

Memorandum of evidence from the British Medical Association to the Health Committee inquiry on regulation of medicines, medical devices and substances of human origin after Brexit

The British Medical Association (BMA) is a voluntary professional association and independent trade union, representing doctors and medical students from all branches of medicine across the UK and supporting them to deliver the highest standards of patient care. The BMA is committed to safeguarding the future of the profession and the patients we serve and it is essential we are consulted and involved in consultations to inform negotiations to leave the European Union (EU) which would affect the medical profession and patients.

Executive summary

- The UK government must seek to negotiate a formal agreement with the EU on the EMA (European Medicines Agency) and the regulation of medicines, medical devices and medical products after the UK leaves the EU. Ongoing collaboration with the EMA's network of post-approval regulation and pharmacovigilance would provide medical professionals with assurances that the medicines they are prescribing are safe and robustly tested.
- Should the UK develop a significantly different regulatory process to the EMA over time, there is a risk that the increased burden incurred by duplication of processes and the associated increased investment in time and costs, would lead the pharmaceutical industry to prioritise launching new medicines in the much larger European market over the UK. This could potentially lead to delays of up to 24 months in new drugs being made available to patients in the UK, as a consequence of becoming a second tier priority market.
- An agreement between the UK and EU on the mutual recognition of the CE ("Conformité Européenne") marking scheme for medical devices would help manufacturers to avoid having to satisfy different safety, health and environment protection standards, thereby reducing delays in devices developed in other European countries reaching the UK market, and vice versa.
- A formal agreement on Euratom would allow the UK to guarantee continuous and timely access to radioisotopes for medical purposes. This is vital to lessening the risk of supply issues.
- Establishing a regulatory regime for clinical trials that diverges significantly from EU standards would increase the burden on UK researchers and pharmaceutical companies. This would make the UK a less appealing destination to conduct trials, particularly for rare diseases, while also creating barriers to collaborating and sharing expertise and facilities.
- It is crucial that the UK continues to work collaboratively with the EU on research to develop new medicines and medical devices. Reduced collaboration risks not only having a significant adverse impact on the UK's capacity to develop new products for the benefit of patients, but also limiting training and career opportunities for medical researchers and making the UK a less attractive destination for key talent and expertise.

Following the UK's withdrawal from the EU, what alternative arrangements for the regulation of medicines, medical devices, medical products and substances of human origin could be introduced? What are the respective opportunities, risks and trade-offs involved?

Regulation of medicines

1. There are a number of potential arrangements for the regulation of medicines which the Government could introduce or negotiate with the EU. It may be possible to reach a formal agreement with the EMA through an MRA (mutual recognition agreement)¹, either on bespoke terms or following a similar model to Switzerland.² Alternatively, the MHRA (Medicines and

¹ www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001843.jsp&mid=wcob (last accessed on 26.09.2017).

² European Medicines Agency press release (22.07.2015) *EU and Swiss regulators sign confidentiality agreement*

Healthcare products Regulatory Agency) could introduce a UK accelerated licence, by developing a divergent licensing process but accepting EMA data to reduce the burden on pharmaceutical companies. Finally, the UK could secure an agreement with an alternative market – for example, Australia, Canada, Singapore and Switzerland have recently established a separate regulatory market.

- 1.1 The BMA believes the best arrangement for ensuring timely access to medicines that are safe and robustly tested throughout their life-span, is for the UK Government to continue to work closely with the EMA after the UK leaves the EU.³ This will require a formal agreement – similar to Switzerland - to continue to support and participate in EMA assessments, and a clear agreement how the UK would approve these assessments domestically.
- 1.2 Doctors are concerned that should the UK develop a significantly different regulatory process after Brexit, the increased burden incurred by a duplication of processes and the associated increased investment in time and costs, would lead industry to prioritise the European market over the UK. This risk was acknowledged by the Government in its recent life sciences industrial strategy, which stated that the UK market would be too small to stand on its own.⁴ A divergent regulatory system would potentially lead to delays of up to 24 months in new drugs being made available to patients in the UK as a consequence of becoming a second tier priority market.^{5,6,7} It would also leave the UK more vulnerable to economic uncertainty and fluctuations in the value of Sterling which may also cause pharmaceutical companies to deprioritise the UK market.
- 1.3 A formal agreement with the EMA would also allow the UK to continue to access the EMA network of post-approval regulation and pharmacovigilance. Crucially this would provide doctors with assurances that the medicines they are prescribing are safe and robustly tested, after they have been licensed. 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. Should the UK reduce its involvement in this network, it would significantly lessen the capacity to detect and manage issues such as adverse drug reactions and cause uncertainty for doctors and their patients who rely on accurate reporting.

Regulation of medical devices

2. In order to guarantee ongoing access to new medical devices, the UK and EU should agree a mutual recognition of the CE marking scheme. This would be in line with similar arrangements in place for non-EU countries, for example, Australia, New Zealand and Switzerland all have MRAs which facilitate regulating and importing medical devices into the single market.⁸
- 2.1 The medical devices market is rapidly evolving as new products are continuously brought to market - for example, in cardiology, a continuous flow of new CIED (cardiac implantable electronic devices) are being developed and approved for use. An MRA would avoid requiring manufacturers

³ British Medical Association (2017) *Medicines and medical devices regulation: maintaining an effective working relationship between the UK and the EU*. London: British Medical Association.

⁴ Bell J (2017) *Life sciences industrial strategy: a report to the Government by the life sciences sector*. London: The Stationery Office.

⁵ www.bbc.co.uk/news/health-38922366 (last accessed 25.09.2017)

⁶ UK EU Life Sciences Steering Committee (2016) *Maintaining and growing the UK's world leading Life Sciences sector in the context of leaving the EU*. London: UK EU Life Sciences Steering Committee.

⁷ Fahy N, Hervey T, Greer S et al (2017) How will Brexit affect health and health services in the UK? Evaluating three possible scenarios. *The Lancet* (17): 31926-31928.

⁸ http://www.ema.europa.eu/ema/index.jsp?curl=pages/partners_and_networks/general/general_content_000214.jsp&mid=WC0b01ac058003176d (last accessed 16.10.2017)

to satisfy different safety, health and environment protection standards,⁹ otherwise there would likely be increased delays in devices developed in other countries reaching the UK market and vice versa. Delays would be particularly detrimental for the UK, as most devices are imported and large domestic manufacturers already prioritise the US market, as it is significantly larger.¹⁰

2.2 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 biotechnology industries. While it is vital that the UK should negotiate a withdrawal deal that works for the ongoing supply of medicines and medical devices, we also believe that it is vital that the Government puts in place contingency plans if no deal can be agreed.

How will withdrawal from the European Union affect the UK's ability to influence international standards in life sciences?

3. The terms of the UK's exit deal from the EU are likely to have a significant impact on the UK's ongoing influence in international standards. It may be possible for the UK to retain some of its current influence in the life sciences by reaching a formal agreement with the EU and EMA, and by aligning closely or adopting EU regulations on medicines and devices licensing, as well as clinical trials.

3.1 The UK currently chairs one of four of the EMA's regulatory committees – the PRAC (Pharmacovigilance Risk Assessment Committee). Pharmacovigilance standards set by the committee are often adopted internationally as best practice¹¹, and shaped by the UK's leadership. The MHRA also handles around 40% of the EMA's decision making on medicines, and is therefore able to influence and enforce standards on a case by case basis, and has been key in developing regulations on medical devices. In addition to this, the UK has played a leading role in the development of the new EU Clinical Trials Regulation (536/2014), which is set to be applied from 2019.

3.2 Without formal membership and ongoing participation with the EMA, it is unlikely the UK will be allowed to continue to chair regulatory committees, formally influence EMA licensing decisions and good practice standards and shape the future development of regulations affecting clinical trials. As well as weakening the UK's international influence, this will likely reduce the appeal of the UK for experts working in these areas.

3.3 The UK has had particular prominence in setting international standards in specific areas. The NISBC (National Institute for Biological Standards and Control) is responsible for developing and producing over 90% of the international standards in use around the world to assure the quality of biological medicines in precision medicine and genomics applied to patients, through globally leading initiatives such as the UK Biobank.¹² Genomics England has already set the global standard for healthcare genomic data in rare diseases, and increasingly in cancer. Should the UK lose influence in setting international life sciences generally, then this will place more pressure on building and retaining influence in specific areas, such as biomedicine.

⁹ Ellingworth P, Williams DA and Bernasconi S (12.09.2017) *Letter to Barnier M and Davis D on joint medical technology association post-Brexit*.

¹⁰ <https://www.pharmafield.co.uk/medtech-features/2011/08/Medtech-market-report-the-UK> (last accessed on 03.10.2017)

¹¹ European Medicines Agency (2017) *Pharmacovigilance Risk Assessment Committee (PRAC) work plan 2017*. London: European Medicines Agency.

¹² Medicines and Healthcare products Regulatory Agency (2016) *Human Medicines Regulations 2012 Advisory Bodies Annual Report 2016*. London: Medicines and Healthcare products Regulatory Agency.

What arrangements are needed to ensure the safe, effective and timely support of medical radioisotopes over the short, medium and long term?

4. It is vital that the UK continues to work closely with Euratom after it exits the EU.¹³ In order to do this, we believe the UK should first establish an SSAC (State System of Accountancy and Control for Nuclear Material) to fulfil our obligations to the International Atomic Energy Agency. This includes obligations to agree regional non-proliferation treaties, export controls, security assurances, and many other unilateral and multilateral initiatives. The Government should also negotiate a formal agreement with Euratom, as is the case for a number of non-EU countries, such as Switzerland, which have associate agreements with Euratom, governing reciprocal rights and obligations, common action and special procedures.¹⁴

4.1 A formal agreement on Euratom would allow the UK to guarantee continuous and timely access to radioisotopes for medical purposes. This is vital as isotopes used in medicine have a short half-life and cannot be stock piled. The UK imports medical radioisotopes from an international supply – for example, its supply of Technetium 99m (the most common radioisotope used in nuclear diagnostic imaging in many UK hospitals) is imported from the Netherlands, France and Belgium.^{15,16} As the UK will not have access to a supply close to the point of use, failing to agree ongoing membership of Euratom will increase the risk of supply issues. Breaks in this supply can lead to delayed diagnosis and treatment, as occurred in 2009 and 2013 when maintenance of reactors resulted in facilities going offline temporarily.¹⁷

4.2 Should the UK fail to negotiate a deal with the EU by March 2019, the UK would have to operate outside of Euratom and source radioisotopes from outside this framework. This would remove the guarantee of consistent and timely access to radioisotopes, potentially resulting in delays in diagnosis and cancelled operations for patients. In the longer term, it would also restrict the ability of the UK and EU to benefit from sharing expertise in radiation research, radiation protection and the disposal of radioactive waste. While the Government should prioritise a deal that guarantees access to radioisotopes, it is also important that contingency plans are in place should no deal be reached.

What are the implications for medical research and development, including for the timely patient access to new medicines, technologies and other relevant medical innovations developed within or outside the UK? How can any adverse consequences be avoided or mitigated and any potential opportunities be enhanced?

5. To ensure researchers and research institutions across the UK and EU continue to collaborate, the UK Government should, at a minimum, negotiate a formal agreement to maintain access to EU research funding programmes.¹⁸ Ensuring close collaboration will require the UK to replicate the new EU Clinical Trials Regulation so there is alignment, as well as reaching an agreement as to how the UK (through the MHRA) participates in the operation of pan-European clinical trials.

5.1. The UK should also negotiate a formal agreement with Euratom to ensure ongoing collaboration on radiation research and long term projects such as the ITER (International Thermonuclear

¹³ British Medical Association: *Euratom and Brexit*. London: British Medical Association.

¹⁴ House of Commons Library (2017) *Euratom*. London: The Stationery Office.

¹⁵ British Nuclear Medicine Society and Science and Technology Facilities Council (2014) *Future supply of medical radioisotopes for the UK*. London: British Nuclear Medicine Society.

¹⁶ www.instituteforgovernment.org.uk/brexit-explained/Euratom (last accessed on 12.07.2017)

¹⁷ www.nature.com/news/radioisotopes-the-medical-testing-crisis-1.14325 (last accessed on 27.09.2017)

¹⁸ British Medical Association (2017) *Medical research: maintaining an effective working relationship between the UK and the EU*. London: British Medical Association.

Experimental Reactor) – the EU hosted international nuclear fusion project - and F4E (JET Fusion 4 Energy) – the EU joint undertaking for ITER and the development of fusion energy.¹⁹

- 5.2. Should the UK cease to work collaboratively with the EU on research, it would create uncertainty for future funding and opportunities for researchers, and therefore damage the UK's scientific appeal, as well as creating barriers to cross-border collaboration and cross-fertilisation of ideas.²⁰ For example, collaboration across the EU on research into diabetes has led to the development of community-based approaches to prevention and management of the disease in the UK and Europe.²¹ Research carried out in isolation would have a limited impact²² and this would in turn limit the UK's ability to translate research into products in the market – the UK currently has the largest pipeline of therapeutic treatments in Europe²², while 25% of the world's top prescription medicines were discovered in the UK.⁵
- 5.3. The UK will also lose access to projects coordinated by EMA. For example, UK universities are key partners in PROTECT (the Pharmacoeconomic Research on Outcomes of Therapeutics by a European Consortium), a project coordinated by the EMA and involving a multi-national consortium of 34 partners, which developed innovative methods to improve and strengthen monitoring of the benefits and risks of EU marketed medicines.²³
- 5.4. Reduced research collaboration may have different consequences in the devolved nations or individual regions. For example, in terms of funding, Scottish physics departments receive a higher allocation from the EU than physics departments in each of the other UK nations, while certain regions of the UK are more dependent on the research and education sector for economic development.²⁴
- 5.5. A divergent approach to research standards would also have consequences for the way the UK conducts clinical trials. This would significantly increase the burden on UK researchers and the industry, such as needing to provide different datasets to the MHRA and EMA, and seeking 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, sharing expertise and facilities, and limit access to datasets. It would have a particularly adverse impact on research into rare diseases, as a result of the small number of trial participants and limited research expertise within individual countries. The vast majority of these clinical trials involve active collaboration with EU countries – 736 paediatric trials and 1,021 rare disease trials by the UK were with other EU countries.²²
- 5.6. Reduced collaboration on research would also limit 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 (for example, between 2007 and 2013, the UK was the top destination for the EU's Marie Skłodowska-Curie action fellowships, with five UK institutions among the top ten organisations).²² This would ultimately result in a loss of key expertise in the UK.

¹⁹ Nuclear Industry Association (2017) *Briefing paper: Euratom*. London: Nuclear Industry Association.

²⁰ RAND Europe (2017) *International mobility of researchers. Supplementary report: perspectives from industry*. London: RAND Europe.

²¹ http://ec.europa.eu/research/infocentre/article_en.cfm?artid=43196 (last accessed on 24.10.2017)

²² Technopolis Group (2017) *Euratom*. London: The Stationery Office.

²³ http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000571.jsp&mid=WC0b01ac0580981013 (last accessed on 16.10.2017)

²⁴ Scottish Parliament Culture, Tourism, Europe and External Relations Committee (2017) *Brexit – what Scotland thinks: summary of evidence and emerging issues*. Edinburgh: Scottish Parliamentary Corporate Body.

5.7. The European Commission has recently announced that, after March 2019, should the UK leave the EU without negotiating an exit deal, UK researchers collaborating on existing EU funded projects will lose access to EU funding from that point onwards and may be required to leave ongoing projects. The potential impact of this is already causing the research community significant uncertainty in terms of future funding sources and opportunities for collaboration. This must be addressed urgently to prevent the UK losing academic expertise and to ensure future demand for researchers to work in the UK. Failure to do so would ultimately damage the UK's research outputs and reputation.