HOUSE OF LORDS Library Briefing

Safety of Medicines and Medical Devices Debate on 28 February 2019

Summary

This House of Lords Library Briefing has been prepared in advance of the debate due to take place on 28 February 2019 in the House of Lords on the motion moved by Lord O'Shaughnessy that "this House takes note of the steps being taken to improve the safety of medicines and medical devices". While the provision of health services is a devolved matter, the regulation of medicines is carried out at the UK level. This briefing therefore contains elements which relate to the UK as a whole and others which relate only to England. These are indicated throughout the briefing.

The regulations for medicines and medical devices in the UK are currently set at a European level. All medicines must be authorised by either the European Medicines Agency (EMA) or the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) on the basis of EU standards. In practice, the two bodies work together to assess medicines before authorisation and to monitor them afterwards. Medical devices must also conform to EU standards.

Medicine regulation in the UK will be affected by its departure from the EU. Under the draft withdrawal agreement, during the transition period, cooperation between the MHRA and the EMA will continue, and following the transition period, the political declaration stated that the UK and EU would "explore the possibility of cooperation". If the UK leaves with no deal, all products authorised at the European level would automatically be authorised in the UK, and the MHRA will take on the functions of the EMA for the UK.

Ongoing developments in medicine safety include the role of technology, for example in analysing multiple databases on patient and drug experiences. Others include new methods of introducing drugs, new processes for clinical trials and enhanced education and training on safety regulation.

In February 2018, following incidents of side effects from three products, the Government launched the Independent Medicines and Medical Devices Safety Review to recommend improvements to the response to patient reports about harmful side effects. The review has so far taken evidence from a variety of sources, but has not announced a date for the publication of its main findings.

Finally, medicine safety can be seen in the context of wider patient safety initiatives. Several government and non-governmental bodies are working in this area, most prominently NHS Improvement, which is developing a new patient safety strategy.

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1. Regulatory Architecture for Medicines and Medical Devices

There has been regulation of medicines in the UK since the 1960s, and of medical devices since the 1990s.[1] In 2017, a pharmaceutical sector publication described pharmaceuticals as "one of the most tightly regulated industries".[2] The aims of this regulation, according to a summary by the European Parliament Research Service, are to protect the health of patients, while not discouraging the development of the industry or the trade in its products.[3]

The laws and guidelines which govern the development and use of medicines and medical devices in the UK are currently set at the European level.[4] To be used in the UK, any medicine must, at present, be authorised by one of two bodies: either the European Medicines Agency (EMA), or the UK national regulator, the Medicines and Healthcare Products Regulatory Agency (MHRA), which follows the standards set by the EU.[5]

This section describes the structure of medicine and medical product regulation in the UK while it remains a member of the European Union. Possible changes to the regime at the point when the UK leaves the EU, whether on the basis of the current draft withdrawal agreement or in the event of a 'no-deal' departure, are discussed in section 4.

1.1 European Medicines Agency

The EMA is an agency of the European Union, but its remit and scope cover members of both the EU and the European Economic Area (EEA).[6] The EMA's role is to advise member states and EU institutions on questions relating to medicines and medical devices, and to coordinate the evaluation and assessment of products before they are granted authorisation to be used. In doing so, it takes advice from around 4,500 experts from across the EU.[7]

While a medicine for use in any member state can be authorised by either the EMA or by the national regulator in that state following EU rules,

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[1] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 3.

[2] Pharmafile, 'What Brexit Means for Drug Regulation', 14 July 2017.

[3] Nicole Scholz, *Medicinal Products in the European Union: The Legal Framework for Medicines for Human Use*, European Parliament Research Service, April 2015, p 5.

[4] British Medical Association, *Brexit Briefing: Medicines and Medical Devices Regulation: Maintaining an Effective Working Relationship Between the UK and the EU*, 2017, p 3.

[5] House of Commons Library, *Brexit and Medicines Regulation*, 20 November 2017, p 4.

[6] European Medicines Agency, 'About Us: Authorisation of Medicines', accessed 18 February 2019.

[7] Nicole Scholz, *Medicinal Products in the European Union: The Legal Framework for Medicines for Human Use*, European Parliament Research Service, April 2015, pp 7–8.

authorisation from the EMA means that the medicine can be made available in all states which are members of the EU or the EEA. Therefore, in practice, most new medicines are now authorised at the European level.[8]

1.2 Medicines and Healthcare Products Regulatory Agency

The MHRA regulates medicines, medical devices and blood products in the UK.[9] It describes its principal aim as being "to safeguard the public's health", by "making sure that medicines and medical devices […] work properly and are acceptably safe".[10] It is largely funded by government and by the fees which pharmaceutical companies pay to be regulated.[11] These include fees for company registrations, licence applications etc.[12]

Historically, the EMA and the MHRA have worked closely together, given the MHRA's status as one of the larger national medicines agencies in Europe.[13] Various sources suggested that the MHRA carried out 40% the EMA's testing, 20% of its scientific work and constituted 15% of its expert base, while payments from the EMA for outsourced work contributed a third of MHRA's income.[14] Similarly, the MHRA noted that it is sometimes asked to take the lead on licensing products in Europe in areas in which it has particular expertise, such as gene therapies.[15]

The MHRA also collaborates with other government agencies involved in healthcare, such as the National Patient Safety Agency and the National Institute for Health and Clinical Excellence (NICE), as well as other international regulators, such as the US Food and Drug Administration.[16] In

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[8] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 6.

[9] Medicines and Healthcare Products Regulatory Agency, 'What the MHRA Does', accessed 18 February 2019.

[10] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 2.

[11] ibid, p 4.

[12] For the current fee structure, see Medicines and Healthcare Products Regulatory Agency, 'Current MHRA Fees', 3 August 2018.

[13] House of Commons Library, *Brexit and Medicines Regulation*, 20 November 2017, p 12. This briefing also suggested that the fact that the EMA was based in London, and therefore close to the MHRA, has been another reason for the close relationship. The EMA is currently in the process of moving from London to Amsterdam (European Medicines Agency, 'Relocation to Amsterdam', accessed 19 February 2019).

[14] House of Commons Health Committee, *Oral Evidence: Brexit and Health and Social Care, HC 640*, 24 January 2017, Q67; European Medicines Agency, *Work Programme 2017*, 9 October 2017, p 116; and Andrew Jack, 'Brexit Briefing: Bitter Medicine', *Financial Times* (£), 4 August 2016. For a further discussion, see House of Commons Library, *Brexit and Medicines Regulation*, 20 November 2017, p 12.

[15] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 6.

[16] ibid, p 3–4. For more information on the US system for medicine safety, see US Food and Drug Administration, 'Development and Approval Process (Drugs)', 13 June 2018.

the UK, the MHRA receives advice from the Commission on Human Medicines, which is an independent, expert group the remit of which includes advising on the "safety, quality and efficacy of human medicinal products".[17]

2. Regulatory Standards for Medicines and Medical Devices

2.1 Medicines

Whether at the European or UK level, the process for obtaining a licence for a medicine includes research, clinical trials and assessment. If the trials are to be conducted in the UK, the MHRA must be satisfied that "strict safety criteria" have been met.[18] The MHRA stated that each year it receives "around 25,000 applications to change the use or format of a medicine".[19]

The assessment of new medicines includes consideration of aspects such as the reliability of the manufacturing operation, good practice in the distribution and transport of medicines and the information supplied to patients. The MHRA is also responsible for preventing fake or unauthorised medicines entering the supply chain.[20] The MHRA described this as an "increasingly lucrative and growing market" but stated that it has been "very active" in the area and has "seized consignments and prosecuted manufacturers and importers".[21]

2.2 Medical Devices

The MHRA suggested that there are around 80,000 devices and pieces of equipment used in UK healthcare.[22] Such devices also have regulatory standards which, as for medicines, are governed by EU regulations.[23] Again, once a product is approved, it can be sold anywhere in the EU and EEA via a scheme known as 'CE marking'. New devices are not automatically subject to clinical trials, but for higher-risk products a trial may be a part of the process.[24]

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[17] Commission on Human Medicines, 'Terms of Reference', accessed 20 February 2019.
[18] ibid, p 5.
[19] ibid, p 8.
[20] Nicole Scholz, *Medicinal Products in the European Union: The Legal Framework for Medicines for Human Use*, European Parliament Research Service, April 2015, pp 20–2; and Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 10.
[21] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 18.
[22] ibid, p 7.
[23] British Medical Association, *Brexit Briefing: Medicines and Medical Devices Regulation: Maintaining an Effective Working Relationship Between the UK and the EU*, 2017, p 3.
[24] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 9.

New EU regulations for medical devices came into force in May 2017, with a period of 'parallel running' of the old and new regulations until May 2020.[25] The new regulations are intended to strengthen the regime in a number of areas, including: enhanced scrutiny of products before they are authorised; the inclusion under the rules of certain, previously excluded, products; and increased traceability of devices. The regulations also impose further requirements on manufacturers to monitor products following the introduction onto the market, and provide for improved coordination mechanisms between EU countries in their post-market surveillance activities.[26]

2.3 'Pharmacovigilance', the General Practice Research Database and the 'Yellow Card Scheme'

The EMA, MHRA and other national regulators are also responsible for monitoring the safety of medicines after they are introduced into the market, in particular to identify any side effects which had not become apparent from the more limited environment of a clinical trial. This area of activity is known as "pharmacovigilance".[27] The MHRA has powers to withdraw a product from the market or suspend its production, prosecute a manufacturer if the law has been broken, issue alerts or warnings to healthcare professionals, or require changes in product labels.[28]

The MHRA described how its monitoring regime included a probationary period of up to two years after the initial launch (or alteration) of a drug, which is intended to prompt healthcare professionals to monitor such medicines closely and report any potential side effects.[29] Other aspects of its pharmacovigilance work included inspections of laboratories and manufacturers, sampling of medicines, reviews of new evidence and commissioning research.[30]

The MHRA also manages the general practice research database (GPRD), which it described as containing "the anonymised records of patients registered at more than 480 family doctor (GP) practices across the UK".[31] It is, the MHRA stated, "the largest/most validated population-based database of its kind in the world", and is used by "academics, pharmaceutical companies, and regulators". The MHRA itself uses the database to "detect healthcare trends and monitor the safety of licensed medicines".

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[25] Medicines and Healthcare Products Regulatory Agency, 'Medical Devices: EU Regulations for Medical Devices and In-vitro Diagnostic Medical Devices', 12 October 2018.
[26] Intertek, 'The EU Medical Devices Regulation (MDR 2017/745)', accessed 20 February 2019.
[27] European Medicines Agency, 'Pharmacovigilance: Overview', accessed 15 February 2019.
[28] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, pp 4 and 13–17.
[29] ibid, p 6.
[30] ibid, p 10.
[31] ibid, pp 10–11.

Finally, the MHRA also operates the "yellow card scheme", whereby patients can report side effects of medicines. It stated that it receives more than 20,000 reports of possible side effects each year.[32]

2.4 MHRA's Standard of "Acceptably" Safe

As described in section 1.2, the MHRA's aim is ensure that medicines and medical products are "acceptably safe". This description, the MHRA stated, recognises that no product is 100 percent safe as all have side effects, whether minor or potentially serious.[33] Therefore, the MHRA assesses a product based on a proportionality test, using the following three questions:

- Do the advantages outweigh the disadvantages of taking the medicine?
- Does the medicine do the most good for the least harm for most people who will be taking it?
- Are the side effects acceptable?[34]

2.5 Herbal Medicines and Homeopathic Remedies

Herbal and homeopathic medicines and remedies are subject to a different regulatory regime.[35] For mass-produced traditional herbal medicines, the MHRA operates a traditional herbal medicines registration scheme which sets out "specific safety and quality standards". The scheme is only used for medicines for "minor health conditions where medical supervision is not required"; herbal medicines for more significant health problems are required to be authorised in the normal way.[36]

For herbal remedies made up on an individual basis, these are currently exempt from the need for a licence. However, the MHRA stated that it is "working with herbal practitioners and government to introduce safeguards for this type of treatment".

The MHRA also operates a specific scheme for homeopathic remedies.[37]

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[32] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 12.
[33] ibid, p 2.
[34] ibid.
[35] ibid, p 8.
[36] Medicines and Healthcare Products Regulatory Agency, 'Apply for a Traditional Herbal Registration (THR)', 22 September 2016.
[37] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 8.

3. Independent Medicines and Medical Devices Safety Review

In February 2018, the then Secretary of State for Health and Social Care, Jeremy Hunt, announced a review into how the health system responds to reports from patients about harmful side effects from medicines and medical devices.[38] The review followed concerns raised about, and problems arising from, three specific products.[39] In announcing the review, the then Secretary of State said the system's response to concerns has "not always been good enough".[40] He continued that the review would "ensure that patient[s'] voices are brought to the table as systematically and consistently as other voices in the system".

The announcement received the support of the Opposition. The Shadow Secretary of State for Health and Social Care, Jonathan Ashworth, stated that a commitment to an inquiry into medical devices and product licensing and regulation had appeared in the Labour Party's 2017 general election manifesto.[41]

3.1 Terms of Reference, Process and Timing

The review's terms of reference include making recommendations on actions in respect of each of the specific products, but also more broadly on what could be done in the future to improve the response to patient reports about harmful side effects. It has been instructed to suggest ways to:

- Identify and acknowledge problems with medicines and medical devices effectively and quickly;
- Strengthen the voice of patients and their families and others so that their concerns are heard in an open, fair and accessible way;
- Ensure that those concerns are recognised and acted upon appropriately, as swiftly as possible and in a coordinated fashion; and
- Ensure that those adversely affected receive the care and support they need.[42]

The review, which is chaired by Baroness Cumberlege (Conservative), is taking written and oral evidence from patients and patient groups, regulators and health professionals. In July 2018, following initial interviews, the review

[38] Independent Medicines and Medical Devices Safety Review, 'Home', accessed 14 February 2019.

[39] The products were: the hormone pregnancy test Primodos; the anti-epileptic drug sodium valproate and pelvic mesh (Independent Medicines and Medical Devices Safety Review, 'Terms of Reference', accessed 14 February 2019).

[40] HC *Hansard*, 21 February 2019, col 165.

[41] ibid, cols 168–9.

[42] Independent Medicines and Medical Devices Safety Review, 'Terms of Reference', accessed 14 February 2019.

called for a pause in the use of one of the products which had prompted the investigation.[43] However, no date has yet been set for the publication of the review's main findings.[44] Regular updates on progress are posted on the review's website.[45]

3.2 Evidence

The review has received some 66 written submissions and held 34 sessions of oral hearings. Submissions were received from four broad categories of respondent: patients and their representative groups; clinicians, academics and their representative bodies; regulators and public bodies; and manufacturers. Copies and video recordings of all evidence are available on the review's website.[46]

In their written submissions, respondents (except manufacturers) were invited to submit ideas for improving medicine safety. While it is impossible to review all the suggestions, the submissions of one respondent from each category are summarised below.

One patient group, the Epilepsy Society, highlighted the difficulty in getting the 'patient voice' heard in the past. It said:

> I would like to draw attention to the question in particular of culture […] I think it would be right for you to consider whether medically qualified professionals gave sufficient weight to information provided to them in part because the source was non-medically-qualified people.[47]

Amongst practitioners and their representative bodies, the Royal College of General Practitioners identified a potential role of new technologies in improving medicine safety, which is discussed further in section 5.1.[48] It also suggested that the 'yellow card scheme', described in section 2.3, needed to be more widely disseminated.

In the category of regulators and public bodies, the MHRA contributed a number of recommendations, including: "a more structured approach to proactive patient engagement and improved safety messaging"; "clear

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[43] Independent Medicines and Medical Devices Review, 'News', accessed 14 February 2019, updated on 10 July 2018.
[44] Independent Medicines and Medical Devices Review, 'Frequently Asked Questions', accessed 14 February 2019, question 7.
[45] Independent Medicines and Medical Devices Review, 'News', accessed 14 February 2019.
[46] Independent Medicines and Medical Devices Review, 'Evidence', accessed 14 February 2019.
[47] Independent Medicines and Medical Devices Review, *Written Evidence: Patient Groups: Sodium Valproate*, January 2019, evidence from the Epilepsy Society.
[48] Independent Medicines and Medical Devices Safety Review, *Written Evidence: Professional and Trade Bodies*, January 2019, pp 185–6.

accountability and leadership", given the complexity of the healthcare system; and collaborative working between practitioners, patient groups and the MHRA itself.[49]

4. Effect of Brexit on Medicines Regulation

As described in section 1, the structure of medicine and medical product regulation in the UK derives from EU regulations and guidelines. These have been implemented in UK law, for example by the Human Medicines Regulations 2012 and the Medical Devices Regulations 2002, and will therefore continue to apply.[50] Further, under the European Union (Withdrawal) Act 2018, all existing rules will be converted into UK law at the moment of exit to the extent they are not already part of UK law.[51]

However, as described in sections 1.1 and 1.2, most medicines for the UK market are currently authorised at the European level, and much of the MHRA's work in practice revolves around its relationship with the EMA. These arrangements will no longer automatically be in place once the UK leaves the EU. This section therefore discusses the possible effects of Brexit on medicinal product regulation. It considers separately the arrangements envisaged should the UK leave on the basis of the draft withdrawal agreement and political declaration published in November 2018, and if the UK were to leave without a deal being agreed.

4.1 Draft Withdrawal Agreement and Political Declaration

Under the draft withdrawal agreement, during the transition period (30 March 2019 to 31 December 2020) cooperation between the MHRA and the EMA will continue and medicines and medical products will be able to move freely between the UK and the EU.[52] However, the UK will not act as "leading authority" on behalf of the EU for any "risk assessments, examinations, approvals or authorisations" of medicines.

Following the transition period, the political declaration stated only that the UK and EU would "explore the possibility of cooperation of United Kingdom authorities with EU agencies such as the European Medicines Agency".[53]

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[49] Independent Medicines and Medical Devices Review, *Written Evidence: Public Bodies*, 31 October 2018, evidence from the MHRA, pp 2–3.
[50] Bonnie Clemence and Jackie Mulryne, 'MHRA Guidance on No-deal Brexit', Arnold and Porter BioSlice Blog, 12 September 2018.
[51] ibid.
[52] House of Commons Library, *The UK's EU Withdrawal Agreement*, 7 December 2018, pp 25–6, 54 and 57.
[53] Department for Exiting the European Union, *Political Declaration Setting Out the Framework for the Future Relationship Between the European Union and the United Kingdom*, 22 November 2018, p 6.

4.2 'No-Deal'

Proposed Arrangements

The MHRA has set out its proposed approach in the event of a no-deal Brexit.[54] It stated that, in respect of the UK market, the MHRA would take on all of the functions of the EMA and the European regulatory framework for medicines. Steps would be taken to ensure that all products authorised at the European level were automatically authorised in the UK as at the departure date. Drug safety reports, risk management plans and reports of suspected adverse reactions to drugs, previously submitted at the EU level, would be submitted to the MHRA.

For assessment of new medicines, the MHRA confirmed that its existing processes would continue, but there would also be certain ways to accelerate applications—including for products which had already received approval by the European authorities.[55] The MHRA then stated that "further detail on the future process for bringing a medical device onto the UK market will be subject to consultation in due course".[56]

Certain aspects of the regime would not, however, be replicated exactly in UK law. For example, the EU introduced specific incentives for companies to develop drugs known as "orphan medicines", which are used to treat very rare diseases, because of a concern that companies were reluctant to invest in research and development when the potential market was small.[57] The MHRA has proposed some changes to these rules as they apply to the UK in the event of a no-deal exit, for example to take account of UK-specific factors such as the prevalence of the disease in question.[58] In addition, there would be requirements for drug companies to have certain appointed individuals established in the UK by certain dates. Some new packaging requirements would also apply.

For medical devices, the MHRA likewise stated that all devices compliant at the EU level would remain allowable in the UK immediately after exit day.[59] However, this would only be for what it called a "time-limited period". After this period, which would vary by type of device, each would need a specific UK registration.[60] The MHRA stated that the "key elements" of the new EU

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[54] Medicines and Healthcare Products Regulatory Agency, 'Further Guidance Note on the Regulation of Medicines, Medical Devices and Clinical Trials if there is No Brexit Deal', 4 January 2019.

[55] ibid, section 1.4.

[56] ibid, section 2.3.

[57] European Commission, 'Orphan Medicinal Products', accessed 15 February 2019.

[58] Medicines and Healthcare Products Regulatory Agency, 'Further Guidance Note on the Regulation of Medicines, Medical Devices and Clinical Trials if there is No Brexit Deal', 4 January 2019, sections 1.5, 1.9 and 1.11.

[59] ibid, section 2.3.

[60] ibid, section 2.7.

regulations for medical devices, discussed in section 2.2, and the transition period for their introduction, would be mirrored in UK law.[61]

The MHRA commented that the arrangements for the monitoring of products which have already been introduced to the market would change: rather than data sharing across countries, with disputes escalated potentially as far as the European Court of Justice, surveillance would be undertaken by the MHRA in the UK only.[62] The MHRA would have sole discretion over decisions relating to the UK market.

Commentaries on Impact of No-Deal

One of the Government's no-deal 'impact assessments' considered the implications of the MHRA being established as a standalone regulator as a result of no-deal on EU exit.[63] It described the proposed approach as maintaining a "high level of public health protection", ensuring "continuity in the safety of medicines and devices in the UK", and doing so "with minimum disruption and burden on businesses and with minimum disruption to the supply of medicines and devices in the UK".[64] However, it did identify additional costs to firms of duplicate authorisations with the EMA and MHRA, and outlined a risk that drugs might therefore not be submitted to MHRA (or take longer to approve). These costs, it suggested, could prevent or delay their availability in the UK.[65]

In 2017, the British Medical Association (BMA) issued warnings about the possible reduction in medicine safety if the UK leaves the EU with no deal. It said:

> Should there be a failure to agree a withdrawal agreement by March 2019, there would be considerable uncertainty about the UK's approach to medicines and medical devices regulation. This would likely lead to a shift away from products being developed for the UK market, with significant ramifications on timely access to new medicines and medical devices, as well as on the UK's pharmaceutical and medical devices industries. There would also be considerable adverse impacts on the future capacity of the UK and EU in relation to

[61] Medicines and Healthcare Products Regulatory Agency, 'Further Guidance Note on the Regulation of Medicines, Medical Devices and Clinical Trials if there is No Brexit Deal', 4 January 2019, section 2.6.
[62] ibid, section 2.5.
[63] Department of Health and Social Care, *Contingency Legislation to Establish MHRA as a Standalone Medicines and Medical Devices Regulator in a Result of No-deal on EU Exit*, 21 September 2018.
[64] ibid, p 1.
[65] ibid, pp 3 and 32.

> pharmacovigilance, which for the UK would be compounded by a potential loss of expertise.[66]

The BMA called for an approach to licensing which was "convergent" with the EMA, a formal agreement for the MHRA to work closely with the EMA in medicine approvals, and mutual recognition of medical device standards.[67] Without these steps, it argued, the UK could face delayed access to new medicines and medical products, weaker monitoring and regulation of drugs post-approval, and a loss of expertise in regulatory processes.

5. Developments in Medicine Safety

This section summarises four areas in which regulators are considering, or trialling, improvements to their processes to enhance medicinal product safety.

5.1 Technology

In its response to the Independent Medicines and Medical Devices Safety Review, the Royal College of General Practitioners commented on possible applications of technology to improve medicine safety.[68] For example, it highlighted the variety of databases which contain relevant information (it named eight and referred to further regional databases). It suggested that linking and analysing these databases together using 'big data' analysis techniques. It also recommended a single system for reporting drug safety issues, linked to GP notes, rather than the multiple systems which currently exist. Finally, it suggested that decision aids, such as those which have been being developed by NICE, can "enhance patient understanding of the risks and potential benefits of interventions".[69]

The EMA has also considered the role of 'big data' in medicine regulation.[70] It noted the variety of sources of health data, including wearable devices, electronic health records, social media, clinical trials and "spontaneous adverse reaction reports". It stated that "there is no doubt that insights derived from this data will increasingly be used by regulators to assess the benefit-risk of medicines across their whole lifecycle". However, it concluded that a "deeper understanding of the data landscape" was necessary to secure any benefits.

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[66] British Medical Association, *Brexit Briefing: Medicines and Medical Devices Regulation: Maintaining an Effective Working Relationship Between the UK and the EU*, 2017, p 2.
[67] ibid.
[68] Independent Medicines and Medical Devices Safety Review, *Written Evidence: Professional and Trade Bodies*, January 2019, pp 185–6.
[69] ibid, p 183.
[70] European Medicines Agency, 'Role of Big Data for Evaluation and Supervision of Medicines in the EU', 15 February 2019.

Artificial intelligence has also been put forward as one of the benefits of the proposed new patient safety incident management system (see section 6.4).

5.2 'Adaptive Pathways'

In its 2015 survey of the legal framework for medicine usage, the European Parliament Research Service considered a concept known as 'adaptive pathways'.[71] This is a method for bringing some new medicines to market more quickly than in the traditional approval process. It involves the 'iterative' or 'progressive' introduction of a product, for example initially only for those with "life-threatening, severely debilitating or very rare conditions for which there is no adequate treatment available". The results of this would supplement clinical trials, prior to a progressive expansion to a wider patient population.

The EMA carried out a pilot of 'adaptive pathways' in 2014 to 2016. It found that the approach can support the development of some medicines, but that it is not suitable for all types.[72] The EMA has since stated that it is "exploring the adaptive pathways concept further".[73]

In the UK, similar approaches were considered in a parallel 'accelerated access review', which was commissioned by the government in 2014 and which reported in 2016.[74] More recently, the Government's proposed arrangements for a no-deal scenario included a new product assessment route described as a "rolling review […] which would allow companies to make applications in stages, throughout the product's development".[75]

5.3 New System for Clinical Trials

The EMA has announced that the way clinical trials are conducted in the EU will undergo a "major change" when a new regulation, the Clinical Trial Regulation, comes into force.[76] The EMA stated that the aim of the regulation was to ensure "the highest standards of safety for participants and increased transparency of trial information". In particular, it would improve "collaboration, information-sharing and decision-making between and within

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[71] Nicole Scholz, *Medicinal Products in the European Union: The Legal Framework for Medicines for Human Use*, European Parliament Research Service, April 2015, p 23.

[72] European Medicines Agency, *Final Report on the Adaptive Pathways Pilot*, 28 July 2016.

[73] European Medicines Agency, 'Adaptive Pathways', accessed 15 February 2019.

[74] Accelerated Access Review, 'Accelerated Access Review: Final Report', 24 October 2016.

[75] Medicines and Healthcare Products Regulatory Agency, 'Further Guidance Note on the Regulation of Medicines, Medical Devices and Clinical Trials if there is No Brexit Deal', 4 January 2019, section 1.4.

[76] European Medicines Agency, 'Clinical Trial Regulation', accessed 19 February 2019. The regulation itself can be found at European Union, Regulation 536/2014, 16 April 2014.

member states", which in turn would help to avoid unnecessary duplication or repetition of trials.[77]

The MHRA has stated that these regulations "will not be in force in the EU at the time that the UK exits the EU and so will not be incorporated into UK law on exit day".[78]

Further discussion on clinical trials and possible improvements to them can be found at:

- Parliamentary Office of Science and Technology, *Regulating Clinical Trials*, October 2017

5.4 Education and Training

The MHRA also contributes to improving safety standards by advising on both regulation and on improving education and training for medical practitioners.[79] For example, it stated that it has worked with the medical royal colleges to introduce a "driving licence" for the safe use of particular pieces of medical equipment. This scheme is now operated by the National Association of Medical Device Educators and Trainers (NAMDET); examples of modules currently provided include defibrillators, electrosurgery, anaesthetic machines and operating tables.[80]

6. Wider Patient Safety Initiatives in the NHS

The Secretary of State for Health and Social Care, Matt Hancock, has argued that "patient safety is the golden thread" that runs through his three stated priorities for the NHS, namely, "workforce, technology and prevention".[81] The initiatives on medicine and medical product safety outlined in the sections above therefore sit within a wider programme of patient safety initiatives in the NHS. This section briefly summarises some aspects of that wider programme.

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[77] European Medicines Agency, 'Clinical Trial Regulation', accessed 19 February 2019.

[78] Medicines and Healthcare Products Regulatory Agency, 'Further Guidance Note on the Regulation of Medicines, Medical Devices and Clinical Trials if there is No Brexit Deal', 4 January 2019, section 3.5.

[79] Medicines and Healthcare Products Regulatory Agency, *Medicines and Medical Devices Regulation: What You Need to Know*, April 2008, p 19.

[80] National Association of Medical Device Educators and Trainers, 'Medical Device Driving Licence'; and 'Devices E-Learning Modules', accessed 19 February 2019.

[81] Department of Health and Social Care, 'Secretary of State Matt Hancock's Address to the Patient Safety Learning Conference on Patient Safety: No Room For Complacency', 26 September 2018.

6.1 NHS Improvement

A key body in this field is NHS Improvement. It was formed in 2016 by bringing together different organisations and initiatives, including a body named "Patient Safety".[82] NHS Improvement has two statutory patient safety duties: collecting information about what goes wrong in healthcare; and developing policy, advice and guidance to maintain and improve the safety of healthcare.[83] NHS Improvement's remit extends to England only.[84]

6.2 Patient Safety Strategy

In December 2018, NHS Improvement's National Director of Patient Safety, Aidan Fowler, published proposals for a new "national patient safety strategy".[85] The consultation document accompanying the announcement described how this strategy would bring together existing work with some "new and wide-reaching" initiatives.[86] A consultation on the strategy closed on 15 February 2019, and NHS Improvement intends to publish a final version of the strategy in Spring 2019.[87] As part of the strategy, all NHS trusts will be expected to appoint a "patient safety director" at a senior level.[88]

6.3 Patient Safety Collaborative

The National Patient Safety Collaborative (PSC) consists of a network of 15 regional PSCs, all in England, which are charged with leading safety improvement projects across their local health and care organisations.[89] It is funded by NHS Improvement, which described the PSCs as "the largest safety initiative in the history of the NHS".[90] The work of the PSCs includes, for example: helping healthcare organisations to "nurture and develop a culture of safety", and improving "early warning systems" to identify where outcomes and experiences of patients are deteriorating.[91]

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[82] NHS Improvement, 'Who We Are', accessed 19 February 2019.
[83] NHS Improvement, *Developing a Patient Safety Strategy for the NHS: Proposals for Consultation*, December 2018, p 3.
[84] ibid.
[85] NHS Improvement, 'Developing a Patient Safety Strategy for the NHS', 14 December 2018.
[86] NHS Improvement, *Developing a Patient Safety Strategy for the NHS: Proposals for Consultation*, December 2018, p 2.
[87] NHS Improvement, 'Consultation on a National Patient Safety Strategy for the NHS', 14 December 2018.
[88] Shaun Lintern, 'Trusts Expected to Create New Patient Safety Director Role', Health Service Journal, 26 November 2018.
[89] NHS Improvement, *Patient Safety Collaboratives: A Retrospective Review*, January 2019, p 10.
[90] NHS Improvement, 'Patient Safety Collaboratives', 16 January 2019.
[91] ibid.

A review of the PSCs, published in January 2019, found that they had contributed to improved safety, but that there was "significant scope for the PSCs to contribute to further improvements in patient safety".[92] The review made recommendations to enhance their effectiveness, including strengthening their oversight, specifying minimum national standards and expectations and identifying where national workstreams would be more effective than local.[93]

6.4 Learning from Errors and 'Near Misses'

In 2014, a report commissioned by the Department of Health and Social Care found that the annual cost of "preventable adverse events" (errors that take place in the course of healthcare) in the NHS was "likely to be more than £1 billion but could be up to £2.5 billion".[94] There are several initiatives in the NHS to ensure such errors are made the subject of learning and improvement, including the following:

- The national reporting and learning system (NRLS), a central database of patient safety incident reports.[95] Under the new national patient safety strategy, the NRLS is being replaced by the patient safety incident management system. The latter will "explore using artificial intelligence to dig deeper into data so patient safety risks and improvements can be identified more quickly".[96]

- In March 2017, the National Quality Board introduced new guidance for NHS providers on learning from deaths of people in their care.[97]

- The Care Quality Commission has carried out reviews of the procedures for investigating deaths of patients in England and of the issues that contribute to what it calls 'never events' (defined as large, preventable safety incidents) in the NHS.[98]

- The Healthcare Safety Investigation Branch was established in April 2017 to undertake "exemplar investigations" of incidents,

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[92] NHS Improvement, *Patient Safety Collaboratives: A Retrospective Review*, January 2019, p 2.
[93] ibid, pp 3–4.
[94] Frontier Economics, *Exploring the Costs of Unsafe Care in the NHS*, October 2014, p 1.
[95] National Reporting and Learning System, 'Welcome to NRLS Reporting', accessed 19 February 2019.
[96] NHS Improvement, 'Avoidable Patient Harm to be Halved in Key Areas as Part of Ambitious Strategy', 14 December 2018.
[97] NHS Improvement, 'Learning from Deaths in the NHS', 14 December 2017.
[98] Care Quality Commission, 'Learning, Candour and Accountability', 10 July 2017; and 'Learning From Never Events', 10 July 2018.

and support skills development in investigators.[99]

- A draft bill which would establish a new investigative body with statutory powers was published in 2017.[100] The bill underwent pre-legislative scrutiny by a joint committee, which published its findings in August 2018.[101] The Government's response committed to bringing forward the legislation "when parliamentary time allows".[102]

6.5 National Institute for Health and Care Excellence

NICE has a range of responsibilities designed to improve patient safety and medicine safety, including assessing the clinical and cost effectiveness of medicines and medical products.[103] In 2015, it published guidance for practitioners and patients on the safe and effective use of medicines. It reported evidence that 5% to 8% of unplanned hospital admissions were due to "medication issues" and provided a review of the evidence on the "systems and processes required to ensure safe and effective medicines optimisation".[104]

6.6 Patient Safety Translational Research Centres

The National Institute for Health Research (NIHR) funds three 'patient safety translational research centres' (PSTRCs) in England, in Manchester, Yorkshire and Imperial College.[105] The Manchester PSTRC stated that it aims to develop and test "new ideas and approaches to patient safety", and ultimately "putting these interventions into practice in routine health and social care settings".[106] The NIHR set out some examples of the possible benefits of PSTRC work, including reducing prescription errors, improving diagnosis of cancer and reducing accidents during surgery.

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[99] NHS Improvement, *The Future of Patient Safety Investigation*, March 2018, p 3.
[100] Department of Health and Social Care, 'Health Service Safety Investigations Bill', 25 September 2017.
[101] Joint Committee on the Draft Health Service Safety Investigations Bill, *Draft Health Service Safety Investigations Bill: A New Capability for Investigating Patient Safety Incidents*, 2 August 2018, HL Paper 180 and HC 1064 of session 2017–19.
[102] Department of Health and Social Care, *The Government Response to the Report of the Joint Committee on the Draft Health Service Safety Investigations Bill*, December 2018, Cm 9737, p 5.
[103] National Institute for Health and Care Excellence, 'What We Do', accessed 19 February 2019.
[104] National Institute for Health and Care Excellence, *Medicines Optimisation: The Safe and Effective Use of Medicines to Enable the Best Possible Outcomes*, 4 March 2015, pp 8 and 11.
[105] University of Manchester NIHR Greater Manchester Patient Safety Translational Research Centre, 'About Us', accessed 14 February 2019.
[106] ibid.

6.7 Non-governmental Initiatives

A new non-political organisation, Patient Safety Learning, was set up in 2017 to provide what it called "an independent voice for improving patient safety".[107] It published a 'green paper' in September 2018, which provided an overview of patient safety issues and made initial proposals for change in the healthcare system.

The Royal College of General Practitioners has published a 'patient safety toolkit' for general practice.[108]

Thinktanks the Health Foundation and the King's Fund have also written on patient safety. The Health Foundation provided a checklist for providers to use when addressing safety improvements.[109] The King's Fund called for a better understanding of behavioural change theories to improve the implementation of patient safety measures in practice.[110]

[107] Patient Safety Learning, 'Patient Safety Learning—Chapter One', 20 September 2017; and *A Patient-safe Future: A Patient Safety Learning Green Paper*, September 2018, p 1.
[108] Royal College of General Practitioners, 'Patient Safety Toolkit for General Practice', accessed 14 February 2018.
[109] For example, John Illingworth, *Continuous Improvement of Patient Safety: The Case for Change in the NHS*, Health Foundation, November 2015.
[110] Suzette Woodward, 'Patient Safety: Closing the Implementation Gap', King's Fund, 30 August 2016.