EUROPEAN
COMMISSION

Brussels, 6.9.2022
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COMMISSION DELEGATED REGULATION (EU) …/...

of 6.9.2022

amending Regulation (EU) No 536/2014 of the European Parliament and of the Council as regards labelling requirements for unauthorised investigational and unauthorised auxiliary medicinal products for human use

(Text with EEA relevance)

EXPLANATORY MEMORANDUM

1. CONTEXT OF THE DELEGATED ACT

Annex VI to the Clinical Trials Regulation (EU) 536/2014[1] introduces a change to the rules under the Clinical Trials Directive (2001/20/EC)[2] for the labelling of unauthorised investigational and auxiliary medicinal products. According to these new requirements, the expiry date must be included on both the immediate and outer packaging of these products, without exception. Excluding the possibility to omit the expiration date from the labelling on immediate packaging when appropriate, such as when the inner packing is too small or always used with the outer packaging, can be associated with increased risk to the quality and safety of clinical trial for example by requiring the disintegration of these products or resulting in prolonged and repeated exposure of sensitive products to light or temperature variations. In addition, these changes might lead to unnecessarily increased complexity of medicine delivery by medicine developers and thus can result in delays in the setting up and conduct of clinical trials and create a more restrictive environment for research in Europe in association with increased risk to clinical trial participants' safety.

2. CONSULTATIONS PRIOR TO THE ADOPTION OF THE ACT

The Commission consulted the Clinical Trials Coordination and Advisory Group ('CTAG'), established in accordance with Article 85 of Regulation (EU) 536/2014 on 4 February 2022 for the position of Member States on modifying the labelling requirements in Annex VI to this Regulation. Member States expressed strong support for such amendment and, based on this feedback, the Commission prepared a draft text. The draft Delegated Regulation was shared with CTAG on 14 March 2022 for review and comments by the group. The text was finalised at an exceptional CTAG meeting on 31 March specifically dedicated to the discussion on the draft Delegated Regulation. Following the meeting, the updated version of the draft Delegated Regulation was shared with CTAG members for final comments by 5 April 2022.

The draft delegated regulation was posted in the European Commission portal "Have your say" to gather the views of citizens and stakeholders from 1 June 2022 to 29 June 2022. Contributions were received from business organisations and companies, the vast majority of which supported the proposed rules. Some of these contributors proposed additional labelling exemptions, which were not considered due to the potential impact on the safety of clinical trial participant this might trigger. Contributions were also received from citizens, who expressed concerns regarding the proposed exemptions. These concerns were mainly due misunderstandings about the proposed rules, which were often understood as exemptions to label the expiry date for medicines put on the market, or exemptions allowing unauthorised medicines to be put on the market. As a consequence, the draft Regulation was not amended after that consultation.

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1 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.

2 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.

3. LEGAL ELEMENTS OF THE DELEGATED ACT

The legal basis for this Delegated Regulation is set out in Article 70 of the Clinical Trials Regulation (EU) 536/2014, which empowers the Commission to adopt delegated acts to amend Annex VI to Regulation (EU) 536/2014 to ensure subject safety and the reliability and robustness of data generated in clinical trials. Consistent high quality of medicinal products across the lifecycle of the clinical trials is seen as a pre-requisite to participants' safety as well as for the comparability and reliability of the generated data.

The Annex to the Delegated Regulation therefore allows the omission of the expiration date from the immediate packaging when it is too small or when it is intended to stay together with the outer packaging. At the same time, it does not remove the legal obligation to include this information on the outer packaging also in these specific cases.

Points 1 and 2 of the Annex to the Delegated Regulation provides for these risk adaptations to unauthorised investigational and auxiliary medicinal products.

Finally, point 3 of the Annex to the Delegated Regulation allows for the expiration date to be omitted from the immediate label when it is too small or when it is intended to stay together with the outer packaging in cases where other means of labelling such as centralised electronic randomisation systems are used.

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THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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[1], and in particular Article 70 thereof,

Whereas:

(1) Regulation (EU) No 536/2014 sets out detailed rules for the labelling of investigational and auxiliary medicinal products, in particular of unauthorised products, in order to eliminate divergences of approach among Member States. That Regulation requires that the immediate and outer packaging of investigational and auxiliary medicinal products must be appropriately labelled in order to ensure subject safety and the reliability and robustness of data generated in clinical trials, and in order to allow for the distribution of those products to clinical trial sites throughout the Union.

(2) In particular, Regulation (EU) No 536/2014 requires sponsors to display the period of use on the outer and immediate packaging of unauthorised investigational and unauthorised auxiliary medicinal products.

(3) Frequent updates of the period of use on the immediate packaging of unauthorised medicinal products used in clinical trials can be associated in certain cases with potential risks affecting the quality and safety of those products. One such potential risk may be damages stemming from the need to open the packaging by breaking tamper evident seals and disassembling the multilayer kit. Another potential risk may stem from the prolonged exposure to light or higher temperatures for medicinal products with specific sensitivities. Those risks apply in particular to medicinal products where the immediate and outer packaging are provided together as well as when the immediate packaging takes the form of blister packs or small units. In those cases, it is appropriate and proportionate to the nature and the extent of the risk that the period of use is omitted from the immediate packaging.

(4) Regulation (EU) No 536/2014 should therefore be amended accordingly,

[1] OJ L 158, 27.5.2014, p. 1.

HAS ADOPTED THIS REGULATION:

Article 1

Annex VI to Regulation (EU) No 536/2014 is amended in accordance with the Annex to this Regulation.

Article 2

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

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

Done at Brussels, 6.9.2022

For the Commission
The President
Ursula VON DER LEYEN