SOIF SCHOOL OF INTERNATIONAL FUTURES

CANCER RESEARCH UK

FUTURE OF CLINICAL TRIALS AFTER BREXIT

FINAL REPORT

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This report was commissioned by Cancer Research UK. It was conducted and authored by School of International Futures and any views expressed do not necessarily reflect the views of the Cancer Research UK

About School of International Futures

School of International Futures (SOIF) was conceived to meet the growing demand for strategic foresight among international policy officials, business leaders, analysts and activists. We help organizations think differently – and more confidently – about the future.

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Executive Summary

This report was commissioned by Cancer Research UK (CRUK) to explore the impacts of Brexit on the future of clinical trials as a whole and cancer trials in particular in the United Kingdom (UK) and European Union (EU).

It was carried out by the School of International Futures (SOIF) and informed by exchanges with participants from across the clinical trials sector, including researchers, industry, patients, policy makers and regulators in the UK, EU and internationally.

Europe is a world leader in the development and running of clinical trials. Over 4,800 UK-EU trials were conducted between 2004 and 2016.

Patients in the UK and Europe benefit from the UK's participation in EU trials and this has helped improve access and patient recruitment in rare disease and paediatric trials.

As the world's largest independent cancer charity, CRUK supports research into all aspects of cancer with the aim to accelerate progress so that three in four people survive their cancer for 10 years or more by 2034. Of the 200 trials directly funded by CRUK, 28% involve patients from countries in the EU. Therefore, to help achieve this ambition, it will be important to reach the best possible outcome for clinical trials after the UK exits the EU.

A future shaped by Brexit has introduced significant uncertainty over the future of clinical trials and the UK's ability to collaborate with and engage in European trials. In particular, delays to the implementation of the EU Clinical Trial Regulation (EU CTR) have resulted in its exclusion from the UK's European Union (Withdrawal) Bill. The EU CTR is now expected to be implemented in the EU in 2019 although there are some concerns that implementation will be further delayed.

The EU CTR has been designed to address existing and future barriers to the conduct of clinical trials in Europe. The UK clinical trial community played a significant role in the development of the CTR, intended to be an improvement from the existing Clinical Trial Directive (CTD). Where the UK is not aligned after Brexit, it may not be able to take advantage of the proposed changes. In addition, the uncertainty presented by Brexit about the possibility of future regulatory divergence risks losing the UK's ability to remain at the forefront of international trials.

However, there were some suggestions that if the UK takes a proportionate approach to regulation that balances alignment with opportunities to innovate it could help the UK to stay internationally competitive.

There are also broader concerns as to how Brexit will impact clinical trials. These include impacts on trade, access to new medicines, data, funding and the workforce. Factors that together will influence the competitiveness of the UK to conduct trials.

Any additional barriers to conducting trials are perceived to be a deterrent to where they are placed. There is the potential for the UK's attractiveness as a hosting country and research partner to be at risk, with negative impacts for patients.

Ensuring a positive outcome for clinical trials over the next decade

As phase II negotiations get under way, it will be critical to ensure that the final Brexit outcome takes into consideration the important role that trials play in supporting research and patient experience, as well as society and the economy to the UK and EU.

It is also important to ensure that short-term uncertainty around Brexit does not distract from the sectors ability to plan for broader changes that are likely to occur – from changes in demand for healthcare, new technologies from gene editing to data, new trial designs, and changes in the social and political environment.

Participants in the project saw a number of opportunities and challenges for the sector associated with these broader shifts. The project used a futures approach based on horizon scanning, trend analysis and scenario planning to explore these within a ten year time horizon (up to 2028) and to identify a set of key recommendations: short- or long-term actions that government and the wider sector need to take to ensure the best possible outcome for trials for the benefit of both the UK and the EU.

Section 1 provides an introduction to the project approach, scope and context

Section 2 outlines the key implications and recommendations

Section 3 reflects on the key insights and messages from the report.

We are grateful to the support and participation of all those who generously took part in the interviews, survey and workshop. Selected quotes from some of the project's participants have been included throughout this report.

Further information on the scenarios and a participant list is provided in the Annexes at the end of the report.

Recommendations:

1. Priorities for negotiations

Regulation

- The UK government should continue to seek full regulatory alignment with the forthcoming EU Clinical Trial Regulation (EU CTR). This should include a bespoke agreement for access to the EU portal and database and to ensure the UK can take part in the centralised assessment process.
- Where full alignment with the provisions of the EU CTR is not possible, the UK government should seek a proportionate approach to regulation that balances alignment with the opportunities to innovate.

Access to medicines, Investigational Medicinal Products (IMPs) and devices

- The UK and EU should work to ensure that trade barriers do not impact the availability or movement of new and existing licensed medicines, Investigational Medicinal Products and devices after Brexit as this is crucial to maintain standard of care on which to build clinical trials.
- The UK government should continue to seek a close partnership between the MHRA and the EMA. An agreement should be sought to allow EMA marketing authorisation decisions to apply to the UK and equivalent safety standards to be maintained after Brexit
- The UK and EU regulators should ensure equivalence of regulation and standards for certification and testing of IMPs and devices.

Funding

- The UK and EU should agree full UK participation in EU framework programmes with access to funding for clinical research.

Workforce

- The UK government should negotiate reciprocal arrangements, where possible, to ensure international mobility, as this is seen as a critical aspect of collaboration and research excellence.

2. Actions to maintain UK attractiveness

Regulation

- The UK should adopt a broad strategy to EU and international engagement to ensure it can continue to influence and drive new regulation and standards across Europe and globally, including through partnership with the EMA.

Workforce

- The UK Government should modernise and streamline its global immigration system as this is also seen as a critical aspect of collaboration and research excellence. In particular, a permissive immigration system should be developed that supports the clinical trials, health and research workforce that allows continued movement across borders.

3. Optimising the landscape long-term

Regulation

- UK and EU regulation and regulators will need to adapt to allow for new trial designs, new devices and technologies, and new approaches to data.

Data

- A more streamlined and efficient approach is required in the UK and internationally to allow the effective collection and sharing of anonymised patient and trial data while protecting patients' rights and interests.

Funding

- A long-term strategic approach to funding of clinical trials is necessary in the UK to both ensure investment and to drive collaboration.

Workforce

- The UK needs to invest in a skilled clinical trials workforce to ensure it can maintain its longer-term competitiveness encouraging UK investment.

SECTION 1

Introduction

The outcome of Brexit will have direct and indirect impacts on the future of clinical trials in the UK and EU.

Perhaps the most immediate and direct impact will be the level of regulatory alignment between the UK and EU with respect to the forthcoming implementation of the EU Clinical Trial Regulation (EU CTR).

More broadly, the shape of Brexit will determine a number of factors that together will affect the clinical trials landscape including access to medicines and Investigational Medicinal Products (IMPs), data, funding and the clinical trials workforce (see Section 2).

Each of these have emerged during this study as key themes for the sector to address in both the short- and long-term as we look out to 2028.

Brexit will determine or limit the options available to the sector, however, in the long-term the UK may have opportunities to adapt to any changes in the environment.

It will also be critical to ensure that decisions made today are in the context of broader shifts in the sector, and the world in which it is operating: to understand the longer-term drivers and shifts, like availability of funding for clinical trials, research and innovation and advances in genomic, personalised and translational medicine.

A positive outcome for patients and the sector

Patients across Europe have benefited from close collaboration between the UK and EU. The UK conducted the highest number of phase I trials in the EU and the second highest number of phase II and III trials (after Germany) in 2015[1]. International collaboration is an essential component of many trials, and particularly for rare disease and paediatric treatments where it can be particularly hard to recruit from a single country.

Collaboration with the EU also brings wider benefits for research and innovation across the life sciences and health care industries. For instance, the UK has the largest therapeutic pipeline in Europe, developing over 800 product candidates in 2016[2].

A future shaped by Brexit

The UK's decision to exit the EU has introduced significant uncertainty around the future of their relationship. Timelines have been set. The UK voted to leave the European Union on 23 June 2016. Prime Minister Theresa May triggered Article 50 on 29 March 2017, and the UK now has until 29 March 2019 to negotiate final terms for its exit.

Both parties have outlined their negotiating positions for any future partnership: positions that are not entirely compatible. A free trade agreement would initially appear to be the only remaining option for a deal, though it is unclear whether this would be as comprehensive or selective as the UK desires.

In the absence of any agreement – a "no deal" scenario- the relationship between the EU and the UK would default to World Trade Organisation terms with uncertain implications for UK and EU citizens, trade, customs and regulations.

(For a summary of potential Brexit shapes please see Figure 1)

[1] Technopolis (2017) The Impact of Collaboration: The Value of UK Medical Research to EU Science and Health

[2] BIA (2016) The UK Life Sciences Industry and the Public Markets, 2016/17

Potential Brexit shapes

No Deal

1. Cliff-edge no deal The UK leaves the EU without any arrangements in place. The UK and EU trade on WTO terms including for drugs. The UK is able to establish its own regulatory standards. Formal freedom of movement ends, but little may change in the short-term. A new UK border system is required from day one, with issues around access to market, regulatory checks and potential damage to supply chains. UK implements legislation and regulation agreed in the Withdrawal bill. Potential negative relationship and lack of cooperation between UK and EU. UK and EU are third countries for services. Potential for a FTA between the UK and US, with the UK moving towards US standards over time.

2. Transitional no deal UK and EU negotiate a transitional arrangement beyond that already agreed in principle for instance for an additional 4 years. UK and EU trade on WTO terms. Potential for other bespoke agreements around e.g. data sharing, regulation and citizens' rights. Warmer relations between EU and UK compared

to the cliff-edge scenario. The UK may be able to negotiate better than third country access to Framework Programmes and other European institutions. Potential for a trilateral FTA between the UK, EU and US, with the UK moving towards US standards over time.

Hard Brexit

3. UK-EU Free Trade Agreement UK exports to the EU would have to satisfy some rules of origin requirements, and customs measures would increase compared to current Single Market membership. To trade in the EU,

UK companies would still need to comply with ECJ legislation and regulation. UK regulations and standards can diverge from those of the EU. UK has reduced access to markets, increased regulatory checks and potential damage to supply chains. The UK may be able to negotiate better than third country access to Framework Programmes and other European institutions. The level of comprehensiveness depends on the final agreement.

Soft Brexit

4. Norway model The UK remains part of the European Economic Area with access to the EU Single Market, but leaves the Customs Union. The UK would have to comply with EU rules on free movement of goods, services, capital and people. It would be able to pursue other FTAs, but would face rules of origin and other Non-Tariff Barriers in trade with the EU, would have to accept EU regulations and contribute to the EU budget, despite being excluded from decision-making. UK is a third country but (like Norway who is attempting to implement the EU CTR) may be able to access the EU CTR.

5. Swiss model The UK remains in the Single market for goods but not services. The UK–EU goods trade would continue to be tariff-free. But non-tariff barriers on trade in services rise. UK is required to contribute to the EU budget and adhere to EU regulations and standards. The UK has no voice in decision-making and would have to accept new regulation from Europe. The UK can negotiate Free trade agreements with other countries. UK is a third country and would need to negotiate a bespoke arrangement to provide access to EU CTR.

6. Customs union covering goods only. The UK maintains a customs union with the EU, but only for goods, not services, while leaving the Single Market. This would restrict the UK's ability to act independently, but would ensure trade with the EU took place free of tariffs and some non-trade barriers, even though non-trade barriers on services would rise. UK a third country.

Figure 1 - Potential Brexit shapes. High-level summary of different "shapes" of Brexit, outlining the key features and differences of each shape.

UK position

The UK government could accept a 'Hard Brexit'[3] (see Figure 2) outside the Single Market and its associated four freedoms (the free movement of goods, capital, services and labour) and outside the Customs Union (a trade agreement in which EU countries decide not to tax imports or goods from inside the Union and prohibits members from negotiating trade agreements separately to the EU).

With this, it aims to limit freedom of movement of EU citizens in the UK, to be less bounded to the jurisdiction of the European Courts of Justice (ECJ), to maintain free and open trade and the ability to negotiate its own trade deals, and to limit any future financial contributions to the EU.

However, the government has stated a preference for a comprehensive and unique free trade agreement[4] and a close ongoing relationship with the EU. Although a 'Soft Brexit' is still possible where the UK may still have access to the Single Market and/ or be part of a Customs Union, this would require a change in policy.

EU position

The EU desires to have the UK as a close partner. However, it is not willing to divide the "four freedoms" of the Single Market, it wants to ensure that non-members do not have the same benefits as members. The EU may agree to some of the UK's negotiating positions, in exchange for a financial or other contribution to the EU, but it has stated the UK would not be able to "cherry pick".

The role of clinical trials

Clinical trials are a key research tool for advancing medical knowledge and patient care. They produce the best available data for healthcare decision- making related to whether a medical strategy, treatment, or device is safe and effective for humans. They offer important information on the cost- effectiveness of a treatment, the clinical value of a diagnostic test and provide patients with early access to experimental treatments and innovations.

> **"The biggest risk will be outcomes for patients, and what the sector will be able to deliver.**

They benefit society by helping identify innovative and cost-effective ways to meet healthcare needs, including challenges associated with an aging population and an increasing prevalence of non-communicable diseases such as cancer.

They have a positive economic impact: the NIHR Clinical Research Network alone was estimated to provide £2.4 billion of gross value added (GVA) to the UK economy and to support 39,500 jobs in the UK in 2014-15[5].

Clinical trials also help support a vibrant health and life sciences ecosystem and contribute to the knowledge economy by attracting talent and facilitating international collaboration.

Europe is a world leader in the development and running of clinical trials. Over 4,800 UK-EU trials were conducted between 2004 and 2016[6].

The UK has played a key role in pan- EU clinical trials providing notable leadership through the Medicines and Healthcare products Regulatory Agency (MHRA), which has helped to develop and guide European regulation. However, it is unclear whether this close relationship will continue after Brexit.

[3] The Guardian (2017) https://www.theguardian.com/.../15/theresa-may-uk-is-prepared-to-accept-hard-brexit

[4] UK government (2018) https://www.gov.uk/government/speeches/trade-and-tariffs-brexit-and-beyond

[5] KPMG (2016) NIHR Clinical Research Network Impact and Value Assessment

[6] Cancer Research UK (2017) The impact of collaboration: The value of UK medical research to EU science and health

An uncertain future for trial regulation

Perhaps the most direct impact of Brexit relates to the EU Clinical Trial Regulation due to be implemented in 2019.

The EU CTR aims to address existing shortcomings of the existing Clinical Trials Directive (CTD), to minimise barriers to the conduct of multinational trials by:

- Ensuring a harmonised approach to the conduct of trials across Member States and reducing duplication of effort in multi-country trials.
- Providing a single coordinated approval process and EU portal and database with the potential to decrease the administrative burden for clinical trials and support transparency, from submission through to assessment and communication between sponsors and participating countries.

Ongoing Uncertainty

Technical delays to the portal and database have delayed its implementation in the EU and there are some concerns that implementation may be further delayed. This has resulted in its exclusion from the UK's European Union (Withdrawal) Bill and there is significant uncertainty as to whether the UK will adopt the provisions of the EU CTR after Brexit, and whether it will remain aligned in the longer-term. A positive sign was seen in a recent Lords debate on alignment with the EU CTR, where the government stated their commitment to "being as aligned with the new EU clinical trials regulation as we possibly can be"[7]

As a third country, the UK would be unable to participate in the EU Portal and Database unless special provisions are made, either during phase II negotiations or through a separate agreement.

In addition, while the EU CTR allows non-EU countries to co-sponsor and participate in pan-EU trials, it requires them to have a legal representative within an EU member state to sponsor trials[8].

> **"We need an extended transition period. Lives matter. Taking as much time as it needs to get this right is really important.**

The UK and EU have both publicly agreed that the UK and the EU have a lot to offer to each other and UK government has announced that a close relationship is preferred. However, whether a close relationship transpires will depend on the outcome of the final negotiations.

UK government[9] and MHRA[10], have both signalled their intention to align with the EU post- Brexit and for the UK to adopt the provisions of the EU CTR at the point that they are implemented in the EU, providing a level of assurance for the sector.

However, despite intentions there is still significant ongoing uncertainty as to the outcome of negotiations, where questions such as the ones below remain to be answered:

- Will there be a transition period? A 21-month period is included in the Transition Agreement, but in the event of a no deal this may not apply. There are also concerns that 21 months will not be long enough to address issues of critical importance to trials, for instance to implement new border systems.
- What will be the future trading relationship between the UK and EU?
- Will the UK be able to participate in the new clinical trials system, including the EU portal and database?

[7] UK Parliament (2018) https://hansard.parliament.uk/Lords/2018-04-18/debates/D572CBF6-A85C-4208-B426-843747A766FA/EuropeanUnion(Withdrawal)Bill#contribution-3E59ACA4-1C9D-4EBF-9941-C297F4A01A6E

[8] European Parliament (2014) Regulation (EU) No 536/2014

[9] Hansard (2018) HL Deb 18 April 2018 vol 790 c1215

[10] MHRA (2018) Corporate Plan. 2018-2023

SECTION 2

Project Findings

Brexit has introduced significant short- and long-term uncertainty in a broad set of areas including regulation, trade, access to medicines, data, the workforce and funding of clinical trials. The UK faces a future that will be influenced by global shifts in values, demographics, innovation and technological change.

Brexit is redefining the relationship between the UK and EU. The clinical trials sector will need to adapt to the opportunities and challenges associated with Brexit.

However, it is also important that any decisions made today are effective and resilient in the longer-term. To do this it is important to understand both the longer-term impacts of Brexit as well as broader changes that may influence how future trials are conducted, and the world in which trials operate.

To do to this, we used a futures approach[11,12] to look out to 2028. We engaged a broad set of participants with a main cancer focus, an international mix of researchers, patients, clinicians, industry, government and regulators to help participants explore the future of trials before surfacing insights for today.

There were four phases to the project:

1. **Horizon scan and interviews.** A broad range of literature was reviewed to identify drivers, trends and weak signals (past or current issues/ developments with ambiguous interpretations) that will shape the future of clinical trials. In parallel, 23 interviews were conducted with a mix of researchers, patients, clinicians, industry, government and regulators to identify different perspectives on the future.
2. **Prioritisation of drivers of change.** An online assessment was conducted to gather sector views on the most important and uncertain drivers of change and to gather additional perspectives.
3. **Scenario development.** Five alternative scenarios were developed for the future of clinical trials. Further information on how the scenarios were developed and their characteristics is provided later in the document and in Annex B.
4. **Identification of implications and recommendations.** A participative workshop was held with 38 participants to explore the scenarios and explore their implications. Following the workshop, we identified 5 themes – regulation, access to medicines and IMPs, data, funding and the workforce – along with a set of recommendations to help ensure a successful future for trials and a positive outcome for patients.

[11] The World Today (2017) Strategic foresight can make the future a safer place

[12] Government Office of Science (2017) The Futures Toolkit

The forces shaping the future of clinical trials

Through the horizon scan and interviews a shortlist of 26 drivers of change were identified that were viewed to be important to the future of clinical trials.

These included a broad set of drivers that would have impacts on the Economy, Society and Technology, as well as a set of issues that would affect regulation, efficiency and collaboration, funding and Brexit, supply chains and migration.

The 26 drivers were then assessed in an online survey, in particular to identify:

- **Critical issues:** high impact and highly uncertain drivers that might impact the sector by 2028. (Figure 2)
- **Short- and long-term priorities:** important drivers in 0-2 year and 5-10 year time-frames. (Figure 3)
- **Emerging issues**: important drivers where there was less consensus on the level of impact or uncertainty among respondents. A lack of consensus can help to identify 'weak signals' of change not yet on most people's radar.

Perhaps due to the uncertainty inherent in Brexit, the critical issues surfaced by respondents included a set of drivers that are highly dependent on the outcome of Brexit negotiations.

Similarly, short-term priorities were focused on the need for regulatory alignment, to maintain effective collaboration and cooperation between the UK and EU, to ensure a skilled workforce, and to maintain funding for the sector.

However, as perspectives shifted to the long-term, funding was seen as the most important driver for the future of clinical trials, although regulatory alignment, collaboration and the workforce continued to be a concern. When thinking about the longer-term, respondents also gave more weight to the transparency and the ease of disclosure of trial data, advances in genomic, personalised and translational medicine, and the need to ensure the competitiveness of the UK and EU.

The key emerging issues were social attitudes to data, privacy and the transparency of trials, patient-centric approaches, the level of clinical innovation, and the impact of aging and non-communicable diseases.

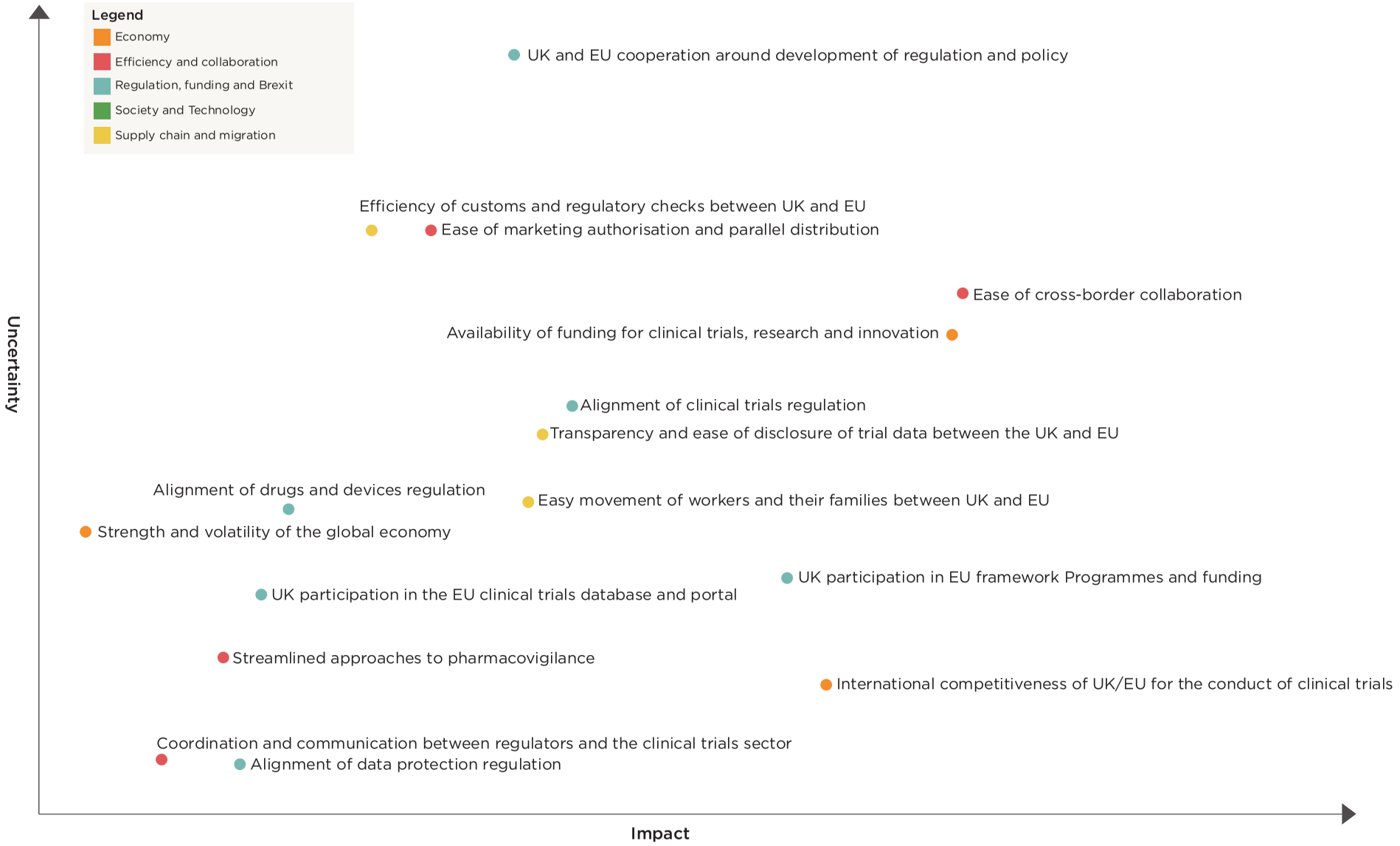


Figure 2 Critical Factors Drivers prioritised by survey respondents as having greater than average impact and uncertainty (See Annex A for more information)

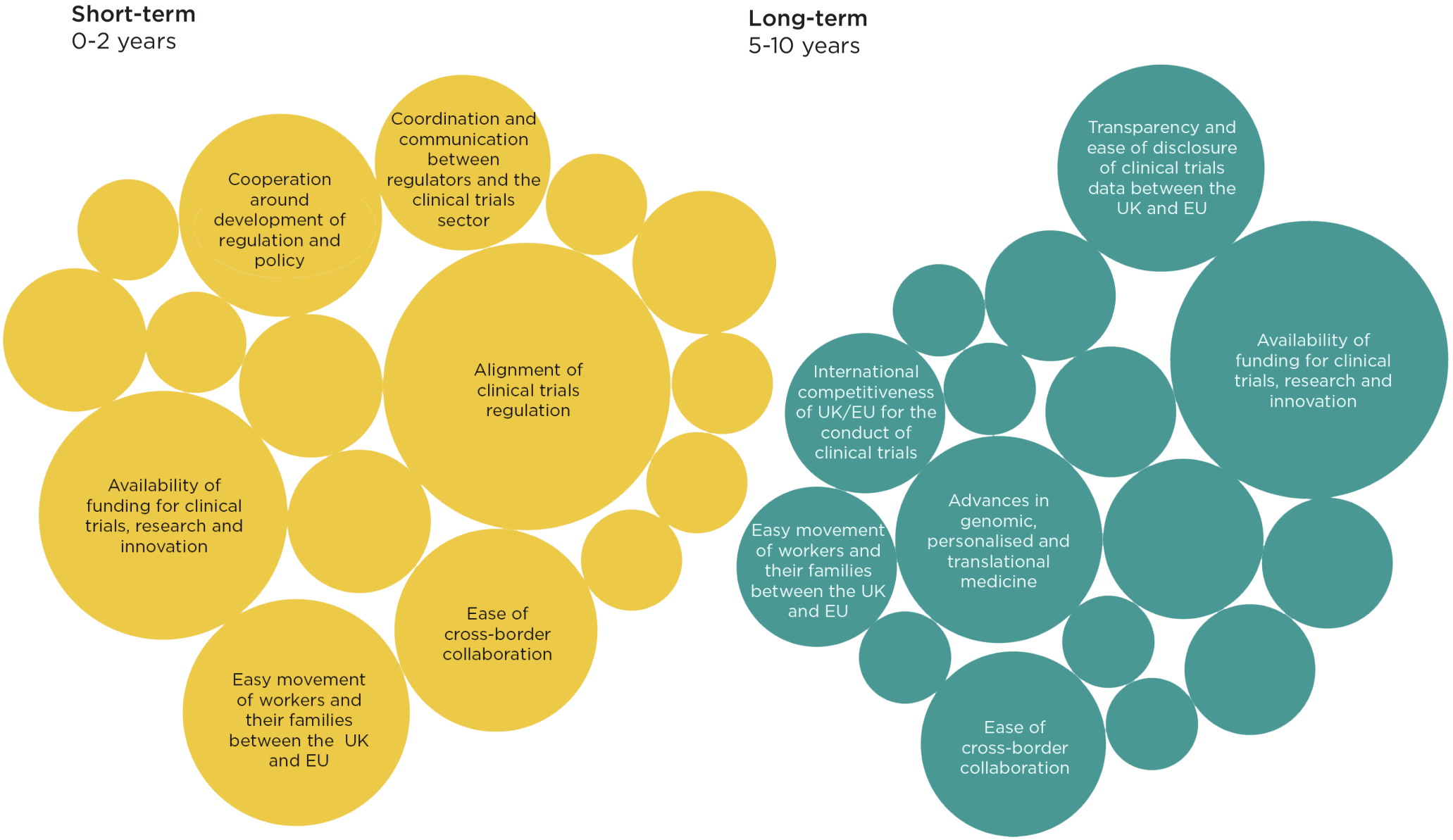


Figure 3 Short-term and long-term priorities. Circle size is proportional to the number of respondents selecting the driver as the most important sector priority.

Five scenarios for the future of clinical trials

Based on the findings of the online survey, a set of scenarios were developed as a framework in which to explore the future of clinical trials.

They describe five possible futures, looking out one decade, written in 2028 in the present tense as if that future has happened.

They are not intended to be predictions, but to help to expose some of the impacts of different Brexit outcomes on the future of clinical trials, while also considering the impact of broader shifts within the trials sector.

The scenarios are just a few of those that can be imagined from a range of possible futures. In fact, it is unlikely that these scenarios will come to pass as described. However, by taking the time to explore alternative futures the sector can start to make strategic choices.

The scenario framework

A scenario framework was developed to help consider the impact of different Brexit shapes, and levels of alignment on the future of clinical trials (Figure 4).

- **The shape of Brexit:** How might different Brexit outcomes impact the future of clinical trials? What does the post-Brexit world look like in 2028? (see Figure 1 for a summary of the different Brexit shapes)
- **The level of regulatory alignment between the UK and EU:** Does the UK implement the provisions of the EU CTR? Will a bespoke agreement be made to allow the UK to participate in the EU database and portal? And will it be possible to stay aligned over time?

  Full alignment assumes a bespoke agreement is agreed between the UK and EU to allow the UK to participate fully in the provisions of the EU CTR and to access the EU portal and database.

  Partial alignment assumes that the UK implements the provisions and processes in the EU CTR as far as possible but is unable to access the portal and database as a third country.

  No alignment assumes that the UK does not implement the provisions of the EU CTR but keeps existing clinical trials legislation in place. The UK may choose to adopt a bespoke regulatory system or align with an alternative market.

Five scenarios

Five scenarios were developed for further exploration (Figures 4 and 5) and a range of outcomes associated with additional drivers were explored.
See Annex B for the full scenario narratives and a summary of the features of each scenario.
The final scenario narratives were used in a participative workshop with 38 participants to start to explore the implications for patients, trials and the sector.

Implications and Recommendations

Following the workshop, five themes were identified as priority areas that would impact the future of clinical trials out to 2028:

- Regulation
- Access to medicines, IMPs and devices
- Data
- Funding
- Workforce

These are explored in the next section along with a set of recommendations to help ensure a successful future for trials and a positive outcome for patients. For each section a table is presented that highlights the key implications and high-level recommendations highlighting key features of different levels of alignment after Brexit.

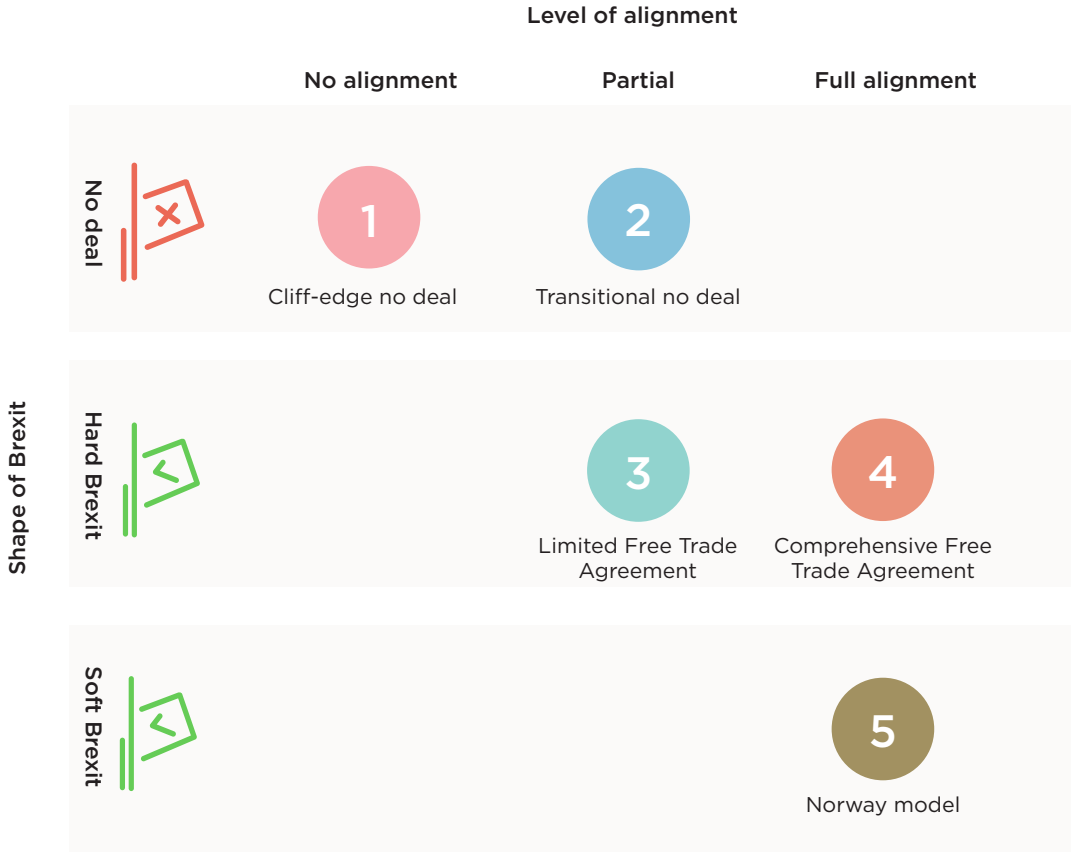


Figure 4 Scenario framework. High-level outline of the scenarios based on the shape of Brexit and corresponding level of alignment with the provisions of the EU Clinical Trials Regulation

SCENARIO 1: No Deal | No Alignment

Brexit talks collapsed at the end of 2018 with the EU and UK failing to reach an agreement during phase II negotiations. As a result, the proposed transition period that was intended to last until 2020 fell through, as this was conditional on Phase II negotiations.

The UK left the EU at the end of March 2019. Trade defaulted to WTO rules, without any agreement between the UK and EU for the free movement of goods, capital, services and labour. Research and scientific collaboration was impacted once the UK became a third country with limited options to participate in EU programmes and access funding to support researcher mobility.

SCENARIO 2 No Deal | Partial Alignment

The UK was unable to secure a comprehensive trade deal with the EU. Instead an amicable no deal was agreed including additional time to implement necessary changes. This provided a level of reassurance to industry and to the workforce. In 2024, bespoke arrangements came into force for data sharing, regulation and citizen rights.

Today, in 2028, the UK is struggling to find its way in a market that is increasingly global and competitive.

SCENARIO 3: Limited Free Trade Agreement | Partial Alignment

As the first country to leave the EU, the UK struck a limited free trade agreement with the EU in 2019. Today in 2028, despite that agreement, cooperation between UK and EU Member States is increasingly reliant on informal networks and back-channels, in a world of closed borders.

UK and EU clinical trials regulation is partially aligned. The UK is unable to access the EU portal and database and has instead established parallel systems and processes. The UK is unable to lead on EU trials, although it can still participate. This has negatively impacted the type and number of trials being conducted in the UK.

SCENARIO 4: Comprehensive Free Trade Agreement | Full Alignment

The UK and the EU agreed a comprehensive free-trade agreement during Phase II Brexit negotiations. Revised financial contributions to the EU secured the continued movement of goods, people, services and capital.

Today, in 2028, the UK continues to cooperate with the EU as a third country. The UK has access to the EU database and has fully implemented the provisions of the EU CTR. Researchers and industry are able to participate in EU programmes and funding though the UK has less influence on future regulation. Bilateral arrangements with non-EU partners are starting to be put in place.

SCENARIO 5: Soft Brexit: UK joins EEA | Full Alignment

The UK government changed their Brexit position during phase II negotiations and the UK and EU negotiated a 'Soft Brexit'. The UK joined the European Economic Area (EEA) with access to the EU Single Market, but outside the Customs Union.

Today in 2028, in return for access to the Single Market, we continue to comply with EU rules on free movement of goods, services, capital and people in return for accepting EU regulations and contributions to the EU budget.

For clinical trials, the precedent set by Norway meant that the UK was able to gain full alignment within 5 years of Brexit.

Figure 5 Scenario descriptors. Please see Annex for full scenario narratives.

Theme 1: Regulation

1.1 Alignment with the provisions of the European Clinical Trial Regulation

Recommendation: The UK government should continue to seek full regulatory alignment with the forthcoming EU Clinical Trial Regulation. This should include a bespoke agreement for access to the EU portal and database and to ensure the UK can take part in the centralised assessment process.

The final shape of Brexit has the potential to influence the level of regulatory alignment between the UK and EU (see Figure 5) and specifically the extent to which the UK replicates the provisions in the EU CTR.

- **Full alignment** is most likely in a 'Deal' or 'Soft Brexit' scenario where the UK is required to adopt EU regulation on an ongoing basis. However, even in these scenarios the UK would be a third country and would not have automatic access to the EU portal and database. This would require a bespoke agreement with the EU, either as part of Phase II negotiations or through a separate or subsequent agreement.
- **Partial alignment** is possible under any scenario, with the UK adopting some or all of the provisions of the EU CTR but without access to the EU portal and database.
- **No (or minimal) alignment** is most likely in a no-deal scenario. The UK would not have access to the EU portal and database and would be free to align or diverge from EU regulation.

Key features of the EU CTR:

- **A simplified process for the application and approval of clinical trials across the EU.** A single application dossier will be submitted for each clinical trial or modification by the Reporting Member State (RMS) who will provide the initial assessment of the trial (Part I approval). Part I approval will then apply to all EU Member States. Member States will then need to undertake Part II approval at a national level to assess ethical requirements. The same process will apply to amendments to trials allowing them to be applied uniformly across Member States.
- **Clinical trials sponsorship.** Where the UK is a third country or no bespoke agreement is in place, it will not be eligible to be a RMS and unable to be the legal lead for clinical trials involving other EU countries. However, the EU CTR allows third countries to co-sponsor and participate in trials where they have a legal representative in the EU to demonstrate and ensure compliance. There are concerns that this may limit UK academic trials or UK businesses who do not have existing sites in the EU from sponsoring trials.
- **A co-ordinated and risk-proportionate approach to assessment, authorisation and supervision.** This is a new uniform procedure that includes the ability to request additional information from a Sponsor when appraising substantial amendments, allowing assessments to proceed where they would be rejected under the CTD, and reduced regulatory burden for low-risk trials using an IMP with an existing Marketing Authorisation.

> **"Regulatory divergence would slow down what is already a laborious and time consuming process for clinical trials. For rare cancers, with smaller and smaller populations, this would become impossible**

- **Increased transparency.** The portal and database will include public registration of all trials and modifications. This will bring increased transparency for patients and the sector but there were concerns about how this would affect industry.
- **The expansion of trials internationally.** There may be additional barriers expanding UK- only trials into Europe and for UK centres to join existing EU trials. This would be particularly important for the treatment of rare and paediatric cancers and as future trials become increasingly stratified and personalised.

Full alignment would lead to a positive outcome for patients and trials

The dominant view was that full alignment is essential to ensure the best possible outcome for trials and patients.

The UK is currently perceived as a costly and slow environment for the conduct of trials compared to other EU and international countries, despite its world-class regulatory, research and trial base. This is particularly due to the costs and timelines associated with the set up and conduct of trials.

Where the UK is unable to benefit from the provisions of the EU CTR, or where regulatory divergence introduces new barriers, there were significant concerns that the UK would become less attractive for the placement of trials.

Any actions that would reduce the UK's competitiveness would ultimately lead to a reduction in the quantity and diversity of trials being conducted in the UK, further impacting patients and research in the EU and beyond.

Ultimately, patients would have fewer options and delayed access to trials and treatments. The UK healthcare system may lose access to and familiarity with new drugs and innovative protocols: innovation may suffer.

As a third country outside the EU, the UK was viewed to be too small a market, with small patient populations, and unable to compete with continental Europe or internationally.

Access to the portal and database will require separate negotiation

Even if regulation is aligned, as a third country the UK would not automatically gain access to the EU portal and database. A bespoke agreement would be required to ensure access to the portal and database.

In the event that an agreement is not reached the UK could either choose to implement:

- **A separate, parallel system** that mirrors the specifications and processes of the EU portal and database. This may minimise duplication, at the initial submission although divergence could occur during parallel reviews or subsequent amendments. The parallel system could still result in increased costs, administrative burden, and delay the speed at which clinical trials can be conducted. Any new database would also have implementation costs and may take time to implement
- **A bespoke system** with separate specifications and processes. Clinical trialists would be required to make multiple submissions with increased costs and delays. The UK would also be unable to access data in the EU clinical trials portal and database

Even if the UK has full access, some participants were concerned that the running of trials in the UK could also be impacted where implementation of the EU CTR is delayed, or the portal and database are hard to use.

1.2 UK influence over future regulation and policy

Recommendation: The UK should adopt a broad strategy to EU and international engagement to ensure it can continue to influence and drive new regulation and standards across Europe and globally, including through partnership with the EMA.

> **"Whether you think regulations are good or bad, you need to be part of the system. Otherwise, who would pay attention to the UK, and what value would it be except to us?**

Deregulation was not seen to be a viable option for the UK, but it was notable during the workshop that 'partial alignment' scenarios, where the UK was able to participate in EU trials and passively inherits legislation without any influence on its development were less preferable than scenarios where the UK had a leading voice. This applied equally where the UK was a rule-taker from the EU or another market such as the United States.

The future relationship between the Medicines and Healthcare products Regulatory Agency (MHRA) and European Medicines Agency (EMA) was seen to be particularly important, and the move of the EMA to Amsterdam, in particular, to have a negative impact on the UK's ability to influence future regulation.

There was a call for clarity over the future relationship and roles of the MHRA and EMA.

The ability for the UK to contribute to and drive new regulation and standards across Europe was viewed to be particularly important, not only for the UK, but to drive innovation across Europe and internationally. In scenarios where the UK is subject to future EU regulation but does not have a formal role in shaping it, there were particular concerns that the EU-27 may take a risk-averse approach to regulation to the detriment of trials and patients.

The MHRA, is broadly well-regarded for its leading role in Europe, and it was acknowledged by many participants that the forthcoming EU CTR is catching the EU up to the UK regulatory standards that the MHRA has developed working closely with the sector and industry.

However, there were also negative perceptions about how the EU CTD had been implemented across Europe, with the MHRA choosing to "gold- stamp" regulation. After Brexit, without a requirement to align, there were concerns that the regulator may choose to overprescribe regulation, missing opportunities to take a more proportionate and innovative approach.

This could be an additional barrier that negatively impacts the UK's competitiveness.

Irrespective of individual sentiments, it was felt that the UK has a lot to offer the EU and international markets in terms of guidance, support and experience in regulation.

Development of a close relationship either through negotiation of membership or associated status with the EMA was seen to be important, both for the benefit of trials, but also to avoid delays to licensing.

However, in the event that this is not achieved, or in the event of a breakdown in UK and EU relations, participants highlighted the need for informal communications to continue outside of official channels.

Suggestions included:

- A role for CRUK, other Clinical Research Organisations and Clinical Trials Units to support cross-border collaboration.
- Track II diplomacy or "backchannel diplomacy" to drive engagement across Europe in addition to the UK government's intent to "strengthen its bilateral and multilateral research

relationships with EU Member States and the UK's other international partners around the world"[13]

- Informal alliances with EU and internationally including through MoUs and confidentiality agreements with other countries.
- Continued membership of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)
- Continued membership and access to European networks and infrastructure including institutions such as the European Strategy Forum on Research Infrastructures (ESFRI), and the European Reference Networks (ERN) which support knowledge sharing in rare diseases for both clinical care and research. Third country participation in some of these networks could be secured through participation in future EU Framework Programmes, or through bespoke agreements. There are a number of non-EU countries with access to these networks and it seems likely the UK will remain involved.
- Informal collaborations with organisations such as the OECD and WHO
- UK representation in leadership roles in international organisations, to help ensure the UK has a voice at an international, if not European level.

Participants also noted that in an increasingly global market, where the UK is outside of the EU, it will be critical for UK government and MHRA to invest time and resources building relationships internationally. This is particularly critical in a no deal scenario.

The option for the UK to align with an alternative market was also seen to be potentially desirable in a no deal scenario, as this would allow the UK to still be part of a larger market for clinical trials. Suggestions included Canada, Japan, Singapore and the United States. However, for most participants, this strategy was viewed as a contingency.

> **"We need to keep contributing to the research agenda of the EU and continue to drive and influence the agenda.**

A few participants fundamentally questioned the need for future alignment with the EU, wondering whether the UK would be better served by seeking alignment and strengthen relations with the US Regulator, the Food and Drug Administration (FDA).

It was suggested that alignment with the US market could allow the UK to benefit from quicker timelines for the setup and assessment of trials, as well as opportunities to access funding. An aligned NHS would be a significant potential market for the extension of US trials, and may encourage pharma to place more trials in the UK. It may also be possible to promote UK excellence and expertise to the US. Yet some participants noted that most of the options for US alignment should only be considered desirable in a no deal scenario as it presents a riskier strategy.

Alignment with the US was suggested in a recent Wellcome Trust report[14]. However, the same report notes the shared values that the UK and EU share around "rights, data privacy and animal welfare" and history as drivers for continued collaboration, and notes that a UK-EU R&I agreement should enable the UK to participate in EU's harmonised clinical trials. Physical proximity has also been flagged as a key priority for future collaboration.

[13] HM government. Collaboration on Science and Innovation. A Future Partnership

[14] Wellcome (2018) Building a Strong Future for European Science: Brexit and Beyond

1.3 Innovation

Recommendation: Where full alignment with the provisions of the EU CTR is not possible, the UK government should seek a proportionate approach to regulation that balances alignment with the opportunities to innovate

Regulation was seen to be both an enabler and barrier to future innovation in clinical trials.

Under a full or partial alignment scenario, the UK would inherit any future regulation from the EU. Depending on the level of influence (see 1.2) that the UK has on development of new regulation, this may limit opportunities for the UK to adopt new regulatory approaches in the face of technological progress, social change, attitudes to data and privacy, and new trial design.

Some participants were concerned that the forthcoming EU CTR would bring additional bureaucracy and red-tape.

Respondents noted that the CTD had slowed and prevented some trials from being conducted. Others felt that the EU CTR is simply catching up with UK excellence.

There were also concerns that EU bureaucracy might limit the pace at which new regulation can be legislated across Europe.

Outside of the EU, the EU CTR and any new legislation would not automatically apply to the UK, this could make it difficult to keep legislation in sync, or result in delays as the UK replicates new legislation.

However, the UK could choose to diverge from EU regulation.

Most participants felt that divergence would harm clinical trials. However, where the UK is outside of the EU, participants saw an opportunity for the UK to stay competitive internationally, by taking a proportionate approach to regulation that balances alignment with opportunities to innovate.

> **How trials are conducted in the future will impact on regulators-adaptive, complex designs. There needs to a review to accommodate these types of clinical trial.**

In particular, there were seen to be opportunities for the UK to build on its expertise – the quality of its research base, and the NHS as a test-bed for trials – to become a home to novel and innovative clinical trials.

However, many viewed a future in which the UK was only attractive to 'niche' trials as damaging to the sector as a whole and to patients.

1.4 Clinical trial design

Recommendation: UK and EU regulation and regulators will need to adapt to allow for new trial designs, new devices and technologies, and new approaches to data.

Perhaps the most consistent message across from interviewees was that regulation and regulators will need to evolve to ensure UK and EU trials can take advantage of advances in healthcare, new devices and technology, and new trial designs, including real-world evidence (RWE) and adaptive trials.

The pace at which biological understanding is progressing, coupled with advances in data were in particular felt to:

- Provide new opportunities to streamline and to stratify patient populations as new approaches to biomarkers and tumour pathology allow for better diagnosis of the taxonomy of illness. However, there were concerns that this would mean

that the number of trials being conducted would decrease as they become increasingly segmented with additional costs and bureaucracy, including around patient access and recruitment.

- Challenge the current, dominant models of clinical trials: while large randomised clinical trials are likely to persist over the next decade, new trials including adaptive and trials focused on real-world evidence (RWE) were viewed to become increasingly important.
- Bring new ethical considerations and challenges for data sharing, with calls for better and more effective data collection and sharing to facilitate new approaches to trials. The need to make better use of anonymised data was highlighted by many participants, though couched against a need to protect patients. There were also additional concerns as to whether patients would continue to consent to their data being used and shared and the effect this would have in the number of patients opt-in to trials.
- Allow for new approaches to the collection of data to allow collection of real-world and other evidence to be gathered remotely, outside of clinical environments. This has potential impacts for trial infrastructure and international collaboration (see theme 3).
- Facilitate new approaches to patient recruitment, enrolment and investigator interactions.
- Require a new approach to the regulation of medical technology and devices. In particular participants were concerned about what would constitute a medical device and be regulated in the future, with a blurring between personal and medical devices.

As these changes impact the industry there were concerns as to whether the UK and EU and their regulators are in a strong position to keep pace with these changes.

For instance, several participants noted that multi-arm, multi-stage trials, such as STAMPEDE have been around since the early 2000s, but that regulation was only now catching up.

With new trial designs on the horizon, including the increasing interest in adaptive trials the need to innovate was felt to be an opportunity for the UK, the EU and beyond.

Adaptive trials require ongoing and prospective modifications to trials, including changes to baseline characteristics e.g. patient survival or efficacy, outcomes, sample sizes, new treatment arms and endpoints, among others. They also require a new approach to statistics, in particular Bayesian statistics. There were concerns as to whether regulators have sufficient skills and expertise at an operational level to design, implement and assess adaptive trials. Participants felt that the forthcoming EU CTR should hopefully remedy these challenges.

On the other hand, participants recognised that where the UK can build these skills and adopt a streamlined approach to the management and conduct of adaptive clinical trials this could help the UK to build its competitiveness leveraging existing strengths in adaptive, observational and real-world studies. It is important to highlight though that as these types of trials often trim down patient populations, the UK could face the challenge to not be able to gather enough patients to carry out them.

In general, this strategy was seen to be particularly important in the event that the UK is no longer aligned with the EU or competitive for the placement of more traditional large-scale and international trials.

	Implication	Full alignment		Partial alignment		No alignment	Recommendation
Regulation	**Alignment with the provisions of the EU Clinical Trials Regulation**	UK replicates provisions of the EU CTR and negotiates access to the EU portal and database through a bespoke agreement Harmonised approach to trials with minimal barriers UK and EU can cooperate on trials maximising patient participation and access to trials and treatments UK seen as an attractive destination for clinical trials as part of a unified UK and EU market	✓	UK can replicate provisions of the EU CTR but does not have access to the EU portal and database UK facing increased complexity and difficulty to sponsor EU trials, particularly for non-commercial trials and increased barriers to expanding trials internationally Quality and frequency of trials conducted in UK decreases Patients have fewer options and delayed access to trials and/or potential innovative treatments UK a less competitive market for the placement of trials as an 'additional' market outside of the EU	✗	UK and EU clinical trials regulation is not equivalent Increased costs and delays to international trials Quantity of trials conducted in UK decreases Patients have fewer options and delayed access to treatments Potential opportunities to innovate, but UK potentially less competitive compared to Full alignment UK may choose to specialise or align with another international market e.g. USA	**The UK government should continue to seek full regulatory alignment with the forthcoming EU Clinical Trial Regulation. This should include abespoke agreement for access to the EU portal and database and to ensure the UK can take part in the centralised assessment process**
	Access to the EU clinical trials portal and database	A bespoke agreement allows the UK to access the portal and database as a third country Risks where implementation of the EU CTR is delayed, or the portal and database are hard to use	✓	Increased costs and potential time delays if the UK implements a parallel system Parallel systems may still be a barrier to the placement of trials in the UK due to increased administrative costs and duplicate systems	?	Time delays and costs to implement a bespoke system Different systems require multiple submissions with increased costs and delays	✗	
	Clinical trials sponsorship	A bespoke agreement allows the UK to lead and sponsor trials as a third country	✓	UK researchers and companies cannot sponsor and lead trials without legal representation in the EU to ensure compliance This may increase complexity and costs and result in fewer trials being conducted in the UK	?	UK researchers and companies cannot sponsor and lead trials without legal representation in the EU to ensure compliance This may increase costs and result in fewer trials being conducted in the UK	?	
	Supervision and assessment	UK can benefit from the streamlined supervision and assessment process in the EU CTR which should result in reduced clinical trial timelines and costs	✓	Increased costs and barriers where the UK is outside of the supervision and assessment process Likely reduction in the number of EU-UK trials being sponsored in UK	✗	Increased costs and barriers where the UK is outside of the supervision and assessment process UK participates in fewer UK-EU trials UK could become a more international market for clinical trials over time	?	
	Transparency	Greater transparency of clinical trials benefits patients. Potential barrier to the placement of industry trials.	?	Less transparency of UK clinical trials with negative impacts on patients.	✗	Less transparency of UK clinical trials with negative impacts on patients	✗	
	Expansion of trials	UK-only trials can be expanded to include European centres (and vice versa) facilitating patient recruitment and access	✓	Limited ability to expand UK-only trials and to join EU trials already underway	✗	Limited ability to expand UK-only trials and to join EU trials already underway	✗	

✓ Positive outcome ✗ Negative outcome ? Risk or uncertainty

Implication	Full alignment	Partial alignment	No alignment	Recommendation
UK influence over future regulation and policy	? Significant risk that the UK will be subject to EU regulation without significant influence around medicines regulation in EU and new CT guidance Potential to negotiate membership or associated status with the EMA Limited international influence	✗ Significant risk that the UK will be subject to EU regulation without significant influence Limited ability to influence as an observer of the EMA Potential to influence regulation internationally	✗ No formal mechanisms for influencing former EU legislation Critical to build influence internationally	**The UK should adopt a broad strategy to EU and international engagement to ensure it can continue to influence and drive new regulation and standards across Europe and globally, including through partnership with the EMA**
Innovation	? UK automatically inherits new regulation. UK may have limited influence and opportunity to drive innovation. EU bureaucracy may limit the speed at which new regulation can be introduced	✗ UK required to take additional steps to implement new regulation UK likely to have limited influence and opportunity to drive innovation. EU bureaucracy may limit the speed at which new regulation can be introduced. Limited opportunities for divergence.	? Outside of the EU, the UK could take an innovative and proportional approach to regulation. Concerns that UK will become too niche, or become a rule-taker from another market e.g. USA	**Where full alignment with the provisions of the EU CTR is not possible, the UK government should seek a proportionate approach to regulation that balances alignment with the opportunities to innovate without compromising patients' safety**
Clinical trial design	? UK researches can influence and drive development of regulation for adaptive and real- world evidence trials UK aligned with Europe which may limit ability to adopt new approaches or benefit from advances internationally	? UK has limited influence for regulation of new trial designs but needs to align with EU legislation	✓ UK is independent and would drive development of regulation for adaptive and real- world evidence trials in the UK or internationally, or benefit from alignment with non- EU countries	**UK and EU regulation and regulators will need to adapt to allow for new trial designs, new devices and technologies, and new approaches to data**

✓ Positive outcome ✗ Negative outcome ? Risk or uncertainty

Table 1 Regulation. Key implications and high-level recommendations highlighting key features of different levels of alignment after Brexit.

Theme 2: Access to Medicines and IMPs and Devices

2.1 Trade barriers

Recommendation: The UK and EU should work to ensure that trade barriers do not impact the availability or movement of new and existing licensed medicines, Investigational Medicinal Products and devices after Brexit as this is crucial to maintain standard of care on which to build clinical trials

The clinical trials sector is reliant on the open and efficient movement of goods, not only for trade with the EU but internationally. 45 million packs of medicines are supplied from the UK to Europe each month, and 37 million in reverse. Internationally, exports of pharmaceutical and medical technologies account for 5.2% of UK goods and services by value[15].

The UK and EU currently cooperate closely and many companies have sites, or suppliers on both sides of the channel. Some medical products and medical devices make multiple border crossings as they move from design to production. The UK currently benefits from preferential trade with EU and other countries through existing schedules set by the EU. This could affect the movement and cost of drug products within the EU, currently distributed without import or export duties.

New barriers to trade may result in increased costs and inefficiencies to the movement of materials, including supplies for clinical research, and medical radioisotopes, potentially jeopardising patient care. Products may be also subjected to new tariff or non-tariff barriers resulting in raising costs.

Desktop research showed that in the event that new trade barriers are introduced, existing supply chains may

> **We need to address customs border issues to allow ease of passage of medicines and components of medicines**

be required to reconfigure, with impacts on the cost and efficiency of existing or planned clinical studies. New trade barriers may also result in small and mid-size biotech organisations outsourcing their manufacturing, packaging and labelling to third-party vendors, with a preference to use suppliers on the continent.

While the UK and EU are working to resolve border issues during Brexit negotiations, the efficiency of customs and regulatory checks and freedom of movement of goods with the EU is likely to be negatively impacted in almost all Brexit scenarios.

There are concerns that the proposed transition period (until December 2020) will not provide sufficient time to put new border arrangements into place. And in the event of a no deal, the transition period would not apply. This would mean the UK may be required to introduce a new border process immediately after it has left the EU, and there are significant concerns that the UK may not be ready, introducing significant delays. Additionally, there is also a potential for a hard border with Ireland.

Immediately following Brexit or during any transition period it will be critical to ensure that certain medicines, including those with short shelf-lives such as those including radioisotopes, can move quickly from production to their site of use in order to make them a reliable option for treatment.

After Brexit, trade with the EU will depend on the final negotiations. In the event of a 'Soft Brexit', the UK may

[15] CBI (2018) Smooth Operations. An A-Z of the EU Rules That Matter for the Economy

continue to comply with EU rules on the free movement of goods and services (Norway model) or just for goods (Swiss model) either outside or inside the Customs Union. In the event of a no deal scenario, trade would default to WTO rules. There has been some reassurance that the UK, under the WTO, would be able to place zero tariffs on some finished pharmaceutical products[16]. However, not all pharmaceutical products are eligible for zero tariffs and the list of agreed products has not been updated since 2010. Industry have voiced considerable concern about relying on WTO rules[16]. This includes concerns about the coverage of products and the disruption of complex product supply chains that have become integrated between the UK and other EU countries. This disruption is expected to add costs and cause delays in access to medicines[17]. It is unclear whether existing schedules with non-EU countries will be respected, or if the UK will need to renegotiate these.

Under all hard or no-deal scenarios, it has been estimated that the UK economy is likely to be depressed due to new trade barriers, with a loss of 1.0 to 3.0 percent of GDP and "even 'Soft Brexit' options are still worse economically than staying in the EU[18].

2.2 Marketing authorisation

Recommendation: The MHRA should work closely with the EMA to ensure equivalence of marketing authorisation processes and safety standards after Brexit

To get from trials to market and to remain there, products are subject to a series of regulations and standards that ensure best practice along the supply chain. Products must achieve marketing authorisation, an assessment of the quality, efficacy and safety of a product, before achieving clinical approval (and in some countries, demonstrating cost-effectiveness) at national level. To move between countries, they are also subject to testing requirements and certification, and are subject to ongoing pharmacovigilance to ensure patient safety.

As with clinical trials regulation (Theme 1) the dominant view was that the closest possible alignment with EU regulation and standards would be of benefit to patients and the sector. Similarly, there were some opportunities for the UK to innovate, for instance around device regulation and authorisation.

As part of the EU, the UK currently takes part in Marketing Authorisation through the EMA. After Brexit, it is unclear whether this will continue[19].

Before a drug can be placed onto the UK or EU market, an application needs to be made to a health authority in the EU. Products can be approved centrally by the EMA, or at a national level. The centralised approach allows for a single marketing authorisation to benefit all Member States and is seen to be an efficient mechanism for rare and paediatric diseases as it supports aggregation of data for market authorisation across countries.

Processes for mutual recognition also allow for a product to be approved for use in one Member State and then subsequently approved across other Member States, while the decentralised process allows simultaneous approval in multiple Member States.

The MHRA has stated that ahead of Brexit and during the transition period it will not seek to make any changes to existing arrangements[20]. The UK will continue to seek a close relationship with the EMA either as a full or "associate" member of the EMA.

[16,17] House of Commons (2018) The impact of Brexit on the pharmaceutical sector

[18] Rand (2018) After Brexit. Alternative forms of Brexit and their implications for the United Kingdom, the European Union and the United States

[19] CBI (2018) Smooth Operations. An A-Z of the EU Rules That Matter for the Economy

[20] MHRA (2018) MHRA update to pharmaceutical companies on exit preparations

However, given the complexity and long lead-times the MHRA has urged Pharma to prepare for a no-deal. In the event of a no-deal the EU (Withdrawal) Bill will convert the existing EU legislative framework into UK law at the moment of exit, so there would be no sudden changes to the processes for market approval in the UK[21]. The UK could choose to replicate and align authorisation processes and replicate any EU approvals, minimising duplication and requirements for submission of multiple approvals.

A rather pressing concern was whether the MHRA and EMA would continue to cooperate and remain aligned in the longer-term. Divergence in regulation could result in the UK becoming a lower priority market compared to the EU which as a combined market receives 25 percent of global sales compared to the UK at 3 percent[22].

The result may be substantial delays to new medicines for UK patients. Studies of Switzerland and Canada (which are cited as potential models for the UK's future relationship with the EU) have shown that Switzerland gains access to new medicines 157 days later on average than the EU, and that Canada sees delays of 6-12 months[23].

As a third country UK data may not be eligible for use in EU marketing authorisation. It was noted that there were some precedents for using international data but that this typically is to support EU data as part of a larger dossier. An inability to use UK data may decrease the appetite for the placement of trials in the UK. Participants also raised concerns about the UK's capacity and capability to independently conduct and maintain a greater number of authorisations outside of the EU.

An additional benefit of the centralised approach to market authorisation is parallel trade, or parallel distribution, namely the distribution of a centrally authorised medicinal product from one Member State to another by a pharmaceutical company independent of the marketing-authorisation holder. Parallel trade is estimated to have saved the NHS €986.2 million between 2004 and 2009 and is the only mechanism through which certain medicines are available in the UK. Loss of parallel trade may result in increased costs, or affect the future supply of these medicines[22].

Safety testing is also currently coordinated by the EU as an important aspect of marketing approval and ongoing pharmacovigilance, although individual countries have a National Competent Authority who are responsible for safety monitoring.

In the short-term there are concerns that after Brexit, patient safety may be compromised, where the UK is no longer able to access and contribute to EU pharmacovigilance databases and processes.

The UK also contributes significantly to pharmacovigilance studies within Europe and has detected the greatest number of "signals" or flaws in medicines since 2012[24]. After Brexit, an inability for the UK and EU to cooperate on pharmacovigilance could have significant negative impacts for patients across the UK and EU.

Approval and Reimbursement

Once marketing authorisation has been given and a drug has an EU or UK licence, it can be prescribed in the UK, however, to be made available on the NHS, or at a national level, it needs to be approved.

[21] MHRA (2018) MHRA update to pharmaceutical companies on exit preparations

[22,23] UK EU Life Sciences Steering Group (2016) Maintaining and growing the UK's world leading Life Sciences sector in the context of the EU

[24] House of Commons (2018) Brexit: medicines, medical devices and substances of human origin. Fourth Report of Session 2017-19

In England, the National Institute for Health Care and Excellence (NICE), provides guidance on whether a drug should be made available based on its cost-effectiveness in terms of the cost per quality-of-life-adjusted year (QALY) with input from interested parties including health professionals, patient organisations and experts.

Respondents perceived that the UK's current approach to NHS approval and reimbursement challenges the translation of drugs from trials to patients, with some drugs developed in UK trials more likely to see approval in international markets.

This issue was also raised by several UK and EU clinicians and pharmaceutical companies, who highlighted this as one of their four key priorities for HM government. A participant noted that this was particularly true for oncology trials, and that while the UK has the third highest launch rate for new medicines globally, it is at the bottom of the EU league table for patient access to medicines[25].

To address this, a new approach to approval was suggested. This would include a shift away from decisions solely made on the basis of QALY estimates made from clinical trials data to include the use of real world evidence.

In scenarios where the UK is no longer aligned and cooperating with the EU the need for the UK to have a competitive approach to market approval and reimbursement without compromising patient safety was seen as important to help companies to commercialise trials, and to incentivise research in the UK.

Participants also called for efforts to reduce the timeline for approval processes to help support commercialisation, as well as a broader review of the standards of evidence and indicators used for approval.

> **"If you limit the drugs that are used and are available for patients – the standard or care may be different to other countries. Patients may not be able to access drugs and solutions may be limited**

Ultimately, the lack of commercialisation of products into the NHS and the UK market was viewed as a risk to patients with concerns that the UK may fall behind other countries for Standard of Care.

[25] Written evidence submitted by workshop participant (Confidential)

2.3 Medical devices, Investigational Medicinal Products and product regulation

Recommendation: The UK and EU regulators should ensure equivalence of regulation and standards for certification and testing of Investigational Medicinal Products and devices

Where the UK is outside of the EU after Brexit, it will initially be aligned with the majority of regulation. However, as with the EU CTR, it is unclear whether alignment can or will be maintained in the longer-term. Any future divergence may have significant impacts on patients and research where it introduces duplication, costs or delays. As stated earlier in the theme, it will also be important to ensure that any new customs barriers around access to medical devices are minimised.

There are precedents to achieve this. The EMA has existing mutual recognition agreements with third countries such as Switzerland, USA and Canada. The UK could build on these, and the government policy paper on Collaboration on Science and Innovation specifically mentions Good Manufacturing Practice (GMP), Good Distribution Practice (GDP) and medical device notified bodies as areas that could be included in any mutual recognition arrangement between the EU and UK[26].

An additional barrier to the conduct of clinical trials and the competitiveness of the UK, cited by participants, is the future requirement for the release and certification of IMPs.

As part of the customs union, IMPs are not subject to additional testing when moving between the UK and EU. A quality control test is performed once in a single member state by a Qualified Person (QP) who is legally responsible for the safe batch release of medicines before they are placed on the market or used in clinical trials.

After Brexit, where the UK does not have arrangements in place, this may cause significant additional barriers to the import and export of IMPs between the UK and EU. New customs checks and requirements may result in inefficiencies, and increased costs, in particular for testing, certification and ongoing market surveillance.

If QPs in the UK will no longer be recognised in other EEA countries, then there will be a requirement for any medicines or devices exported from Britain to have a QP based in each customer's country[27].

The fear expressed by many participants was that this will increase the cost of doing business and thus dissuade companies from investing in British trials, as well as leading to those QPs currently residing in the UK moving to other EEA states.

For medical devices, there are three existing directives, which the UK has already adopted. However, two new directives designed to improve health and safety for patients, support fair trade and to modernise existing directives are due to come into force in 2020 (medical devices) and 2022 (in vitro diagnostic medical devices).

[26] CBI (2018) Smooth Operations. An A-Z of the EU Rules That Matter for the Economy

[27] IQVIA (2018) Personal communication

Access to medicines, IMPs and devices	Implication	Full alignment	Partial alignment	No alignment	Recommendation
	Trade barriers	? Outcome dependent on the shape of Brexit. Products may be subject to new tariff or non-tariff barriers resulting in raising costs Increased costs and inefficiencies to the movement of materials, including supplies for clinical research, and medical radioisotopes.			**The UK and EU should work to ensure that trade barriers do not impact the availability or movement of new and existing licensed medicines, Investigational Medicinal Products and devices after Brexit as this is crucial to maintain standard of care on which to build clinical trials**
	Marketing authorisation	✓ UK participates in EU marketing authorisation processes Aggregation of data for market authorisation supports rare and paediatric diseases Rapid access to drugs authorised in Europe UK benefits from parallel distribution of medicine and IMPs UK and EU can share signals and safety information for Pharmacovigilance	✗ UK may be able to participate in EU marketing authorisation processes Potential delays in access to and availability of medicines and IMPs UK unable to benefit from parallel distribution, raising costs of some medicines Additional costs and delays in sharing safety data	✗ UK unable to participate in marketin authorisation process Significant delays to the availability and access to drugs No parallel distribution resulting in increased costs Barriers to the placement of trials Additional costs and delays in sharing safety data	**The UK government should continue to seek a close partnership between the MHRA and the EMA. An agreement should be sought to allow EMA marketing authorisation decisions to apply to the UK and equivalent safety standards to be maintained after Brexit**
	Medical devices, IMP's and regulation	✓ UK adopts EU regulation for medical products including GMP, GDP. Mutual recognition of standards, certification requirements and Qualified Persons No additional testing requirements. Free movement of medical products (including IMPs) and devices.	? UK adopts EU regulation for medical products including GMP, GDP. Equivalence of standards and certification but no mutual recognition. Additional barriers to the import and export of IMPs between the UK and EU.	✗ UK and EU standards diverge. No recognition of standards and certification. Significant additional barriers to the import and export of medical products, IMPs and devices between the UK and EU.	**The UK and EU regulators should ensure equivalence of regulation and standards for certification and testing of Investigational Medicinal Products and devices.**

✓ Positive outcome ✗ Negative outcome ? Risk or uncertainty

Table 2 Access to Medicines and Investigational Medicinal Products. Key implications and high-level recommendations highlighting key features of different levels of alignment after Brexit.

Theme 3: Data

Recommendation: A more streamlined and efficient approach is required in the UK and internationally to allow the effective collection and sharing of anonymised patient and trial data while protecting patients' rights and interests.

> **If we are not aligned, our data counts for nothing. Why would we do trials if data counts for nothing?**

The ability to share data across borders was seen to be an imperative in all scenarios and crucial to a successful future for clinical trials. Participants were concerned that delays in sharing data would ultimately reduce the effectiveness of research, prevent timely commissioning of clinical studies and delay access for patients to treatments and research.

The need for data was seen to be particular acute over the next decade as clinical trials evolve. In particular, in response to:

- new approaches to devices and diagnosis
- a need to capture and share new types of data to support real-world evidence trials
- increasingly personalised and stratified trials
- a need to ensure an efficient and harmonised approach to data across the UK
- a need to drive international collaboration.

Transparency and ease of disclosure of clinical trial data between UK and EU was a particular concern. After Brexit it is expected that the MHRA will align in its majority with the new CTR, and the UK will adopt the provisions of the GDPR.

However, there were concerns that a lack of harmonisation in the long term might mean that UK data is not accepted across Europe or Internationally.

The use and access to data around observational trials, was also viewed to be critical to understanding how best to optimise clinical trials and treatments for patients in the future. Access to EU data and patient populations was again seen to be critical for the conduct and design of observational trials, designed to better understand the real-world impact of trials on patients.

Data portability and transparency is also critical for ensuring appropriate patient recruitment. Patient recruitment and retention are a major challenge for those running trials, with a high percentage not meeting targets and drop-out rates increasing. Data portability and transparency is seen as critical to overcome this as it aids with patient perception of the effectiveness of trial care.

For paediatric and rare diseases where recruitment can already be a challenge, the ability for the UK to share and access data internationally was seen to be especially important.

Regarding data regulation, there was a broad call for the UK to continue to align with future EU CTR regulation, as well as the provisions of the General Data Protection Regulation 2016/679/EU ("GDPR") which has come into effect in May 2018 and introduces new requirements for genetic and genomic data.

Under the GDPR, data subjects have new rights to help ensure their data are processed securely and with adequate

protections, and clearer responsibilities and obligations are placed on companies using such data. In particular, the GDPR raises some important questions for clinical trials, where the new rights to erasure of personal data and to data portability need to be managed appropriately by sponsors and regulators. After Brexit, the level of alignment chosen by the UK on data protection will affect how data is shared and handled both within the UK and across borders, and ultimately how clinical trials are performed.

Were the UK to become unaligned with EU regulation, this would result in increased bureaucracy and costs, or fundamentally prevent data from being shared across borders, with negative impacts of the conduct and placement of trials. Investment in data infrastructure was seen as an imperative. There was also significant concerns that public attitudes to data may limit their participation in trials.

While the sector should do everything it can to explain the need and benefits of data sharing, it was acknowledged that it may have limited ability to shape the societal dialogue especially where impacted by developments in the use of data in other domains, for instance a backlash against social media.

Participants also saw a requirement to get ready for changes to global data standards with any shift towards greater international harmonisation of standards a positive outcome.

Specific suggestions included:

- **Support for sharing of anonymised patient level data** and to make it available to support clinical and commercial research. In the UK, the NHS was viewed as an important national asset for collecting and accessing patient-level data for trials, which could be unlocked through a streamlined and unified approach to data sharing. To this end, the planned improvements to the health data infrastructure in the Life Sciences Industrial Strategy[27] were supported by participants. The Clinical Practice Research Data Link was also noted as important for supporting the collection and use of observational data.
- **Harnessing big data.** With the increasing focus on Big Data this will be a valuable resource for driving future discoveries in cancer research. Interviewees noted that predictive clinical trials were increasingly being used by some pharmaceutical companies and investors to identify in advance what drugs may be worth investing in or targeting to different markets. With all the data available, it is important, however, that clinical trial management and data analytics software keep pace.
- **Incentivising patient participation** by ensuring patients understand their rights and the benefits of sharing their data for clinical research, with certainty over what data is used.

> **We need a more mature understanding of consent over "donating data" "who gets access" and "who benefits". We currently err on the side of safety so data is not fully shared. Regulation should support access and transparency.**

[28] HM government (2017) Life Sciences: Industrial Strategy

Theme 4: Funding

Recommendation: The UK and EU should agree full UK participation in EU framework programmes with access to funding for clinical research.

A long-term strategic approach to funding of clinical trials is necessary in the UK to both ensure investment and to drive collaboration.

Funding was the voted as most critical factor for the sector to address over a 5-10 year timeframe and the availability of funding for trials, research and innovation was the second highest ranked factor based on impact out to 2028 (Figure 2).

There were concerns about the ongoing commitment of the UK government to support and fund clinical trials after Brexit. Participants welcomed commitments to date including government ambitions to increase investment in UK research and development to 2.4% of UK GDP by 2027[29] and planned initiatives to encourage industry investment, as well as government commitment to provide funding for the lifetime of existing projects that are funded by EU Framework Programmes. A recent speech from the Prime Minister on science and the modern Industrial Strategy highlighted the government commitment to invest in science and research to keep the UK at the forefront of new technologies and the benefit their bring[30].

However, there were concerns about the longer-term commitment of this, or future governments, where faced with other pressures, such as an economic downturn or global recession.

A strategic approach to funding was suggested, one that would take a long-term and cross-party approach to provide additional certainty.

> **The UK should ensure that they remain involved in EU Framework Programmes to ensure that there is a continuous funding stream for clinical research coming into the UK. This will be important for continuing successful collaborations between UK and EU researchers and to build on the successes of previous trials.**

This would include the closest possible association to existing and future EU programmes after Brexit, such as Horizon Europe (FP9). The UK was a net contributor to the EU budget between 2007 and 2013, but was one of the largest recipients of research and innovation funding and is believed to have received a greater amount of EU research funding than it contributed[31].

There are signs, that the EU is keen to retain close ties with the UK in relation to research and innovation: the European Commission's LAB – FAB – APP: Investing in the European Future We Want report, July 2017[32], calls for 'full and continued engagement' with the UK, recognising that cooperation and ongoing engagement has benefits for the EU.

Continued participation in future framework programmes was also viewed to provide non-financial benefits by supporting the quality of the UK research environment, driving opportunities for collaboration and supporting the movement of researchers and the workforce into the UK, with benefits to trials and its workforce.

[29,30] HM Government (2018) PM speech on science and modern Industrial Strategy: 21 May 2018

[31] Royal Society (2015) UK research and the European Union: The role of the EU in funding UK research

[32] European Commission (2017) LAB – FAB -APP. Investing in the European Future we want

There are a variety of existing mechanisms to access EU funding and to facilitate participation in EU framework programmes that may be available to the UK, but any agreement will need to be agreed as part of Brexit negotiations:

- 16 countries have Associated Country status for H2020, including Switzerland, Norway and Israel. These countries have full access to H2020 under the same conditions as EU Member States[33].
- Some non-associated third countries are also eligible for full participation: Enlargement Countries (those seeking to join the EU), Neighbourhood Countries (close Eastern and Southern neighbours to the EU), and developing countries are automatically eligible.
- Other third countries may obtain access through a bilateral agreement. These agreements have different requirements in terms of a country's wider relationship with the EU - for example in terms of single market access, freedom of movement of people and budgetary contributions.
- Third countries with no bilateral agreement who do not qualify for full access are still able to participate in H2020, but they are not usually eligible for any EU funding.
- Many countries also hold bilateral science and technology cooperation agreements with the EU (e.g.Brazil, Canada and Egypt) but the mechanisms vary. They may include participation in joint projects, sharing of facilities, staff exchanges, or the organisation of specific regional or thematic events.

In addition to ensuring access to EU funding, participants also surfaced a number of other suggestions for how to support funding for clinical trials and research including:

- New strategic funding calls in the UK designed to encourage investment in UK priorities. This would need to be linked to a clear strategy for the sector.
- Establishing a budget for research including strategic funding for the NHS and research infrastructure. There were concerns that NIHR were providing less support for research infrastructure within the NHS than in the past.
- Driving investment in priority areas through philanthropic funding or grand challenges.
- Investing in an innovation ecosystem that can support SMEs and start-ups to support clinical trials and the broader life science and data ecosystem and encourage venture capital funding through initiatives like the Patient Capital Investment Vehicle (PCIV)[34]
- Encouraging efficiencies to support existing funding by investing in emerging technologies and automation.
- Prioritising new international schemes to drive international collaboration.

[33] European Commission (2017) Associated Countries

[34] Royal Society (2015) UK research and the European Union: The role of the EU in funding UK research

Theme 5: Workforce

Recommendation: The UK government should negotiate reciprocal arrangements, where possible, to ensure international mobility, as this is seen as a critical aspect of collaboration and research excellence.

The UK Government should modernise and streamline its global immigration system as this is also seen as a critical aspect of collaboration and research excellence. In particular, a permissive immigration system should be developed that supports the clinical trials, health and research workforce that allows continued movement across borders.

The UK needs to invest in a skilled clinical trials workforce to ensure it can maintain its longer-term competitiveness encouraging UK investment.

Participants recognised that to stay competitive in a global market it would be necessary to protect the clinical trials workforce in the short-term, as well as to invest in developing the necessary skills for the future to support new trial designs and to keep pace with advances in technology and research.

An ideal outcome was viewed to include a permissive migration system that allows continued movement of workers with skillsets relevant to clinical trials, health and research.

Mobility is also an important driver of collaboration and innovation. Additionally, ease of movement of workers and their families helps countries to attract talent and specialist skills which greatly contributes to economic growth and development.

Freedom of movement of UK workers within the EU, and the reverse, is likely to be impacted in almost all Brexit scenarios. Ongoing uncertainty around freedom of movement and negative perceptions about the UK's intentions is already impacting people's decisions to move to or remain in the UK.

> **We need to be able to attract the brightest minds to innovate and staff to deliver. It's already difficult to recruit high quality triallists and trial delivery is affected by resource issues in the NHS**

EU migrants make a significant contribution to clinical trials in the UK and a loss of freedom of movement could:

- Affect the UK's ability to attract and retain talent and specialist skills - not only to ensure recruitment of the best staff, but also to foster collaborations with leading researchers in other countries.
- Reduce the pool of available workers who are not subject to immigration rules – hindering recruitment. There was a view that the UK is already struggling to recruit personnel to deliver trials in the UK and to support the healthcare system, so a restrictive immigration policy might worsen the situation.
- Increase the administrative burden and cost of relocation where migration is still possible.
- Reduce the attractiveness of the UK as a destination for overseas researchers, with the potential to lose skills to other European and international destinations limiting the UK's ability to attract and train the researchers of tomorrow

- Limit the ability of UK researchers to participate in career-enhancing collaborations and knowledge hubs, and to participate in EU and international research networks
- Reduce expertise in the UK for the delivery of trials and development of innovative therapies and trial designs
- Potentially limit or add additional barriers to patient recruitment for some rarer and paediatric disease trials

Positive indications have recently been provided by the UK government[35] including through The Life Sciences: Industrial strategy[36] and Life Sciences sector deal[37] which acknowledge the importance of global science and recommends that the government establish a system for fast recruitment and retention of highly skilled workers from around the world.

It also sets strategic goals of attracting 2000 new scientists as well as developing a programme to attract 100 top-class researchers to the UK over the next ten years. However, it is unclear whether the mandate or political will exist in the UK to continue to deliver on these goals.

It is essential to train scientists with the relevant skills for the future in order for the UK to remain globally competitive. The emerging field of Big Data will also require a new generation of scientists with skills to adapt to rapidly changing technologies. The Life Science Industry Strategy includes recommendations to increase apprenticeships in data sciences as well as allocated funding for cross-sectoral partnerships and exchanges across industry. This will open up a range of opportunities for young people and early career researchers, while ensuring that the next generation have the relevant skills to carry out innovative multidisciplinary research.

There have been calls for the UK to not only focus on replacing existing arrangements with the EU, and minimising UK-EU barriers, but also to seek to harmonise and reduce barriers internationally. This applies equally to the UK immigration system, as it does to arrangements with other countries who may have more bureaucratic, costly or confusing visa systems.

Recognising this, participants called for:

- Urgent clarity on future immigration, and in the long term for new approaches that facilitate migration.
- A change of immigration policy including mechanisms such as Visas, and routes for students, researchers and workers to come to the UK, without necessarily facilitating residency.
- Targeted recruitment from particular countries or focused on attracting particular skill sets. This requires the sector to better understand what the future skills and requirements of the clinical workforce will be.
- Investment in education and opportunities to support skills development, including by increasing the number and type of courses available and investing in vocational education and workforce development.
- Investment in new incentives to attract and keep workers in the UK, including new opportunities for career progression and increased transparency and new opportunities for research.

[35] HM government (2018) PM speech on science and modern Industrial Strategy: 21 May 2018

[36] HM government (2017) Life Sciences Industrial Strategy

[37] HM government (2017) Industrial Strategy. Life Sciences Sector Deal

- Efforts from both the government and the research community to ensure a welcoming and inclusive culture and to actively promote opportunities for people to work in the UK.
- An assessment of pay and conditions in the NHS and research with a view to addressing barriers to the retention of staff. Skilled staff are already viewed to be leaving the NHS, whether clinical staff, research nurses or other workers. Unless the UK invests in the workforce, this is likely to place increased demands on the remaining workforce, and require retraining and redeployment, or new approaches to streamlining work through the use of new technologies and automation.

Ultimately, where additional constraints are placed on the workforce and where other countries become more attractive there is a real concern that the UK will lose its workforce and become less diverse, less competitive and less innovative.

Patients may lose confidence in the NHS and may have poorer patient outcomes, experiences and opportunities to participate in trials.

	Implication	Full alignment	Partial alignment	No alignment	Recommendation
Data	**Data**	✓ Data protection remains aligned between UK and EU UK influences new standards and approaches to data sharing Permissive environment for real-world evidence Effective patient recruitment	? UK likely to remain aligned with EU data protection Lack of influence may limit UK's ability to drive new standards and approaches UK may be unable to participate in databases	✗ UK and EU regulation may diverge with negative impacts on the ability for data sharing, patient recruitment, pharmacovigillance and trials Opportunity to innovate	**A more streamlined and efficient approach is required in the UK and internationally to allow the effective collection and sharing of anonymised patient and trial data while protecting patients' rights and interests.**
Funding	**Funding**	✓ UK can participate in EU Framework programmes and funding either as an Associated country or through a bilateral agreement	? UK can participate in EU framework programmes as a Third Country but is unlikely to be eligible for funding New strategies may be required to support funding and investment in the longer-term	✗ UK can participate in EU framework programmes as a Third Country but is ineligible for funding New strategies will be required to support funding and investment in the longer-term	**The UK and EU should agree full UK participation in EU framework programmes with access to funding for clinical research.** **A long-term strategic approach to funding of clinical trials is necessary in the UK to both ensure investment and to drive collaboration.**
Workforce	**Workforce**	? Short-term uncertainty likely to persist until Brexit outcome known with negative impacts on workforce. Freedom of movement of UK workers within the EU, and the reverse, is likely to be impacted in almost all Brexit scenarios with negative impacts on the availability of skilled workers in trials and the health sector. Negative impact on UK talent and international competitiveness Opportunities to harmonise migration internationally.			**The UK government should negotiate reciprocal arrangements, where possible, to ensure international mobility, as this is seen as a critical aspect of collaboration and research excellence.** **The UK Government should modernise and streamline its global immigration system as this is also seen as a critical aspect of collaboration and research excellence. In particular, a permissive immigration system should be developed that supports the clinical trials, health and research workforce that allows continued movement across borders.** **The UK needs to invest in a skilled clinical trials workforce to ensure it can maintain its longer-term competitiveness encouraging UK investment.**

✓ Positive outcome ✗ Negative outcome ? Risk or uncertainty

Table 3 Data, Funding and Workforce. Key implications and high-level recommendations highlighting key features of different levels of alignment after Brexit.

SECTION 3

Conclusions and Next Steps

The implications and recommendations outlined in this report are those that participants surfaced as critical to address as the UK and EU work towards a positive future for trials: a future where patients have the best possible outcomes and benefit from a thriving clinical trials sector.

As explored in Sections 1 and 2, the shape of Brexit has the potential to influence and limit what options are available to the sector. As the UK and EU enter phase II negotiations, the sector needs to ensure that clinical trials and patients remain a priority for the UK and EU.

Regulatory alignment in itself will not be sufficient to ensure the best possible outcome. The UK will need special agreements to access the EU portal and database and to simplify UK ability to lead and sponsor trials. It will also need to ensure it can fully participate in pharmacovigilance databases and seek mutual recognition for standards and certification.

Without this, patient safety could be compromised, and industry may be disincentivised from setting up and running trials in the UK.

It will also be necessary to ensure that funding and a skilled workforce are available to support trials, and to address structural barriers to the conduct of trials in the UK. Many of these barriers are not new, but were viewed by participants to have become more apparent and urgent due to Brexit.

A systemic and strategic approach is needed, one that will help to address the implications outlined in Section 2. An approach that will ensure that the sector is best equipped to meet future challenges as well as those apparent today, and to take advantage of new approaches to healthcare, data and trials.

> **If we don't have new ideas, therapies, devices then the sector won't advance. In the NHS we have a perfect test put with patients who are keen to participate in innovative treatment and trial design**

It was positive that participants sought to find opportunities and solutions to the challenges for the future of clinical trials. They reflected a genuine and open desire to mobilise and collaborate towards a positive future for regulation, trials and patients.

It is also encouraging to see the broader sector – patients, clinicians, research, policy makers and regulators – in agreement around the need for future alignment and participation in EU clinical trials regulation and associated systems.

However, the political processes inherent in Brexit, and the "all or nothing" approach that many see around future engagement with Europe, means that it is even more critical than ever to prepare for alternative outcomes. In particular to be ready for a no deal scenario where the UK may end up outside the EU and without a transition period.

It is understood that the MHRA and UK government are preparing for alternative outcomes, but the view from many participants is that this has been happening behind closed doors, without details being communicated to the sector.

While acknowledging the political sensitivities inherent in Brexit, there was a view that more could be done to provide assurance and support.

In the event that the UK is no longer aligned with the EU, the biggest concern was around a lack of UK influence on the future development of standards and regulation. There was a strong consensus that a future in which the UK is unable to share its experience and drive innovation is undesirable.

Under these circumstance, the UK may be better to diverge from EU regulation to foster innovation and help develop a competitive environment for trials, in particular to support new trial designs, including Real-World Evidence and adaptive design.

Some respondents also suggested that a relationship with the United States could bring access to greater patient populations and a more enlightened approach to regulation.

In addition, participants also identified a number of "no regrets" strategies, that would be worth exploring in all scenarios.

These include:

- The need for UK government to invest in an NHS that is fit for the future, one with a unified data infrastructure, a strong workforce and a focus on research.
- The need for the sector to do to more to communicate the economic and social value of trials and ensure its prominence in phase II negotiations. In particular to promote the contribution of trials to the broader life sciences sector including its positive impact on patient outcomes.
- The need for UK government to develop a long-term, strategic vision for the clinical trial sector that provides early and ongoing assurance for UK triallists and industry. Workshop participants suggested the Vision needed to look out beyond the electoral cycle, and to take a cross-party approach to ensure strategic investments are prioritised for the long-term
- The need for the UK and EU to ensure a smooth transition to any new arrangements to minimise disruption to patients and trials, resulting from new systems
- The need for the UK to develop an approach to immigration that will support clinical trials and the broader health and life sciences sector

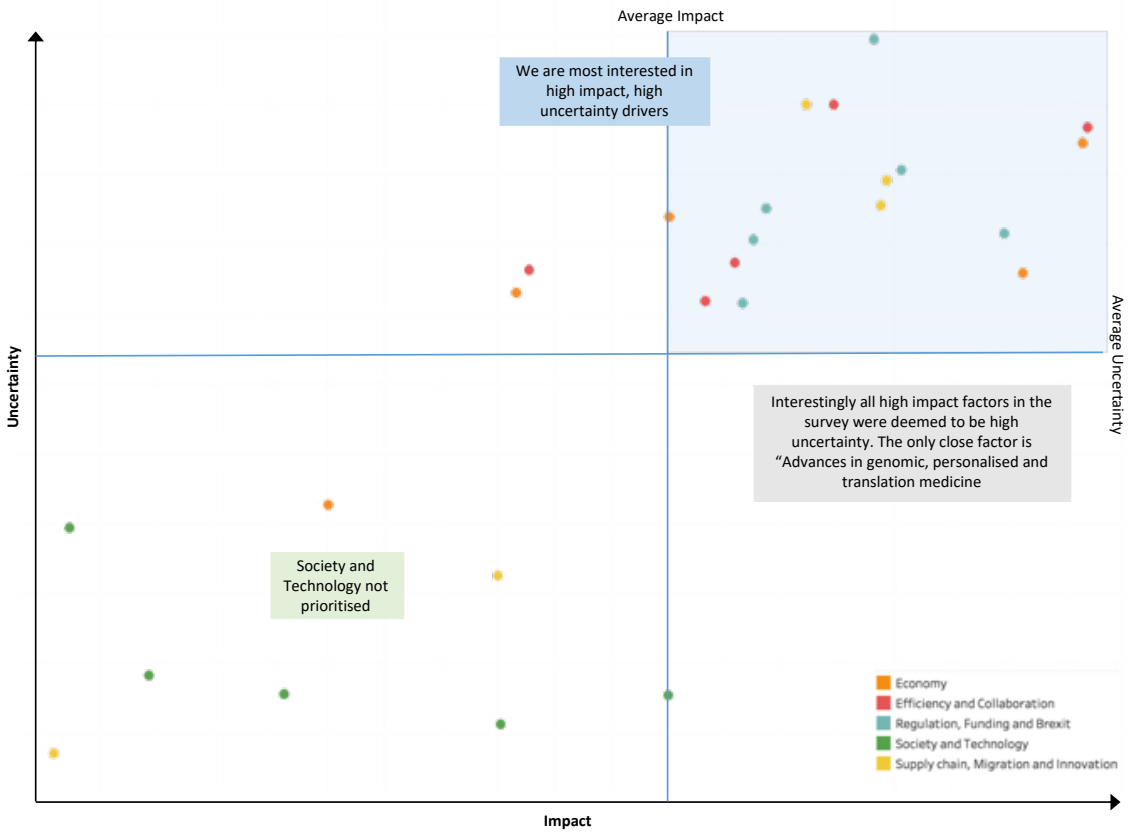
As negotiations progress, and more clarity is gained as to the outcomes of negotiations – the shape of Brexit and the level of alignment between the EU and the UK – we encourage CRUK to continue to push debate on the future of clinical trials, and to revisit the findings of this project.

A successful future for patients will require an ongoing and committed focus of the sector to addressing the broader and longer-term issues outlined in the report, regardless of the Brexit outcome.

ANNEX A

Driver Prioritisation

During the online assessment exercise, participants were asked to assess 26 drivers of change (identified on the horizon scan) to select those that (a) were likely to have a high impact on the sector out to 2028 and (b) where there was a high level of uncertainty as to what that impact would be (see Figure 6).



Top 10 Drivers by Impact

1. Ease of cross-border collaboration
2. Availability of funding for clinical trials, research and innovation
3. International competitiveness of UK/EU for the conduct of clinical trials
4. UK participation in EU Framework programmes and funding
5. Alignment of clinical trials regulation
6. Transparency and ease of disclosure of clinical trial data between UK and EU
7. Easy movement of workers and their families
8. UK and EU cooperation around development of regulation and policy
9. Ease of marketing authorisation and parallel distribution
10. Efficiency of customs and regulatory checks between the UK and EU

Top 10 Drivers by Uncertainty

1. UK and EU cooperation around development of regulation and policy
2. Ease of marketing authorisation and parallel distribution
3. Efficiency of customs and regulatory checks between the UK and EU
4. Ease of cross-border collaboration
5. Availability of funding for clinical trials, research and innovation
6. Alignment of clinical trials regulation
7. Transparency and ease of disclosure of clinical trial data between UK and EU
8. Easy movement of workers and their families
9. Alignment of devices and drugs regulation
10. Strength and volatility of the global economy

Figure 6 – Results of the prioritisation exercise showing the highest impact and high uncertainty drivers

ANNEX B: Scenarios

Overview

Having gathered and explored perspectives on the critical issues facing the future of clinical trials out to 2028, SOIF developed a set of alternative scenarios exploring the future of clinical trials out to 2028 in the context of Brexit.

The scenarios are not intended to be predictive, but consider a range of potential developments that might take place over the next decade.

The scenarios are one to two-page narratives that describe alternative possible futures, looking out one decade to help shift perspectives away from immediate Brexit concerns to consider longer term issues around future alignment of clinical trials regulation in an evolving sector.

The scenarios assume that Brexit has happened and build on inputs from the CRUK Policy Team around potential future levels of alignment with the EU CTR.

We have chosen to consider five scenarios, designed to reflect a broad range of possible Brexit outcomes. In each of these scenarios we have considered as a starting point, what the most likely level of alignment will be between the UK and EU for clinical trials regulation, and specifically access to the EU database and portal.

For each scenario, and alignment option, we have mapped out the key features that will determine the future world in 2028. We are now considering how each scenario might develop by 2028, based on how a wider set of drivers might interact to shape the future, namely:

- The broader regulatory environment
- Cooperation and collaboration
- Trade barriers and supply chains
- Skills and migration
- Funding and the economy
- Future competitiveness of the UK and EU
- A vision for the sector

The resulting scenarios are just a few of those that could be imagined from a range of possible futures. They are not meant to be predictive, but by taking the time to explore alternative futures, this will allow us to identify some of the critical issues and strategic choices that need to be made. For instance, by developing and prioritising policies that are resilient in multiple futures, or those that are effective in a particular future.

The scenarios

Scenario 1: No Deal / No alignment with EU Clinical Trials Regulation

Scenario 2: No Deal / Partial alignment with EU Clinical Trials Regulation

Scenario 3: Limited Free Trade Agreement (Hard Brexit) / Partial alignment with EU Clinical Trials Regulation

Scenario 4: Comprehensive Free Trade Agreement (Hard Brexit) / Full Alignment with EU Clinical Trials Regulation

Scenario 5: Soft Brexit with UK joining the EEA / Full alignment with EU Clinical Trials Regulation

Scenario 1

Brexit Shape: No Deal
Alignment: No Alignment with EU Clinical Trials Regulation

Brexit talks collapsed at the end of 2018 with the EU and UK failing to reach an agreement during phase II negotiations. As a result, the proposed transition period that was intended to last until 2020 fell through, as this was conditional on Phase II negotiations.

The UK left the EU at the end of March 2019. Trade defaulted to WTO rules, without any agreement between the UK and EU for the free movement of goods, capital, services and labour. Research and scientific collaboration was impacted once the UK became a third country with limited options to participate in EU programmes and access funding to support researcher mobility.

Relationships with the EU are still tense, though the EU and UK have struck some deals in areas of mutual benefit, for instance to address the Irish border question and to support aviation.

Tough choices and long-term solutions have been necessary. The UK faced political pressures to restrict migration and today there is still limited free movement between the UK and the EU, while geopolitical tensions have led to a more complicated visa system globally.

Skills shortages still bite

Today, overseas workers do not see the UK as an attractive destination. The UK still faces significant skills and labour shortages, which have impacted healthcare, research and clinical trials. A significant numbers of EU workers left the UK following Brexit and a smaller pool of skilled workers is available.

Fast tracked trade with the US

The UK government saw an opportunity to establish trading relationships with new international partners including countries in Asia, the US and Canada. The 2024 UK-US Free Trade Agreement being the most significant – the product of four years of accelerated negotiations.

Cooperation with the EU is now mostly through bilateral agreements with individual Member States or through cooperation with non-governmental European networks. The UK is outside of most decision-making and as has limited access to EU funding and programmes. This has had a negative impact on UK research in a suppressed economy.

The number and variety of clinical trials conducted in the UK has been impacted. The UK has not implemented the provisions of the EU CTR, is not able to access the EU database and portal, or to lead or participate in clinical trials that include European countries. However, the MHRA took steps to develop a bespoke regulatory approach to support innovation and reduce barriers for the conduct of clinical trials. This has helped make the UK a more attractive partner for novel trials and the UK benefits from a closer alignment with the United States.

Fewer clinical trials are taking place in the UK and despite demand, patients are sometimes unable to access innovative clinical trials taking place in the EU, as the UK and EU are not collaborating by running parallel sites in the UK and EU.

A mixed Clinical Trials sector

With the UK outside the EU many international businesses shifted their attention to other, larger markets. However, the exodus was not as big as some had expected, possibly due to the early and ambitious vision set out by UK and US governments on their intentions to collaborate.

In the short-term, there were some issues around the availability of existing medicines and investigational products, in part due to new customs and regulatory requirements. The loss of parallel trade within Europe has also made it harder for the UK to benefit from cross-border sales of drugs from the EU.

Scenario summary

Brexit	No deal. The UK leaves the EU without any trade agreement in place. UK and EU negotiate a transitional period beyond that already agreed in principle for an additional 4 years. The UK is outside the Single Market and its associated four freedoms (the free movement of goods, capital, services and labour) and outside the Customs Union (a trade agreement in which EU countries decide not to tax imports or goods from inside the Union and prohibits members from negotiating trade agreements separately from the EU).
Regulatory environment	The UK and EU have no alignment around EU CTR. The UK has distinct processes, a bespoke approval system and is unable to access the database or lead on European trials. The UK cooperates with the EU as a third country with no additional agreements around research, scientific collaboration or clinical trials. There are opportunities for UK to prioritise regulatory alignment and cooperation with international markets.
Cooperation and collaboration with the EU	Reasonable co-operation with the EU. Strong non-government cooperation. Bespoke agreements agreed for data sharing, regulation and citizens rights and access to EU Framework Programmes and funding. Government funding to reinforce existing research and attract international investment has minimal impact. UK prioritises early career and other travel. In the absence of any specific agreement, however, the UK would have limited opportunities to collaborate on Framework Programmes and would need to provide funding to resource any collaboration.
Trade and supply chains	UK free to negotiate trade agreements. UK and EU trade on WTO terms, which means no preferential tariffs. Goods have to meet each jurisdiction's regulatory requirements. A new UK border system would be required as soon as Brexit happens, with issues around access to market, regulatory checks and potential damage to supply chains.
Skills and migration	No rights agreed. UK can make unilateral offer to EU citizens living in the UK. EU member states can make offers to UK citizens resident in EU countries. Formal freedom of movement ends, but in practice little may change until a new permanent regime is put in place.
Clinical trials	The impacts on the clinical trials sector include: • A potential reduction in numbers and types of trials, and industry investment due to increased costs and bureaucracy for the conduct of clinical trials • UK and EU losing competitiveness in a global clinical trials market • Loss of skilled workers in trials and healthcare may limit quality of research base and innovation • Potential for reform of drug licensing and market approval • There is a potential for regulation to further diverge over time

Scenario 2

Brexit Shape: No Deal
Alignment: Partial Alignment with EU Clinical Trials Regulation

The UK was unable to secure a comprehensive trade deal with the EU. Instead an amicable no deal was agreed including additional time to implement necessary changes. This provided a level of reassurance to industry and to the workforce. In 2024, bespoke arrangements came into force for data sharing, regulation and citizen rights.

Today, in 2028, the UK is struggling to find its way in a market that is increasingly global and competitive.

Tough times

The economy is suffering. Locked outside of the EU Customs Union and Single Market but with warm relations with the EU, the UK government spent most of the 2020s seeking to strengthen and build its trade relations with Europe.

Early signs were promising. During the 5-year transition period, the UK prioritised industry, healthcare and research. Access to EU Framework Programmes and funding was secured in return for a continued contribution to the EU budget, but the agreement fell short of the comprehensive research and innovation settlement the UK had pushed for during phase II negotiations.

The UK took steps to align with the provisions of the EU CTR. However, while regulation is aligned, the UK still has distinct processes, a bespoke approval system and is unable to access the database or lead on European trials. Instead, the UK and EU regulators have worked to promote mutual recognition of standards in an attempt to minimize disruption and bureaucracy.

Today, the UK attempts to follow EU developments, but has little influence on the development of new EU regulation.

In a global context, the EU and UK have been slower to innovate than other countries including the US and China, who have taken advantage of advances in devices and diagnostics, fast-tracking innovative approaches to clinical trials and the handling and sharing of patient data in a world in which treatment and care is increasingly stratified and personalised.

Supply chains and skills

Locked out of the customs union, access to physical resources, goods and medicine has become one of the UK's most significant issues. New tariffs and regional restrictions on exports have disrupted supply chains. High inflation means the population is suffering. From finance to technology, companies depending on a high-skilled workforce have left the UK for Continental Europe, Asia, the Americas and Africa. Meanwhile data protection and a lack of harmonized global data standards have limited the UK's ability to share and access international trial data, including observational data.

An increasingly global outlook

A continuing UK priority has been research and innovation. The UK has introduced fiscal and domestic incentives to target industry sectors, including pharma, data and technology companies. This has included reform of drug licensing and market approval, and efforts to reduce barriers to clinical trials.

The government is pushing hard to develop new industry partnerships and funding instruments. Bilateral and multilateral agreements with trusted partners around the globe are a priority. 'Global UK' is the new marketing campaign, aimed at establishing collaboration and attracting investment.

Simplifying international visas has also been a priority, and in 2022, the UK ratified a new visa regime. Short-stay and long-term visas for skilled workers have been fast-tracked. Extra funding was also made available to boost industry and international collaborations and attract early-career researchers from India, China and elsewhere in Asia.

Scenario summary

Brexit	No deal. The UK leaves the EU without any trade agreement in place. UK and EU negotiate a transitional period beyond that already agreed in principle for an additional 4 years. The UK is outside the Single Market and its associated four freedoms (the free movement of goods, capital, services and labour) and outside the Customs Union (a trade agreement in which EU countries decide not to tax imports or goods from inside the Union and prohibits members from negotiating trade agreements separately from the EU).
Regulatory environment	The UK and EU have partial alignment around EU CTR. The UK can take steps to align with the provisions of the EU CTR, however, while regulation is aligned, the UK has distinct processes, a bespoke approval system and is unable to access the database or lead on European trials. Bespoke data sharing agreement, and efforts to align regulation in the short-term, with some divergence in the longer term as UK looks to build on broader trade agreements.. Some agreement between the MHRA and EMA to promote mutual recognition of standards in an attempt to speed up and reduce barriers to trials.
Cooperation and collaboration with the EU	Reasonable co-operation with the EU. Strong non-government cooperation. Bespoke agreements agreed for data sharing, regulation and citizens rights and access to EU Framework Programmes and funding. Government funding to reinforce existing research and attract international investment has minimal impact. UK prioritises early career and other travel. In the absence of any specific agreement, however, the UK would have limited opportunities to collaborate on Framework Programmes and would need to provide funding to resource any collaboration.
Trade and supply chains	UK free to negotiate trade agreements. UK and EU trade on WTO terms, which means no preferential tariffs. Goods have to meet each jurisdiction's regulatory requirements. A new UK border system would be required as soon as Brexit happens, with issues around access to market, regulatory checks and potential dam-age to supply chains.
Skills and migration	No rights agreed. UK can make unilateral offer to EU citizens living in the UK. EU Member States can make offers to UK citizens resident in EU countries. Formal freedom of movement ends, but in practice little may change until a new permanent regime is put in place.
Clinical trials	The impacts on the clinical trials sector include: • A potential reduction in numbers and types of trials, and industry investment due to increased costs and bureaucracy for the conduct of clinical trials • UK and EU losing competitiveness in a global clinical trials market • Loss of skilled workers in trials and healthcare may limit quality of research base and innovation • Potential for reform of drug licensing and market approval • There is a potential for regulation to further diverge over time

Scenario 3

Brexit Shape: Deal / Limited Free Trade Agreement
Alignment: Partial Alignment with EU Clinical Trials Regulation

As the first country to leave the EU, the UK struck a limited free trade agreement with the EU in 2019. Today in 2028, despite that agreement, cooperation between UK and EU member states is increasingly reliant on informal networks and back-channels, in a world of closed borders.

UK and EU clinical trials regulation is partially aligned. The UK is unable to access the EU portal and database and has instead established parallel systems and processes. The UK is unable to lead on EU trials, although it can still participate. This has negatively impacted the type and number of trials being conducted in the UK.

Restrictions on trade

EU-UK trade was hit hard after the transition period. The UK did not have enough time to prepare for the new border arrangements. Goods moving between the UK and EU were suddenly subject to extra rules of origin requirements (to prove that the UK was not being used by third countries to gain low tariff access to the single market). It became more difficult to clear customs and a lack of equivalence for Qualified Persons added to the time and cost of pharmacovigilance.

In the short-term access to medical supplies and drugs became a significant concern. There were also impacts on the availability of medical radioisotopes.

Having addressed some of these barriers, supply is less of an issue nowadays. The bigger impact is cost – with some treatments and drugs in the UK considerably more expensive than on the continent.

It can also take time for new medicines available on the continent to be authorized and marketed in the UK.

Healthcare and Trials are impacted

For clinical trials, the UK tried but failed to reach an agreement with the EU for access to the clinical trials database and portal. The UK implemented the provisions and processes in the EU CTR as far as possible but now operates separate, parallel approval systems, leading to extra costs and bureaucracy, slowing down trials. UK researchers are no longer able to lead EU clinical trials.

International ambitions are unsuccessful

In the years following the transition, the UK looked to establish new trade agreements internationally, but with limited success. Trade agreements could only be made with countries that did not already have a preferential deal with the EU. And in a resource-constrained world, many trading blocs had taken steps to restrict migration and protect their resources.

Political tensions are high and in 2026 the latest water crisis has put pressure on global institutions.

Driving clinical innovation

Today, although most of the UK research and innovation community sees itself as part of Europe, the UK participates in framework programmes and funding remains as a third country.

This has reduced the appetite for researchers to move to the UK and in the 2020s there was an exodus of industry and researchers to EU and Asia, beset by perceptions that the UK was closed for business. Invitations to join consortia and attend conferences declined and options for collaboration were limited.

Healthcare and clinical trials sectors have suffered, with reduced skills, lower industry investment, and increased bureaucracy.

The government reacted by announcing new funding for research and coordinated efforts between government and the UK regulator have started to reverse this trend.

New light-touch approaches to legislation and regulation are now helping the UK conduct novel trials building on our regulatory, healthcare and research expertise. A focus has been placed on data collection and a new shared digital infrastructure joining up the NHS and private sector was established, opening patient data to new uses. However, this has been met by concerns about privacy and permissions, data ownership and remuneration, and a growing number of patients are opting out.

Scenario summary

Brexit	Deal. The UK exits the EU having agreed a comprehensive free trade agreement with the EU and with a transition period until 2020. UK regulations and standards can diverge from those of the EU. UK has reduced access to markets, increased regulatory checks and potential damage to supply chains.
Regulatory environment	The UK tried but failed to reach an agreement with the EU for access to the clinical trials database and portal. The UK implemented the provisions and processes in the EU CTR as far as possible but now operates separate, parallel approval systems, leading to extra costs and bureaucracy, slowing down trials. UK researchers are no longer able to lead EU clinical trials. The UK trials light-touch approaches to legislation and regulation to drive clinical innovation, with a focus on data collection and a new shared digital infrastructure. There are concerns about patient rights and access to data.
Cooperation and collaboration with the EU	Reasonable level of co-operation with the EU. The UK participate as a third country in EU research programmes but is unable to negotiate a bespoke arrangement. The UK looks to collaborate internationally but with limited success. UK government decides to fund and invest in research. UK increasingly self-sufficient for trials, science and research.
Trade and supply chains	UK and EU agree new terms for trading on preferential terms. Bespoke bilateral trading deal. UK exports to the EU would have to satisfy some rules of origin requirements, and customs measures would increase compared to current Single Market membership. To trade in EU, UK companies would still need to comply with ECJ legislation and regulation.
Skills and migration	A new migration regime can be introduced, in line with any deal provisions, after exit.
Clinical trials	The impacts on the clinical trials sector include: • UK supply chains may be disrupted by increased regulatory checks and potential damage to supply chains with impacts for availability and cost of drugs • UK is unable to lead on EU clinical trials • Potential loss of access to patient populations • New regulatory and data approaches can drive innovation if barriers can be overcome • Concerns around patient rights and data

Scenario 4

Brexit Shape: Deal / Comprehensive Free Trade Agreement
Alignment: Full Alignment with EU Clinical Trials Regulation

The UK and the EU agreed a comprehensive free-trade agreement during Phase II Brexit negotiations. Revised financial contributions to the EU secured the continued movement of goods, people, services and capital.

Today, in 2028, the UK continues to cooperate with the EU as a third country. The UK has access to the EU database and has fully implemented the provisions of the EU CTR. Researchers and industry are able to participate in EU programmes and funding though the UK has less influence on future regulation. Bilateral arrangements with non-EU partners are starting to be put in place.

UK dependent on EU and losing influence

In return for access to EU markets, the government agreed to remain subject to the conditions of the majority of EU legislation. Contributions to the EU budget continued in return for broad market access including EU Framework programmes, infrastructure and funding, and to support mobility and reciprocal social and healthcare.

Following Brexit, the UK was increasingly dependent on the EU. Unable to influence new legislation or policy during transition, it has continued to lose direct influence, with UK interests increasingly represented on a proxy basis through advocacy and lobbying other individual EU Member States.

Bridging the innovation gap

Science, research and innovation remained a UK priority during Brexit negotiations and the UK secured specific agreements for clinical trials, science and research as part of phase II negotiations. government has continued to recognize the value of these sectors in securing new and longer-term UK growth, and made ongoing commitments to increasing the availability of funding in real terms out to 2030.

The UK has been able to participate in all thematic areas as part of Horizon Europe. It has also been successful in developing new global research partnerships across Asia, the Middle East and the Americas. The UK continued to be competitive as a host for future European and international research infrastructures

Improved access to trials

The implementation of the pan-EU database and portal has allowed greater cooperation and harmonisation of clinical trials. The new flexibility to modify and expand trials has helped streamline data collection and access for patients across UK and EU sites.

Additionally, the UK implemented a new immigration system, it became easier for UK workers to move overseas and for skilled international workers to move to the UK. In Europe, new regulations were introduced to support the growing global demand for health tourism with patients increasingly able to travel to access treatments and clinical trials across Europe.

We witnessed a continuing shift towards greater patient empowerment in relation to clinical trials. Greater transparency and accountability over the speed, quality and efficacy of trials was introduced, but persistent concerns were expressed from clinicians and patients alike that regulation continued to hold back innovation.

Universities rise to the competition

Today, industry and research have benefited from the continued flow of people and ideas and industry continues to secure a larger share of global investment in Research and Development. New Grand challenges and innovation prizes have arisen to help drive contemporary research agendas.

Research institutions have been quick to take advantage of the new visa system. With preferential access for EU students, researchers and workers, talent has flooded into the UK over this period, helping to drive a vibrant research ecosystem.

Scenario summary

Brexit	Deal. The UK exits the EU having agreed a comprehensive free trade agreement with the EU and with a transition period until 2020. UK regulations and standards can diverge from those of the EU. The UK may be able to negotiate better than third country access to Framework Programmes and other European institutions. The level of comprehensiveness depends on the final agreement.
Regulatory environment	EU and UK agree the UK can fully implement and participate in the EU CTR system, with access to the portal and database, resulting in total alignment. This would be part of a wider agreement on health with the EMA, achieving a level of harmonisation close to that the UK would have if it were an EU Member State as possible. UK researchers able to lead on clinical trials and have access to the database. Reduced barriers around the conduct of EU clinical trials. The UK is likely to be fully aligned with drug licensing, with a Mutual Recognition Agreement for Good Manufacturing Practice and data sharing. UK working effectively with EMA around market authorisation and clinical trials. Free to focus on new challenges, but UK potentially held back by EU regulation.
Cooperation and collaboration with the EU	UK and EU agree new terms for trading on preferential terms. Bespoke bilateral trading deal. UK exports to the EU would have to satisfy some rules of origin requirements, and customs measures would increase compared to current Single Market membership. To trade in EU, UK companies would still need to comply with ECJ legislation and regulation.
Trade and supply chains	UK and EU agree new terms for trading on preferential terms. Bespoke bilateral trading deal. UK exports to the EU would have to satisfy some rules of origin requirements, and customs measures would increase compared to current Single Market membership. To trade in EU, UK companies would still need to comply with ECJ legislation and regulation.
Skills and migration	A new migration regime can be introduced, in line with any deal provisions, after exit.
Clinical trials	The impacts on the clinical trials sector include: • UK supply chains may be disrupted by increased regulatory checks and potential damage to supply chains with impacts for availability and cost of drugs • UK can lead and participate in EU clinical trials • Where the UK is unable to influence and support development of new regulation there may be negative impacts on innovation for clinical trials and research – impacting patient access to new therapies • UK and EU competitiveness may be negatively impacted

Scenario 5

Brexit Shape: Deal / Soft Brexit with UK joining the EEA
Alignment: Full Alignment with EU Clinical Trials Regulation

Contrary to expectations, the UK government changed their Brexit position during phase II negotiations and the UK and EU negotiated a 'Soft Brexit'. The UK joined the European Economic Area (EEA) with access to the EU Single Market, but outside the Customs Union.

Today in 2028, in return for access to the Single Market, we continue to comply with EU rules on free movement of goods, services, capital and people in return for accepting EU regulations and contributions to the EU budget.

For clinical trials, the precedent set by Norway meant that the UK was able to gain full alignment within 5 years of Brexit.

Supply chain and custom delays

As part of the EEA, the UK has benefited from access to the Single Market and its associated four freedoms (the free movement of goods, capital, services and labour). The UK also benefited from passporting rights for sectors such as finance.

However, the transition to the new arrangements was problematic. After Transition the UK was outside of the Customs Union and was required to put in place new checks and processes to satisfy rules of origin requirements to facilitate trade and prove that it was not being used by third countries to gain low tariff access to the single market. EU- UK trade suffered from new customs delays and increased paperwork.

Industries which relied on 'just in time' manufacturing were particularly impacted. In Ireland, a soft border with Ireland was agreed, but did not become operational until 2026 as part of wider reform of UK customs and regulatory checks.

In Europe, but limited influence

Under a 'Soft Brexit' the UK was free to negotiate new trade details with other countries, however, the UK chose not to do this, prioritising its relationships with the EU and the other EEA members, to build the strongest possible relationship with Europe.

As with the EFTA countries, the UK can't directly amend or influence new legislation or regulation developed by the EU, but we retained the option as to whether the UK would accept new rules, standards and processes. In reality, though, to ensure as frictionless a relationship as possible, the UK continues to adopt the majority of the substantive legislatory and regulatory changes from Europe, although there can be a time lag in implementation in the UK.

Norway was the first EFTA member to gain access to the EU clinical trials portal and database in 2024, and the UK followed the next year, having taken the necessary steps to implement the provisions and processes in the EU Clinical Trials Regulation. At this point the UK was fully aligned with the EU.

Permissive migration

The anticipated 'brain drain' and loss of skilled workers from the UK's healthcare and research system was largely avoided, in part due to agreements with the EU. The UK Home Office fast-tracked a new international immigration system as part of a government focus on innovation and industry as the UK recognized the need to invest in its strengths.

A changing world

Today, the UK has taken advantage of its alignment with the EU to invest in shared data and infrastructure platforms. In the health sector this has included new approaches to how data is handled and shared across the NHS and private healthcare sector. Together with fast-tracked regulation for new devices and remote monitoring, this has allowed for improvements to patient access, patient recruitment and trial design both in the UK and across Europe. In an increasingly global world of pharma and research, this has helped drive inward investment and boost trials in the UK

Scenario summary

Brexit	Deal. The UK remains part of the European Economic Area with access to the EU Single Market but leaves the Customs Union. The UK would have to comply with EU rules on free movement of goods, services, capital and people. The UK would have to accept EU regulations and contribute to the EU budget, despite being excluded from decision-making.
Regulatory environment	UK implements the provisions and processes in the EU CTR as far as possible but is initially unable to access the portal and database. As with Norway (who is currently attempting to implement the EU CTR) the UK may not be able to access the EU portal and database initially. Strong cooperation, UK accepts new regulatory changes, with limited influence in Europe, except through informal channels. EU and UK prioritise alignment but differences may occur over time if the UK seeks to innovate.
Cooperation and collaboration with the EU	The UK could participate as a third country in EU research programmes but would have limited opportunities to collaborate on Framework Programmes and would need to provide funding to resource any collaboration.
Trade and supply chains	The UK would be able to pursue other free trade agreements, but would be required to operate as part of the EEA. Potential for streamlined processes around customs and regulatory checks. In the short-term, there were some issues around the availability of existing medicines and investigational products, in part due to new customs and regulatory requirements
Skills and migration	Equal rights and obligations for citizens and economic operators between UK and EU New UK international migration system
Clinical trials	The impacts on the clinical trials sector include: • Short-period of partial alignment may impact conduct of clinical trials, but over time the UK and EU will be fully aligned • UK will need to adopt EU regulations, but may be able to innovate in some areas including to fast-track regulation for new devices and remote monitoring, this has allowed for improvements to patient access, patient recruitment and trial design

ANNEX C: Participants

Interviewees

Adrienne Clarke	GlaxoSmithKline
Angela McFarlane	IQVIA
Christopher Banford	IQVIA
Christine Phillips	IQVIA
Claire Snowdon	Institute of Cancer Research's Clinical Trials and Statistics Unit
Craig Johnson	GlaxoSmithKline
Denis Lacombe	European Organisation for Research and Treatment of Cancer (EORTC)
David Webb	The University of Edinburgh
Emma du Four	AbbVie
James Brooks	IQVIA
Francois Doz	Institut Curie/SIREDO Oncology Centre
Gary Patou	MPM Capital
John Reeve	Patient Representative, The National Cancer Research Institute (NCRI)
Jonathan Ledermann	Cancer Research UK and University College London Cancer Trials Centre
Jonathan Montgomery	Health Research Authority (HRA)
Kent Woods	Academy of Medical Sciences (AMS)
Laurent Degos	Federation of European Academies of Medicine (FEAM)
Matt Seymour	National Institute for Health Research (NIHR)
Martin Gore	Royal Marsden Hospital
Max Parmar	Medical Research Council (MRC)
Mike Rawlins	Medicines and Healthcare Products Regulatory Agency (MHRA)
Peter Johnson	The Francis Crick Institute/University of Southampton
Richard Stephens	Patient Representative, The National Cancer Research Institute (NCRI)
Robert Jones	Cancer Research UK Clinical Trials Unit Glasgow
Ruth Plummer	Newcastle University
Sheuli Porkes	Association of the British Pharmaceutical Industry (ABPI)
Toby Toward	Immunocore
Virginia Acha	Merck

Workshop Participants

Alastair Nicholson	Health Research Authority (HRA)
Ali Hansford	Association of the British Pharmaceutical Industry (ABPI)
Andrea Harkin	Cancer Research UK Clinical Trials Unit, Glasgow
Benoit Aigret	Barts Clinical Trials Unit, Queen Mary University of London
Bettina Ryll	Melanoma Patient Network Europe
Brian Duggan	NHS England
Christiane Abouzeid	BioIndustry Association (BIA)
Christos Gatsios	Office for Life Sciences
Claire Snowdon	Institute of Cancer Research's Clinical Trials and Statistics Unit (ICR-CTSU)
Dave Murphy	Health Research Authority (HRA)
Emma Du Four	AbbVie
Gene Matthews	Leigh Day
James Larkin	Cancer Research UK / The Royal Marsden NHS Foundation Trust
Kelly Gleason	Cancer Research UK Imperial Centre, Imperial College
Ilaria Mirabile	Cancer Research UK / Experimental Cancer Medicine Centres (ECMC)
Libby Dixon	Academy of Medical Sciences
Liz Flackett	European Organisation for Research and Treatment of Cancer (EORTC)
Martin Landray	University of Oxford
Martin O'Kane	Medicines and Healthcare Products Regulatory Agency (MHRA)
Martyn Ward	Medicines and Healthcare Products Regulatory Agency (MHRA)
Matt Sydes	Medical Research Council Clinical Trials Unit at University College London (UCL)
Michelle Sleeth	Barts Clinical Trials Unit, Queen Mary University of London
Mike Rawlins	Medicines and Healthcare Products Regulatory Agency (MHRA)
Natlie Kempston	UK Department of Health & Social Care (DHSC)
Nick Meade	Genetic Alliance UK
Nick Skyes	Pfizer
Nicky Gower	Cancer Research UK and UCL Cancer Trials Centre
Nina Spencer	Merck
Pam Kearns	Cancer Research UK / University of Birmingham
Renata Crome	Centre for Drug Development, Cancer Research UK
Richard Baird	Addenbroke's hospital, Cambridge University Hospitals
Richard Stephens	Patient Representative, The National Cancer Research Institute (NCRI)
Rick Kaplan	Medical Research Council Clinical Trials Unit at University College London
Ruth Roberts	Leigh Day
Sarah Collen	NHS Confederation Office
Stéphane Lejeune	European Organisation for Research and Treatment of Cancer (EORTC)
Angel Yiangou	Cancer Research UK
Emlyn Samuel	Cancer Research UK
Mark Heffernan	Cancer Research UK
Zoe Martin	Cancer Research UK

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