the rights, safety and well-being of trial subjects are protected, and the results of clinical trials are credible. Although the authorisation of clinical trials occurs at member state level, the EMA plays a key role in ensuring that the standards of good clinical practice (GCP) are applied across the EU in accordance with clinical trial legislation. Clinical trials outside the EU have to comply with equivalent ethical principles where they are included in applications for EU marketing authorisation.

The way clinical trials are conducted in the European Union will undergo a major and positive change when the Clinical Trial Regulation comes into force in 2019. The Regulation harmonises the assessment and supervision processes for clinical trials throughout the EU, via an EU portal and database. The EMA will set up and maintain the portal and database, in collaboration with the Member States and the European Commission.

In its response to the Health and Social Care Select Committee's Fourth Report, the Government stated that if the Clinical Trials Regulation does not come into force during the transition or implementation period *"we will give priority to taking the steps necessary to bring into UK law, without delay, all relevant parts of the EU regulation that are within the UK's control, so that those planning clinical research can do so with certainty."* (May 2018)

This commitment is welcome as the new Regulation would be a significant improvement on existing legislation, in terms of simplification and speed of work, and has been strongly supported by the UK life science sector. Any unnecessary delay in implementing the regulation in the UK would be damaging and the target should be to implement it at the same time as it comes into practice in the EU.

Current EU regulations specify that no batch of medicinal product can be released for sale or supply prior to certification by a Qualified Person (QP) who is legally responsible for certifying that each batch of a medicinal product is suitable for release for sale, or for use in a clinical trial, and will be named on the manufacturer's authorisation. The QP is typically a licensed pharmacist, biologist or chemist, who has several years' experience working in pharmaceutical manufacturing operations and has passed relevant examinations attesting to their knowledge.

A 'no-deal' scenario would mean that clinical trial supplies from the UK/EU would be subject to an extra Qualified Person (QP) release on import into the other territory. This may cause unnecessary delays in getting an Investigational Medicinal Product to trial sites.

As clinical trials being conducted in the EU must be sponsored by an EU-based legal entity, UK-based sponsors using a UK-based legal representative would therefore need to establish a legal representative in the EU (if not already existing) to continue to conduct such trials.

The UK conducts numerous GCP inspections on behalf of the EU. When the UK leaves the EU, GCP inspections conducted by the UK may be duplicated by the EU, and vice versa. As GCP standards are common, this would create extra regulatory burden and delays with no benefit to patients.

These difficulties would undermine the Life Sciences Sector Deal (December 2017) which outlined ambitious proposals to promote inward investment in the life sciences, including UK clinical research trials, through the streamlining of clinical trial approvals processes, and further investment in NHS research infrastructure.

Against this unattractive no-deal scenario, it is reported that Recardo, a clinical-stage life science company based in California, has ceased all its drug trials of its heart drug dutogliptin in the UK, on the grounds that data collected in the UK may not be acceptable to the EMA after March 2019. This applies to Clydebank, as well as Leeds and Exeter. (Source: Pharmaforum, 3 October 2018)

Again, the simplest solution would be to extend any UK/EMA MRA, or to create a new MRA if necessary, for continuity of supply and trials, avoiding duplication of resources and involving mutual recognition of GCP inspections.

Science

Public Policy Projects

"The life sciences industry…has the advantage of very high productivity compared to other sectors, and generates a wide range of products including drugs, medical technology, diagnostics and digital tools, as well as products for consumer health. It is also widely distributed across the whole of the UK and brings significant jobs and growth to virtually every region." (Professor Sir John Bell, author of Life Sciences Industrial Strategy, 2017)

In August 2017 the Life Sciences Industrial Strategy was published in partnership with both the Department of Health and Social Care and the Department for Business, Energy and Industrial Strategy. This was followed by a Life Sciences Sector Deal in December 2017 designed to take this strategy forward.

The Strategy *"places an emphasis on putting the UK in a world-leading position to take advantage of the health technology trends of the next 20 years"* 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 medicines and devices. It 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.

Indeed, the UK has gained far more from EU science grants than it has paid out. To mitigate the risk to funding in the immediate term, the Government quickly committed to underwriting funding from EU Horizon 2020 projects secured while the UK is in the EU.

One area of concern, however, is that where high class universities have benefitted most from EU grants, the future distribution of grants by government bodies is likely to be more evenly spread across all universities. As a result, the most pre-eminent universities in science could lose up to half their income from this source.

Equally as important as funding, is the future of the UK's involvement in EU collaborative projects. The UK and its universities, including the University of Edinburgh, are active participants in Horizon 2020 and rank second in the EU in the number of participants with signed Horizon 2020 contracts. The UK's continued involvement in successor programmes, both under Horizon 2020 and in other EU areas, must be a high priority. There is a fear that such collaboration will involve the UK to a much lesser extent in the future (indeed there are reports that this is already happening) on the reasonable grounds that the UK will be outside the EU when many projects will still be underway.

Although UK access to EU funding beyond Horizon 2020 is still unknown, it is helpful that through the Life Sciences Industrial Strategy 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% of the GDP by 2027 and 3% over the longer term. This has given some confidence to the sector that the UK Government will continue to support life sciences as the UK leaves the EU.

One part of the Life Sciences Industrial Strategy is especially welcome, namely its recommendation for the creation of the Health Advanced Research Programme. This would:

- Establish a coalition of funders to create the Health Advanced Research Programme to undertake large research infrastructure projects and high risk 'moonshot programmes', that will help create entirely new industries in healthcare
- Offer continued support for genomics in medicine, including advancing proposals by the Chief Medical Officer for increasing genomic testing and screening
- Create a platform for developing effective diagnostics for early, asymptomatic chronic disease
- Use digitalisation and artificial intelligence to transform pathology and imaging
- Support projects around healthy ageing.

Given the importance of the digitalisation of healthcare, the Strategy proposed the creation of regional digital innovation hubs to ensure access and to integrate data from across the UK from local integrated care records and national datasets. This would realise the benefits of the UK's unique and patient-level data system.

The Sector Deal, which is part of the Strategy, included clinical trials, which are an important area for the industry. It outlined proposals to promote inward investment in UK clinical trials

through the streamlining of clinical trial approval processes, and further investment in NHS research infrastructure.

Looking ahead, the Life Sciences Industrial Strategy needs to be implemented in full, with a final deadline of 2023. This should be supported with commitments to other domestic measures such as the Accelerated Access Review of 2016, which also set out recommendations to speed up access to innovative healthcare and technologies, to improve efficiency and outcomes for NHS patients.

Life Science Staff

"Medium sized member companies in the UK tell us that up to 30% of their research and development staff are non-UK EU nationals. Multinational companies' research and development facilities in the UK have a non-UK EU national workforce of about 20%. We are aware of university spin-outs where 60%+ of their researchers are non-UK EU workers." (Life Sciences Industry Coalition Position Paper, 2017)

As the paper emphasises, EU migrants make a significant contribution to life sciences in the UK, including research and development, manufacturing and distribution. A potential cessation in the rights of these professionals to work in the UK may cause a staffing crisis within the NHS and lead to disruption in the life science sector more broadly, leading to longer waiting times for patients. Equally, the UK is a key contributor to the European life sciences ecosystem. The UK contributes to life sciences internationally through various means, including leading universities, a developed technology transfer system, funds to support the commercialisation of science and the work of institutes and research charities.

The UK and EU are home to numerous multinational companies with international functions. Companies seek a multinational workforce to reflect their multinational nature. Both UK and EU based companies should ensure that inter-company transfers remain simple post-Brexit. The intra-company transfer process should facilitate movement of people employed overseas by life science companies into the UK, and for UK nationals to spend time in other company sites in the EU.

The Government has acknowledged that *"a significant number of EU nationals are vital to the country's health research landscape in universities and the NHS. These include academic clinicians working at all levels from doctoral researchers to professional[s] and across all research disciplines, and research support and delivery staff."* (Government response to the Health and Social Care Fourth Report, May 2018)

An early agreement on citizens' rights in the negotiating process between the UK and the EU is crucial in order to provide an element of certainty for EU citizens working in the UK. An early agreement would also ensure that healthcare providers and life science professionals, including their families and spouses, are able to prepare for, and adapt to, a future agreement. International collaboration and multi-national working environments should continue to be fostered to facilitate the exchange of expertise between life-science professionals.

Intellectual Property

The UK is 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 benefits to UK pharma industry are twofold: the single application procedure has substantially reduced the cost of obtaining a patent, and the single body of law which has grown under the EPC has allowed the UK to influence the shape of European IP law.

The EPC does not create a one-stop patent per se, however. A European Patent is in fact a bundle of national patents which must be enforced or challenged on a country-by-country basis: pharma innovators therefore face the challenge of policing national patents in up to 38 separate jurisdictions. A solution to this problem has emerged after more than 40 years of negotiations in the form of the Unified Patent (UP) overseen by a Unified Patent Court (UPC). UPs would be truly European patents, enforceable across 25 EU member states in a single court. 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 Government delighted the business world in November 2016 when it announced that it would ratify the UPC agreement, and in April 2018 the Government deposited the instrument of ratification with the European Commission. An unexpected problem is that German ratification has been delayed by a complaint filed with the German Constitutional Court, but, assuming that this can be sensibly decided, the treaty will then come into force.

A separate issue concerns the supplementary patent certificate (SPC) that extends the duration of certain rights associated with a patent. A supplementary protection certificate comes into force only after the corresponding general patent expires and normally has a maximum lifetime of 5 years, although this may be extended under certain circumstances to 5.5 years. SPCs provide crucial extended protection for certain patented medicines which have unusual barriers to marketing – for example, particularly lengthy or onerous regulatory requirements. Currently the proposed UP system does not have provision for SPCs, although this is still under discussion.

If the UP system does not include SPCs, companies face a situation where exclusivity is longer in one country than another, leading to double the litigation. It is therefore imperative for UK pharma that, post-Brexit, the SPC regulations either remain in force as a feature of the UK's relationship with the Single Market or are transposed entirely into UK domestic law.

The Supply Chain

As previously explained, the production of medicines involves complicated supply chains in which the goods used in the research, development, manufacture and packing are transported between facilities in different countries.

There are currently no declarations on the movement of goods between EU member states. Once goods from outside the EU have been cleared in customs at the EU border, they are in free circulation within the EU. Many UK biotechnology and pharmaceutical companies rely on this free movement of goods within the EU in their supply chains and vice versa. As stated earlier, it is estimated that every month 45 million packets of medicines are supplied from UK to the EU, with 37 million medicines packets going from the EU to the UK.

The Customs Freight Simplified Procedure (CFSP) fast-tracks arrivals by air within the UK for laboratories receiving samples for testing. Administered by Her Majesty's Revenue and Customs, CFSP is an electronic customs system for imported third country goods. It allows the faster release of goods from countries that are not members of the European Union at the frontier or inland, the use of simpler customs declarations and cash flow benefits to importers.

In the event of a no-deal Brexit, CFSP could be extremely useful. There are two CFSP procedures. The Simplified Declaration Procedure is used for releasing goods at the frontier to most customs procedures and is particularly useful for importing time-sensitive goods such as those used in clinical trials. The Local Clearance Procedure is used for moving goods from the frontier to storage and then releasing them to a customs procedure

Even with this CFSP qualification, a withdrawal from the EU without agreement ahead of 29 March 2019 would mean that UK-EU trade would fall under World Trade Organisation (WTO) terms.

The main points are:

- There will be no financial tariffs (subject to the paragraphs below), but it is vital that no non-tariff barriers are imposed between the two sides
- Customs controls at UK-EU borders will be imposed if the UK is not within the Customs Union or the Single Market. These controls will be costly and time-consuming, with serious risks of limiting and delaying patient access to medicines; to avoid this, the parties will need to find a solution to deliver frictionless trade after Brexit
- Value Added Tax (VAT) will be one of the most complex and challenging areas after the exit of the UK. VAT will need to be pre-funded by pharmaceutical companies. This will have a significant cash-flow impact on pharmaceutical companies

- In the context of the Free Trade Agreements (FTAs) concluded by the EU with third countries, which include preferential measures for goods developed in EU member states, the exclusion of the UK from FTAs would automatically exclude all operations undertaken in the UK from this preferential treatment and have an impact on EU exports. The UK also risks losing the benefits of Mutual Recognition Agreements (MRAs) between the EU and third countries. If the UK were to operate under a WTO framework, customs declarations would be required for exported and imported goods to and from the EU, as well as from non-EU states. This includes investigational medicinal products, intermediate goods, finished goods, research goods and services.

Crucially the WTO's Pharmaceutical Tariff Elimination Agreement means that finished pharmaceutical products and certain components are subject to zero per cent tariffs. The Pharmaceutical Tariff Elimination Agreement is based on a negotiated list of finished products and ingredients. The agreement has not been updated since 2010.

It has been estimated by IQVIA that, as a result, up to 1,000 finished products and 700 ingredients are not currently included in the list and would therefore be subject to tariffs when traded on WTO terms. IQVIA MIDAS data shows that New Active Substances launched since 2010 have generated sales of around $12bn in the past five years. Tariffs could therefore present a risk to NHS budgets in the case of a no deal and could cost manufacturers extra where the product crosses the UK/EU border multiple times during manufacture.

Increasingly time-consuming customs controls in medicine supply chains will have an economic impact on the medicines trade. More importantly, however, customs controls and additional administrative requirements on companies to seek any form of additional authorisation would increase burdens on both the UK and European authorities, as well as businesses, meaning that patients will have to wait longer to receive important medication; more critically some medicines require cold storage or have short shelf lives, and thus cannot sit at borders.

If companies are required to obtain Authorised Economic Operator status, the concern is that neither the UK authorities nor business would be able to handle the additional workload in the short term. In terms of administrative requirements, importers and exporters will be required to file Customs Declarations with the EU and UK. Traders will also need to hold additional data to support the correct completion of these declarations. The costs and time required to complete these declarations (including fees paid to customs agents) will be substantial.

Finance

Financing for biotech companies, particularly those starting up, but also existing SMEs, is often their overriding concern.

A company that runs up considerable R&D costs, whilst still having no product income, is exceptionally vulnerable. If drug development takes longer than planned in either the research or regulatory phases, biotech companies will seek follow-on funding or enter strategic partnerships with pharmaceutical companies looking to improve their pipeline.

The financial system in the UK has advantages and disadvantages. Private equity is equity capital provided to enterprises quoted on a stock market. The amount of private equity investment in the UK in 2016 was £756m, virtually unchanged since 2013, with the number of companies receiving private equity investment falling from 80 in 2016 to 67 in 2016. The amount raised in global life sciences Initial Public Offerings fell from £1.6bn in 2016 to just £22m in 2017, although it should be noted that this is an area notorious for its extreme volatility, so too much should not be read into one year's figures. (Source: Life Science Competitiveness Indicators, Office for Life Sciences, May 2018)

Indeed, the UK BioIndustry Association has provided more encouraging recent news, with the Biotech Financing Update June-August 2018 showing an acceleration in venture capital fundraising and an increase in the amounts raised in Initial Public Offerings in the second half of the year. The Update also found that that UK biotech companies had already raised more than £1.5 billion in 2018, surpassing the 2017 annual total of £1.2 billion.

One of the main sources of income, which has been adopted by many large biopharmaceutical companies, is corporate investment or corporate venture capital (CVC), where

corporate funds are invested directly into external start-up companies. This form of capital has played a role in venture financing since the 1960s, but has grown in importance, particularly in the biomedical sector, since the 1990s.

From the perspective of the investee biotech, CVC investment may bring access to sector-specific expertise, contacts and resources, which other finance routes may not provide. Importantly, CVC investment is also often more patient than venture capital, as corporate investors recognise and understand the timelines involved in bringing new medicines to the clinic, and often have strategic rather than purely financial drivers for investment.

Since 2000 some $34bn of investment has been made by pharmaceutical equity investors and their syndicate partners in biotech companies globally, however only a relatively small proportion of this has been invested in UK companies. A higher success rate could potentially result in an increased R&D footprint from these operations in the UK.

As the Association of the British Pharmaceutical Industry noted:

"Between 2014 and 2017, $2.9bn was raised by privately owned emerging companies compared to $1.2bn raised in the previous three years. The scale of the increase in corporate equity investment in UK biotech has been phenomenal. The amount of capital invested alongside CVCs into UK companies increased six-fold between 2010 and 2015, so that about 60% of financing rounds in 2016 included a CVC, or $567m of $965m invested. The UK's share of European financing rounds involving a CVC reached 60% by mid-2016, up from about a fifth a decade ago. The growth in validating investment by pharma is arguably leveraging record levels of investment, but the potential is even greater." (The rise of corporate venture capital investment in *UK Biotech*, December 2017)

The main disadvantage of CVC, as explained in the Life Sciences Industrial Strategy, is that whilst the UK has relied heavily on angel investment (i.e. that by individuals) and CVC support for its SME sector, those who fund the latter typically seek to exit their investment within the life of their funds. To realise their profits within 5-7 years after investing leaves little time for companies to grow and scale. Given that the time taken from the patenting of a new medicine to production will normally be some 12 years, sometimes longer, the disadvantages are obvious.

This is why there has been increasing interest in Patient Capital, defined as investment supporting entrepreneurs and investors in order to make a return from the substantial growth of a business rather than through short-term profits from low-risk projects. Although these have been growing, the UK continues to lag the USA on a per capita basis, by billions of pounds of the capital necessary to grow solid and sustainable companies.

As the Chancellor of the Exchequer pointed out, the barrier:

"continues to be access to long-term investment. This slows these firms' growth, dampens their ambition and means that some firms are sold to trade buyers rather than growing to maturity in the UK. Overall levels of productivity are reduced as a result because some firms do not fulfil their economic potential." (August 2017)

This has led the Government to publish a consultation paper on "Financing growth in innovative firms" (August 2017) with reference to Patient Capital, to which the industry has already responded.

The review considered the European Investment Bank, of which the European Investment Fund is part. This is Europe's largest single source of venture capital, has been very successful in encouraging entrepreneurs to operate in this sector, and accounts for more than one-third of investment in UK-based venture capital funds across all sectors. If Brexit means there will be much less money for the UK – it may not be zero, but it will become a trickle (Forbes, 21 November 2016) then, as the Life Sciences Industry Strategy paper recommends, it must be replaced by another source of capital.

In his Budget speech of November 2018, the Chancellor announced that a new £2.5 billion Investment Fund would be established. It would be incubated in the British Business Bank with the intention to float or sell once it has established a sufficient track record. By co-investing with the private sector, a total of £7.5 billion of investment will be supported. This is an important first step, but it will need to be built upon.

In looking to improve the efficiency of UK public markets for life science companies, it is instructive to look at the USA's 'Prudent Person Rule' in 1979, which allowed pension funds to invest in higher risk assets, creating a flood of new risk capital into the sector. Most UK CVC companies lack the deep pools of risk capital seen in their American equivalents which, in turn, appears to condition the ambitions of UK life science companies and their approaches to raising private and market finance.

As the Life Sciences Industrial Strategy review concluded:

"Conservatism amongst UK investors appears widespread and underpins the challenges in raising long-term capital funds. Pension funds that invest in this sector actively in the US are not participants in this sector in the UK and influencing and educating gatekeepers for these funds to consider this sector should be a priority."

A final point here, which relates to one mentioned above, is that the UK needs to address the free movement of skilled workers, as this could otherwise undermine future investment and the financial attractions of the UK. At present, the UK provides excellent access to experienced senior management as well as to skilled and specialist staff, so, if this were to be put into question by Brexit, the implications for funding the life science sector would be adverse and financially damaging.

Q² Solutions – A Case Study

Q² Solutions is an example of the kind of company which both contributes to and benefits from the strengths of Scottish life sciences.

With the combined resources of IQVIA and Quest Diagnostics, the Q² Solutions joint venture was formed in 2015 by combining the best of each parent organisation's capabilities in clinical trials and laboratory services.

As set out in the Background section, Scotland is already a leading global cluster for life sciences, employing over 37,000 people across some 700 organisations. Q² Solutions have almost 900 employees in Livingston, making it the largest employer in Scotland in the life sciences sector.

The sections below explain why Q² Solutions came to Scotland, what it does and how it can expand.

The general attractions of Scotland were set out in a section earlier in this paper, but the specific benefit was that it is an ideal location in which to conduct clinical research.

Q² Solutions was also drawn to Scotland because of its positive tax incentives, a highly educated workforce, favourable costs and excellent logistics.

The key work of Q² Solutions lies in its laboratories. In Livingston it carries out 4 million clinical trials tests a year, with 900,000 custom sample collection kits assembled and shipped annually.

Around 70% of shipments at Livingston are within the EU countries. Others involve Russia (13%), the Ukraine (9%) and other non-EU countries. Interestingly, the UK itself accounts for just 6%, which underlines the European nature of the Q² Solutions services.

The process begins with pharmaceutical companies sharing their clinical trial protocols with

Q² Solutions. The latter then sets up the studies in their systems, builds specimen solution kits and ships the kits to investigator (medical doctor) sites. The investigator site personnel collect specimens (mostly blood) from patients, which are delivered to Livingston; the boxes of specimens are unpacked, processed and analysed; and the results conveyed back to the investigators, so they can treat the patient, and results data is electronically transferred to the pharmaceutical company for analysis and regulatory filings.

Oncology accounts for 30% of Q² Solutions work; immune and infectious diseases comprise 11%, as do endocrine and metabolic disorders; the central nervous system and pulmonary each account for 8%; and the remainder is spread over a wide therapeutic field.

Quality control is critical to the whole process, which is why the Livingston site is modern, has top quality equipment and operates within well-developed protocols.

The Alba Campus facility comprises 115,000 square feet and has seven main functions:

- Full service laboratory
- Translational science laboratory
- Sample management
- Kit production, logistics, warehouse
- Project services

- Support functions
- Management team for Europe, the Middle East and Africa.

The future expansion of Q² Solutions could be affected in the first instance by the result of the Brexit negotiations.

The service depends upon the free movement of investigative medicines and biological samples and being able to turn around biological samples flown into Livingston from across Europe in 24 to 48 hours. The optimal delivery of clinical trials samples combined with research institutions has the potential to facilitate the next evolution of delivery.

As explained in this paper, the Customs Freight Simplified Procedure (CFSP) fast-tracks arrivals by air for laboratories like those of Q² Solutions, which receive samples for testing.

In the event of a no-deal Brexit, CFSP will enable the continued frictionless movement of human biological samples. There are two CFSP procedures. The Simplified Declaration Procedure is used for releasing goods at the frontier to most customs procedures, particularly useful for importing perishable goods. The Local Clearance Procedure is used for moving goods from the frontier to storage and then releasing them to a customs procedure.

Almost as important will be the continued ability to attract highly qualified scientific staff from abroad, as companies like Q² Solutions have a multinational workforce. Whilst only a very small percentage of the Livingstone workforce is from abroad, the importance of this issue is explained at length in this paper, with a recommendation that the UK Government reviews how the Scotland specific shortage occupation list is agreed and considers including a Scottish representative in the decision-making process, as recommended by the House of Commons Scottish Affairs Committee.

The main purposes of this paper have therefore been to emphasise the complexity and importance of the Brexit vote for the life sciences industry, and the key need for as free a trading partnership as possible to emerge from the negotiations.

It is vital for the UK to obtain a special trading relationship with the EU, securing the trade and free movement of medicines, biological supplies and investigative medicines and diagnostics, and retaining the flexibility to attract professional staff.

In the meantime, the potential growth of Q² Solutions is reflected by the size of the clinical trials market, which accounts for one-third of total biopharmaceutical R&D spending and is constantly expanding.

Q² Solutions has not only created the Alba Campus, making it a premier global clinical research site, but it is expanding its Scottish workforce, which has increased by 12% since Q3 2017. The company's future growth plans include the development of the genomic services being provided by the Alba Campus.

Genomics is where the future lies and brings together academic research, practising clinicians and commercial experts to understand more about how our genes affect our health and risks of disease. This research is finding new personalised treatments and medicines which will benefit patients in Scotland as well as in other countries.

The Scottish Genomes Partnership is a good example of what is happening. It involves a major Scotland-wide research programme between the Universities of Edinburgh, Glasgow, Aberdeen and Dundee, with NHS Scotland, NHS Lothian, NHS Greater Glasgow & Clyde, NHS Grampian and NHS Tayside. It offers a range of genomic services to support drug discovery, precision medicine and clinical development.

The programme is funded by the Scottish Government's Chief Scientist Office and the UK's Medical Research Council.

The research includes a collaboration with the Genomics England 100,000 Genomes Project. Recruitment to this study is through the four nationally designated NHS Scotland regional Clinical Genetics units and Genetic laboratories in Aberdeen, Dundee, Edinburgh and Glasgow. These sites provide genetic services across Scotland and are able to recruit participants to the study from all NHS Scotland Board areas.

The Scottish Genomes Partnership has prioritised patients with rare diseases and cancer, working alongside the Scottish NHS and the partner project at Genomics England. These patients will have their whole genome (their entire genetic makeup) mapped, leading to precise diagnoses of the causes of their disease. This often involves patients whose diagnoses have eluded medical investigation by other means for many years.

Q² Solutions provides a range of genomic services to support drug discovery, precision medicine and clinical development. This will be done by supporting others in their clinical trials and research efforts across the industry spectrum, working also with academia, government bodies and voluntary bodies. It also means that 'big data' solutions will enable precision medicine, resulting in shorter clinical trials and increased benefit-risk profiles for patients.

In this, the 70th anniversary of the founding of the NHS, there is a great opportunity for the life science industry and the NHS, together with academia and government, to enhance the current collaborative efforts in Scotland for the benefit of patients and the wider economy.

Next Steps for Scotland

The attractions of Scotland for life sciences were set out in the section headed "Why Scotland?" The aims and implications around the Brexit negotiations and the consequential results for the UK, including Scotland were set out in the next stage.

The purpose of this section is to review what else the Scottish Government may wish to consider about how best to support its life science base.

On the major issue of the single market and customs union, the First Minister said:

"Most of you already know the position I take – I deeply regret the UK's decision to leave the EU. And I believe the absurdity of the on-going UK Cabinet discussions and disputes over post-Brexit customs arrangements strengthens one of the basic arguments that the Scottish Government, together with many businesses, has been making. And that argument is that in our view the best approach - if the UK is determined to leave the EU – is to remain in the single market and the customs union.

It is the obvious democratic compromise, in a UK where 48% of voters – and two out of four nations - chose to remain in the EU. And it's also the least damaging solution economically. So, my government will continue to make common cause with allies - including other political parties and governments and businesses across the UK, for a measured, sensible approach." (16 May 2018)

The Prime Minister, Mrs May, has made clear that the UK will leave both the single market and the customs union, however given the Parliamentary arithmetic in the House of Commons, it is extremely difficult to predict the outcome. The possibilities range from a no-deal Brexit to a Chequers-style compromise, from a Canada style trade deal to staying in the single market and customs union like Norway, to the question of a second referendum.

Whilst it is easy and sometimes enjoyable to speculate, the First Minister concluded that:

"However, the prospect of Brexit reinforces the importance of all of the other steps we are taking to create a strong business environment. Scotland is working hard to attract inward investment. We are already the most successful part of the UK outside London and the south east when it comes to attracting inward investment." (Ibid)

Attracting New Investment

According to a Scottish Enterprise economic trends survey, companies in the life sciences sector are among the least optimistic about Scotland's economic outlook (only 33% expressed a positive view), although only 3% expressed an outright negative view. Political uncertainty is the main reason clouding the economic outlook, quoted by 56% of respondents. (Source: Scottish Parliament Report, March 2018)

This is a worrying if understandable development, and the best response is for the Scottish Government to continue – as it has been doing – to meet and encourage life science companies already in Scotland, setting out all the country's advantages, and seeking to attract companies elsewhere in the UK and from abroad. This requires a thought-out campaign, going further than what has been done to date.

The life science focus in Scotland is already on medtech/ diagnostics companies, which comprise nearly half the life sciences sector in Scotland, with pharmaceuticals at about 5%. It therefore makes sense for Scotland to focus where it is strongest, and where growth prospects are high compared with pharmaceuticals. Many of these companies will also come from the USA, where Scotland is already developing good links and has language advantages compared to other EU counties.

The financial support that Scotland can offer is crucial, as it is one of the main drivers of innovation and attracting new investment.

According to a Life Sciences Scotland survey published in July 2018, getting the right financial support will be the biggest challenge facing the sector over the next five years, as this is needed to accelerate revenue, attract the right people with the correct skills and increase customers and sales.

The Scottish Government has a good record in investing in life sciences, and last year the First Minister announced a £45m boost for business research which, spread over three years, represents a 70% increase in Scottish Government funding for businesses to conduct new R&D projects. (Source: Daily Business, 31 August 2017)

The UK Government's decision to invest an extra £20bn in the NHS by 2023/4 means an increase in funding of around £2bn for Scotland. The then Scottish Health and Sport Minister, Shona Robison, pledged that "every penny" of the extra funds would be allocated to the Scottish health service, which is understandable given the pressures on GP practices and hospitals, but within this allocation emphasis could be put on encouraging life sciences development within the NHS. (Source: The Telegraph 17 June 2018)

If the UK economy is stabilised over the next years, then more resources should become available to build upon the grants and investments being made by the Scottish Government.

The Scottish Enterprise Board is important in that it can offer to match accredited investment partners up to a maximum of 50% of the total funding package on a commercial basis, however the operative word is "can" – there are no certainties.

A further measure to encourage investment has been the announcement by the Scottish Government that a Scottish Investment Bank will be set up in 2019 to provide some £2bn for Scottish firms over the next ten years (Source: The Scotsman 8 May 2018). This is a useful start in helping to offset the loss of funding from the European Investment Bank, although some may think that the £2bn will need to be increased.

Immigration

Between 2016 and the next quarter century the number of deaths in Scotland is projected to be higher than the number of births every year. Any increase in population will be due to net immigration. (Source: National Records of Scotland, October 2017)

This helps explain the very great concern that Scotland cannot sustain the future population which it needs to achieve economic growth and to meet the needs of an ageing population. It has led to calls for a more formal role to be given to Scotland by the UK Government in commissioning and determining what occupations have shortages in Scotland. This issue is particularly relevant to the life sciences industry, which is so dependent on professional expertise from abroad, whether in universities, NHS Scotland, company management, or of analysts or other professional staff.

The House of Commons Scottish Affairs Committee endorsed this concern and made important recommendations as set out below:

"The Scottish Government pointed out that currently it has no formal role in determining which occupations are on the shortage occupation list for Scotland and that Scottish Ministers cannot commission the MAC [Migration Advisory Committee] to consider changes to the list. Instead the Scottish Government contributes to calls for evidence in the same way as any other stakeholder. It supports the proposal in Dr Hepburn's report that the UK Government should give it a formal role in commissioning and determining what occupations are in shortage in Scotland but has also expressed reservations about whether the shortage occupation list is a helpful measure in the longer term. Dr Allan told us that: We feel that Scottish Ministers could

not unreasonably have some role in the say on what the Scottish shortage occupation list is. At the moment, we can be consulted in the same way as a trade union or a business interest can be consulted, but Scotland is a bit more than that and we feel that we should have more of a role....

We recommend that the UK Government reviews how the Scotland specific shortage occupation list is agreed, including considering having a Scottish representative involved in the decision-making process. We also recommend that the UK Government reviews how it engages with the devolved administrations on areas of policy—such as immigration—which are reserved but of clear importance to the devolved administrations." (July 2018)

The Committee also commented on the inclusion of students in the immigration totals:

"The Higher Education sector is an important asset to the Scottish economy and encouraging international students to live and study in Scotland is an effective way of bringing new talent to the country. We do not believe it makes sense for the Government to include student numbers in the net migration target, whilst at the same time investing in ways of encouraging more students to come to the UK. Whilst we accept that the actual impact of student numbers on the target may well be minimal, we believe that the message given by current policy is confused and counterproductive. We recommend that student numbers are removed from the figures used to monitor the net migration target, and that the Government clarifies its message to welcome international students to the UK."

In these circumstances, it is widely recommended that the Scottish Government takes up this approach. Scotland should be represented in the decision-making immigration process. EU migrants make a significant contribution to life sciences, including research and development, manufacturing and distribution, so access to overseas highly-skilled talent is a major issue. Indeed, the Select Committee felt that the UK Government was reconsidering its stance on students, for which pressure has been building across the country and within the Westminster Parliament.

Digital Technology

Digital technology has the potential to change the face of health and social care delivery.

In March 2017 the Scottish Government published 'A Digital Strategy for Scotland'. This aims to *"ensure that Scotland is recognised throughout the world as a vibrant, inclusive, open and outward-looking digital nation". It also comments "The Scottish Government will create the conditions which encourage continuous innovation and improvement in our public services."*

The Health and Sport Committee of the Scottish Parliament issued a report in February 2018 on "Technology and innovation in health and social care." The report reached several conclusions:

- Evidence showed a disconnect between Scottish Government strategies and local delivery. This was considered by some to have contributed to the slow adoption of mobile devices and medical technologies. Some respondents felt that variations at NHS board level hampered the delivery and implementation of the eHealth strategies. The Information Commissioner's Office (ICO) noted that the implementation of strategies has been impacted by an imbalance of decision making between technical leaders and clinical leaders
- A disconnect was also found between Scottish Government strategy and local delivery, and unwanted variation between NHS boards
- There is an absence of financial information on how the strategy will be funded. There should be a financial framework to accompany the strategy.

The Committee was surprised to find a culture that was reluctant to adopt new ways of working and where innovation was not encouraged. Heavily out-dated IT systems still caused major barriers. Because decisions were made on a board-by-board basis there was little leadership in technology and innovation. Often the boards or specialities that showed strength in technology and innovation only did so because of a clinician who had a personal interest.

The Report's key conclusions are so important that they are set out below:

"This cannot continue. The Scottish Government must take ownership and ensure the nature of the NHS changes to welcome new and innovative ways of working. Only by having a "once for Scotland" approach can any meaningful changes happen. It is no longer acceptable in this age that our health service is still using multiple incompatible systems and various platforms. In all our work we have heard repeated concerns around data sharing and interoperability.

Nurses, pharmacists, allied health professionals, social care services, primary care services, prison health services and more, are all highlighting the fact they do not have timely access to relevant health records. This is an area the Scottish Government must tackle urgently to ensure appropriate medical care can be given in the right place at the right time. Work must be done to update systems, so they can interact, whilst work must also be carried out to ensure data protection requirements and opportunities to share data are better understood...

The uptake of technology in the NHS that offers remote monitoring and new time and cost saving ways of working seems very slow and inconsistent. This seems surprising when people so readily use such equipment in their personal lives for health and other areas such as banking. More must be done by the Scottish Government to increase the use of technology across NHS boards and social care. This cannot be left to be agreed on a board by board basis. Such a piecemeal process leads to increased variation in health outcomes across Scotland. We expect the use of technology should also lead to a reduction rather than an increase in health inequalities."

One reason why Scotland is attractive for life science companies, is because it has a unified NHS and access to some of the best data in the world, but if the system is as weak as the Committee found, this undermines its claim to be at the forefront of technology in the healthcare field. This needs to be addressed.

This challenge is also an opportunity. If the issues are addressed, with a robust and effective system as the end result, this would add considerably to the attractiveness of Scotland for future investment by life science companies.

Glossary

Authorised Economics Operator - the Authorised Economic Operator (AEO) certification is an internationally recognised quality mark indicating that your role in the international supply chain is secure, and that your customs controls and procedures are efficient and compliant.

It is seen by the UK Government as a means of reducing post-Brexit delays. The scheme is available to any company involved in the international supply chain which carries out customs related activities in the EU, including manufacturers, exporters and importers. The benefits include simplified customs procedures and the possibility of fast-tracking shipments in some cases. Demand for AEO status has seen the timeframe for approvals increase and it can take months for approval from the UK authorities. The scheme may not be appropriate to every company, particularly when additional procedures (such as veterinary checks) need to be carried out at the border.

Good Clinical Practice - Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and wellbeing of trial subjects are protected, and that clinical trial data is credible. The protection of clinical trial subjects is consistent with the principles set out in the Declaration of Helsinki. This is a statement of ethical principles developed by the World Medical Association. Requirements for the conduct of clinical trials in the European Union (EU), including GCP and good manufacturing practice (GMP) and GCP or GMP inspections, are implemented in the Good Trial Directive (2001) and the GCP Directive (2005).

Horizon 2020 Associated Countries - Associated countries participate in Horizon 2020 under the same conditions as the 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 to, 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.

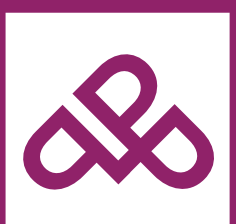
Mutual recognition agreements (MRAs) involving the EMA are trade agreements with the EU that aim to facilitate market access and encourage the greater international harmonisation of compliance standards while protecting consumer safety. They can vary from one MRA to another, but broadly they allow EU authorities and their counterparts to rely on each other's inspection systems; share information on inspections and quality defects; and waive batch testing of products on import into their territories. MRAs are already in place with Australia, Canada, Japan, New Zealand and Switzerland, and the USA has a transitional MRA.

NHS Research Scotland - formed through a partnership of Scottish NHS Boards and the Chief Scientist Office, NHS Scotland works to ensure that NHS Scotland provides the best environment to support clinical research. It's work includes helping to deliver high quality studies in the NHS; providing a solid infrastructure to deliver trials to meet deadlines and targets; and connecting NHS, industry and academia to accelerate the development of new treatments, devices and diagnostics to tackle complex healthcare needs.

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 their business, and/or equity investment from external investors, such as business angels, venture capital funds or the public markets. In addition, some forms of debt instruments (e.g. venture debt) may meet this definition, and some forms of equity investment may not (e.g. some approaches to leveraged investment). Patient capital supports entrepreneurs in bringing 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.

The Prudent Person Rule refers to a legal maxim in the USA that is also called the "reasonable man rule". Under this rule, a person need not possess exceptional investment skills, but must exercise discretion and average intelligence while making investments that would be considered proper or sound. In 1978, the attractiveness of venture capital received a shot in the arm when the 1978 Revenue Act reduced the capital gains rate from 49 1/2% to 28%. The flow of monies into venture capital funds jumped from $68 million to nearly $1 billion. In 1979, Congress passed the "Prudent Person" Rule that allowed pension funds to invest in venture capital. By 1983, new commitments exceeded $5 billion.

Scottish Genomes Partnership - the Scottish Genomes Partnership is a major Scotland-wide research programme between the Universities of Edinburgh, Glasgow, Aberdeen and Dundee, with NHS Scotland, NHS Lothian, NHS Greater Glasgow & Clyde, NHS Grampian and NHS Tayside. The programme is funded by the Scottish Government's Chief Scientist Office and the UK's Medical Research Council. The research includes collaboration with the Genomics England 100,000 Genomes Project. Recruitment to this study is through the four nationally designated NHS Scotland Regional Clinical Genetics Units and Genetic Laboratories in Aberdeen, Dundee, Edinburgh and Glasgow. These sites provide genetic services across Scotland and are able to recruit participants to the study from all NHS Scotland Board areas.



Public Policy Projects