EXPLANATORY MEMORANDUM TO

THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) (AMENDMENT) (EU EXIT) REGULATIONS 2019

2019 No. 744

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 – and is laid before Parliament by Act.

1.2 This memorandum contains information for the Joint Committee on Statutory Instruments.

2. Purpose of the instrument

2.1 This instrument amends the Medicines for Human Use (Clinical Trials) Regulations 2004 ("the 2004 Regulations") to ensure they are fit for purpose in a no-deal EU-exit scenario.

Explanations

What did any relevant EU law do before Exit Day?

2.2 The requirements and procedures for clinical trials are harmonised across the EU by Directive 2001/20/EC on the approximation of laws, regulations, and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials. This has been implemented in the UK through the 2004 Regulations. These regulations require: all interventional clinical trials of medicines to be authorised by the MHRA, as the national competent authority in the UK; to have a favourable ethics opinion; and, to be conducted according to Good Clinical Practice (GCP). They also include requirements for the assessment and supply of investigational medicinal products (IMPs),[1] and for safety reporting.

Why is it being changed?

2.3 In a No Deal scenario, the MHRA needs to operate as a regulator outside the EU system and take on roles formerly conducted by the EMA and wider EU regulatory framework.

What will it now do?

2.4 This instrument will modify the 2004 Regulations to address deficiencies arising from the withdrawal of the United Kingdom from the European Union and ensure that the regulation of clinical trials continues to operate effectively.

[1] Medicinal products which are being tested or used as a reference, including as a placebo, in a clinical trial.

3. Matters of special interest to Parliament

Matters of special interest to the Joint Committee on Statutory Instruments

3.1 The instrument contains provisions which anticipate prospective changes to be made by the Human Medicines (Amendment etc.) (EU Exit) Regulations 2019 which are laid in draft alongside this instrument. Footnotes in the instrument indicate where this is the case. Both instruments will be made at the same time to come into force on exit day.

Matters relevant to Standing Orders Nos. 83P and 83T of the Standing Orders of the House of Commons relating to Public Business (English Votes for English Laws)

3.2 The territorial application of this instrument includes Scotland and Northern Ireland.

3.3 The powers under which this instrument is made cover the entire United Kingdom (see section 8(1) of the European Union (Withdrawal) Act 2018) and the territorial application of this instrument is not limited either by the Act or by the instrument.

4. Extent and Territorial Application

4.1 This instrument extends to all of the United Kingdom.

4.2 This instrument applies to all of the United Kingdom.

5. European Convention on Human Rights

5.1 Stephen Hammond has made the following statement regarding Human Rights:

5.2 "In my view the provisions of The Medicines for Human Use (Clinical trials) (Amendment) (EU Exit) Regulations 2018 are compatible with the Convention rights."

6. Legislative Context

6.1 The regulation of human medicines, including clinical trials of medicines for human use, is an area of shared competence between the EU and Member States under article 4 of the Treaty on the Functioning of the EU (TFEU). However, considering the EU's comprehensive exercise of the competence, Member States are effectively precluded from exercising the competence nationally.

6.2 The EU has created a comprehensive scheme for the regulation of clinical trials for human use. This is set out in: Directive 2001/20/EC of the European Parliament and of the Council relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (the Clinical Trials Directive); and, tertiary Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products (the GCP Directive).

6.3 The Clinical Trials Directive and the GCP Directive have been transposed into UK law by the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) (the 2004 Regulations). The 2004 Regulations are made under section 2(2) of the European Communities Act 1972 (ECA).

6.4 On 16 April 2014, Regulation (EC) No 536/2014 was adopted and subsequently entered into force on 16 June 2014. This new EU Regulation replaces the Clinical

Trials Directive and the GCP Directive but will only apply - the EU term for when a measure becomes operative – from six months after the EU IT is declared ready. This is estimated to be December 2020.

6.5 The EU (Withdrawal) Act 2018 (EUWA) provides at section 2 that domestic legislation made under section 2(2) ECA continues to have effect in domestic law on or after Exit Day (notwithstanding that the ECA is repealed by section (1). "Exit Day" is defined at section 20 to mean 11pm on 29th March 2019. By being saved under section 2 EUWA, the 2004 Regulations form part of "retained EU law" as defined in section 6(7) EUWA.

6.6 Section 3 EUWA provides that EU Regulations that are in force and apply immediately before Exit Day also continue to form part of domestic law on or after Exit Day and form part of retained EU law. This means that the new EU Regulation does not form part of domestic law after Exit Day by virtue of section 3 EUWA on the basis that it does not apply immediately before Exit Day.

6.7 Section 8 EUWA provides that a Minister of the Crown may by regulations make such provision as the Minister considers appropriate to prevent, remedy or mitigate: (a) any failure of retained EU law to operate effectively; or, (b) any other deficiency in retained EU law arising from the withdrawal of the UK from the EU.

6.8 These Regulations exercise the power at section 8 EUWA to amend the 2004 Regulations to ensure that all aspects of retained EU law in relation to clinical trials of medicines for human use operate effectively and are not deficient after Exit Day because of the UK's withdrawal from the EU.

6.9 The Medicines and Healthcare products Regulatory Authority (MHRA), an executive agency of the Department of Health and Social Care, carries out the functions of a competent authority in the UK in the area of clinical trials on behalf of the "licensing authority": a body established under the HMRs. The power in section 8(6)(a) of EUWA is exercised in these Regulations to confer on the MHRA those functions in relation to clinical trial regulation, including legislative functions, that are currently carried out by EU bodies

6.10 During the passage of the EUWA through Parliament, a Government commitment was made in relation to the implementation of the new EU Regulation. The Government committed to being as aligned with the new EU Regulation as possible and said it would give priority to taking the steps necessary to bring into UK law, without delay, all relevant parts of the EU Regulation that are within the UK's control (see Hansard, 18th April 2018, column 1216). This commitment is not addressed in these Regulations which are limited to correcting deficiencies in retained EU law (i.e. the 2004 Regulations) arising from the withdrawal of the UK from the EU. The commitment in relation to the new EU Regulation will be delivered through a separate legislative vehicle which will brought forward when the application date of the new EU Regulation is known.

7. Policy background

What is being done now and why?

Legal presence

7.1 At present, the sponsor of a clinical trial must be established in an EEA State or have a legal representative who is established in an EEA state. This instrument will allow the

sponsor (or legal representative) of a clinical trial to remain established in an approved country, which on Exit Day, will include all EEA states. This is being done to ensure continuity of the existing clinical-trials landscape and to maintain the UK as an attractive, open environment in which to conduct trials.

Reporting suspected adverse reactions

7.2 Currently, a clinical-trial sponsor can report a suspected, unexpected, serious, adverse reaction (SUSAR) which occurs during the course of a clinical trial in the UK through the EU database. Similarly, all SUSARs originating outside the UK where the sponsor has an ongoing trial in the UK involving the same medicinal product currently must be entered into the EU database. This instrument will ensure that, post-Exit, such events must be reported to the licencing authority: the MHRA.

Import of IMPs

7.3 For an IMP to be supplied in the EU, including the UK, it must have been certified by a Qualified Person (QP certified), and that Qualified Person must be based in the EEA. This is true whether the IMP is manufactured in the EEA or a third country.

7.4 For IMPs manufactured in a third country the importer must hold a Manufacturers Authorisation for Import for IMPs (MIA(IMP)) and QP-certify the product before supplying it in the EEA. When the UK becomes a third country to the EU, there will be no obligation under EU law that ensures IMPs coming from the EU into the UK will have been QP-certified.

7.5 QP certification is a critical part of ensuring that an IMP has been manufactured to the correct standard. For this reason, this instrument will require the importation of IMPs from approved countries (which, on Exit Day, will encompass all EEA states) to be overseen by the holder of an MIA(IMP) licence to ensure that the IMP has been QP-certified within an approved country.

Transparency

7.6 Information on clinical trials carried out in the EU is made public in the EU Clinical Trials Register. This is done via Member States supplying the EU with data on the clinical trials in their territories.

7.7 To ensure continued transparency of clinical trials, this instrument provides the licensing authority with the power to publish information on UK trials, in line with what is currently made available.

Updates to good clinical practice and associated guidance

7.8 This instrument will transfer the powers currently exercised by EU bodies to update the conditions and principles of good clinical practice to take account of technical and scientific progress. The MHRA will also have the power to publish its own guidance on clinical trial applications and applications for an ethics committee opinion, as well as the declaration of the end of the clinical trial and the content of documents forming the trial master-file. This will ensure standards and guidelines for clinical trials in the UK can be kept up to date.

8. European Union (Withdrawal) Act/Withdrawal of the United Kingdom from the European Union

8.1 This instrument is being made using the power in section 8 of the European Union (Withdrawal) Act 2018 in order to address failures of retained EU law to operate effectively or other deficiencies arising from the withdrawal of the United Kingdom from the European Union. In accordance with the requirements of that Act, the Minister has made the relevant statements as detailed in Part 2 of the Annex to this Explanatory Memorandum.

9. Consolidation

9.1 There are no plans to consolidate at this time.

10. Consultation outcome

10.1 The MHRA and DHSC conducted informal consultation with industry and the third sector over a series of deep dives to develop No Deal proposals. Informal consultation at official level was also conducted with the Devolved Administrations. The Secretaries of State in Scotland and Wales, and the Permanent Secretary in Northern Ireland, in the respective health departments, were informed of the proposed positions ahead of formal consultation.

10.2 Some of the proposed changes to medical devices regulations were included in the formal written consultation alongside the proposals for medicines and clinical trials. This consultation lasted 4 weeks (4th October – 1st November 2018 inclusive). There were 168 responses through the online portal and 9 via email. Responses were received from a range of interests including medical devices companies (including SMEs), trade bodies, NHS trusts, universities, research organisations, charities, health-related professional bodies (including from the Devolved Administrations), law firms, and learned societies.

10.3 The proposal regarding allowing the sponsor or their legal representative to be established in a country included on the approved list was supported in relation to flexibility. However, concerns were raised around the proposal to require the Chief Investigator to be available as a UK contact point. This additional requirement has consequently not been introduced.

10.4 All stakeholders supported the provision to be made to allow the MHRA to publish information on UK clinical trials, as currently done in the EU Clinical Trials Register. Companies requested that the UK align transparency requirements with those in the EU to eliminate duplication of efforts.

10.5 Consultees were broadly supportive of the pragmatic approach of having a list of approved countries, for the purpose of recognising QP certification, which would initially include all EEA countries, so as to ensure immediate continuity. However, there were requests for additional countries which meet appropriate standards to also be considered. The list of approved countries will be subject to regular review and so the MHRA will consider the appropriateness of further countries at a later date.

11. Guidance

11.1 The MHRA has published guidance to prepare for EU exit, following the No Deal consultation. This can be accessed here:

https://www.gov.uk/government/publications/further-guidance-note-on-the-regulation-of-medicines-medical-devices-and-clinical-trials-if-theres-no-brexit-deal.

11.2 Additional guidance will be provided, in particular to give further clarity on IMP importation and the practicalities of becoming, or contracting, an authorised importer of IMPs to ensure that there are no bottlenecks in any clinical trial settings.

12. Impact

12.1 The impact on business, charities or voluntary bodies is included in the published Impact Assessment

12.2 The impact on the public sector is included in the published Impact Assessment.

12.3 A full Impact Assessment is submitted with this memorandum and published alongside the Explanatory Memorandum on the legislation.gov.uk website

13. Regulating small business

13.1 The legislation applies to activities undertaken by small businesses. The MHRA will seek to minimise the legislation's impact by providing guidance to relevant stakeholders.

14. Monitoring & review

14.1 As this instrument is made under the EU Withdrawal Act 2018, no review clause is required.

15. Contact

15.1 Ian King at the Medicines and Heath products Regulatory Agency can be contacted with any queries regarding the instrument (+44 7825 256 320, ian.king@mhra.gov.uk)

15.2 Patrick Carey at the Medicines and Heath products Regulatory Agency can confirm that this Explanatory Memorandum meets the required standard.

15.3 Stephen Hammond, Minister of State for Health 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

Part 1

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 clauses 8(1), 9 and 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/ESIC
Appropriate-ness	Sub-paragraph (2) of paragraph 28, Schedule 7	Ministers of the Crown exercising clauses 8(1), 9 and 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 clauses 8(1), 9 and 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 clauses 8(1), 9 and 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 77	Ministers of the Crown exercising clauses 8(1), 9 and 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 Exit 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 clauses 8(1), 9, and 23(1) or jointly exercising powers in Schedule 2 to create a criminal offence	Set out the 'good reasons' for creating a criminal offence, and the penalty attached.
Sub-delegation	Paragraph 30, Schedule 7	Ministers of the Crown exercising clauses 10(1), 12 and 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 4 or 14, Sch 7.	Statement of the reasons for the Minister's opinion that the SI is urgent.
Explanations where amending regulations under 2(2) ECA 1972	Paragraph 13, Schedule 8	Anybody making an SI after Exit 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 Exit Day, and explaining the instrument's effect on retained EU law.

Scrutiny statement where amending regulations under 2(2) ECA 1972	Paragraph 16, Schedule 8	Anybody making an SI after Exit Day under powers outside the European Union (Withdrawal) Act 2018 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.

Part 2

Statements required when using enabling powers under the European Union (Withdrawal) 2018 Act

1. Appropriateness statement

1.1 The Minister of State for Health, Stephen Hammond, has made the following statement regarding use of legislative powers in the European Union (Withdrawal) Act 2018:

"In my view the Medicines for Human Use (Clinical Trials) (Amendment) (EU Exit) Regulations 2019 do no more than is appropriate". This is the case because: the changes to the law made by these Regulations are limited to making provision which is appropriate to prevent, remedy, or mitigate deficiencies arising out of EU exit. Those deficiencies result from the UK no longer being part of the EU medicines regulatory network and the amendments enable the UK licensing authority (acting through the MHRA) to act as a stand-alone regulator in the area of clinical trials for the UK, whilst maintaining, so far as possible, the existing regulatory position.

2. Good reasons

2.1 The Minister of State for Health, Stephen Hammond, has made the following statement regarding use of legislative powers in the European Union (Withdrawal) Act 2018:

In my view there are good reasons for the provisions in this instrument, and I have concluded they are a reasonable course of action". These are: to address deficiencies arising from the withdrawal of the United Kingdom from the European Union; and, to ensure that the regulation of clinical trials continues to operate effectively, in line with the need for the MHRA to operate as a regulator outside the EU system.

3. Equalities

3.1 The Minister of State for Health, Stephen Hammond, has made the following statement:

"The draft instrument does not amend, repeal or revoke a provision or provisions in the Equality Act 2006 or the Equality Act 2010 or subordinate legislation made under those Acts".

3.2 The Minister of State for Health, Stephen Hammond, has made the following statement regarding use of legislative powers in the European Union (Withdrawal) Act 2018:

"In relation to the draft instrument, I, Stephen Hammond, Minister of State for Health, have had due regard to the need to eliminate discrimination, harassment, victimisation and any other conduct that is prohibited by or under the Equality Act 2010.".

4. Explanations

4.1 The explanations statement has been made in paragraph 2 of the main body of this explanatory memorandum.

5. Criminal offences

5.1 The Minister of State for Health, Stephen Hammond, has made the following statement regarding use of legislative powers in the European Union (Withdrawal) Act 2018:

"In my view there are good reasons for maintaining the existing criminal offence (and penalty for that offence) in regulation 49(1)(k) of the 2004 Regulations of contravening the prohibition on importing an investigational medicinal product from a country outside the European Economic Area without a manufacturing authorisation, but widening the scope of that offence to include the activity of importing such products from any country outside the United Kingdom."

5.2 The reasons are that the activity of importing an investigational medicinal product from an EEA state is not currently an activity that requires a manufacturing authorisation, on the basis that the UK is a Member State of the EU and therefore such products being sold between EEA states must undergo qualified-person certification. Once the UK is a third country in relation to the EU, there is no obligation for investigational medicinal products imported into the UK from an EEA State to have been QP certified. Requiring persons who import from EEA states to have a manufacturing authorisation and an assurance system in relation to QP certification is an appropriate way to address this issue and it is appropriate for the same level of sanction to apply to contravention of this new requirement as currently applies to any breach of the existing requirements.

6. Legislative sub-delegation

6.1 The Minister of State for Health, Stephen Hammond, has made the following statement regarding use of legislative powers in the European Union (Withdrawal) Act 2018:

"In my view it is appropriate to create a relevant sub-delegated power in Medicines for Human Use (Clinical Trials) (Amendment) (EU Exit) Regulations 2019."

6.2 This is appropriate in relation to the amendments made by this instrument giving the licensing authority a duty to publish lists of countries which are relevant for the purposes of certain provisions mentioned in section 8. The list mechanism is appropriate because it provides flexibility to respond to developments as countries can, or can no longer, demonstrate equivalence with the UK, when the UK is no longer bound by EU law in relation to clinical trials. It is also appropriate in relation to the power for the licensing authority to publish a list of the information which may be made accessible to the public in relation to clinical trials carried out in the UK. Including the lists in the 2004 Regulations would be a cumbersome way of addressing these technical and potentially fluctuating issues.