BMA

BREXIT BRIEFING

Medical research

Maintaining an effective working relationship between the UK and the EU

Key points

- The EU (European Union) provides a unique platform for medical research collaboration by supporting the sharing of research staff and expertise, cross border trials, and the development of world-class facilities. The UK has been a leading partner in this.

- While the UK's decision to leave the EU does not prevent collaboration, it has the potential to significantly limit the ability of researchers and institutions to work together because:
  - the loss of access to EU health-related research funding programmes undermines the development of new or improved medicines and medical devices in the UK; damages the UK's scientific reputation and appeal for researchers; limits the UK's ability to translate research into medicines and medical devices into products to bring to the market; and reduces training and career opportunities for research; and
  - it would increase the burden of conducting multi-centre clinical trials and create barriers to working collaboratively and sharing expertise, facilities and datasets, ultimately delaying the development of and access to new medicines and devices across Europe.

- To minimise these potential impacts, the UK should:
  - negotiate a formal agreement to maintain access to EU funding programmes; and
  - to ensure consistency and close alignment with clinical trials regulations in the EU, as well as agree how the MHRA (Medicines and Healthcare Products Regulatory Agency) participates in pan-European clinical trials.

- For the UK, this approach would:
  - provide assurances on the long-term source of funding for UK medical researchers collaborating with EU research institutions to develop and access new therapies and technologies;
  - provide timely access to therapies and technologies developed in other EU countries;
  - support access to expertise, knowledge and capability within the EU, alongside tapping into international research to develop effective drugs for UK patients; and
  - secure the UK's leading reputation for medical research, ensuring international partners continue to seek access to UK infrastructure and collaborate with UK researchers.

- For the EU, this approach would:
  - underpin continued collaboration with UK research institutions in developing and accessing new therapies and technologies, as well as timely access to those under development in the UK. This is particularly important for areas where the UK has a track record, for example, in breast cancer research; and
  - facilitate participation in UK-led clinical trials, particularly in relation to rare diseases and children, where EU expertise is limited.

- Should there be a failure to agree a withdrawal deal by March 2019, the research community would face significant uncertainty about future funding sources and opportunities for collaboration. This would potentially lead to the UK losing academic expertise and a decline in demand from researchers to work in the UK, thereby damaging the UK's research outputs and reputation. After March 2019, UK researchers collaborating on existing EU funded projects may also lose access to EU funding from that point onwards and may have to leave ongoing projects.

Background

The EU provides a unique platform for medical research collaboration between countries. This has improved health across Europe and worldwide through the development of new medicines, therapies and medical technologies. It facilitates sharing of research staff and expertise, supports cross-border clinical trials, the development of world-class facilities, and provides a high-quality training environment.

A central feature of this research collaboration is the provision and distribution of funding by the EU, through programmes such as the EU Framework Programme for Research and Innovation (known as Horizon 2020), and the EIB (European Investment Bank). This vital investment provides wider benefits to the UK economy – for example, it is estimated that for every £1 invested in public research, the private sector invests an extra 20p into research and development every year in perpetuity.[1] Specifically, EU funding supports research opportunities across the biomedical research community and drives collaboration, making the EU a world-leading hub for science.[1] The EU's commitment to creating a European Research Area is likely to further deepen collaboration.[2] Its five key priorities are:

- more effective national research systems;
- optimal transnational co-operation and competition;
- an open labour market for researchers, facilitating mobility, supporting training and ensuring attractive careers;
- gender equality and gender mainstreaming in research; and
- optimal circulation and transfer of scientific knowledge to guarantee access to and uptake of knowledge by all.

Please note: while this briefing considers the key issues around medical research, this closely links to issues relevant to the licensing of medicines and medical devices, which is covered in a complementary briefing, 'Maintaining an effective working relationship between the UK and the EU on medicines and medical devices regulation'.

The UK's relationship with the EU on medical research

The UK is a leading partner in the EU's science and research programme, and provides significant value to this collaborative effort (see **Box 1**).

Box 1 – The value of UK medical research to EU science and health
A report from eight leading UK medical research funders and charities has highlighted how the UK plays a vital role in the following areas.[3]

1. **Contributions to advisory bodies, collaborations and networks** – the UK contributed almost 20% of the total research work carried out within EU health programmes between 2007 and 2016. The UK has a lead role in Europe's key research networks (eg the European Strategy Forum on Research Infrastructures),[a] coordinates six of the 24 European Reference Networks[b] that pool knowledge and share research expertise, and hosts headquarters for several important institutions (such as the European Life Science Infrastructure for Biological Information).[c] UK experts provide valuable input to individual research institutions, such as Germany's Max Planck Institutes.[d]
2. **Participating in and leadership of pan-EU clinical trials** – the UK has the highest number of phase I trials in the EU and the second highest number of phase II and III trials, after Germany. It has led or participated in trials for rare diseases and paediatric conditions where international collaboration is vital. The MHRA is recognised as one of the leading national authorities for clinical trial regulation, and the UK now has established networks of patients and professionals for rare diseases, making it easier to recruit patients for clinical trials.
3. **Co-ordinating and hosting large-scale infrastructures for medical research** – the UK provides major research assets accessible to the EU, such as the Wellcome Trust Sanger Institute.[e] It supports the collection of large-scale population cohort studies (such as the 1946 Birth Cohort – the longest continually running study of its kind) that are used in many EU studies and policy development. It provides access to large NHS datasets of high quality and completeness (eg the National Cancer Data Repository).
4. **The development of new therapies and medical technologies** – around 25% of the world's top 100 prescription medicines were discovered and developed in the UK, and three of the five top-selling drugs globally act on a mechanism discovered by UK researchers. The UK has expertise in quickly translating innovative solutions into commercial products. 500 new biotechnology-based drugs are currently under development and 600 innovative pharmaceutical product candidates are in the pipeline in the UK.
5. **Training early career researchers from across the EU** – the UK trains the second highest number of science graduates after the USA, and UK training is noted for its focus on teaching graduates to think analytically and innovatively. Students from EU member states make up 8% of all postgraduate and 4% of all undergraduate students in the UK studying subjects relevant to biomedicine. In comparison, Germany, France and the Netherlands each host about 2-4% of its undergraduate 'biomedical' student population from other EU countries.

a The European Strategy Forum on Research Infrastructures identifies and sets the EU's strategy for research facilities over a 10-20 year time frame. The UK leads on the health and food aspects of the Forum and therefore has significant influence in shaping policy.
b European Reference Networks, formed in 2017, aim to link up leading specialised healthcare providers across the EU to pool knowledge and expertise, particularly in tackling rare diseases.
c The European Life Science Infrastructure for Biological Information is an initiative that allows life science facilities across Europe to share and store research data as part of an organised network, while exchanging expertise and agreeing on best practice.
d The Max Planck Society is a series of over 80 world leading research institutes supporting work in the natural, life and social sciences.
e The Wellcome Trust Sanger Institute is one of the leading centres of genomic discovery and understanding in the world. It collaborates across the globe to provide the foundations for further research and transformative healthcare innovations.

Although the UK's decision to leave the EU does not in itself prevent collaboration, there are a number of areas which have the potential to limit the ability of researchers and institutions to work together, which would significantly diminish the impact of medical research in the UK and the EU.

Potential consequences of the UK's exit from the EU on medical research

– **Loss of access to EU health-related research funding programmes, creating barriers to collaboration**

The level of EU funding the UK receives for health-related research projects is substantial and demonstrates the importance of maintaining access to this source of funding, as well as the quality of UK-based researchers.[4] Between January 2007 and March 2017, the UK received the highest level of funding (£1.2 billion), among all EU countries, for health-related research projects from EU funding programmes FP7 (Framework Programme 7) (2007-2013) and Horizon 2020 (2014-2020).[3] This investment stimulates further significant industry funding (£1.6bn in 2015-16) from bodies such as Cancer Research UK, the British Heart Foundation and the Wellcome Trust.[1]

Beyond providing financial resources, these programmes facilitate and actively promote international collaboration between researchers and research institutions. For example, over the same period, the UK was actively involved in 1,000 EU health-related projects, involving over 2,300 UK participations,[f] and delivering health-related research work worth €4,800 per researcher.[3] Similarly, the £110 million of funding provided by FP7 for UK-coordinated health-related projects generated 351 UK participations, alongside large participations from Germany (231), the Netherlands (153), France (145) and Italy (124), bringing €203m of research funding to these countries.[3] These collaborative links with EU countries greatly enhance the quality and breadth of medical research by both partners.

If the UK no longer had access to these EU research funding programmes, it would significantly adversely effect its capacity to undertake medical research, and would create barriers to partnership working with the EU and to international collaboration more generally. This in turn would:

– undermine the development of new or improved medicines, therapies and medical devices in the UK and EU, and their impact on clinical guidelines and medical practice – the UK has the largest pipeline of therapeutic treatments in Europe, developing more than 800 product candidates in 2016, compared to around 600 in Germany and 550 in France.[3] For example, research conducted in the UK on the role of statins in cardiovascular disease prevention has led to the adoption of their use throughout the EU,[5,6,7,8] while cross-border collaboration and EU funding has led to the development of innovative therapies for personalised breast cancer treatments;[9]
– damage the UK and EU's scientific reputation and appeal for researchers, by creating psychological and actual barriers to cross-border collaboration and cross-fertilisation of ideas. This is an issue as research collaboration increases the impact of publications, as the MNCS (Mean Normalised Citation Score)[g] demonstrates. The average number of citations a published article receives is higher for articles published by authors coming from UK and other EU countries compared to those published by EU26 authors only (without UK co-authors) or UK authors only (without EU26 co-authors) and the MNCS score of joint UK and EU26 publications (1.98) is nearly twice the world average;[3]

f 'Participations' means the act of involvement of a legal entity in a project. A single participant can be involved in multiple projects.
g A measure of the impact of a research publication that takes into account the average number of citations received by all articles published in the same subject field over a specific time period.

– reduce training and career opportunities – researchers across the UK and EU are able to train and develop in world-class research networks and facilities offered by all Member States, with the UK seen as a highly attractive destination (eg between 2007 and 2013, the UK was the top destination for the EU's Marie Sklodowska-Curie action fellowships, with five UK institutions among the top 10 organisations).[3] The EIB also invests heavily in UK research facilities – for example at universities in Oxford, Edinburgh, Swansea, Bangor, Newcastle and UCL in 2016 – which makes a significant contribution to ensuring UK facilities remain world leading.[10]

– **Adopting a divergent approach to conducting clinical trials and creating delays in developing new medicines and medical devices**

The UK has worked closely with the EMA (European Medicines Agency) in recent years to overhaul the framework for conducting clinical trials across the EU. The existing regulations – the Clinical Trials Directive (2001/20/EC) and the Good Clinical Practice Directive (2005/28/EC)[11] – will be replaced by the Clinical Trials Regulation (536/2014) during 2019. This is expected to provide streamlined procedures for assessment and authorisation of new clinical trials, a lighter regulatory regime for trials conducted with medicines already authorised, and simplified reporting requirements for results of clinical trials. These developments have been welcomed by Cancer Research UK, the MHRA and the NHS Confederation,[12,13,14] as they will provide a more favourable environment for researchers and aim to reduce the decline in the number of clinical trials being conducted across Europe.

Establishing a regulatory regime for clinical trials that diverges significantly from the new EU regulations would significantly increase the burden on UK researchers and pharmaceutical companies. For example, they would need to provide different datasets to the MHRA and EMA, and researchers would need to seek individual permissions for trials in the UK, as well as the EU. This would make the UK a less appealing destination to conduct clinical trials, create barriers to working collaboratively and sharing expertise and facilities, and limit access to datasets for other EU countries – over 660,000 patients were recruited to clinical trials in the UK in 2016/17[1] – such as the unique National Survey of Health and Development[h] and the UK Biobank study.[i] The ageing demographic of the UK (which is ahead of much of the rest of Europe in this regard), particularly in the South of England, increases the value of these datasets for research into similar population groups across Europe. This divergent approach would ultimately weaken the UK's research framework and capacity, and therefore delay the development of and access to new medicines and devices across Europe by removing collaboration between the UK and EU, while creating an additional burden of developing new and existing facilities across Europe.

The establishment of a different regulatory framework would have a particularly adverse impact on research into medical devices and research into rare diseases and clinical trials for children. In 2009, the EU recommended each Member State should have a rare diseases strategy and the UK's response was published in 2013.[15,16] The strategy emphasised the need to collaborate, reflecting the way in which this type of research requires international collaboration as a consequence of the small number of trial participants and limited research expertise within individual countries. The UK is a world leader in this area, for example in paediatric cancer, haematologic rare neoplasms and neurodocrine tumours – it participates in the highest number of clinical trials for rare diseases (n=1,349) and paediatric patients (n=1,193) within the EU.[3] The vast majority of these clinical trials involve active collaboration with EU countries – 736 paediatric trials and 1,021 rare disease trials conducted by the UK were with other EU countries.[3]

h The National Survey of Health and Development is one of the oldest running cohort studies in the world providing data on development, childhood, IQ, socioeconomic factors, health behaviours and measures of health.

i The UK Biobank Study is the most detailed national study of demographic, genetic and health related data as well as biological samples and analytic pharmacological, environmental biology and molecular biology data available to researchers.

Ensuring close collaboration between the UK and the EU on medical research

To ensure researchers and research institutions across the UK and EU are able to continue to collaborate closely, the UK Government should, at a minimum, negotiate a formal agreement to maintain access to EU research funding programmes. This could be similar to the arrangements that several non-EU countries have for participation in Horizon 2020, known as Association Agreements[17] – for example, Switzerland, Norway and Israel are among the highest net recipients of funding from the programme.[18] Ensuring close collaboration will also require the UK to replicate the new EU Clinical Trials Regulation so there is alignment, as well as an agreement as to how the UK (through the MHRA) participates in the operation of pan-European clinical trials. The UK will also need to endeavour to participate in the development of the European Research Area to ensure that it shares in the benefits derived from it.

For the UK, this approach would:
- provide assurances on the long-term source of funding for UK medical researchers collaborating with EU research institutions to develop and access new therapies and technologies;
- provide timely access to new therapies and technologies developed in other EU countries;
- support access to expertise, knowledge and capability within the EU, alongside tapping into international research to allow the UK to develop effective drugs for UK patients;
- ensure the UK is able to continue to access diverse European population groups in coordinating clinical trials (particularly in relation to rare diseases and children), as well as limit the burden of conducting cross-border clinical trials by ensuring permission does not have to be sought on an individual basis for the UK;
- continue to attract future generations of researchers to the UK for education, training and career development; and
- secure the UK's reputation as a world leader in medical research, ensuring international partners continue to seek to access UK infrastructure and collaborate with UK researchers.

For the EU, this approach would:
- underpin continued collaboration with UK research institutions in developing and accessing new therapies and technologies, as well as timely access to those under development in the UK. This is particularly important for areas where the UK has a particular track record, for example, in breast cancer research;
- support access to expertise, knowledge and capability within the UK, including comprehensive NHS datasets such as the Birth Cohort Study;
- facilitate participation in UK-led clinical trials, particularly in relation to rare diseases and children, where EU expertise is limited; and
- allow EU researchers to continue to train and work in the UK and access world-leading and unique UK research facilities (such as the Wellcome Trust Sanger Institute).

Key developments

- In August 2016, the Chancellor announced that where UK organisations bid for EU funding projects, such as Horizon 2020, the Treasury would underwrite all payments of awards signed before the Autumn Statement 2016 (23 November 2016), even when specific projects continue beyond the UK's departure from the EU.[19]
- In September 2017, the UK Government published a position paper setting out its objectives for a science and innovation agreement with the EU. This includes an ambition to build on the uniquely close relationship with the EU, to strengthen collaboration on science and innovation and to forge a more ambitious and close partnership with the EU than any other agreement that has been reached between the EU and a non-EU country. The paper also sets out examples of where the UK sees potential mutual benefit in a close future relationship, exploring precedents for each.[20]

Summary

Collaboration on medical research has bought wide-ranging benefits as part of the UK's membership of the EU. Supporting coordinated research and development activities between European countries, as well as an aligned approach to clinical trials has meant that patients in the UK and across Europe have accessed new and innovative medicines faster. The UK's decision to leave the EU has the potential to limit the benefits of this collaborative approach and presents a substantial risk to the continued success of European medical research, and to the successful development of the European Research Area. It is vital that the UK Government's negotiations with the EU prioritise the ability for the UK and EU to work closely across these areas.

References

1 Bell J (2017) *Life sciences industrial strategy: a report to the Government by the life sciences sector.* London: the Stationery Office.

2 http://ec.europa.eu/research/era/era_communication_en.htm (last accessed on 09.08.2017).

3 Technopolis Group (2017) *The impact of collaboration: the value of UK medical research to EU science and health.* London: Technopolis Group.

4 Royal College of Physicians (2017) *Brexit: what does it mean for medical research?* London: Royal College of Physicians.

5 Shepherd J et al (1995) Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia, the West of Scotland Coronary Prevention Study. *New England Journal of Medicine.* 333(20):1301-07.

6 Ford I. et al (2007). Long term follow up of the West of Scotland Coronary Prevention Study. *New England Journal of Medicine.* 357(15):1477-1486.

7 REF 2014 Impact Case Studies. Global adoption of statins for cardiovascular disease prevention. Webpage. Available from: impact.ref.ac.uk/CaseStudies/CaseStudy.aspx?Id=41155. [Accessed 31 March 2017].

8 Packard C. J., Ford I., Murray H., McCowan C (2014) Lifetime clinical and economic benefits of statin-based LDL lowering in the 20-year follow-up of the West of Scotland Coronary Prevention Study. *Circulation.* 130:2105-2126.

9 European Commission press release (27 October 2014) EU breast cancer research targets personalised treatment.

10 European Investment Bank (24.01.2017) *EIB confirms GBP 5.5 billion backing for investment across the UK in 2016.*

11 www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000072.jsp (last accessed on 01.08.2017).

12 House of Commons Health Committee (2016) *Brexit and health and social care – people and processes.* Written evidence submitted by Cancer Research UK (BRE0074).

13 House of Commons Health Committee (2016) *Brexit and health and social care – people and processes.* Written evidence submitted by the Medicines and Healthcare Products Regulatory Agency (BRE0087).

14 www.nhsconfed.org/regions-and-eu/nhs-european-office/influencing-eu-policy/clinical-trials (last accessed on 01.08.2017).

15 Council of the European Union (2009) *Council Recommendation on action in the field of rare diseases.* Luxembourg: Council of the European Union.

16 Department of Health (2013) *The UK strategy for rare disease.* London: The Stationery Office.

17 http://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/hi/3cpart/h2020-hi-list-ac_en.pdf (last accessed 09.08.2017).

18 European Commission (2015) *Horizon 2020: first results.* Brussels, Belgium: European Commission.

19 HM Treasury press release (13 August 2016) *Chancellor Philip Hammond guarantees EU funding beyond date UK leaves the EU.*

20 HM Government (2017) *Collaboration on science and innovation: a future partnership paper.* London: The Stationery Office.

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