

BREXIT BRIEFING

Medicines and medical devices regulation

Maintaining an effective working
relationship between the
UK and the EU



Key points

- The UK has developed a well-functioning medicines and medical devices regulatory system, working with the EMA (European Medicines Agency) and built on EU (European Union) regulations and directives.
- Adopting a divergent approach to licensing would lead to:
 - delayed access to new medicines and medical devices – it has been suggested a separate regulatory system for medicines could lead to delays of 12 to 24 months in accessing life-saving drugs;
 - weaker post-approval regulation and pharmacovigilance, by lessening capacity to manage and detect issues such as adverse drug reactions; and
 - loss of expertise in regulatory processes and pharmacovigilance.
- To minimise these potential impacts, the UK Government should:
 - work closely with the EMA through a formal agreement to continue to support and participate in their assessments for medicines approvals; and
 - agree mutual recognition of the CE-mark (“Conformité Européene”) scheme.
- For the UK, negotiating a formal agreement on medicines and continuing to collaborate on medical devices would:
 - limit potential delays incurred by pharmaceutical companies and device manufacturers seeking a licence for their products in the UK, and thus ensure timely access to medicines and medical devices;
 - minimise the risk of pharmaceutical companies based in the UK from re-locating to a country working within the jurisdiction of the EMA, and the consequential impact on the UK’s research community and its economy; and
 - prevent any lessening of the UK’s capacity for pharmacovigilance by providing access to the EMA’s networks.
- For the EU, negotiating a formal agreement on medicines and continuing to collaborate on medical devices would:
 - maintain access to the extensive network of expertise in the UK in medicines and medical devices regulation and pharmacovigilance;
 - ensure pharmaceutical companies based in the EU can readily access the UK market; and
 - ensure medicines and devices developed in the UK reach EU citizens quickly, well in advance of the rest of the world.
- Should there be a failure to agree a withdrawal agreement by March 2019, there would be considerable uncertainty about the UK’s approach to medicines and medical devices regulation. This would likely lead to a shift away from products being developed for the UK market, with significant ramifications on timely access to new medicines and medical devices, as well as on the UK’s pharmaceutical and medical devices industries. There would also be considerable adverse impacts on the future capacity of the UK and EU in relation to pharmacovigilance, which for the UK would be compounded by a potential loss of expertise.

Background

The regulation of medicines in the UK – including those under development and approved for use – derives from EU regulations and directives, and is overseen by the MHRA (Medicines and Health Products Regulatory Agency). Working with the Agency, the UK has developed a well-functioning medicines regulatory system which ensures that patients have timely access to safe and effective drugs.

The EMA is responsible for ensuring that all medicines available on the EU market are safe, effective and of a high quality. In particular, it provides a centralised approval procedure for licensing to allow pharmaceutical companies to submit a single marketing authorisation to the EMA, which once granted is valid across the EU and EEA (European Economic Area).^a It also has a lead role in harmonising the regulation of clinical trials – which are often undertaken on a cross border basis across the EU – and agreeing post approval regulation to monitor the safety of medicines across their life-cycle.

The licensing of medical devices^b is also governed by EU regulations, and works via a system where they are approved by a registered notified body in a Member State. Once approved, devices can be sold across the EU and EEA through the CE marking scheme.^c Products made in countries outside the EU must be compliant with these requirements if they are to be made available on the EU market. Medical devices can be interpreted to include medical informatics^d which are impacted by the EU GDPR (General Data Protection Regulation). The Government confirmed in the 2017 Queen's speech that the GDPR will be transposed into UK law.¹

Please note: while this briefing considers the key issues around medicines and medical devices regulation, these aspects are closely linked to the research activities that underpin their development. The impact of the UK's exit from the EU on medical research is considered in a complementary briefing, 'Maintaining an effective working relationship between the UK and the EU on medical research'.

a EEA countries include Iceland, Lichenstein and Norway.

b There are over 500,000 types of medical devices and in-vitro diagnostic medical devices on the EU market. Examples include contact lenses, x-ray machines, pacemakers, breast implants and hip replacements and sticking plasters. In-vitro diagnostic medical devices, which are used to perform tests on samples, include HIV blood tests, pregnancy tests and blood sugar monitoring systems for diabetics.

c The CE mark is a labelling system which signifies that products sold in the EU and EEA have been tested and assessed to meet safety, health and environmental protection requirements set by EU regulations.

d Medical informatics are the resources, devices and methods required to retrieve, store and use information in health and biomedicine.

The UK's relationship with the EU on medicines and medical devices regulation

As a Member State and by adopting EU regulations, the UK has access to the EMA-wide centralised approval procedure for medicines and medicinal products, to influence regulations affecting clinical trials across the EEA, and to work closely with the EU on pharmacovigilance.^e The EMA is currently based in London, which reflects and bolsters the importance of the pharmaceutical industry in the UK. It has also helped ensure an interlinked relationship between the UK and the European Agency – for example, the MHRA handles around 40% of the EMA's decision making on medicines.²

The MHRA is the designated competent authority in the UK for administering and enforcing the law on medical devices in accordance with EU regulations on accreditation and market surveillance. It ensures these devices are safe to use and meet required standards for CE marking. This is a significant role for the MHRA, given the UK medical device market is the third largest in Europe, behind Germany and France, and the sixth largest in the world. It was valued at \$10.1 billion in 2016.^{3,4} Approval of medical devices in the UK automatically extends to approval to the rest of the EU for products with a CE-mark.

In a speech in September 2017, Lord O'Shaughnessy confirmed that some elements of EU Regulations which allow medical devices to be legally placed on the UK market, had been directly applied in UK law since May. Therefore, as it stands the EU (Withdrawal Bill) would maintain this position beyond March 2019.⁵ The ABHI (Association of British Healthcare Industries), BIVDA (British In Vitro Diagnostics Association) and MedTech Europe wrote to Michel Barnier and David Davis in September 2017, to raise concerns that beyond March 2019 the UK could become increasingly divergent from the CE marking scheme which may mean the UK does not fully adopt the EU Regulations.⁸

Potential consequences of the UK's exit from the EU on medicines and medical devices licensing

– Delayed access to new medicines and devices

While the regulatory process is different for medicines and medical devices, the impact of moving away from the existing collaborative approach would be the same. The centralised processes reduce the burden on the regulatory authority in each Member State and create a larger European market for the pharmaceutical industry and medical device manufacturers – for example, the EMA accounts for 25% of world sales of medicines, second only to the United States.⁶ The UK in comparison accounts for only 3% of the total world market.

Should the UK develop a significantly different regulatory process to the EMA for medicines regulation, the increased regulatory burden on pharmaceutical companies would lead them to prioritise the much larger EEA market over the UK. This was acknowledged by the Government in its recent life sciences industry strategy, which stated that the UK market would be too small to stand on its own.⁴ This would potentially cause delays in new drugs being made available for patients in the UK. For example, it has been suggested that a separate regulatory system to the EMA could lead to delays of 12 to 24 months for UK patients being able to access life-saving cancer drugs.⁷ It would also mean that medicines developed in the UK do not reach patients in the EU market as quickly.

^e The WHO (World Health Organization) define pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse drug effects or any other drug-related problems.

Establishing a separate system for accreditation of medical devices in the UK (away from the CE marking scheme) would also increase the burden on device manufacturers through the need to satisfy different safety, health and environmental protection requirements.⁸ This would likely lead to delays in devices developed in other countries reaching the UK market, and vice versa. This would be particularly detrimental for the UK, as most medical devices are imported. The UK has a limited number of large manufacturers, and those that do exist tend to concentrate on the US market. The strength of UK manufacturers lies in orthopaedics but also in imaging, diagnostics and cardiovascular disease. Those manufacturers that do exist often rely on components made in the rest of the EU and would thus face higher costs if the UK was outside the customs union.

– **Weaker post-approval regulation and pharmacovigilance**

The EMA coordinates a large network of pharmacovigilance, including post-approval regulation, surveillance and information sharing of medicines and medical devices across their life-cycle. This operates through cooperation between EU Member States, the EMA and the EC. By collecting and sharing real-time data on approved medicines and devices, the EMA is able to identify trends and quickly take action to inform patients and healthcare professionals about any safety concerns. The specific advantage of this collaboration at an EU level is the wider coverage area for surveillance and reporting of adverse effects, as there is a greater number of patients using a drug compared to within an individual country. This increases the likelihood of the data collected being more accurate, as well as concerns being picked up at an earlier stage.

Should the UK reduce its involvement in this network and adopt a more selective approach to pharmacovigilance data and information sharing, it would significantly lessen the capacity to detect and manage issues such as adverse drug reactions. This would potentially cause harm and uncertainty for patients and their doctors who rely on accurate reporting. While this would have an impact on both the EU and the UK, it would be particularly significant for the UK given the smaller population size for detecting problems.

– **Loss of expertise in regulatory processes and pharmacovigilance**

As a result of the key role that the MHRA plays in supporting the EMA, there is a significant network of medicines and medical devices regulation and pharmacovigilance expertise based in the UK. The ABHI view the MHRA as the pre-eminent competent global authority for medicines and medical devices regulation.⁹ The UK's expertise includes specialists from across Europe working for the MHRA, as well as those employed by pharmaceutical companies – each company has to employ a QPPV (qualified person for pharmacovigilance) working within the EU, and many are based in the UK to facilitate close working with the EMA.¹⁰

While a move away from working collaboratively with the EMA, coupled with its re-location away from London, will increase the likelihood of expertise moving abroad, this would be particularly challenging should the UK decide to establish its own, separate regulatory systems. The impact of the UK's loss of expertise would be reflected in a loss of regional and international influence in pharmacovigilance practice and make the UK reliant on other countries for sharing expertise.

Ensuring close collaboration between the UK and the EU on medicines and medical devices regulation

To ensure timely access to medicines, maintain robust pharmacovigilance systems, and minimise the loss of expertise, the UK Government should continue to work closely with the EMA after the UK leaves the EU. This will require a formal agreement to continue to support and participate in EMA assessments, and a clear agreement how the UK would approve these assessments domestically. The latter will be particularly important given the EMA is subject to the ECJ (European Court of Justice),¹¹ and that the UK Government has stated its intention to work outside the jurisdiction of the ECJ.¹²

A number of non-EU countries (eg Switzerland)¹³ have set a precedent for working on an individual arrangement basis on medicines licensing with the EMA, either through a MRA (mutual recognition agreement) to align regulatory processes,¹⁴ or through membership of the centralised authorised medicines procedure, as is the case with EEA countries.¹⁵ While the role of the ECJ is unclear in these circumstances, any ongoing involvement by the European Court should not be a barrier to future partnership working.

To prevent delays in medical devices reaching the UK and EU markets, and facilitate coordinated post-approval surveillance, the UK Government should agree mutual recognition of the CE-mark between the UK and the EU. This is in line with the arrangements in place for a number of non-EU countries for regulating and then importing medical devices into the single market. For example, Australia, New Zealand and Switzerland have MRAs with the EU to promote trade by providing easier access to conformity assessments. Each MRA has a list of approved conformity assessment bodies within the EU, which carry out testing and certification to show compliance with EU regulations and thus allowing it to apply the CE mark.¹⁶

For the UK, negotiating a formal agreement on medicines and continuing to collaborate on medical devices would:

- limit potential delays incurred by pharmaceutical companies and device manufacturers seeking a licence for their products in the UK, and thus ensure timely access to medicines and medical devices;
- avoid the burden and cost of establishing an independent regulatory and pharmacovigilance system;
- minimise the risk of pharmaceutical companies based in the UK from re-locating to a country working within the jurisdiction of the EMA, and the consequential impact on the UK's research community and its economy;
- prevent any lessening of the UK's capacity for pharmacovigilance by providing access to the EMA's networks; and
- support close collaboration with clinical research institutions across the EU.

For the EU, negotiating a formal agreement on medicines and continuing to collaborate on medical devices would:

- maintain access to the extensive network of expertise in the UK in medicines, medical devices regulation and pharmacovigilance;
- continue the close working relationship with the UK's world-leading clinical research institutions;
- ensure pharmaceutical companies based in the EU can readily access the UK market;
- ensure medicines and devices developed in the UK reach EU citizens quickly, well in advance of the rest of the world; and
- maintain the EU's current capacity for pharmacovigilance by providing access to the UK's networks.

Key developments

- In June 2017, the EU formally confirmed the relocation of the EMA away from London and set out the process for doing so.¹⁷ A decision on its future location is expected in November 2017.
- In July 2017, the UK Secretaries of State for Health and Business set out the Government's plans for the regulation of medicines post exiting the EU.¹⁸ This included the Government's intention to find a way to collaborate with the EU, in the interests of public health and safety. It set out three key principles for medicines regulation in the UK: patients should not be disadvantaged; innovators should be able to get their products into the UK market as quickly and simply as possible; and the UK should continue to play a leading role promoting public health.
- In August 2017, the Government set out its position and principles to ensure minimal disruption on withdrawal from the EU, with regards to the availability of goods.¹⁹ A position paper stated the Government would be negotiating on the key principles of ensuring continued availability of products in the EU and UK market, at the date of withdrawal and ensuring goods in circulation continue to comply with product legislation and market surveillance authorities can take the necessary action with respect of non-compliant goods. This includes a specific proposal that assessment bodies should continue to be recognised to fulfil any ongoing obligations (pharmacovigilance) for the lifetime of products and activities (medicines and medical devices).

Summary

Collaboration across borders on the way medicines and medical devices are regulated has been a key advantage of the UK's membership of the EU. Establishing a robust common framework for assessing and monitoring drug safety and efficacy has meant patients across Europe have timely access to new therapies and technologies. The CE marking system for medical devices has facilitated access to innovative medical devices from across Europe. The UK's decision to leave the EU has the significant risk of limiting the benefits of this harmonised approach. 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 www.gov.uk/government/publications/queens-speech-2017-what-it-means-for-you/queens-speech-2017-what-it-means-for-you (last accessed on 06.09.2017).
- 2 <https://pharmaphorum.com/news/ema-expects-uk-march-2019/> (last accessed on 26.05.2017).
- 3 www.pharmafield.co.uk/medtech-features/2011/08/Medtech-market-report-the-UK# (last accessed 06.09.2017).
- 4 Bell J (2017) *Life sciences industrial strategy: a report to the Government by the life sciences sector*. London: the Stationery Office.
- 5 Department of Health press release (14.09.2017) *Lord O'Shaughnessy on medical technologies and Brexit*.
- 6 Nuffield Trust (2017) *General Election 2017: Getting a Brexit deal that works for the NHS*. London: Nuffield Trust.
- 7 www.bbc.co.uk/news/health-38922366 (last accessed on 19.07.2017).
- 8 Ellingworth P, Williams DA and Bernasconi S (12.09.2017) *Letter to Barnier M and Davis D on joint medical technology association post-Brexit*.
- 9 Association of British Healthcare Industries (2017) *Healthy outside the EU: Strategy for a thriving midtech industry*. London: Association of British Healthcare Industries.
- 10 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.
- 11 www.instituteforgovernment.org.uk/printpdf/blog/government-hamstrung-its-position-european-court-justice (last accessed on 20.07.2017).
- 12 European Union (Withdrawal) Bill, 2017-19.
- 13 European Medicines Agency press release (22.07.2015) *EU and Swiss regulators sign confidentiality agreement*.
- 14 www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001843.jsp&mid=WC0b01ac058005f8ac (last accessed on 02.08.2017).
- 15 www.ima.is/licences/marketing_authorisations/ (last accessed on 02.08.2017).
- 16 https://ec.europa.eu/growth/single-market/goods/international-aspects/mutual-recognition-agreements_en (last accessed on 07.09.2017).
- 17 www.consilium.europa.eu/en/press/press-releases/2017/06/22-euco-agencies-relocation/ (last accessed on 02.08.2017).
- 18 Financial Times (4.7.2017) *We will continue to work with EU on medicines*.
- 19 HM Government (2017) *Continuity in the availability of goods for the EU and the UK: Position paper*. London: the Stationery Office.

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