EUROPEAN
COMMISSION

Brussels, 24.3.2021
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COMMISSION DELEGATED REGULATION (EU) …/...

of 24.3.2021

amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products

(Text with EEA relevance)

EXPLANATORY MEMORANDUM

1. CONTEXT OF THE DELEGATED ACT

Article 23b of Directive 2001/83/EC[1] and Article 16a of Regulation (EC) No 726/2004[2] empower the Commission to adopt delegated acts specifying the categories in which variations to authorised human medicinal products are to be classified; and establishing procedures for the examination of applications for variations to the terms of marketing authorisations.

This Delegated Regulation amends Commission Regulation (EC) No 1234/2008[3] by adding provisions to deal with variations to the active substance of authorised COVID-19 vaccines.

2. CONSULTATIONS PRIOR TO THE ADOPTION OF THE ACT

Member States' experts were consulted in the context of the Pharmaceutical Committee[4], which discussed the matter on 19 February 2021.

3. LEGAL ELEMENTS OF THE DELEGATED ACT

The legal basis of this Delegated Regulation is Article 23b of Directive 2001/83/EC and Article 16a of Regulation (EC) No 726/2004, which empower the Commission to adopt delegated acts specifying the categories in which variations are to be classified; and establishing procedures for the examination of applications for variations to the terms of the marketing authorisation.

The delegated powers should be used to amend Commission Regulation (EC) No 1234/2008, which governs the examination of variations for medicinal products for human use and veterinary medicinal products.

The proposed changes to Commission Regulation (EC) No 1234/2008 address the need to specify the applicable provisions for adaptations of the active substance of authorised COVID-19 vaccines in order to ensure their effectiveness against mutations or variants of the virus that may evolve over time. In this regard, it seems appropriate to use procedures that have been established for human influenza vaccines in the context of a pandemic. This will ensure the streamlined handling of any variation and enable the competent authorities to respond to specific needs arising from the COVID-19 pandemic and the associated public health crisis. It seems appropriate to extend the coverage of the new provisions to all coronaviruses, again building on the approach used in the past for human influenza vaccines, where the provisions are applicable to all forms of human influenza.

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1 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).

2 Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1).

3 Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7).

4 Council Decision of 20 May 1975 setting up a pharmaceutical committee (OJ L 147, 9.6.1975, p.23).

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THE EUROPEAN COMMISSION,

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

Having regard to 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[5], and in particular Article 23*b* thereof,

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[6], and in particular Article 16*a*(3) thereof,

Whereas:

(1) Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus (SARS-CoV-2). On 30 January 2020, the World Health Organization (WHO) declared the outbreak of COVID-19 a public health emergency of international concern. On 11 March 2020, it characterised COVID-19 as a pandemic.

(2) The COVID-19 pandemic has given rise to an unprecedented public health emergency that has claimed hundred thousands of lives worldwide, affecting in particular older people and those with underlying or pre-existing health conditions.

(3) COVID-19 is a complex disease that affects multiple physiological processes. COVID-19 vaccines are considered an efficient medical countermeasure during the ongoing pandemic, for the protection of particularly vulnerable groups and the population as a whole.

(4) Based on the scientific assessment by the European Medicines Agency, the Commission has thus far authorised several COVID-19 vaccines.

(5) Mutations of the SARS-CoV-2 virus are a natural phenomenon and to be expected. Authorised vaccines are not necessarily less effective against mutations, but there is a risk that they may be.

(6) In order to ensure the continued effectiveness of authorised COVID-19 vaccines, it may be necessary to modify them in ways that involve changing their composition so as to protect against new or multiple variant strains in the context of the pandemic or otherwise. Such changes, which include the replacement or addition of a serotype,

[5] OJ L 311, 28.11.2001, p. 67.
[6] OJ L 136, 30.4.2004, p. 1.

strain or antigen or a combination of serotypes, strains or antigens, should be considered as variations to the marketing authorisation in accordance with Commission Regulation (EC) No 1234/2008[7]. Some vaccines are based on nucleic acid technology to produce an immune response. Modifications of those vaccines may include changes to the coding sequence.

(7) The same approach should be followed for all human coronaviruses.

(8) The provisions on such variations should be streamlined, especially during a pandemic. In line with the approach taken with human influenza vaccines, the procedures should apply to all human coronavirus vaccines and follow an accelerated timetable. However, where the competent authorities request additional data in the course of their assessment, they should not be required to take a decision until the assessment of that data has been finalised.

(9) During a pandemic, it may be in the interest of public health to process variations on the basis of less comprehensive data than is normally the case. However, this approach should be subject to a requirement that the data be complemented subsequently, with a view to confirming that benefit-risk balance remains favourable.

(10) Regulation (EC) No 1234/2008 should therefore be amended accordingly,

HAS ADOPTED THIS REGULATION:

Article 1

Regulation (EC) No 1234/2008 is amended as follows:

(1) Article 21 is replaced by the following

'*Article 21*

Pandemic situation with respect to human influenza and human coronavirus

(1) By way of derogation from Chapters I, II, IIa and III, where a pandemic situation with respect to human influenza or human coronavirus is duly recognised by the World Health Organization or by the Union in the framework of Decision No 1082/2013/EU of the European Parliament and of the Council[*], the relevant authorities, or in the case of centralised marketing authorisations, the Commission may, where certain pharmaceutical, non-clinical or clinical data are missing, exceptionally and temporarily accept a variation to the terms of a marketing authorisation for a human influenza vaccine or a human coronavirus vaccine.

(2) The relevant authority may request the applicant to provide supplementary information in order to complete its assessment within a time limit set by it.

(3) Variations may be accepted pursuant to paragraph 1 only if the benefit-risk balance of the medicinal product is favourable.

[7] Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7).

[*] Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC (OJ L 293, 5.11.2013, p. 1).

(4) Where a variation is accepted pursuant to paragraph 1, the holder shall submit the missing pharmaceutical, non-clinical and clinical data within a time limit set by the relevant authority.

(5) In the case of centralised marketing authorisations, the missing data and the time limit for submission or compliance shall be specified in the conditions to the marketing authorisation. Where the marketing authorisation has been granted in accordance with Article 14-a of Regulation (EC) No 726/2004 this may be done as part of the specific obligations referred to in paragraph 4 of that Article.'

(2) In point (a) of Article 23(1*a*) the following point (ix) is added:

'(ix) variations related to changes to the active substance of a human coronavirus vaccine, including replacement or addition of a serotype, strain, antigen or coding sequence or combination of serotypes, strains, antigens or coding sequences;'

(3) In point 1 of Annex I, point (c) is replaced by the following:

'(c) replacement of a biological active substance with one of a slightly different molecular structure where the efficacy and/or safety characteristics are not significantly different, with the exception of:

– changes to the active substance of a seasonal, pre-pandemic or pandemic vaccine against human influenza;

– replacement or addition of a serotype, strain, antigen or coding sequence or combination of serotypes, strains, antigens or coding sequences for a human coronavirus vaccine;

– replacement or addition of a serotype, strain, antigen or combination of serotypes, strains or antigens for a veterinary vaccine against avian influenza, foot-and-mouth disease or bluetongue;

– replacement of a strain for a veterinary vaccine against equine influenza;'

(4) In point 2 of Annex II the following point (l) is added:

'(l) variations related to the replacement or addition of a serotype, strain, antigen or coding sequence or combination of serotypes, strains, antigens or coding sequences for a human coronavirus vaccine.'

Article 2

This Regulation shall enter into force on the third 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, 24.3.2021

For the Commission
The President
Ursula VON DER LEYEN