EXPLANATORY MEMORANDUM TO

THE HUMAN MEDICINES (AMENDMENTS RELATING TO THE EARLY ACCESS TO MEDICINES SCHEME) REGULATIONS 2022

2022 No. 352

1. Introduction

1.1 This explanatory memorandum has been prepared by The Medicines and Healthcare products Regulatory Agency ("MHRA"), an executive agency of the Department of Health and Social Care ("DHSC") and is laid before Parliament by Command of Her Majesty.

1.2 This memorandum contains information for the Joint Committee on Statutory Instruments and for the Northern Ireland Assembly (and its Health Committee) which must debate and agree this instrument before it is made.

2. Purpose of the instrument

2.1 This instrument amends the Human Medicines Regulations 2012 (S.I. 2012/1916, as amended) ("the HMRs") and the Medicines for Human Use (Clinical Trials) Regulations 2004 (S.I. 2014/1031, as amended) ("the 2004 Regulations") to provide a statutory basis for the Early Access to Medicine Scheme ("EAMS") – there has previously been a non-statutory version of the Scheme. The EAMS has the purpose of giving patients with life threatening or seriously debilitating conditions access to medicinal products that are either not authorised or not authorised for that particular clinical use.

3. Matters of special interest to Parliament

Matters of special interest to the Joint Committee on Statutory Instruments

3.1 This instrument is made under the Medicines & Medical Devices Act 2021 ("the MMDA") (c. 3). It amends the HMRs, which were made under section 2(2) of the European Communities Act 1972. This instrument is subject to the draft affirmative procedure and is being made under powers conferred after 21st June 2017. The procedural and publication requirements of paragraphs 13 and 14 of Schedule 8 to the European Union (Withdrawal) Act 2018 therefore do not apply. The statement required by paragraph 15 of Schedule 8 to that Act is set out in the Annex to this memorandum.

Matters of special interest to the Northern Ireland Assembly

3.2 Section 2(6)(b)(ii) of the MMDA provides that in relation to Northern Ireland, regulations under section 2 can be made by the Department of Health in Northern Ireland and the Secretary of State acting jointly. Section 47(6)(c) of the MMDA provides that in the case of the regulations being made jointly the regulations must be laid before and approved by a resolution of each House of Parliament, and the Northern Ireland Assembly.

4. Extent and Territorial Application

4.1 The territorial extent of this instrument is the whole of the United Kingdom.

4.2 The territorial application of this instrument is the whole of the United Kingdom.

5. European Convention on Human Rights

5.1 The Parliamentary Under Secretary of State for Technology, Innovation and Life Sciences at the Department of Health and Social Care, Lord Kamall has made the following statement regarding Human Rights:

"In my view the provisions of the Human Medicines (Amendments Relating to the Early Access to Medicines Scheme) Regulations 2022 are compatible with the Convention rights."

6. Legislative Context

6.1 The MMDA now provides enabling powers to make provisions amending or supplementing the "law relating to human medicines", which includes the HMRs and the 2004 Regulations.

6.2 The HMRs govern the arrangements across the United Kingdom for the licensing, manufacture, wholesale dealing and sale or supply, advertising and post-marketing monitoring of medicines for human use. The 2004 Regulations govern the conduct of clinical trials of medicinal products for human use. Together, they set the essential framework, alongside the surviving provisions of the Medicines Act 1968 and the relevant fees regulations, for the regulation of medicines for human use in the United Kingdom.

6.3 There is currently no specific legislative provision for the EAMS and the scheme has operated on a non-statutory basis.

6.4 In placing the EAMS on a statutory footing, regard has been had to the continuing need for the regulatory framework in Northern Ireland to be reflective of the requirements of Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to products for human use (OJ L 311, 28.11.2001, p. 67, as amended). In practice, this has meant that the arrangements for the ordering, manufacture sale and supply of EAMS medicinal products are similar to those already in place across the United Kingdom for the ordering etc. of unlicensed products known as 'special medicinal products' or 'specials'. These arrangements take as their starting point Article 5(1) of Directive 2001/83/EC.

7. Policy background

What is being done and why?

7.1 EAMS was launched in April 2014 following a public consultation and government response. EAMS aims to give patients with life threatening or seriously debilitating conditions access to medicines that are either not authorised or not authorised for the particular clinical use proposed, where there is a clear unmet medical need, that is, that there is no other suitable medicine. This instrument does not change this core aim of EAMS. EAMS provides an important regulatory flexibility for earlier patient access and significant numbers of patients from across the UK have benefited from the scheme. For example, in England, over 1600 patients have benefitted from EAMS medicines in a variety of both common and rare diseases.

7.2 Currently, there is no legislative provision that covers or specifically mentions EAMS. The new statutory framework operation will provide a clear legal basis for the

delivery of the EAMS and there has been simplification of its requirements where feasible. This statutory instrument builds on experience of the scheme gained through its operation on a non-statutory basis since 2014 and recommendations from a Government commissioned independent review of the scheme carried out in 2016.

7.3 In particular, this instrument will provide legal clarity for those pharmaceutical companies who may be considering using the EAMS to place products on the market in the UK – and it will also provide a clear framework for requirements for safety monitoring and collection of data. At the same time, the aim is to enhance the flexibility of the scheme and maximise benefits to patients and participating pharmaceutical companies, ensuring that the EAMS remains an attractive option for companies to provide medicines to patients prior to licensing.

7.4 A specific statutory basis for the EAMS will also help to improve understanding of regulatory requirements and enhance the visibility of this important patient access route. The EAMS-specific legislative provisions should help contribute to the innovation agenda by supporting the collection of real-world data and facilitating earlier regulatory engagement with medicine developers. Most importantly it should provide a more visible regulatory framework to support earlier patient access to medicines in areas of high unmet patient medical need.

Operation of the EAMS

7.5 Companies apply to the MHRA for the EAMS in a two-step process. The first step is the Promising Innovative Medicine (PIM) designation. The PIM designation gives an indication that a medicinal product may be eligible for EAMS based on early clinical data. When the company has sufficient data to support patient access, it can apply for the second step, the EAMS scientific opinion. When considering granting a scientific opinion, MHRA will consider the risks and benefits of the medicine based on data gathered from clinical trials. The scientific opinion supports prescribers and patients to use the medicine under the EAMS framework before the medicine has received a marketing authorisation (product licence).

7.6 The MHRA may place specific conditions on the issue of the scientific opinion, as appropriate. Should the holder of a scientific opinion breach those conditions or the new statutory conditions, or sufficient reasons no longer exist for including the product in the scheme (for example, a better treatment becomes available), then the MHRA may revoke the scientific opinion. Otherwise the scientific opinion will lapse once the medicine receives a marketing authorisation, or the variation of an existing authorisation valid in the territory of its use (United Kingdom, Great Britain or Northern Ireland), or at the end of a period of one year from the scientific opinion being issued, where MHRA has not renewed the opinion. However, there is also provision for a winding down period, allowing an opinion to continue to apply after it generally ceases to have effect for certain limited purposes, to prevent disruption of patient care.

Supply of EAMS products

7.7 Provisions in this instrument are intended to simplify regulatory requirements for the supply of EAMS products (compared to the supply of 'specials') and encourage use of UK sites in manufacturing those products.

7.8 Currently in the UK, the type of manufacturing licence held by the EAMS supply chain differs depending upon whether the EAMS medicine is not authorised

("unlicensed") or an authorised medicine being used for an indication which is not currently part of its marketing authorisation ("off-label use"). The majority of EAMS medicines are unlicensed.

7.9 In the UK, under existing legislation, manufacture and assembly of unlicensed medicines require the site to hold a Manufacturing Specials (MS) licence and a Manufacturing and Importation Authorisation (MIA) for licensed medicines. The importation of unlicensed medicines from an EEA member state may be performed under a Wholesale Dealer's Licence (WDA(H)), and importation from a non-EEA country requires a Manufacturing Specials (MS) Licence. However, UK sites involved in the manufacture, assembly and importation of EAMS medicines do not typically hold a Manufacturing Specials Licence, but rather hold a manufacturing licence for the manufacture and assembly of clinical trial supplies (MIA(IMP)). The need to obtain an additional manufacturing licence for an EAMS medicine increases burden and cost, and disincentivises the use of UK sites of manufacture/assembly.

7.10 The quality standards and requirements are essentially similar across the various UK manufacturing licences (MIA, MS and MIA(IMP)). The new legislation recognises this and enables a more proportionate and flexible approach that allows EAMS medicines to be manufactured or assembled under any valid manufacturing licence (MIA, MS or MIA(IMP)), provided that the proposed activity is authorised under that manufacturing licence.

Advertising

7.11 The HMRs (regulation 279) include a general prohibition on advertising unlicensed products. Whilst this is applied to the non-statutory EAMS, it is not currently explicit in legislation that this applies for EAMS. This instrument makes it clear that no advertisement relating to an EAMS medicinal product may be published by any person as a result of the EAMS scientific opinion. The EAMS scientific opinion could be withdrawn if this requirement is breached and withdrawal was the reasonable sanction in the circumstances.

Pharmacovigilance (safety monitoring)

7.12 The monitoring of medicines when they are in use (pharmacovigilance) is essential for the MHRA to identify risks or evolving concerns and assure the continued safe use of those medicines.

7.13 Supply of a medicine through EAMS is generally short term and fairly limited in scope by the nature of the medicine's use in areas of unmet clinical need. As such, the public health implications of any new safety concerns that arise may be relatively low.

7.14 Currently, the recommended pharmacovigilance activities for EAMS are specified in guidance. This instrument makes clear in legislation the specific pharmacovigilance provisions that apply for EAMS, including: a risk management system must be agreed with the licensing authority; the EAMS scientific opinion holder must record and maintain adverse reaction reports; the EAMS scientific opinion holder must report on all serious suspected adverse reactions that occur within 15 days; and the EAMS scientific opinion holder must submit periodic reports to the licensing authority.

7.15 The pharmacovigilance provisions in this instrument are designed to be proportionate to EAMS medicinal products, whilst still supporting safe use, and ensuring both patients and healthcare professionals have confidence in the safety of EAMS products.

Framework for real world data collection

7.16 A key recommendation from the 2016 Government-commissioned independent review of EAMS was that the EAMS should become a vehicle to support the collection of real-world data. Real-world data is clinical data that better reflects the use of a drug in clinical practice outside of formal clinical trials. The benefits of collecting real-world data to supplement data derived from clinical trials are increasingly being recognised.

7.17 Currently, the collection of real-world data in relation to an EAMS medicinal product may fall under the requirements of the 2004 Clinical Trial Regulations and therefore a clinical trial authorisation (CTA) application might be required. It is not beneficial from a public health perspective to consider EAMS data collection to fall under the requirements of the 2004 Clinical Trial Regulations, and the need for a CTA application may act as a disincentive to scientific opinion holders to collect real world data.

7.18 This instrument provides a statutory gateway for a company that holds an EAMS scientific opinion to collect real world data in the context of EAMS without the need for a CTA. Data collection will be dependent on MHRA approval, and on the basis that patients must give informed consent. A patient must have access to the medicine regardless of whether they consent to their data being collected. This will retain regulatory oversight through the consideration of the EAMS scientific opinion and pharmacovigilance requirements but remove the additional burden of CTA applications and the need to implement formal clinical trial standards.

Miscellaneous and transitional provisions

7.19 In line with the new flexibilities for manufacturers and importers outlined above, a number of consequential changes have been made to the standard conditions for their licences, and to the arrangements for product release, to ensure that these new flexibilities will work appropriately.

7.20 This instrument will apply to all new EAMS applications once the provisions have come into force.

7.21 However, EAMS products that have a valid scientific opinion received prior to this instrument coming into force, may continue to be supplied under the conditions of that scientific opinion. At the time of renewal of the scientific opinion (one year after the opinion was issued or earlier at the MHRA's discretion), the EAMS products will transition into the statutory scheme.

8. European Union Withdrawal and Future Relationship

8.1 This instrument does not relate to withdrawal from the European Union/trigger the statement requirements under the European Union (Withdrawal) Act 2018.

9. Consolidation

9.1 This instrument makes amendments to the HMRs and the 2004 Regulations. There are no plans to consolidate the legislation this instrument amends.

10. Consultation outcome

10.1 The MMDA requires that, before making regulations under section 2, a public consultation be carried out in accordance with section 45(1) MMDA. As part of the

development of the proposals being given effect to by this instrument in a public consultation was carried out from 6th August 2021 to 17th September 2021. There were 59 complete responses; 66% of responders were from organisations (69% of these organisations cover the UK) and 34% were individuals (81% of were from England, 10% from Northern Ireland). Responders from organisations included industry trade associations, individual pharmaceutical companies, not for profit organisations involved in drug development, patient advocacy groups, regulatory / professional representation bodies and health delivery organisations.

10.2 The responses were generally supportive of the proposals to introduce a bespoke EAMS provision within the HMRs. A summary of the consultation responses and the Government's response can be found here: https://www.gov.uk/government/consultations/early-access-to-medicines-scheme-eams-consultation

10.3 This instrument is being made on a UK-wide basis. The Devolved Administrations have been consulted on the development of this instrument. The regulation of medicines is a devolved matter for Northern Ireland. This instrument has therefore been made jointly with the Northern Ireland Department of Health, and the public consultation was also carried out jointly.

11. Guidance

11.1 EAMS has been in operation since April 2014. EAMS processes and procedures are supported by a variety of MHRA guidance documents and templates, which can be found here: https://www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams. We fully recognise that guidance accompanying the legislation will be critical for proper implementation and interpretation of this instrument. The MHRA will work with stakeholders through established connections to produce updated EAMS guidance, with the intent to publish new guidance by the time the statutory provisions come into force.

12. Impact

12.1 The impact on business, charities or voluntary bodies of this instrument can be considered insignificant.

12.2 As this instrument provides a statutory basis for EAMS, which is already in operation and requirements for which are currently outlined in guidance, there will not be significant changes in the requirements for businesses who utilise the scheme.

12.3 There is no, or no significant, impact on the public sector.

12.4 An economic impact analysis identified the level of impact to be less than £5 million a year, therefore in line with government guidance a full Impact Assessment has not been carried out. A Regulatory Triage Assessment was undertaken in place of a full Impact Assessment.

13. Regulating small business

13.1 The legislation applies to activities that are undertaken by small businesses.

13.2 Following economic analysis of the proposed changes, no specific action is considered necessary to minimise the regulatory impact on small businesses.

14. Monitoring & review

14.1 The approach to monitoring of this legislation is for the MHRA to monitor EAMS on an ongoing basis to ensure operation of the scheme remains effective and the statutory basis continues to be fit for purpose.

14.2 This instrument does not include a statutory review clause but does contain an amendment to the review clause embedded in the HMRs. In line with the requirements of the Small Business, Enterprise and Employment Act 2015 Lord Kamall has made the following statement:

"The Human Medicines Regulations 2012 are subject to a regular review by the Secretary of State".

15. Contact

15.1 Daniel O'Connor at the Medicines and Healthcare products Regulatory Agency, Telephone: 02030806305 or email: daniel.oconnor@mhra.gov.uk can be contacted with any queries regarding the instrument.

15.2 Rachel Arrundale, Deputy Director for Policy at the Medicines and Healthcare products Regulatory Agency can confirm that this explanatory memorandum meets the required standard.

15.3 Lord Kamall, Parliamentary Under Secretary of State at the Department of Health and Social Care can confirm that this explanatory memorandum meets the required standard.

Annex

Statements under the European Union (Withdrawal) Act 2018 and the European Union (Future Relationship) Act 2020

Part 1A

Table of Statements under the 2018 Act

This table sets out the statements that may be required under the 2018 Act.

Statement	Where the requirement sits	To whom it applies	What it requires
Sifting	Paragraphs 3(3), 3(7) and 17(3) and 17(7) of Schedule 7	Ministers of the Crown exercising sections 8(1) or 23(1) to make a Negative SI	Explain why the instrument should be subject to the negative procedure and, if applicable, why they disagree with the recommendation(s) of the SLSC/Sifting Committees
Appropriate-ness	Sub-paragraph (2) of paragraph 28, Schedule 7	Ministers of the Crown exercising sections 8(1) or 23(1) or jointly exercising powers in Schedule 2	A statement that the SI does no more than is appropriate.
Good Reasons	Sub-paragraph (3) of paragraph 28, Schedule 7	Ministers of the Crown exercising sections 8(1) or 23(1) or jointly exercising powers in Schedule 2	Explain the good reasons for making the instrument and that what is being done is a reasonable course of action.
Equalities	Sub-paragraphs (4) and (5) of paragraph 28, Schedule 7	Ministers of the Crown exercising sections 8(1) or 23(1) or jointly exercising powers in Schedule 2	Explain what, if any, amendment, repeals or revocations are being made to the Equalities Acts 2006 and 2010 and legislation made under them. State that the Minister has had due regard to the need to eliminate discrimination and other conduct prohibited under the Equality Act 2010.
Explanations	Sub-paragraph (6) of paragraph 28, Schedule 7	Ministers of the Crown exercising sections 8(1) or 23(1) or jointly exercising powers in Schedule 2 In addition to the statutory obligation the Government has made a political commitment to include these statements alongside all EUWA SIs	Explain the instrument, identify the relevant law before IP completion day, explain the instrument's effect on retained EU law and give information about the purpose of the instrument, e.g., whether minor or technical changes only are intended to the EU retained law.
Criminal offences	Sub-paragraphs (3) and (7) of paragraph 28, Schedule 7	Ministers of the Crown exercising sections 8(1) or	Set out the 'good reasons' for creating a criminal offence, and the penalty attached.

		23(1) or jointly exercising powers in Schedule 2 to create a criminal offence	
Sub-delegation	Paragraph 30, Schedule 7	Ministers of the Crown exercising section 8 or part 1 of Schedule 4 to create a legislative power exercisable not by a Minister of the Crown or a Devolved Authority by Statutory Instrument.	State why it is appropriate to create such a sub-delegated power.
Urgency	Paragraph 34, Schedule 7	Ministers of the Crown using the urgent procedure in paragraphs 5 or 19, Schedule 7.	Statement of the reasons for the Minister's opinion that the SI is urgent.
Scrutiny statement where amending regulations under 2(2) ECA 1972	Paragraph 14, Schedule 8	Anybody making an SI after IP completion day under powers conferred before the start of the 2017-19 session of Parliament which modifies subordinate legislation made under s. 2(2) ECA	Statement setting out: a) the steps which the relevant authority has taken to make the draft instrument published in accordance with paragraph 16(2), Schedule 8 available to each House of Parliament, b) containing information about the relevant authority's response to— (i) any recommendations made by a committee of either House of Parliament about the published draft instrument, and (ii) any other representations made to the relevant authority about the published draft instrument, and, c) containing any other information that the relevant authority considers appropriate in relation to the scrutiny of the instrument or draft instrument which is to be laid.
Explanations where amending regulations under 2(2) ECA 1972	Paragraph 15, Schedule 8	Anybody making an SI after IP completion day under powers outside the European Union (Withdrawal) Act 2018 which modifies subordinate legislation made under s. 2(2) ECA	Statement explaining the good reasons for modifying the instrument made under s. 2(2) ECA, identifying the relevant law before IP completion day, and explaining the instrument's effect on retained EU law.

Part 1B

Table of Statements under the 2020 Act

This table sets out the statements that may be required under the 2020 Act.

Statement	Where the requirement sits	To whom it applies	What it requires
Sifting	Paragraph 8 Schedule 5	Ministers of the Crown exercising section 31 to make a Negative SI	Explain why the instrument should be subject to the negative procedure and, if applicable, why they disagree with the recommendation(s) of the SLSC/Sifting Committees

Part 2

Statements required under the European Union (Withdrawal) 2018 Act or the European Union (Future Relationship) Act 2020

1. Explanations

1.1 The explanations statement has been made in section 7 of the main body of this explanatory memorandum.