EUROPEAN
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COMMISSION DELEGATED REGULATION (EU) …/...

of 26.5.2021

supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council by establishing the criteria for the designation of antimicrobials to be reserved for the treatment of certain infections in humans

(Text with EEA relevance)

EXPLANATORY MEMORANDUM

1. CONTEXT OF THE DELEGATED ACT

Regulation (EU) 2019/6 of the European Parliament and of the Council lays down rules for the placing on the market, manufacturing, import, export, supply, distribution, pharmacovigilance, control and use of veterinary medicinal products.

Antimicrobial resistance to medicinal products for human use and to veterinary medicinal products is a major health threat that is growing both at Union and global levels. In order to preserve as long as possible the efficacy of certain antimicrobials in the treatment of infections in humans, including those of 'last resort', it has become necessary to reserve these antimicrobials for use in humans only and subsequently to ban their use in animals. It is the scope of the present Delegated Regulation to establish the criteria to designate such antimicrobials to be reserved for the treatment of certain infections in humans, in accordance with Article 37(4) of Regulation (EU) 2019/6.

It is worthwhile mentioning that, in line with Article 37(5) of Regulation (EU) 2019/6, a list of antimicrobials to be reserved for treatment of certain infections in humans shall be established in an implementing act, based on the criteria defined in the present Delegated Regulation. Those antimicrobials, which will have been designated in the Union as reserved for human use will not be authorised for use in animals in the Union. In addition, given the international dimension of antimicrobial resistance, they will not be authorised for use in animals or in products of animal origin to be exported from Third Countries into the Union, in accordance with Article 118 of Regulation (EU) 2019/6.

2. CONSULTATIONS PRIOR TO THE ADOPTION OF THE ACT

In accordance with Article 147(5) of Regulation (EU) 2019/6, the Commission has carried out substantial consultation with Member States' experts on veterinary medicines, who generally supported the content of the present Delegated Regulation.

In addition, the Commission consulted the European Medicines Agency (EMA) for scientific advice. The advice took into account the views from the European Centre for Disease Prevention and Control (ECDC) and from the European Food Safety Authority (EFSA). It also took into account relevant recommendations from international organisations, such as the World Health Organization (WHO) and the World Organisation for Animal Health (OIE). Moreover, the Commission carried out targeted stakeholder consultations on the scientific advice provided by EMA.

This Delegated Regulation was also made available to the European Parliament and the Council.

There were no comments received from the Council.
There were no comments received from the European Parliament.

In addition, stakeholders' comments on the draft Delegated Regulation were collected in the context of the Better Regulation feedback mechanism during the period between 26 March 2021 and 23 April 2021. Comments from five non-governmental organisations representing veterinarians, one medical association, two business associations and one citizen representing the pharmaceutical industry, six associations/organisations representing the agri-food sector, two consumer organisations, one citizen and three non-EU countries were received via the online

platform 'Have your Say'[1]. Comments from an additional non-EU country and a public authority from an EU country were sent by email to the relevant Commission services.

A sizeable proportion of the comments requested to add new provisions to clarify the process that would be followed by the Commission to establish the list of antimicrobials to be reserved for use in human medicine, based on the criteria described in the present Delegated Regulation. The comments also included the request to describe, as part of this process, the mechanism that would be followed to determine whether there would be an overriding public health interest that would justify that an antimicrobial is reserved for use in human medicine, provided that the absence of its use in veterinary medicine would only trigger limited morbidity or mortality. Comments indicated that this process should be transparent and that relevant stakeholders should be consulted. The Commission fully agrees that it is essential to have a science-based assessment of which antimicrobials should be reserved for use in human medicine and that national authorities, together with relevant stakeholders, should be consulted on the list of antimicrobials proposed. The list itself will be established in an Implementing Regulation, based on the criteria defined in the present Delegated Regulation. However, this process is outside the scope of the present Delegated Regulation. The scope is indeed, in accordance with Article 37(4) of Regulation (EU) 2019/6 to define the criteria that will be used to establish a list of antimicrobials to be reserved for the treatment of certain infections in humans. For this reason, the Commission did not include any provisions describing the process of the application of these criteria.

Other comments underlined that the criteria partially rely on measurable parameters, such as 'significant morbidity or significant mortality' or 'the limited treatment alternatives available', without specifying a corresponding numerical value that would allow to indisputably determine whether the criterion is fulfilled or not. The Commission wishes to emphasise that it did not provide such numerical values within the present Delegated Regulation, as these would vary depending on a range of parameters considered, such as, for example, the antimicrobial considered, the micro-organism and disease considered or the animal species concerned, making it unrealistic to draw up an exhaustive list. The Commission, in line with Article 37(6) of Regulation (EU) 2019/6, will take into account the scientific advice of the EMA, the EFSA and the ECDC, whose experts will jointly evaluate on a case-by-case basis, which antimicrobials fulfil the three criteria set in the present Delegated Regulation and should thus be included in the Implementing Regulation establishing the list of those antimicrobials to be reserved for use in human medicine. This scientific assessment will be published by the EMA in a scientific advice report, which will be available to the general public to ensure transparency.

It was also mentioned in some comments that the criterion of 'risk of transmission of resistance' was too strict and would likely result in no new antimicrobials being authorised for the veterinary market in the future, as all antimicrobials theoretically have a 'potential' for cross-resistance or co-selection of resistance to other antimicrobials. The Commission wishes to clarify that for this criterion to be met, there should be scientific evidence showing that there is such a potential but also scientific evidence showing that this transmission from animal sources to humans would likely be significant and linked to the use of this antimicrobial or group of antimicrobials in animals. In addition, the Commission underlines that an antimicrobial cannot be included in the list of antimicrobials to be reserved for use in human medicine on the sole basis of the fulfilment of this criterion; indeed all three criteria defined in the present Delegated Regulation should be met.

Some stakeholders indicated their regret that the criteria do not make any distinction between the assessment of antimicrobials used in food-producing animal species and the assessment of antimicrobials used in companion animal species. The Commission wishes to specify that Regulation (EU) 2019/6 does not foresee that any distinction should be made in the drafting of the

[1] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/11570-Establishment-of-Criteria-for-the-designation-of-antimicrobials-reserved-for-human-use

criteria, depending on the animal species in which the antimicrobial may be used. However, Article 107(6) of Regulation (EU) 2019/6 foresees the possibility of restricting the use of certain antimicrobials outside the terms of their marketing authorisation to certain conditions and provides the possibility for the Commission to establish a list of antimicrobials subject to these conditions in an Implementing Regulation. Such conditions could include the restriction of the use of certain antimicrobials outside the terms of their marketing authorisation to certain animal species only, allowing, for example, the use of certain antimicrobials outside the terms of their marketing authorisations in companion animal species, but not in food-producing animal species. This provision thus provides for a very useful complementary tool to promote a prudent and responsible use of antimicrobials in veterinary medicine, while allowing for a more targeted approach.

3. LEGAL ELEMENTS OF THE DELEGATED ACT

In accordance with Article 37(4) Regulation (EU) 2019/6, the present delegated act is to establish the criteria for the designation of the antimicrobials, which are to be reserved for treatment of certain infections in humans in order to preserve the efficacy of those antimicrobials. These criteria should not only apply to antimicrobials that have not yet been authorised for the veterinary market but should also apply to antimicrobials in existing veterinary medicinal products, in line with Article 152(1) of Regulation (EU) 2019/6.

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THE EUROPEAN COMMISSION,

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

Having regard to Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC[2], and in particular Article 37(4) thereof,

Whereas:

(1) Regulation (EU) 2019/6 of the European Parliament and of the Council aims to enhance the internal market and increase the availability of veterinary medicinal products, while guaranteeing the highest level of public and animal health and environmental protection. In particular, it aims to contain the spread of antimicrobial resistance with concrete measures to promote a prudent and responsible use of antimicrobials in animals, in line with the 'One Health' approach[3].

(2) Although the efficacy of all antimicrobials is important to preserve public health, some antimicrobials are deemed more crucial than others, based on being preferred options for the treatment of serious infections in humans and the availability or lack of alternative treatment options. When antimicrobial resistance develops to an antimicrobial agent used to treat a specific infection for which there are no treatment alternatives and that resistance spreads, the consequences to public health are significant and potentially life-threatening. Human health, animal health and the environment are interlinked and are all essential parts of the 'One Health' approach, thus antimicrobial management in one sector may affect antimicrobial resistance in the other sectors.

(3) Article 37(4) of Regulation (EU) 2019/6 requires the Commission to adopt delegated acts establishing criteria that will allow the Commission to determine which antimicrobials or groups of antimicrobials should be reserved for human use.

(4) Various international organisations and countries have developed criteria for specifying or ranking the importance of antimicrobials or antimicrobial classes for human and veterinary medicine. Those criteria were developed for use in risk management strategies related to antimicrobial use in human healthcare settings and animal use. Prioritising critically important antimicrobials for humans is a valuable tool to support an evidence-based approach to risk management.

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2 OJ L 4, 7.1.2019 p. 43.

3 Commission Communication of 29 June 2017 on a European One Health Action Plan against Antimicrobial Resistance (COM(2017)0339).

(5) The criteria to determine which antimicrobials are to be reserved for human use should be clear and pertinent whilst reflecting the latest scientific evidence. Pursuant to Article 37(6), the Commission received advice from the European Medicines Agency ('the Agency') on 31 October 2019[4]. The Agency's advice has taken account of expert opinions from national competent authorities, the European Food Safety Authority and the European Centre for Disease Prevention and Control. In the context of the preparation of that advice, a scientific workshop involving members of the Agency's expert group and international organisations was organised in Brussels on 14 June 2019. The workshop allowed participants to exchange views and share expertise from a global perspective on the topic of how to establish such criteria. The outcome of those discussions was taken into consideration by the Agency's expert group in completing its advice and the Commission has taken into account that advice in accordance with Article 37(6) of Regulation (EU) 2019/6.

(6) While a number of countries within and outside the Union have implemented measures to restrict the use of certain antimicrobials, few have specific legislation for banning their use in veterinary medicine. Banning the use of an antimicrobial in animals is one of the most severe risk management measures that can be taken, thus such measures should be taken cautiously. Whenever possible, other existing risk management measures should be favoured, such as improving animal husbandry, biosecurity and herd or flock management, making a better use of vaccination and restricting the use of antimicrobials to specific circumstances.

(7) Antimicrobials to be used only for treatment of certain infections in humans should be designated on the basis of sound criteria. Those criteria should allow to identify those antimicrobials that are of high importance to preserve human health and that should therefore be considered for use in human medicine exclusively. The criteria should also enable to identify those antimicrobials, whose use in animals could accelerate the spread of antimicrobial resistance, or present a risk thereof, by allowing for the transmission of resistance, which may include cross-resistance or co-selection of resistance to other antimicrobials, from animals to humans. Finally, the criteria should allow to identify antimicrobials that do not represent an essential need for animal health, and whose absence of use in veterinary medicine would not lead to any significant negative impact on animal health.

(8) While assessing whether an antimicrobial could be reserved for the treatment of certain infections in humans, it is important to determine whether its absence of use in veterinary medicine would result in significant morbidity or significant mortality or would have a major impact on animal welfare and public health. In the latter case, the availability of adequate alternative medicinal products for the treatment of the diseases concerned in the animals species concerned should be considered.

(9) When considering the use of alternative medicinal products instead of certain antimicrobial medicinal products, it is important that those products are adequate and available. Such alternatives should be authorised medicinal products in suitable formulations for the treatment of the disease in the animal species requiring treatment. Their use should lead to a lower risk to public health in terms of antimicrobial resistance than the antimicrobial medicinal product it aims to replace.

[4] Advice on implementing measures under Article 37(4) of Regulation (EU) 2019/6 on veterinary medicinal products – Criteria for the designation of antimicrobials to be reserved for treatment of certain infections in humans (EMA/CVMP/158366/2019)

(10) In exceptional cases where there is scientific evidence showing an overriding public health interest, the criterion of non-essential need to animal health should envisage the possibility for an antimicrobial to be reserved for human use, even if no alternative medicinal product is available for veterinary medicine, provided that not using such an antimicrobial would only result in limited morbidity or limited mortality. In such exceptional cases, the fulfilment of the other two criteria (high importance to human health and risk of transmission of resistance) should be still required for such an antimicrobial to be reserved for human use.

(11) Article 152(1) of Regulation (EU) 2019/6 indicates that existing products authorised in accordance with the previous legislation is to be deemed to be authorised in accordance with the Regulation, with the exception of authorisations of veterinary medicinal products containing antimicrobials that have been reserved for human use only. The criteria in the present act apply to antimicrobials that have not yet been authorised for the veterinary market but also apply to antimicrobials in existing veterinary medicinal products.

(12) It is recognised that the necessary available evidence to assess the fulfilment of the criteria may vary depending on the marketing authorisation status of the antimicrobial or group of antimicrobials considered: (1) authorised in human medicine only; (2) authorised in veterinary medicine only; (3) authorised both in human and veterinary medicine; (4) authorised neither in human nor veterinary medicine. For that reason, the available evidence should be taken into account while applying the criteria.

(13) This Regulation should apply from 28 January 2022 in accordance with Article 153(2) of Regulation (EU) 2019/6,

HAS ADOPTED THIS REGULATION:

Article 1

1. The criteria for the designation of antimicrobials to be reserved for the treatment of certain infections in humans are set out in the Annex.

2. An antimicrobial or a group of antimicrobials shall meet all three criteria set out in Parts A, B and C in the Annex in order to be designated as reserved for treatment of certain infections in humans.

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*.

It shall apply from 28 January 2022.

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

Done at Brussels, 26.5.2021

For the Commission
The President
Ursula VON DER LEYEN