



**BRIEFING PAPER**

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# Brexit and medicines regulation

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**Contents:**

1. Current regulation of medicines and medical devices
2. UK medicines industry and trade
3. Impacts of Brexit on medicines regulation and supply
4. No-deal Brexit
5. Further reading



# Contents

<b>Summary</b>	<b>3</b>
<b>1. Current regulation of medicines and medical devices</b>	<b>4</b>
1.1 The regulatory bodies	4
The European Medicines Agency	4
The Medicines and Healthcare Products Regulatory Agency	5
1.2 Regulation of medicines	6
Medicines production	7
Pharmacovigilance	7
1.3 Regulation of medical devices	8
New EU regulations for medical devices	9
Medical device vigilance	10
<b>2. UK medicines industry and trade</b>	<b>11</b>
2.1 The pharmaceutical Industry	11
2.2 Contribution to the economy	11
2.3 Employment	12
2.4 Trade	13
<b>3. Impacts of Brexit on medicines regulation and supply</b>	<b>15</b>
3.1 What are the options for future regulation?	15
3.2 Legislation after Brexit	16
3.3 Negotiations on the future relationship with the EU	17
Government White Paper on the future relationship between the UK and the EU (July 2018)	18
Withdrawal Agreement November 2018	18
Political Declaration	20
3.4 Views on regulating medicines outside of the EU	20
3.5 The regulator's preparations for Brexit	22
EMA	22
MHRA	23
<b>4. No-deal Brexit</b>	<b>24</b>
4.1 Impacts of a no-deal Brexit	24
4.2 Government preparations	27
Technical notices	27
Stockpiling and other preparations	28
A proposed accelerated licencing route for medicines	30
Orphan medicines	31
4.3 Medical devices	32
CE markings	32
Notified Bodies	32
Post market surveillance of devices	32
4.4 No deal Brexit legislation	32
Serious Shortage Protocol	33
<b>5. Further reading</b>	<b>35</b>

## Summary

How and when we get access to medicines and how their safety is ensured is one area which has been subject to debate and analysis since the EU referendum.

Currently, the European Medicines Agency (EMA) provides and coordinates licensing, expertise and support for medicines and medical devices throughout the EU. Pharmaceutical companies may choose to licence a medicine only in one EU country, or to use the centralised, or mutual recognition procedure, that allows them to sell a product throughout the EU.

The Medicines and Healthcare products Regulatory Agency (MHRA) is the body responsible for licensing and regulating medicines and medical devices in the UK. It currently works with the EMA as part of a regulatory network and undertakes a significant amount of assessments and other work on behalf of the European agency.

It is still not known how medicines will be regulated when the UK leaves the EU. The Government have stated that it is seeking a close future relationship with the EMA. The November 2018 Political Declaration said that the Parties would “explore the possibility of cooperation” with EU agencies such as the EMA. There have been calls from health organisations, healthcare professionals, pharmaceutical companies and others for the Government to ensure regulatory alignment with the EMA on medicines in order to guarantee patient safety, public health and support the industry in the UK.

Concerns have been expressed about the impacts of a no deal Brexit on medicines supply and future medicine regulation in the UK. The Government have undertaken a range of actions to prepare for this scenario, including requiring pharmaceutical companies to stockpile medicines, securing new freight options for transporting medicines, and introducing new measures for supplying medicines in the event of serious shortages.

The paper is narrowly focused on medicines regulation and does not discuss potential changes to research funding and clinical trials regulation following Brexit.

The European Medicine Agency was based in London until 1 March 2019. Following the referendum result it has now moved to Amsterdam.

Contributing authors: Chris Rhodes: UK Medicines Industry and trade

# 1. Current regulation of medicines and medical devices

This section provides an overview of the current medicine regulatory bodies and processes in the UK and throughout the European Union (EU) and the European Economic Area (EEA).

For a more detailed description of the regulation of medical products in the EU, see the 2015 European Parliament Research Service briefing, [Medicinal products in the European Union: The legal framework for medicines for human use](#).

## 1.1 The regulatory bodies

There are currently two regulatory bodies through which UK medicines can be licensed, medical devices are regulated, and a medicine's safety is monitored. The European Medicines Agency performs all these roles on an EU and EEA (European Economic Area) country wide basis. The Medicines and Healthcare Products Regulatory Agency is the UK-based regulator. These two bodies currently work together in the UK market.

### The European Medicines Agency

The [European Medicines Agency \(EMA\)](#) is an agency of the European Union (EU) responsible for the scientific evaluation, supervision and safety monitoring of human and veterinary medicines.

The EMA works across the European Union (EU), performing a number of functions, including:

- Assessing both human and animal medicines for marketing authorisations;
- Providing independent evidence-based information on medicines;
- Monitoring the safety of medicines post authorisation; and
- Assessing and regulating medical devices.

[National medicines authorities](#) from EU Member States and EEA countries and others collaborate with the EMA. The EMA describes this as a "*unique regulatory framework*" that it states offers the following benefits:

- Enables Member States to pool resources and coordinate work to regulate medicines efficiently and effectively;
- Creates certainty for patients, healthcare professionals, industry and governments by ensuring consistent standards and use of best available expertise;
- Reduces the administrative burden through the centralised authorisation procedure, helping medicines to reach patients faster;
- Accelerates the exchange of information on important issues, such as the safety of medicines.<sup>1</sup>

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<sup>1</sup> EMA, [European medicines regulatory network](#) [accessed 14 March 2019]

The majority (about 90%) of the EMA budget comes from fees and charges. These include fees for processing marketing authorisation applications, and for scientific advice. In 2018 the total budget of the EMA was €337.8 million:

- approximately €304.5 million will come from fees and charges levied for regulatory services;
- approximately €22.4 million is expected in income from the EU, mainly to support the policies for orphan and paediatric medicines, advanced therapies and micro, small and medium-sized enterprises.<sup>2</sup>

The EMA reports that in 2018, it is estimated that €127.6 million will be paid to national medicines regulators from the EMA.<sup>3</sup>

More detailed information on the work of the EMA can be found in a 2017 European Parliament Research service briefing, [European Medicines Agency: A look at its activities and the way ahead](#).

## The Medicines and Healthcare Products Regulatory Agency

The [Medicines and Healthcare products Regulatory Agency](#) (MHRA) is the Department of Health and Social Care executive agency responsible for licensing and regulating medicines and medical devices in the UK.

Its responsibilities include:

- ensuring that medicines, medical devices and blood components for transfusion meet applicable standards of safety, quality and efficacy
- ensuring that the supply chain for medicines, medical devices and blood components is safe and secure
- promoting international standardisation and harmonisation to assure the effectiveness and safety of biological medicines
- helping to educate the public and healthcare professionals about the risks and benefits of medicines, medical devices and blood components, leading to safer and more effective use
- supporting innovation and research and development that's beneficial to public health
- influencing UK, EU and international regulatory frameworks so that they're risk-proportionate and effective at protecting public health.<sup>4</sup>

The budget of the MHRA for the 2017/18 period was £168.8 million. As with the EMA, most of this (£157.5) comes from trading activities such as income from fees.<sup>5</sup>

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<sup>2</sup> EMA, [Funding](#), [accessed 14 March 2019]

<sup>3</sup> Ibid.

<sup>4</sup> MHRA, [About us \[accessed 18 March 2019\]](#)

<sup>5</sup> MHRA, [Annual Report and Accounts 2017/18](#), July 2018

### Box 1: The International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

The International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is an influential organisation that works to harmonise medicines registration globally, and brings together the regulators and pharmaceutical industry on this issue.<sup>6</sup> The ICH comprises of the regulatory bodies of the EU, the US and Japan. The Council sets guidelines regarding the requirements for medicines registration that whilst not legally binding, are required for any company wishing to import medicines into the EU, Japan or the US. Currently, the UK participates in the ICH as part of the EU delegation, and also plays a role in several ICH expert working groups.

## 1.2 Regulation of medicines

Before a medicine can be sold or prescribed in the UK it must usually receive a marketing authorisation (see box 2) either from the EMA or MHRA.

A marketing authorisation will only be issued if [clinical trials](#) have proved that the medicine:

- successfully treats the condition it was developed for;
- has acceptable side effects; and
- meets high safety and quality standards.

### Box 2: Types of marketing authorisations

Marketing authorisations are the European licensing system for medicines. There are several routes that applicants can take to obtain a marketing authorisation, at the EU and national level:

- **Centralised procedure:** This is set out in [Regulation \(EC\) No 726/2004](#) and allows applicants to apply for a marketing authorisation to the EMA which will then apply across the EU and EEA countries. This approach is compulsory for certain medicines such as orphan medicine products (see box 3 below) and biotechnology products.
- **Mutual recognition procedure:** This is set out in EU [Directive 2001/83/EC](#) and applies to most medicines that do not have to be licenced through the centralised procedure. This process means that if a medicine has been assessed and licenced in one EU Member State (the 'Reference Member State'), this can then be recognised throughout the EU and in EEA countries under the EMA.
- **Decentralised procedure:** This is set out in [Directive 2004/27/EC](#) which amended Directive 2001/83/EC. The procedure can be used for most conventional medicines. An application for a marketing authorisation application is submitted to several Member States at one time. One of these Member States is allocated to be the 'Reference Member State' and will undertake the assessment. When the licence is granted it will apply in the Reference and other concerned Member States.
- **National procedure:** An application for a marketing authorisation may be made to one national authority, to apply only in that Member State (eg. the MHRA in the UK)

For more information on licencing procedures, the following sources may be useful:

- MHRA, [Guidance: Apply for a licence to market a medicine in the UK](#)
- European Commission, [Authorisation procedures for medicinal products](#)
- Taylor Wessing, [Types of marketing authorisation](#)

<sup>6</sup> [ICH website](#)

Initial marketing authorisations are valid for five years and then may be renewed on the basis of a re-evaluation.

## Medicines production

Licences are required in order to manufacture or supply a medicine in the UK.<sup>7</sup> These are granted by the MHRA in the UK.

Rules on the manufacture and supply of medicinal products are set out in [European Commission Directive 91/356/EEC](#), implemented through the [Human Medicines Regulations 2012](#). Under current rules, medicines manufacturers in the UK must meet a minimum standard of Good manufacturing practice (GMP) which requires the medicine to be of a high quality, appropriate to its intended use and meet the requirements of its licence.<sup>8</sup>

Good Distribution practice (GDP) puts further requirements on manufacturers and dealers to ensure that medicines are obtained from a licenced supply chain, are stored, transported and handled as required by the marketing authorisation.

The MHRA is responsible for undertaking inspections to ensure that the rules on GDP and GMP are met in the UK. More information on GDP and GMP is provided on [the MHRA website](#).

Under EU Directive 2001/83/EC a manufacturer must appoint a Qualified Person (QP). The QP is responsible for ensuring that every batch of medicines has been manufactured and checked in accordance with legal requirements. The MHRA provide further information on this in a [guidance note](#):

The QP's duties are specific and are intended to ensure that every batch of medicinal product has been manufactured and/or assembled and checked in accordance with legal requirements.

[...]A QP has a personal responsibility for ensuring that the required tests and controls are carried out and must sign or certify, for each batch, that the appropriate tests have been carried out and that it complies with the relevant marketing authorisation (MA), Article 126a authorisation, certificate of registration or traditional herbal registration. More than one QP may be named on a Manufacturer's Licence.<sup>9</sup>

Under EU law, the marketing authorisation holder of a medicine and the Qualified Person must be based in an EU/EEA country.

## Pharmacovigilance

Following the granting of a marketing authorisation, and wide use of that medicine, certain adverse effects might be noted that were previously unknown. Post authorisation monitoring is an important feature of medicines safety.<sup>10</sup>

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<sup>7</sup> MHRA, [Guidance: Apply for manufacturer or wholesaler of medicines licences](#), 2018

<sup>8</sup> MHRA, [Guidance: Good manufacturing practice and good distribution practice](#), February 2019

<sup>9</sup> MHRA, [Notes for applicants and holders of a Manufacturer's Licence](#), 2014

<sup>10</sup> EMA, [Pharmacovigilance \[accessed 9 April 2019\]](#)

The ongoing safety of drugs is monitored across the EU regulatory network by the EMA. The [Pharmacovigilance Risk Assessment Committee](#) (PRAC) is the EMA committee responsible for monitoring safety issues for medicines, and undertaking assessments. The Committee is made up of representatives from regulatory bodies across the EU and EEA, including the MHRA.<sup>11</sup>

PRAC also coordinates an EU wide system for reporting suspected adverse effects in medicines, [Eudravigilance](#). It can be used by Member States, the EMA and the pharmaceutical industry.

The MHRA conducts safety monitoring of medicines on a UK-wide basis. This includes undertaking inspections of UK-based marketing authorisation holders to ensure that they have an effective system for monitoring medicines, maintain documentation on this, and have sufficient staff to undertake this work.<sup>12</sup> The MHRA also runs the [Yellow Card Scheme](#), which is used to collect evidence on medicines safety issues. Reports on side effects, defective products and adverse incidents on medicines, device and vaccine can be made through this scheme.

### 1.3 Regulation of medical devices

A medical device is any instrument (other than a medicine) that is used to diagnose or manage a medical condition. The definition covers a wide range of products including syringes, dressings, surgical tools, scanners and some medical apps.<sup>13</sup>

Currently, all medical device products must meet the essential requirements of all relevant European medical device directives. The directives outline the safety and performance requirements for medical devices in the EU. The CE mark is a legal requirement to place a device on the market in the EU and EEA.

The regulatory procedures for medical devices are currently set out in the [Medical Devices Regulations 2002](#) (as amended) which implement the following three EU Directives:

- Medical Devices Directive (93/42/EEC);
- Active Implantable Medical Devices Directive (90/385/EEC); and
- In Vitro Diagnostic Medical Devices Directive (98/79/EC).

Medical devices that are certified under the regulations as conforming to the Directives are CE marked and can be marketed and sold anywhere in the EU.

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<sup>11</sup> EMA, [Pharmacovigilance Risk Assessment Committee \(PRAC\) \[9 April 2019\]](#)

<sup>12</sup> MHRA, [Guidance: Good pharmacovigilance practice \(GPvP\)](#), July 2016

<sup>13</sup> More detail on the definition of medical devices is provided in MHRA, [Guidance on legislation: Borderlines between medical devices and medicinal products](#), May 2016

### Box 3: CE Marking

- The letters "CE" on a product which is traded in the EU and EEA signifies that it has been assessed to meet safety, health and environmental protection requirements.
- By affixing the CE marking to a product, a manufacturer declares that the product meets all the legal requirements for CE marking and can be sold throughout the EU and EEA.
- Not all products must bear CE marking; only those product categories subject to specific directives that provide for the CE marking are required to be CE marked.

Devices are classified according to [guidance set out by the European Commission](#) and the certification process is different for each class of device. These processes are set out in detail in [MHRA guidance on the gov.uk website](#).

Higher-risk devices (such as Class IIa, IIb and III medical devices and in vitro diagnostic devices in list A and list B in Annex II of the EU Directive, plus those for self-testing) must be certified by an independent conformity assessment body, called EU Notified Bodies. A [notified body](#) is an organisation that has been designated by an EU Member State (the designating authority in the UK is the MHRA) to assess whether manufacturers and their medical devices meet the requirements set out in legislation. There are currently around 50 notified bodies in the EU - five of these are in the UK.<sup>14</sup>

### New EU regulations for medical devices

In April 2017, two [new EU regulations](#) were adopted by the European Parliament and the Council.<sup>15</sup> [Regulation \(EU\) 2017/745](#) will regulate general medical devices and will apply after a 3 year transition period, and [Regulation \(EU\) 2017/746](#) will regulate in vitro diagnostic medical devices and will apply after 5 years.

The European Commission website provides information about the changes introduced by the new Regulations:

The new Regulations contain a series of extremely important improvements to modernise the current system. Among them are:

- [stricter ex-ante control for high-risk devices](#) via a new pre-market scrutiny mechanism with the involvement of a pool of experts at EU level;
- [the reinforcement of the criteria for designation and processes for oversight of Notified Bodies](#);
- [the inclusion of certain aesthetic devices](#) which present the same characteristics and risk profile as analogous medical devices under the scope of these Regulations;
- [the introduction of a new risk classification system for in vitro diagnostic medical devices](#) in line with international guidance;

<sup>14</sup> MHRA, [Guidance: Notified bodies for medical devices](#), December 2014

<sup>15</sup> European Commission, [Revisions of Medical Device Directives \[accessed 9 April 2019\]](#)

## 10 Brexit and medicines regulation

- improved transparency through the establishment of a comprehensive EU database on medical devices and of a device traceability system based on Unique Device Identification;
- the introduction of an “implant card” containing information about implanted medical devices for a patient;
- the reinforcement of the rules on clinical evidence, including an EU-wide coordinated procedure for authorisation of multi-centre clinical investigations
- the strengthening of post-market surveillance requirements for manufacturers;
- improved coordination mechanisms between EU countries in the fields of vigilance and market surveillance.<sup>16</sup>

### Medical device vigilance

The MHRA is the competent authority in the UK for monitoring the safety of medical devices. It explains its responsibilities in this role on its website:

To ensure that medical devices placed on the market and put into service in the UK meet these regulatory requirements we perform the following activities:

- assess all allegations of non-compliance brought to us, using a risk-based system.
- monitor the activity of notified bodies designated by MHRA to assess the compliance of manufacturers
- investigate medical devices as a result of adverse incident reports or intelligence indicating a potential problem
- carry out proactive risk-based projects with other member states in Europe to identify emerging risks<sup>17</sup>

Post-marketing safety information on medical devices is shared across the EU through the [National Competent Authority Report Exchange](#).

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<sup>16</sup> Ibid.

<sup>17</sup> [MHRA, Guidance: Medical devices: the regulations and how we enforce them](#), February 2019

## 2. UK medicines industry and trade

### 2.1 The pharmaceutical Industry

The following table summarises the economic contribution of the UK pharmaceuticals industry.<sup>18</sup>

The UK pharmaceutical industry in 2018		
		% of UK total
Economic contribution	£13.8 billion	0.7%
Employment (2017)	39,000	0.1%
Businesses	630	0.02%

Source: Economic contribution: ONS, [GDP estimates Q4 2018](#), Low Level Aggregates Table

Employment: ONS, [Business register and employment survey](#), 2018, via NOMIS database

Businesses: ONS, [Business counts](#), via NOMIS database

The industry contributed £13.8 billion to the economy in 2018, down 24% in real terms since 2010.<sup>19</sup>

There are around 600 pharmaceuticals manufacturing businesses in the UK, employing 39,000 people.

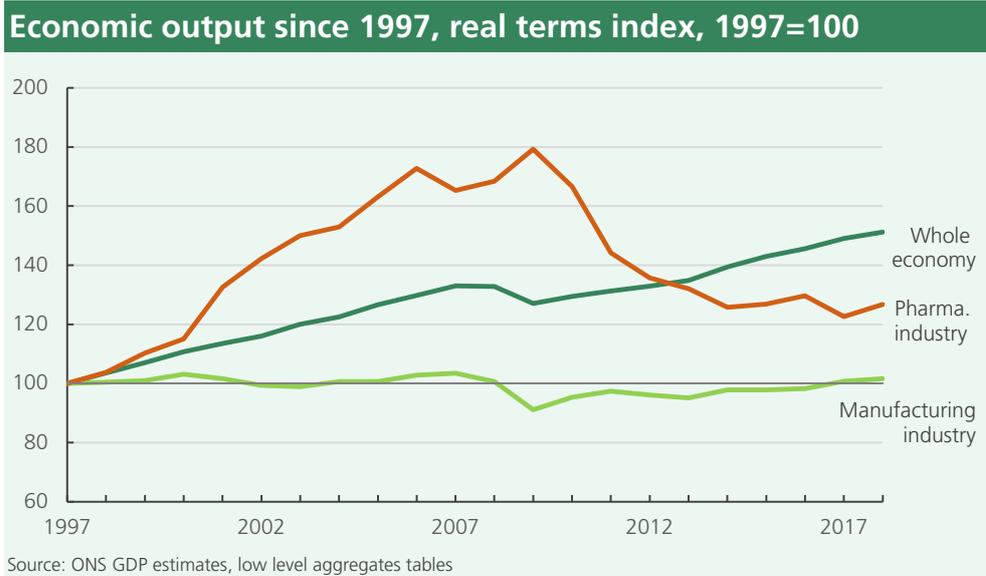
### 2.2 Contribution to the economy

The pharmaceuticals industry contributed £13.8 billion to the UK economy in 2018, 0.7% of total economic output, and 7% of total manufacturing output.

The following chart shows how the economic output of the pharmaceuticals industry has changed over the last 20 year in real terms, compared to the economic output of the whole manufacturing industry, and the whole UK economy.

<sup>18</sup> The pharmaceuticals industry is defined as Standard Industrial Classification (SIC) code 21, the manufacture of basic pharmaceutical products and pharmaceutical preparations

<sup>19</sup> Economic contribution is Gross Value Added (GVA); Employment is for Great Britain in 2016; Businesses excludes small businesses with no employees



Output from the pharmaceuticals industry grew strongly from 1997 and 2007. Whilst the whole economy grew by 32% in real terms, the pharmaceuticals industry grew by 65%. The manufacturing sector as a whole grew by only 3% over this period. <sup>20</sup>

However, since 2009 these trends have been reversed. From 2009 to 2018, the pharmaceuticals industry's economic output fell by 29%, whilst the whole economy grew by 19% and the manufacturing sector grew by 11%.

Over the whole period from 1997 to 2018, the pharmaceutical industry's economic output has grown by 27%. The whole economy has grown by 51%, whilst the manufacturing sector is 2% higher.

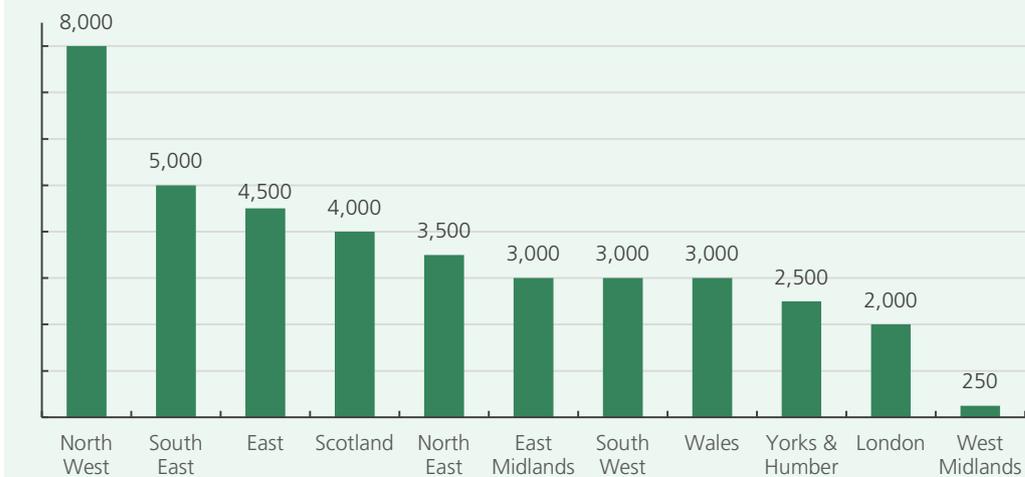
## 2.3 Employment

There were 39,000 people employed in the pharmaceuticals industry in Great Britain in 2018. Employment is not evenly distributed around the country. The following chart shows the number of people employed in the pharmaceuticals industry in each region and country of Great Britain. <sup>21</sup>

<sup>20</sup> The chart uses real terms GVA data from ONS, series KLA8, KL8V, KL5X

<sup>21</sup> Employment data are from the ONS, *Business register and employment survey*, 2018, via [NOMIS database](#). Data for Great Britain only.

### Employment in the pharmaceuticals industry by region, 2017



Source: ONS, Business register and employment survey, 2018, via NOMIS database

In the North West of England there are 8,000 people employed in the industry, 21% of pharmaceutical employment in Great Britain. The South East has the next highest number of people employed in the pharmaceutical industry – 5,000 or 13% of Great Britain.

## 2.4 Trade

There is considerable trade in pharmaceuticals – by value, medicine and pharmaceutical products account for 6.5% of goods exported from the UK and 4.7% of goods imported to the UK.<sup>22</sup>

### UK pharmaceutical trade as a % of all UK trade, 2018

	Exports	Imports
EU	6.3%	6.7%
Non-EU	6.6%	2.4%
<i>Total</i>	<i>6.5%</i>	<i>4.7%</i>

Source: HMRC, [UK Trade Info](#), SITC code 24

UK exports of pharmaceutical products were worth £23.5 billion in 2018, 46% of which went to EU countries.

UK imports of pharmaceutical products were worth £23.4 billion in 2017, 76% of which came from EU countries.

### UK pharmaceutical trade, 2018, £ billions

	Exports	Imports	Balance
EU	10.9	17.7	-6.9
Non-EU	12.7	5.7	7.0
<i>Total</i>	<i>23.5</i>	<i>23.4</i>	<i>0.1</i>

Source: HMRC, [UK Trade Info](#), SITC code 24

<sup>22</sup> HMRC data extracted from the [UK Trade Info database](#) on 15 August 2018. Standard International Trade Classification (SITC) code 54: medicinal and pharmaceutical products.

## 14 Brexit and medicines regulation

Almost a quarter (23%) of UK pharmaceutical exports were to the US in 2018, totalling £5.4 billion. Germany was the UK's next biggest export destination for pharmaceutical products, totalling £4.0 billion.

The UK's biggest pharmaceutical import partner was the Netherlands (20% of UK pharmaceutical imports, worth £4.7 billion). Imports to the UK from Germany were worth £3.4 billion, 14% of all UK pharmaceutical imports.

UK trade in pharmaceutical products: top 10 partners, 2018					
Exports			Imports		
	£ billions	% of total		£ billions	% of total
United States	5.4	23%	Netherlands	4.7	20%
Germany	3.0	13%	Germany	3.4	14%
Netherlands	1.6	7%	Switzerland	3.1	13%
Irish Republic	1.2	5%	Belgium	2.3	10%
France	1.1	5%	Irish Republic	2.1	9%
China	1.0	4%	United States	2.1	9%
Italy	1.0	4%	France	1.4	6%
Spain	0.9	4%	Italy	1.1	5%
Japan	0.8	3%	Denmark	0.5	2%
Belgium	0.7	3%	Spain	0.5	2%
<b>EU</b>	<b>10.9</b>	<b>46%</b>	<b>EU</b>	<b>17.7</b>	<b>76%</b>
<b>Non-EU</b>	<b>12.7</b>	<b>54%</b>	<b>Non-EU</b>	<b>5.7</b>	<b>24%</b>
<b>World</b>	<b>23.5</b>	<b>100%</b>	<b>World</b>	<b>23.4</b>	<b>100%</b>

Source: HMRC, [UK Trade Info](#), SITC code 24

## 3. Impacts of Brexit on medicines regulation and supply

We do not yet know what kind of relationship the UK will have with the EU on medicines after exit day as negotiations are ongoing. However, this section provides an overview of what options have been proposed and what has been discussed in negotiations between the UK Government and the EU on this issue.

### 3.1 What are the options for future regulation?

Future possible outcomes for regulation of medicines in the UK following Brexit could range from an ongoing close cooperation and alignment with the EMA to an entirely separate standalone regulatory system in the UK.

In 2017, the Chairman of the MHRA, Professor Sir Michael Rawlins set out that there were two broad options – one where the UK remains within the EU regulatory system and another where the MHRA becomes a sovereign regulator. He said that even as a sovereign regulator, the UK would need mutual recognition arrangements with the EU:

Even as a sovereign regulator we would still need to have some mutual recognition arrangements with the EU. For example, we would want to have mutual recognition arrangements over inspections. We contribute to the EU's inspectorate going around India, China, wherever, looking at manufacturing sites, but we cannot do it all on our own; we need to share out the burden. It has to be two-way traffic.<sup>23</sup>

#### **Box 4: What is a mutual recognition agreement?**

MRAs are bilateral agreements that are primarily used in trade negotiations to promote trade and facilitate market access in goods between the EU and third countries. They set out where regulators will accept the test results/licencing processes of another country and vice versa.

A potential MRA between the UK and the EMA could involve recognition of:

- Good Manufacturing Practice (GMP) - a code of standards for the manufacture, packaging and supply of a medicine;<sup>24</sup>
- Good Distribution Practice (GDP) - standards for the quality of the medicine to be maintained throughout the supply chain from manufacturer to wholesaler, to pharmacist to patient;<sup>25</sup>
- Medical devices – for the UK to continue its role in appointing notified bodies and participating in assessing medical devices.

<sup>23</sup> House of Lords Select Committee on Science and Technology, [Corrected oral evidence: Brexit: regulation and standards \(Question 4\)](#), 10 January 2017

<sup>24</sup> European Commission, [Good Manufacturing and Distribution Practices \[accessed 9 April 2019\]](#)

<sup>25</sup> *ibid*

There are a number of other countries where standalone regulatory bodies work with the EMA through mutual recognition agreements – these include Switzerland, Canada and the United States.<sup>26</sup>

There is no existing provision for third countries to become members or observers at the EMA, but under Article 77 of the EU Regulation establishing the agency, “representatives of international organisations” may participate as observers in the EMA.<sup>27</sup>

Another option that has been suggested is that the UK could also seek to align with, or use the medical assessments of another regulatory system, such as the US Food and Drug Administration.<sup>28,29</sup>

### 3.2 Legislation after Brexit

Section 3 of the [European Union \(Withdrawal\) Act 2018](#) intends to convert existing EU law that applies in the UK into domestic law.

Section 3 (1) states that it converts all EU law that is ‘operative’ prior to exit day. Section 3 (3) defines ‘operative’ as any provision which, if it is stated to come into force at a particular time and then apply from a later date, actually applies immediately before Brexit day.

EU legislation on medicines regulation is already operative and would therefore be converted into UK law. However, there has been some uncertainty about the new EU regulations on medical devices ([Regulation \(EU\) 2017/745](#) and [Regulation \(EU\) 2017/746](#)) which are due to come into force in 2020 and 2022.<sup>30</sup>

The general medical devices regulations will become operative during the proposed transition period (May 2020), and so will apply under the *EU (Withdrawal) Act* but the in vitro diagnostic medical devices regulations will come into force after 5 years (May 2022).

However, the MHRA has reported that its preparations to implement both medical devices regulations continue.<sup>31</sup> The Government have said that it intends to fully align the UK with the new EU regulations and in vitro diagnostic medical devices regulations. In response to a debate on the safety of medicines and medical devices, the Parliamentary Under-Secretary of State for Health, Baroness Blackwood of North Oxford, provided further information on this:

We will do this even though we are leaving the EU institutions because we are confident that doing so will drive system-wide improvement, including to the levels of clinical data that are mandated before products can be placed on the market, the scrutiny placed on notified bodies, the level of post-market

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<sup>26</sup> EMA, [Mutual recognition agreements \(MRA\)](#), [accessed 9 April 2019]

<sup>27</sup> [EC Regulation No. 726/2004](#)

<sup>28</sup> Health and Social Care Select Committee, [Brexit: medicines, medical devices and substances of human origin](#), HC 352, March 2018

<sup>29</sup> Nuffield Trust, [How will our future relationship with the EU shape the NHS?](#) November 2017

<sup>30</sup> Field Fisher, [It's all a question of timing: Medical Devices, In Vitro Diagnostic Devices, EU Regulations, and Brexit](#), 19 July 2017

<sup>31</sup> MHRA, [MHRA and making a success of Brexit](#), updated January 2019

surveillance conducted and the traceability of medical devices. We think this will improve the safety of medical devices.<sup>32</sup>

### 3.3 Negotiations on the future relationship with the EU

The UK Government has said that it would like to pursue a close relationship with the EMA and EU regulatory network on medicines and medical device regulation.

A Government policy paper on Collaboration on Science and Innovation, published in September 2017 stated that the UK would look to continue working closely with the EMA, and that existing agreements between the EMA and third countries such as Switzerland, USA and Canada provided a precedent which the UK could build on.<sup>33</sup>

In March 2018 the Prime Minister set out that the UK Government would like to remain an 'associate member' of a number of EU agencies after Brexit, including the European Medicines Agency.<sup>34</sup> She has said that this would mean "abiding by the rules of those agencies and making an appropriate financial contribution" and said the following about the benefits of an associate membership of these agencies:

First, associate membership of these agencies is the only way to meet our objective of ensuring that these products only need to undergo one series of approvals, in one country.

Second, these agencies have a critical role in setting and enforcing relevant rules. And if we were able to negotiate associate membership we would be able to ensure that we could continue to provide our technical expertise.

Third, associate membership could permit UK firms to resolve certain challenges related to the agencies through UK courts rather than the ECJ.

[...]

Fourth it would bring other benefits too. For example, membership of the European Medicines Agency would mean investment in new innovative medicines continuing in the UK, and it would mean these medicines getting to patients faster as firms prioritise larger markets when they start the lengthy process of seeking authorisations. But it would also be good for the EU because the UK regulator assesses more new medicines than any other member state. And the EU would continue to access the expertise of the UK's world-leading universities.<sup>35</sup>

However, March 2018 European Council guidelines set out that UK would be excluded from participation in EU Institutions, agencies or bodies, while under Article 11 it may be able to participate in certain EU

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<sup>32</sup> [HL Deb 28 February 2019 c357](#)

<sup>33</sup> Department for Exiting the European Union, [Collaboration on science and innovation: a future partnership paper](#), 6 September 2017

<sup>34</sup> Prime Minister's Office, [PM speech on our future economic partnership with the European Union](#), 2 March 2018

<sup>35</sup> Prime Minister's Office, [PM speech on our future economic partnership with the European Union](#), 2 March 2018

programmes on a conditional basis.<sup>36</sup> There is no existing provision for third countries to become members or observers at the EMA.

### **Government White Paper on the future relationship between the UK and the EU (July 2018)**

The Government Statement on the future EU-UK relationship provided further information about the UK's proposals on medicines following Brexit.

This set out the UK Government's proposal for a common rulebook with regards to manufactured goods, such as medicines, to allow frictionless trade at the border. The paper states that to achieve this, the common rules would apply to all compliance activity required for goods to be sold and supplied across the EU and UK. With specific regards to medicines, it stated that this would include those specific provisions for these products, including "the release of individual batches by a qualified person based in the UK or EU, and the role of the qualified person for pharmacovigilance, responsible for ongoing safety monitoring of potential side effects."<sup>37</sup>

The paper went on to set out that in some areas a greater than usual regulatory control is applied, such as with medicines and chemicals. It set out that the UK was seeking participation in the EMA and other agencies and acknowledged that it would not have voting rights.

The paper states that the UK would seek a future relationship with the EMA that would ensure routes to market for medicines stayed available and meant that the UK could continue to conduct technical work on behalf of the agency, act as a 'leading authority on medicines assessments and participate in ongoing medicines safety monitoring.'<sup>38</sup>

A few days after the publication of the White Paper, at Commons Report Stage of the *Trade Bill 2017-19*, Dr Phillip Lee tabled [New Clause 17](#). This amendment had cross party support and aimed to ensure that continued participation with the EMA was an objective of the UK Government negotiations with the EU. The amendment went to a division and was agreed.<sup>39</sup>

The government have confirmed they have accepted this amendment, and that it reflects the Government policy as set out in the July 2018 White Paper.

### **Withdrawal Agreement November 2018**

The EU UK Withdrawal Agreement was negotiated between the EU and UK and finalised on 14 November 2018. However, the House of Commons declined to approve the deal on 15 January 2019 and 12 March.

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<sup>36</sup> European Council, [European Council \(Art. 50\) guidelines on the framework for the future EU-UK relationship](#), 23 March 2018

<sup>37</sup> HM Government, [The Future Relationship Between the United Kingdom and the European Union, July 2018](#)

<sup>38</sup> Ibid

<sup>39</sup> [HC Deb 17 July 2018, c336](#)

In general, the Withdrawal Agreement would mean that goods can continue to circulate between the UK and EU during the transition period which means authorised medicines and medical products would be able to move freely until the end of the transition.

The Agreement makes several relevant provisions in relation to medicines which relate to the management of them in the future:

- The UK has to transfer documentation relating to ongoing assessments of new medical (and other) products led by UK authorities under EU regulations (article 44);
- The UK must make available the marketing authorisation dossier of a medicinal product previously authorised by the UK (when requested by the end of the transition period for an application made to a Member State or the European Medicines Agency (article 45);
- EU Member States must make available to the UK the marketing authorisation dossier of a medicinal product previously authorised by that body (when requested by the end of the transition period for an application made in the UK) (article 45);
- Exchanges of information for conformity assessments, which would apply to medical devices, are covered by article 46.

The Government explainer set out that these articles “require the UK authorities to transfer files or documents related to certain ongoing product assessments to an EU Member State Authority. This applies to assessments of medicines and chemicals being carried out by the Medicines and Healthcare products Regulatory Agency (MHRA) [and others]”.<sup>40</sup> It also states that it:

...provides for the transfer of information related to testing between relevant testing bodies in the UK and the EU. For example, if a manufacturer chooses to apply for a new certificate in the EU when they already have a certificate in the UK, the title provides for the transfer of information related to tests carried out before the end of the implementation period by the UK testing body to the EU testing body.

The Withdrawal Agreement makes specific provision (**clause 128 (6)**) that the UK shall not act as leading authority on behalf of the EU for risk assessments, examinations, approvals or authorisations in relation to a number of areas, including the regulation of medicines from exit day.

The Withdrawal Agreement was welcomed by the Association of the British Pharmaceutical Industry who said it would allow for the continued supply of medicines during the transition period ‘without delay or disruption’.<sup>41</sup>

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<sup>40</sup> HM Government, [Explainer for the agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union](#), 14 November 2018

<sup>41</sup> ABPI, [“Pharmaceutical industry responds to Brexit ‘draft agreement’”](#), 15 November 2018

[Detailed technical information](#) on what the withdrawal agreement means for pharmaceutical companies in the transition period is provided by the MHRA.

### Political Declaration

More generally, on the subject of goods, the Draft Political Declaration (on the future framework) sets out that the parties will “*put in place provisions to promote regulatory approaches that are transparent, efficient, promote avoidance of unnecessary barriers to trade in goods and are compatible to the extent possible.*” It goes on to state that the Parties will also “explore the possibility of cooperation” with EU agencies such as the European Medicines Agency.

In December 2018, the Minister of State for the Department for Exiting the European Union, Lord Callanan reiterated the aims set out in the political declaration and said that the exact arrangements for future UK participation were subject to future negotiations.<sup>42</sup>

## 3.4 Views on regulating medicines outside of the EU

Industry bodies and commentators have raised a number of potential impacts of the UK moving away from the EMA/EU led system.<sup>43</sup> There has been support from across health organisations and other stakeholders for the UK to secure close regulatory alignment with the EU after Brexit. This section provides a number of these views but is not comprehensive, further resources are provided in section 5.

In its March 2018 report, [Brexit: medicines, medical devices and substances of human origin](#), the Health and Social Care Select Committee called on the Government to secure the closest possible regulatory alignment with the EU on medicines and medical devices regulation:

The overriding message from almost all of the evidence received in this inquiry is that the UK should continue to align with the EU regulatory regimes for medicines, medical devices and substances of human origin both during any transition period and afterwards. Evidence submitted from large pharmaceutical companies, SMEs, academics, healthcare and workforce charities was all almost unanimous in the view that regulatory alignment with the EU would be the best post-Brexit option for the NHS, for patients, and for the UK life sciences industry.

The UK must look to secure, as a priority in the next round of negotiations, the closest possible regulatory alignment with the EU. The continued supply of safe and effective medical devices, medicines and substances of human origin currently on the UK market will depend on continued alignment with European regulations.<sup>44</sup>

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<sup>43</sup> See for example: [Brexit Health Alliance, Brexit and the impact on patient access to medicines and medical technologies, January 2018](#), and [ABPI, Brexit](#)

<sup>44</sup> Health and Social Care Select Committee, [Brexit: medicines, medical devices and substances of human origin](#), HC 352, March 2018

It advised that if full regulatory alignment with the EU was not achieved, the UK should look to establish alignment with another market such as the Food and Drug Administration in the US. The Committee stated that whilst this “would raise significant financial and patient safety issues, it remains preferable to the UK endeavouring to create a standalone regulatory system after leaving the EU.”<sup>45</sup>

Pharmaceutical and medical devices industry bodies have said that close cooperation with the EU would ensure patients can access safe and effective medicines. In a response to an MHRA consultation on no deal legislation, the Association for the British Pharmaceutical Industry (ABPI) and the Bioindustry Association (BIA) stated that:

The ABPI and BIA position is and remains that close cooperation with the EU in the regulation of medicines, including mutual recognition of regulatory activities and quality testing, is essential in ensuring that patients in the EU and the UK can continue to access safe and effective medicines.

The ABPI and BIA believe that a no-deal Brexit would significantly damage public health and the UK life sciences sector and that this must be avoided at all costs. We continue to advocate this position.

The Brexit Health Alliance (a coalition of industry, healthcare providers, patients and public health organisations) has called for post Brexit alignment with the EU’s regulation on medicines and medical devices in order to guarantee patient safety and public health. It warned that delays in accessing new medicines may occur in the UK if regulatory alignment does not continue between the UK and the EU:

There could also be additional delays for UK patients in accessing new medicines, as the experience of Switzerland, which is not a member of the EMA, shows. Despite having a number of bilateral trade agreements with the EU, it is estimated that Switzerland gains access to new medicines on average 157 days later than the EU. In Australia and Canada new medicines come to market on average 6–12 months later than in the EU or USA. The EMA currently represents 25 per cent of the global pharmaceutical sales market, compared to the UK’s 3 per cent share.<sup>46</sup>

Professor Sir Michael Rawlins, Chairman of the MHRA, has expressed a concern that the UK could be at the “back of the queue” when it comes to access to new medicines after Brexit.<sup>47</sup> In response to questions from the Lord’s Science and Technology Select Committee in January 2017, he said that there may be ways in which the UK could try and ensure they were not at the back of the queue for new medicines. These could include making the drug licencing process quicker and undertaking it in parallel with the assessment by the National Institute

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<sup>45</sup> Health and Social Care Select Committee, [Brexit: medicines, medical devices and substances of human origin](#), HC 352, March 2018

<sup>46</sup> [Brexit Health Alliance, Brexit and the impact on patient access to medicines and medical technologies, January 2018](#)

<sup>47</sup> House of Lords Select Committee on Science and Technology, [Corrected oral evidence: Brexit: regulation and standards](#), 10 January 2017

for Health and Care Excellence which could speed up patient access to medicines.<sup>48</sup>

Other issues that have been raised with regards to future regulatory approaches in the UK, include:

- the impact on pharmacovigilance in the UK and whether continued membership of the EU [Pharmacovigilance Risk Assessment Committee](#) and access to the Eudravigilance database will be possible. It has been reported that this could lead to delays in the detection and management for pharmacovigilance in the UK and the EU27/EEA;<sup>49</sup>
- The potential loss of the UK's role in the ICH. This would require the UK to apply to be an observer at the ICH, and then apply to be a member two years later.<sup>50</sup> The Government have said this issue is subject to future negotiations;<sup>51</sup>
- The potential impact on the assessment and licencing of orphan medicines (medicines for rare diseases) which could lead to delays in accessing these medicines.<sup>52</sup>

There are a number of wide-ranging potential impacts on how medicines are regulated and supplied in the UK after Brexit. This paper does not provide detail on all of these but links to further reports and comment are provided in section 5.

### 3.5 The regulator's preparations for Brexit

#### EMA

The EMA has said it working on the scenario that the UK will become a third country on 30 March 2019.

The European Commission and the EMA have published a Notice to all licence holders of medicines with a centrally authorised medicines marketing authorisation. This stated that, in view of uncertainties in relation to a possible withdrawal agreement, marketing authorisation holders need to take action to ensure they could continue to supply medicine in the event of the UK becoming a third country.<sup>53</sup>

A Q&A document provides guidance on these actions. It advises that the marketing authorisation holder would need to be located within the

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<sup>48</sup> House of Lords Select Committee on Science and Technology, [Corrected oral evidence: Brexit: regulation and standards](#), 10 January 2017

<sup>49</sup> Brexit Health Alliance, [Protecting the public's health across Europe after Brexit](#), June 2018

<sup>50</sup> Mark Flear, [Brexit and Pharmaceuticals' Regulation: Optimising the UK's post-Brexit influence in global standards-setting](#), October 2017

<sup>51</sup> Health and Social Care Select Committee, [Brexit: medicines, medical devices and substances of human origin](#), HC 352, March 2018

<sup>52</sup> ABPI, [ABPI and BIA input to MHRA consultation on EU Exit 'no deal' contingency legislation for the regulation of medicines and medical devices](#), 1 November 2018

<sup>53</sup> EMA and European Commission, [Notice to marketing authorisation holders of centrally authorised medicinal products for human and veterinary use](#), 29 January 2019

EEA; and that from the date of withdrawal, products coming from the UK into EU Member States would be considered as imported products.<sup>54</sup>

In April 2018, the EMA also completed the redistribution of work on over 370 centrally authorised products from the UK to other EU27 countries.<sup>55</sup>

More information on the future plans for the EMA in relation to the UK are provided on its [United Kingdom's withdrawal from the European Union webpage](#).<sup>56</sup>

The EMA provide information in [a March 2019 FAQ document about EU actions to prevent medicine shortages due to Brexit](#).

## MHRA

The MHRA [responded to the referendum](#) result in June 2016 (updated in January 2019). It stated that playing a full and active role in European regulatory arrangements remained a priority for the regulator. It has highlighted areas such as medicines and medical device regulation, where it currently plays a significant contributory role.<sup>57</sup>

The MHRA has provided [technical information](#) on what the implementation period means for the life sciences sector.

The MHRA has also been making preparations for a no deal Brexit scenario. More information on these is provided in Section 4 of this paper.

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<sup>54</sup> EMA and European Commission, [Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the Centralised Procedure](#), 1 February 2019

<sup>55</sup> EMA, [United Kingdom's withdrawal from the European Union](#)

<sup>56</sup> EMA, [United Kingdom's withdrawal from the European Union](#)

<sup>57</sup> MHRA, [News story: MHRA and making a success of Brexit](#), August 2016

## 4. No-deal Brexit

In the event of a no-deal Brexit, and without other arrangements in place, the UK could not continue to participate in the shared regulatory framework with the EMA. This could have wide-ranging impacts on the future regulation of medicines in the UK, and more immediately, the maintenance of medicines and medical device supply between the UK and the EU.

The Government have undertaken actions to address potential impacts relating to the supply of medicines and to ensure medicines will continue to be licenced and available in the UK. A February 2019 Ministerial statement from the Minister of State at the Department of Health and Social Care set out some of the actions that had been taken, including:

- Securing additional roll on, roll off freight capacity away from Dover and Folkstone;
- Purchasing extra warehouse space for storage;
- Booking space on aeroplanes for the transport of products with short shelf lives;
- Working with pharmaceutical companies to ensure the increase in buffer stocks of 7000 prescription only or pharmacy medicines<sup>58</sup>; and
- Making changes to regulatory requirements to allow medicines and medical products to continue to be sold in the UK in event of no deal.

This section provides an overview on both immediate and long term concerns related to a no deal Brexit scenario and action that has been taken to address these.

### 4.1 Impacts of a no-deal Brexit

In the event of a no-deal Brexit where the UK is no longer part of the EU regulatory network, the Government has confirmed that the MHRA would take on responsibility for functions currently undertaken by the EMA and that this would require changes to the [Human Medicines Regulations 2012](#).<sup>59</sup> Legislation to do this has already completed its Parliament stages (see below).

For those medicines that are to be licensed and supplied in the EU, the EMA has set out that, in the event of a no-deal Brexit, there will be requirements for marketing authorisation holders and batch testing of medicines to be based in the EU from 30 March 2018.<sup>60</sup> New medicines in the UK would need to be licensed separately. Concerns have been

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<sup>58</sup> Medicines that can only be sold in pharmacies

<sup>59</sup> Department of Health and Social Care, [Guidance: How medicines, medical devices and clinical trials would be regulated if there's no Brexit deal](#), 23 August 2018

<sup>60</sup> EMA, [Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the Centralised Procedure](#), 1 February 2019

expressed that this could mean delays in applications for licences because the UK would represent a much smaller market, and that this could impact on how quickly medicines would be available.<sup>61,62</sup> A no deal Brexit would also impact on the way medicines safety is monitored in the UK in the future.

More immediate concerns relate to the maintenance of supply of medicines in the event of no deal. Currently supply chains for medicines are integrated across the EU, and often involve complicated movement between countries during the medicines production process.<sup>63</sup> Medicines can currently easily cross borders between the UK and other EU countries.

There are concerns about an increase in non-tariff barriers in the event of no deal, and the potential delays this could mean for medicines supply, especially for those products with a short shelf life, such as medical radioisotopes.<sup>64</sup> In evidence to the Health and Social Care Committee, Mark Dayan from the Nuffield Trust provided further information about the potential delays at the border:

At the border, which for me is a huge issue in and of itself, a no-deal Brexit means a huge leap in the amount of red tape that companies have to go through to bring things into the UK. Some of it is being waived, but not all of it, and not all of it is within the power of the UK Government to waive. That raises two problems.

First, there is the direct delaying effect of additional requirements, declarations, and so on; there is the effect they have on the way companies run things when they are used to being able to get goods through on a lorry that rolls on and off a ferry. Secondly, there is a risk that the people who sign things off and implement the additional checks and regulations—in the UK's case, HMRC and the Border Force—will simply buckle under the strain of the huge leap upward in the amount of work they have to do. That is where I come from on the border side.<sup>65</sup>

The Government have acknowledged that a no deal Brexit could lead to delays at the borders on the usual routes for medicines import and export and have taken a number of actions to address these. In a letter to pharmaceutical companies in December 2018, the Secretary of State for Health and Social Care, Matt Hancock, said that whilst the Government had made plans to control arrangements at the UK border to ensure the flow of goods, the European Commission had made clear that in the event of no deal, it will impose third country controls on goods entering the EU from the UK. He advised that in the worst-case scenario, the cross government planning assumptions showed that there could “be significantly reduced access across the short straits, for

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<sup>61</sup> House of Lords Select Committee on Science and Technology, [Corrected oral evidence: Brexit: regulation and standards](#), January 2017 (Q7)

<sup>62</sup> BMA, [Brexit Briefing: Medicines and medical devices regulation](#), October 2017

<sup>63</sup> Health and Social Care Select Committee, [Brexit: medicines, medical devices and substances of human origin](#), HC 352, March 2018

<sup>64</sup> Dayan M, [Over the edge: a no deal Brexit and the NHS](#), Nuffield Trust comment, August 2018

<sup>65</sup> Health and Social Care Committee, [Impact of the Brexit withdrawal agreement on health and social care: Oral evidence](#), 27 November 2018 (Q7)

up to six months.”<sup>66</sup> More information about Government preparations to ensure continued medicines supply is provided in the following section.

#### Box 4: Medical radioisotopes

Radioisotopes are used in the diagnosis and treatment of a range of conditions<sup>67</sup> and are imported to the UK from (mainly EU) research reactors.<sup>68</sup> Although radioisotopes can be sourced from beyond the EU, the materials often have short half-lives, meaning they can decay rapidly and cannot be stored for very long. In the UK around 700,000 nuclear medicine procedures using radioisotopes are carried out each year.<sup>69</sup>

Concerns have been raised that Brexit could affect the supply of radioisotopes<sup>70</sup> by causing import delays<sup>71</sup> and causing the UK to leave the Euratom Observatory which manages supply chains in times of shortages.<sup>72</sup> A no-deal Brexit could mean that any potential customs agreement and cooperation with the Observatory which might be sought as part of a deal would not be realised.

On 6 March 2019, the Royal College of Radiologists reiterated concerns about immediate shortages of medical radioisotopes in the event of a no deal Brexit in guidance to nuclear medicines teams.<sup>73</sup>

The Government has said that they have been working closely with industry to ensure the continued supply of medical radioisotopes in the event of a no deal Brexit:

[...] The Government has been working closely with industry to ensure the supply of medicines, including medical radioisotopes to diagnose and treat breast cancer, can continue uninterrupted in the event of a ‘no deal’ EU exit.

For any products that require air freight, such as medical radioisotopes, we are continuing to work with all suppliers to ensure this occurs. The Department can confirm that companies supplying the vast majority of medical radioisotopes medicines by volume have air freight routes that are currently operational.

The Department wrote to all suppliers of medicines to the United Kingdom on 26 March to advise them of the changes to EU exit dates, and ask them to continue with preparations to protect patients in all possible outcomes.

We are confident that, if everyone does what they need to do, the supply of medicines and medical products will be uninterrupted.<sup>74</sup>

For further information on the impact of Brexit on the supply and regulation of nuclear material see the library briefing paper, [Euratom](#).

A February 2019 Lancet article, [How will Brexit affect health services in the UK? An updated evaluation](#), provided an analysis of different Brexit outcomes and their impacts on health services. On the impacts of a no deal scenario, it reported that:

Under a No-Deal Brexit, the absence of a legal framework for imports and exports is expected to have an immediate and drastic effect on supply chains. The UK Government has sought to reassure patients that its contingency plans with the pharmaceutical industry are robust, but shortages are likely because stockpiling arrangements cannot cope for more than a

<sup>66</sup> Letter from the Secretary of State for Health, [Medicines supply contingency plans for a no-deal Brexit scenario](#), December 2018

<sup>67</sup> European Commission, [Supply of medical radioisotopes](#), Accessed 13 August 2018

<sup>68</sup> World Nuclear News, [Radioisotopes in Medicine](#), May 2017

<sup>69</sup> [Supply of Medical Radioisotopes](#), POSTnote 558, July 2017

<sup>70</sup> Dr Nicola Strickland, [‘RCR statement on the potential impact of leaving the Euratom treaty’](#), Royal College of Radiologists, 10 July 2017

<sup>71</sup> Lords Select Committee on the EU, Home Affairs Sub-Committee, [Brexatom: the health implications of leaving Euratom. Oral Evidence](#), 22 November 2017, Q3

<sup>72</sup> Ibid Q4

<sup>73</sup> RCR, [No-deal Brexit guidance for nuclear medicine teams](#), 5 March 2019

<sup>74</sup> [HC Written question 236430 \[Radioisotopes\]](#) 28 March 2019

few weeks. The Government is proposing that general practitioners prescribe “best alternative medication”, which can be distressing and confusing for some patients. Some products, such as radioisotopes, cannot be stockpiled. The UK would immediately be treated as a third country for licensing and manufacture purposes. Some firms might not have transferred licences to EEA-based entities in time.

In February 2019, doctors and representatives of health organisations and charities wrote to the Prime Minister to ask her to rule out a no deal Brexit. They said that a “no deal Brexit poses grave risks to public health and patient safety and would require extraordinary measures in mitigation.” The letter also stated that “the Government’s contingency plans are unlikely to cover all eventualities and work for all patients, carers and citizens.”<sup>75,76</sup>

## 4.2 Government preparations

In July 2018, the Secretary of State for Health and Social Care Matt Hancock said the Department was preparing for range of outcomes, including a no deal scenario.<sup>77</sup> He said that:

We are focusing on the importance of a continuous supply of medicines that have a short shelf life; some of the medicines that would be most difficult to provide in a no-deal scenario where there was difficult access through ports would need to be flown in, for instance. I hope that, even under a no-deal scenario, there will still be smooth movement in through ports, because it is not our intention to provide barriers to that, and the work will take that into account. But you can imagine that it is incredibly important for me, as Secretary of State, to ensure that people will have access to the medicines they need.<sup>78</sup>

He reported that the Department was working with industry on the stockpiling of medicines and that he was “confident that with the right amount of work we can mitigate the worst of the circumstances”.

### Technical notices

In August 2018, the Government published ‘technical notices’ relating to medicines regulation in the event of no deal:

- [How medicines, medical devices and clinical trials would be regulated if there’s no Brexit deal \[now withdrawn\]](#)
- [Batch testing medicines if there's no Brexit deal](#)
- [Submitting regulatory information on medical products if there’s no Brexit deal](#)

The technical notice, How medicines, medical devices and clinical trials would be regulated if there’s no Brexit deal, has now been replaced by an MHRA guidance document (last updated in February 2019):

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<sup>75</sup> [Letter to Prime Minister, No deal Brexit and health](#), 22 February 2019

<sup>76</sup> Jenny Cook, [Top UK GPs urge government to rule out no-deal Brexit](#), GPonline, 25 February 2019

<sup>77</sup> Health and Social Care Committee, [Oral evidence: Work of the Secretary of State, HC 523](#) (Q209), 24 July 2018

<sup>78</sup> *Ibid*, Q308

- [Further guidance note on the regulation of medicines, medical devices and clinical trials if there's no Brexit deal](#)

The technical notices stated that in the event of no deal:

- existing EU law on medicines would be converted into UK law under the [EU Withdrawal Act 2018](#);
- the UK will recognise medical devices that are CE marked and approved for the EU market and will comply with new EU medical devices regulations due to come into force in 2020 and 2022;
- current marketing authorisations granted through the centrally authorised product route will be converted to UK marketing authorisations, but after 29 March 2019, all new applications for a marketing authorisation in the UK would have to be made to the MHRA;
- batch testing of imported medicines from the EEA and named third countries will continue to be recognised in the UK;
- marketing authorisation holders and those responsible for pharmacovigilance (Qualified Persons) should be established in the UK by the end of 2020; and
- new systems for the submission and processing of regulatory information are being developed for March 2019.

The Government said that the MHRA would:

...take a streamlined approach to approving UKMA applications that places no greater burden on industry and ensures that patients can access new and innovative medicines at the same time as EU patients.<sup>79</sup>

## Stockpiling and other preparations

On 23 August 2018, alongside the publication of the technical notices, Mr Hancock wrote to hospitals, GPs, pharmacies and pharmaceutical companies, setting out what action would need to be taken to ensure medicines supply to patients continues in the event of a no-deal Brexit. The letter requested that pharmaceutical companies ensure that by 29 March 2019 they have an additional six weeks' supply of medicines on top of the normal buffer stock held and that for products with short shelf lives, suppliers should make plans to air freight these to avoid border delays.<sup>80</sup>

The letter also informed pharmacists and hospitals that they should not stockpile medicines and asks clinicians to advise patients about Government plans to maintain medicines supply - and that they too should not stockpile medicines.<sup>81</sup>

As set out above, in December 2018, Matt Hancock wrote again to medicines suppliers to update on progress.<sup>82</sup> He said that the Government had been working to design customs controls at the

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<sup>79</sup> DHSC, [Guidance: How medicines, medical devices and clinical trials would be regulated if there's no Brexit deal](#), 23 August 2018

<sup>80</sup> DHSC, [Letter from Secretary of State for Health and Social Care to pharmaceutical companies](#), 23 August 2018

<sup>81</sup> DHSC, [Letter to the health and care sector: preparations for a potential no-deal Brexit](#), 23 August 2018

<sup>82</sup> DHSC, [Letter: Medicines supply contingency plans for a no-deal Brexit scenario](#), 7 December 2018

borders to ensure that goods can continue to flow into the UK and not be delayed by additional controls and checks. However, planning assumptions had now been revised to show that access across the short strait crossings could now be reduced for six months. This meant that additional measures would need to be introduced by pharmaceutical companies on top of stockpiling.

The DHSC's [Medicines Supply Contingency Planning Programme](#) requires medicines' manufacturers and suppliers to provide information to the Department on their contingency plans for medicines imported from the EU.

### **EU Exit Operational Readiness guidance**

The Department of Health and Social Care (DHSC) published its [EU Exit Operational Readiness Guidance](#) in December 2018. This set out a range of actions that were being taken by the Department to prepare for a no deal scenario and set out what action was required by commissioners, healthcare providers and pharmaceutical companies. It included the following:

- Ongoing work to ensure sufficient roll on, roll off freight capacity to enable medicines and medical products to move freely to the UK, and that these products would be prioritised on alternative routes to ensure unimpeded movement into the UK;
- In the the event of delays, contingency planning was continuing with pharmaceutical companies and other government departments;
- DHSC and NHS England and NHS Improvement were working on measures to enable the local and regional monitoring of stock levels of medicines;
- DHSC would introduce a "Serious Shortage Protocol" through changes in medicines legislation to address potential medicines shortages (see below); and
- Public Health England was leading a UK wide programme to ensure the supply of centrally procured products such as vaccines.<sup>83</sup>

The guidance also reiterated that there was no need for stockpiling by hospitals, pharmacists or patients.

### **Ministerial Statement**

In a February 2019 Ministerial statement, the Department said that there were 7000 prescription only and pharmacy medicines<sup>84</sup> where the Department had been working with suppliers to ensure extra stock was being held, and in some cases, new routes were being secured. He said that the 'vast majority' of companies had confirmed stockpiling plans were in place.<sup>85</sup>

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<sup>83</sup> DHSC, [EU Exit Operational Readiness Guidance](#), December 2018

<sup>84</sup> Medicines that can only be sold in pharmacies.

<sup>85</sup> [HC Written Statement HCWS1358](#)

Mr Hammond also reported that additional roll on, roll off freight capacity had been secured, and medicines and medical products would be prioritised on these routes:

Securing, via the Department of Transport (DfT), additional roll on, roll off freight capacity (away from the short straits) from 29 March.

- Contracts have been signed by DfT with two ferry companies for the next six months. These routes are away from the Dover Straits where most goods flow from the EU and will run from the following routes: Cherbourg – Poole, Le Havre – Portsmouth, Roscoff – Plymouth, Caen – Portsmouth, Vlaardingen – Immingham, Cuxhaven – Immingham and Vlaardingen – Felixstowe. The Government has purchased the tickets from the shipping freight operators, and these will be sold on at market rate.

- There is cross Government agreement that all medicines and medical products will be prioritised on these alternative routes to ensure the flow of all these products may continue unimpeded.

- Companies which supply medicines or medical goods will be offered the option of buying tickets on these routes and my Department is currently engaging with industry to ascertain the likely uptake levels.

- We have worked with the pharmaceutical industry to ensure that planes are contracted to bring in medical radioisotopes under the appropriate specialist conditions.<sup>86</sup>

The Government has also invested in additional warehouse space for the stockpiling of medicines, at an estimated cost “in the low tens of millions of pounds.” This warehouse space is due to be in place by February 2019.<sup>87</sup>

## A proposed accelerated licencing route for medicines

In the event of a no deal Brexit, the MHRA has proposed offering a new accelerated assessment process for products containing active new substances and for biosimilars.<sup>88</sup>

The new application review for those products that have already been approved by the EMA would be completed within 67 days (compared with the current 210-day assessment process). For a full assessment process, the timeline would be 150 days.

The MHRA has also committed to work with industry to “identify options to reduce the current national licensing timetable from 210-days to 180 days.” It will also review whether these accelerated processes could be extended to generic medicines.

These new processes have been welcomed by pharmaceutical industry bodies.<sup>89</sup>

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<sup>86</sup> [HC Written Statement HCWS1358](#)

<sup>87</sup> [Written Question: 203449 \[Drugs\]](#), 7 January 2019

<sup>88</sup> MHRA, [Guidance note on new assessment routes in a no deal scenario](#), March 2019

<sup>89</sup> ABPI & BIA, [ABPI-BIA submission to MHRA consultation on EU Exit no-deal contingency legislation for the regulation of medicines and medical devices](#), 1 November 2018

## Orphan medicines

Orphan medicines are medicines produced to treat rare diseases. These are regulated by the European Medicines Agency. The EMA can give a medicine an 'orphan designation' which means that the company producing it will have access to assistance and incentives from the EU agency.<sup>90</sup>

Orphan medicines are granted a marketing authorisation through the EMA centralised procedure which means that the product benefits from a 10-year period of marketing exclusivity from competition from similar products. More information is provided on the EMA website, [Orphan designation: Overview](#)

The MHRA have said that, in the event of a no deal Brexit, there will be a UK system for orphan medicines. This means that orphan status for medicines will be assessed when an application for a marketing authorisation is made (based on current EU criteria with some UK specifics) and when a medicine is granted orphan status the following will apply:

[...] the initial MA application fee will be refunded at 100% for SMEs and 10% for all other manufacturers. For these medicines SMEs will also receive a fee waiver for variations in the first year after the MA is granted.

The 10 years market exclusivity from competition from similar products in the approved orphan indication would be retained. If criteria for orphan status are met, this incentive would be awarded following grant of a UK orphan MA (see section below on Data and market exclusivity for MAs).<sup>91</sup>

### Box 5: The Falsified Medicines Directive

The EU Falsified Medicines Directive (2011/62/EU) (FMD) introduced new measures to ensure the safe trading of medicines in the EU. It was adopted in 2011 and the final part of the Directive, delegated regulations relating to safety features came into force in February 2019. This requires two safety features to be used on medical products:

- A unique identifier which can be scanned at different points on the supply chain; and
- An anti-tamper device.<sup>92</sup>

Manufacturers upload this information onto a central EU data hub which is part of an end to end medicines verification system. Wholesalers may then scan the codes on the products during the supply chain, and hospitals or pharmacies can scan this information again when the products are delivered to verify authenticity and then the codes are checked out before being dispensed.<sup>93</sup>

The Government have said that in the event of a no deal Brexit, the UK would not have access to this central EU data hub and therefore UK based organisations would not be able to scan products to verify authenticity. The Government have said the legal obligation regarding safety features would be removed in the UK. It has said that:

<sup>90</sup> [EMA, Orphan designation: Overview](#) [accessed 3 April 2019]

<sup>91</sup> MHRA, [Further guidance note on the regulation of medicines, medical devices and clinical trials if there's no Brexit deal](#), 26 February 2019

<sup>92</sup> [MHRA, Guidance: Implementing the Falsified Medicines Directive: Safety Features](#), 27 March 2019

<sup>93</sup> [EMA, Falsified medicines: overview](#)

In the interests of public safety, we will evaluate the options around a future national falsified medicines framework, which would inform the detail of any short or longer-term modifications.<sup>94</sup>

### 4.3 Medical devices

The Government has said that the UK will recognise medical devices approved for the EU market and CE-marked. Should this change in future the Government has said that adequate time will be provided for businesses to implement any changed new requirements.<sup>95</sup>

The UK will comply with all key elements of the Medical Devices Regulation (MDR) and the in vitro diagnostic Regulations (IVDR), which will apply in the EU from May 2020 and 2022 respectively.

However, formal UK presence at EU committees in respect of devices will cease.<sup>96</sup>

#### CE markings

For a time-limited period, the UK would continue to recognise the CE Mark on medical devices, which demonstrates their conformity with EU regulatory requirements. During this period, devices would be accepted on the UK market if they meet all EU requirements, which for all but the lowest-risk devices would include certification by EU Notified Bodies.

The Government has said that further detail on the future process after this temporary situation of bringing a medical device onto the UK market will be subject to consultation in due course.

#### Notified Bodies

UK-based Notified Bodies would, in a 'no-deal' scenario, no longer be able to assess the conformity of medical devices for devices to receive the CE mark and enter the EU market. Therefore, the MHRA would no longer be able to oversee Notified Bodies in the way that it does now.<sup>97</sup>

#### Post market surveillance of devices

In the event of a no deal Brexit, the MHRA continue to perform national post-market surveillance of medical devices on the UK market. It would no longer be able to be involved in the assessment of medical device safety through the EU regulatory network.

### 4.4 No deal Brexit legislation

Two pieces of affirmative procedure draft legislation have now been passed in Parliament which aim to enable the continued regulation of medicines and medical devices in the event of a no deal Brexit:

- [\*The Human Medicines \(Amendment etc\) \(EU Exit\) Regulations 2019\*](#) (completed all Parliamentary stages by 11 March 2019)

<sup>94</sup> MHRA, [A Consultation on implementing 'safety features' under the Falsified Medicines Directive –Government response](#), December 2018

<sup>95</sup> MHRA, [Regulating medical devices in the event of a no deal scenario](#), March 2019

<sup>96</sup> MHRA, [Further guidance note on the regulation of medicines, medical devices and clinical trials if there's no Brexit deal](#), 26 February 2019

<sup>97</sup> MHRA, [Further guidance note on the regulation of medicines, medical devices and clinical trials if there's no Brexit deal](#), 26 February 2019

includes provisions to enable the MHRA to act as a standalone regulator in the event of a no deal Brexit.<sup>98</sup> More information on the Parliamentary consideration of the regulations is provided on the Parliament [SI website](#).

- [The Medical Devices \(amendment\) \(EU exit\) Regulations 2019](#) (Completed all parliamentary stages on 11 March 2019) amends UK legislation that implements EU legislation on medical devices and confirms that the UK will implement a system that mirrors (as much as possible) the new EU regulations on medical devices that will apply from 2020 and 2022. More information on the Parliamentary consideration of the regulations is provided on the Parliament [SI website](#).

## Serious Shortage Protocol

Another piece of Secondary Legislation, the [Human Medicines \(Amendment\) Regulations 2019](#) introduced the “Serious Shortage Protocol” measures highlighted in the EU Exit Operational Readiness Guidance. These makes provision for Ministers to issue a “Serious Shortage Protocol” in the event of a shortage of a prescription-only medicine.<sup>99</sup> This would allow pharmacies to dispense against a protocol instead of a prescription without going back to the prescriber first. This may allow a pharmacist to dispense a different quantity or strength of medicine or a generic or therapeutic equivalent.<sup>100</sup>

The Government have said the protocols would not be suitable for all medicines, and that robust safeguards would be put in place to ensure this is used safely. This is a negative Statutory Instrument, as such it did not require active approval in Parliament and came into force on 9 February 2019.<sup>101</sup>

However, some medical organisations have expressed concerns about the potential impacts of the use of serious shortage protocols on patient safety and have called for further consultation on the plans.<sup>102,103</sup> The Opposition leader, Jeremy Corbyn, tabled a motion to annul the negative Statutory Instrument. This was debated on the 18 March where the motion to annul was not passed.<sup>104</sup>

On 27 February 2019, the Good law Project launched Judicial Review proceedings against the Secretary of State for Health and Social Care on serious shortage protocols in the *Human Medicines Regulations 2019*. This application for Judicial review was [rejected by the High Court](#) on 18 March 2019.

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<sup>98</sup> The Human Medicines (Amendment etc.) (EU Exit) Regulations 2019, [Explanatory Memorandum](#)

<sup>99</sup> The Human Medicines (Amendment) Regulations 2019, [Explanatory Memorandum](#)  
<sup>100</sup> [Letter from Chief Pharmaceutical Officer at NHS England](#), 17 January 2019

<sup>101</sup> [The Human Medicines \(Amendment\) Regulations 2019](#)

<sup>102</sup> [AoMRC, Consultation on changes to HMR2012 in relation to supply and the UK's exit from the EU: A response from the Academy of Medical Royal Colleges, December 2018](#)

<sup>103</sup> Henry Zeffman, Chris Smyth, [Ministers will order pharmacists to ration drugs if UK crashes out](#), The Times, 7 December 2018, and Jenny Cook, [BMA safety warning as pharmacists gain power to switch prescriptions](#), GPonline, 21 January 2019

<sup>104</sup> [HC Deb 18 March 2019 c845](#)

## 34 Brexit and medicines regulation

More information for patients on getting medicines in the event of a no deal Brexit is provided in a [NHS guidance document](#).<sup>105</sup>

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<sup>105</sup> NHS, [Getting your medicines if there's a no-deal EU Exit](#), 28 February 2019

## 5. Further reading

### Department of Health and Social Care

- Collection: [Planning for a possible no-deal EU Exit: information for the health and care sector](#), February 2019
- [Further guidance note on the regulation of medicines, medical devices and clinical trials if there's no Brexit deal](#), February 2019
- [How medicines, medical devices and clinical trials would be regulated if there's no Brexit deal](#), 3 January 2019
- [Batch testing medicines if there's no Brexit deal](#), 14 September 2018
- [Submitting regulatory information on medical products if there's no Brexit deal](#), 14 September 2018
- [Medicines Supply Contingency Planning Programme](#), 23 August 2018
- [Brexit operational readiness guidance for the health and care system in England](#), December 2018
- [Getting medication](#), 18 January 2019

### MHRA

- [Making a success of Brexit](#), January 2019
- [MHRA guidance and publications on a possible no deal scenario](#), March 2019

### NHS England

- [Continuity of supply](#)
- [Preparing for EU exit: Medicines frequently asked questions](#)

### EMA

- [United Kingdom's withdrawal from the European Union \('Brexit'\)](#)
- [Questions & answers: EU actions to prevent medicine shortages due to Brexit](#), 26 March 2019

### Select Committee Inquiries

#### Health and Social Care Select Committee

- [Brexit: medicines, medical devices and substances of human origin \(March 2018\)](#)
- [Impact of a no deal Brexit on health and social care inquiry](#) (October 2018)
- [Impact of the Brexit withdrawal agreement on health and social care inquiry](#) (November 2018)

### Commons Business, Energy and Industrial Strategy Select Committee

- [Brexit and the implications for UK business: Pharmaceuticals inquiry](#) (May 2018)

### Reports and articles

- Kings Fund, [Brexit: the implications for health and social care](#), 22 February 2019
- Fahy et al, [How will Brexit affect health services in the UK? An updated evaluation](#), The Lancet, February 2019
- Nuffield Trust, [Deconstructing the deal: what the Brexit agreement with the EU means for the NHS](#), December 2018
- Nuffield Trust, [Deconstructing the deal: what the Brexit agreement with the EU means for the NHS](#), December 2018
- UK in a Changing Europe, [The NHS and health law post Brexit](#), December 2018
- McHale, J. V. Health law, [Brexit and medical devices: A question of legal regulation and patient safety](#). Medical Law International, November 2018
- Nuffield Trust, [Over the edge: a no deal Brexit and the NHS](#), August 2018
- Brexit Health Alliance, [Protecting the public's health across Europe after Brexit](#), June 2018
- UK in a Changing Europe, [Brexit and the NHS](#), March 2018
- Mark Flear, [Brexit and Pharmaceuticals' Regulation: Optimising the UK's post-Brexit influence in global standards-setting](#), Queen's University Brexit Briefing Series October 2017

[Health law outside the EU, immediate, intermediate, and long term impacts](#) is a ESRC UK in a Changing Europe initiative funded project looking at a number of issues on health law and Brexit, including the regulation of medicines and medical devices. Some of the reports and articles produced by this project are listed above but for a full list of these outputs see [the project website](#).

### Industry and health organisation views

- The Association of the British Pharmaceutical Industry (ABPI), [Brexit](#)
- BMA, [BMA briefing: medicine and medical device regulation](#), December 2018
- Brexit Health Alliance, [Brexit and the impact on patient access to medicines and medical technologies](#), January 2018
- Royal College of Physicians, [RCP policy: Brexit](#)
- Royal College of Radiologists, [Medicines and radioisotope supply in the event of a no-deal Brexit](#), February 2019
- Royal College of General Practitioners, [Brexit](#)

- Royal Pharmaceutical Society, [Brexit](#)
- Royal College of Nursing, [Brexit: RCN priorities overview](#), March 2019
- UK Bioindustry Association, [The BIA Brexit Portal](#)
- Association of British Healthtech Industries, [Brexit resources](#)

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