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Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending Regulation (EU) No 536/2014 as regards a derogation from certain obligations concerning investigational medicinal products made available in the United Kingdom with respect to Northern Ireland as well as in Cyprus, Ireland and Malta

(Text with EEA relevance)

EXPLANATORY MEMORANDUM

1. CONTEXT OF THE PROPOSAL

• Reasons for and objectives of the proposal

Pursuant to the Protocol on Ireland/Northern Ireland ("the Protocol") of the Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community[1] (the 'Withdrawal Agreement'), the importation of investigational medicinal products from third countries into the Union or Northern Ireland is subject to the possession of a manufacturing and import authorisation. These shall be in compliance with the obligations of the EU acquis for clinical trials.

During these last years, the United Kingdom in respect of Northern Ireland as well as the small markets of the European Union (i.e. Malta, Ireland and Cyprus) that are dependent on supply of medicinal products from the United Kingdom, have raised issues with respect to the ability of economic operators to comply with all provisions of the acquis for **medicines after the end of the transition period provided for in the Withdrawal Agreement, including medicines used in clinical trials, having regard in particular to the importation requirements**.

The Commission Notice of 25 January 2021[2] provides for a grace period of one year (until end-December 2021), including for the importation requirements for investigational medicines, to ensure undisrupted supply of medicines to Northern Ireland, Cyprus, Ireland and Malta.

Despite the transition period, it still proves very difficult for certain operators currently based in parts of the United Kingdom other than Northern Ireland to adapt as required by the Protocol. The main reasons are the too high adjustment costs relative to the small size of the Northern Irish market and the complex logistics involved, for which no viable alternative logistical hubs in Northern Ireland have been identified.

For the markets of Cyprus, Malta and Ireland, the same issues arose, and in addition, difficulties were seen with to ensure that clinical trial participants have access to certain medicinal products due to supply chains reliance on other parts of the United Kingdom than Northern Ireland.

Disruption in supply of investigational medicinal products would pose potential risk to the safety and well-being of participants in ongoing clinical trials as well as hinder the setting up of new clinical trials in these Member States and in Northern Ireland.

The objectives of this proposal are to address the issues related to investigational medicinal products, to prevent an adverse impact on their supply and, as a result, on the execution of clinical trials authorised under Regulation (EU) 536/2014[3] in Northern Ireland, Cyprus, Ireland and Malta.

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1 OJ L 29, 31.1.2020, p. 7.

2 Commission Notice of 25 January 2021 on the application of the Union's pharmaceutical *acquis* in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period, (OJ C 27, 25.1.2021, p. 11).

3 Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (OJ L 158, 27.5.2014, p. 1).

This proposal allows exceptionally that the manufacturing and import authorisation is not required for investigational medicinal products imported into Cyprus, Ireland, Malta and Northern Ireland from parts of the United Kingdom other than Northern Ireland, provided that certain conditions are fulfilled. For Cyprus, Ireland and Malta, this derogation is of a temporary nature as it is expected that these markets will gradually be supplied through Member States. A transition period of 3 years seems sufficient.

Although Regulation (EU) 536/2014 entered into force in 2014, its applicability was made dependent on the full functionality of the European Portal and Database. The Commission published the notice of full functionality on 31 July 2021, triggering a 6-month period before applicability on 31 January 2022.[4] As a transitional measure, during the first year (until 31 January 2023), sponsors can chose to submit a clinical trial application in line with the rules of Regulation (EU) 536/2014 or through the rules of Directive 2001/20/EC[5]. Trials authorised under that Directive can continue until 31 January 2025.

Therefore, this proposal should be read in conjunction with the conceptually identical changes to Directive 2001/20 proposed in COM(2021)997 of 17 December 2021 as both legal acts can apply to different clinical trials in the EU until 31 January 2025. For this reason, this separate proposal was given an exemption from an additional fiche for the agenda planning. Considering the urgency needed to address the issues, the roadmap for this initiative will not be provided.

- **Consistency with existing policy provisions in the policy area**

A comprehensive Union medicinal products legislative framework was established, in particular Directive 2001/83/EC[6], Directive 2001/20/EC and Regulation (EU) No 536/2014, which are of relevance for this initiative that will complement and amend them.

This proposal is consistent with the objective to protect participants of clinical trials and public health in the small markets of the Union and in Northern Ireland.

- **Consistency with other Union policies**

This proposal does not affect other Union policies, except for the health and internal market rules. As a consequence, the assessment of the consistency with other Union policies is not considered necessary.

2. LEGAL BASIS, SUBSIDIARITY AND PROPORTIONALITY

- **Legal basis**

As this proposal amends Regulation (EU) No 536/2014, the same legal basis – Articles 114 and 168(4)(c) TFEU – are considered the appropriate legal basis for this proposal as well.

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4 Commission Notice of 25 January 2021 on the application of the Union's pharmaceutical *acquis* in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period, (OJ C 27, 25.1.2021, p. 11).

5 Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (OJ L 121, 1.5.2001, p. 34).

6 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67).

- **Subsidiarity (for non-exclusive competence)**

  This proposal provides exemptions from the provisions of the EU pharmaceutical legislation and can only be achieved by an amendment of the basic act at EU level.

  This proposal aims to provide derogations for medicinal products distributed to Northern Ireland, Cyprus, Ireland and Malta that are used as investigational medicinal products in clinical trials in those countries.

- **Proportionality**

  The proposal covers the exemption from the importation requirements for investigational medicinal products to ensure their continued supply and avoid delays or interruptions to the setting up and conduct of clinical trials in the Union and in Northern Ireland.

  The proposal is restricted to investigational medicines made exclusively available in Northern Ireland and the small markets of those EU Member States – Cyprus, Malta and Ireland – that are dependent on the UK market.

- **Choice of the instrument**

  As the initiative amends Regulation (EU) No 536/2014, a proposal for a Regulation of the European Parliament and Council is considered the appropriate instrument.

3. RESULTS OF EX-POST EVALUATIONS, STAKEHOLDER CONSULTATIONS AND IMPACT ASSESSMENTS

- **Ex-post evaluations/fitness checks of existing legislation**

  Not applicable

- **Stakeholder consultations**

  This initiative is proposed following bilateral discussion with the concerned national authorities and industry associations, who have expressed strong concerns due to the risk of interruptions of ongoing or future clinical trials due to the requirements for importation of investigational medicinal products.

  Considering that targeted consultations with the Member States concerned and the stakeholders took place, another open public consultation will not be carried out.

- **Impact assessment**

  The proposal is exempted from the impact assessment due to the urgency of the situation, to ensure public health through the continued supply of investigation medicinal products for clinical trials in Northern Ireland and the small markets of the EU Member States that are dependent on the United Kingdom for their supplies.

- **Regulatory fitness and simplification**

  By waiving certain regulatory requirements for the importation of investigational medicinal products, provided certain conditions are fulfilled, the proposal reduces compliance costs in particular as regards SMEs.

- **Fundamental rights**

  The proposed Regulation contributes to achieving a high level of human health protection as set out in Article 35 of the EU Charter of Fundamental Rights.

4. BUDGETARY IMPLICATIONS

No budgetary implications are foreseen.

5. OTHER ELEMENTS

- **Implementation plans and monitoring, evaluation and reporting arrangements**

  The initiative applies to the United Kingdom in respect of Northern Ireland that must implement it and notify to the Commission the implementation planning associated with this initiative. The Member States concerned as well must take the necessary measures to implement the initiative. The Commission will further monitor its implementation.

- **Detailed explanation of the specific provisions of the proposal**

  Not applicable for this proposal.

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(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Articles 114 and 168(4), point (c), thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee[1],

Having regard to the opinion of the Committee of the Regions[2],

Acting in accordance with the ordinary legislative procedure,

Whereas:

(1) The Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community[3] (the 'Withdrawal Agreement') was concluded on behalf of the Union by Council Decision (EU) 2020/135 [4] and entered into force on 1 February 2020. The transition period referred to in Article 126 of the Withdrawal Agreement, during which Union law continued to apply to and in the United Kingdom in accordance with Article 127 of the Withdrawal Agreement (the 'transition period'), ended on 31 December 2020. On 25 January 2021, the Commission issued a Notice[5] ('the Notice') on the application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain (i.e. Cyprus, Ireland, Malta and Northern Ireland) after the end of the transition period. This Notice includes explanations of how the Commission would apply the Union's pharmaceutical acquis in those markets with regard to investigational medicinal products. The Notice is to cease to be applied on 31 December 2021.

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1 OJ C , , p. .

2 OJ C , , p. .

3 OJ L 29, 31.1.2020, p. 7.

4 Council Decision (EU) 2020/135 of 30 January 2020 on the conclusion of the Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community (OJ L 29, 31.1.2020, p. 1).

5 Commission Notice – Application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period (2021/C 27/08)(OJ C 27, 25.1.2021, p. 11).

(2) In accordance with the Protocol on Ireland/Northern Ireland, which forms an integral part of the Withdrawal Agreement, investigational medicinal products used in clinical trials in Northern Ireland are to comply with Union law.

(3) Regulation (EU) No 536/2014 of the European Parliament and of the Council[6] lays down the rules for investigational medicinal products intended to be used in clinical trials in the Union. That Regulation applies from 31 January 2022.

(4) In accordance with Article 61(1) of Regulation (EU) No 536/2014, read in conjunction with the Protocol on Ireland/Northern Ireland, the import of investigational medicinal products from third countries into the Union or Northern Ireland is subject to the holding of a manufacturing and import authorisation. Cyprus, Ireland, Malta and Northern Ireland have historically relied on supply of medicinal products, including investigational medicinal products, from or through parts of the United Kingdom other than Northern Ireland, and the supply chains for these markets have not yet been fully adapted to comply with Union law In order to ensure that clinical trial participants in Cyprus, Ireland, Malta and Northern Ireland continue to have access to new, innovative or improved treatments, it is necessary to amend Regulation (EU) No 536/2014 to provide for a derogation from the requirement of the holding of a manufacturing and import authorisation for investigational medicinal products imported into those markets from parts of the United Kingdom other than Northern Ireland. However, both in order to ensure the quality of those investigational medicinal products and to avoid compromising the integrity of the internal market, certain conditions should be laid down.

(5) Regulation (EU) No 536/2014 should therefore be amended accordingly.

(6) In light of the requirement of uniform application of Union law in the Member States, the derogations applicable in Cyprus, Ireland and Malta should be of a temporary nature only.

(7) In order to ensure legal continuity for operators active in this sector and to guarantee the continuous access of participants in clinical trials in Cyprus, Malta, Ireland and Northern Ireland to investigational medicinal products from the date of application of Regulation (EU) No 536/2014, this Regulation should enter into force as a matter of urgency and apply retroactively from the date at which Regulation (EU) 536/2014 becomes applicable,

HAVE ADOPTED THIS REGULATION:

Article 1

In Article 61(1) of Regulation 536/2014, the following subparagraph is added:

"However, the import of investigational medicinal products from other parts of the United Kingdom into Northern Ireland and, until 31 December 2024, into Cyprus, Ireland and Malta shall not be subject to the holding of a manufacturing and import authorisation~~,~~ provided that the following conditions are fulfilled:

(a) the investigational medicinal products have undergone certification of batch release either in the Union or in parts of the United Kingdom other than Northern Ireland to verify compliance with the requirements set out in Article 63(1)***;***

[6] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (OJ L 158, 27.5.2014, p. 1).

(b) the investigational medicinal products are only made available to clinical trial participants in the Member State into which the investigational medicinal products are imported or, if imported into Northern Ireland, are only made available to clinical trial participants in Northern Ireland."

Article 2

This Regulation shall enter into force on the day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 31 January 2022.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels,

For the European Parliament	*For the Council*
The President	*The President*