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DISCUSSION DOCUMENT

Implementing Act under Article 107(6) of Regulation 2019/6

1. Legal basis

Article 107(6) of Regulation 2019/6

The Commission may, by means of implementing acts, and taking into consideration scientific advice of the

Agency, establish a list of antimicrobials which:

- (a) shall not be used in accordance with Articles 112, 113 and 114; or
- (b) shall only be used in accordance with Articles 112, 113 and 114 subject to certain conditions.

When adopting those implementing acts, the Commission shall take account of the following criteria:

- (a) risks to animal or public health if the antimicrobial is used in accordance with Articles 112, 113 and 114;
- (b) risk for animal or public health in case of development of antimicrobial resistance;
- (c) availability of other treatments for animals;
- (d) availability of other antimicrobial treatments for humans;
- (e) impact on aquaculture and farming if the animal affected by the condition receives no treatment.

Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 145(2).

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2. Preamble

Whereas:

- (1) Regulation (EU) 2019/6 lays down, among others, the rules for use of veterinary medicinal products, including the requirement to use them in accordance with the terms of their marketing authorisations. Where there is no veterinary medicinal product authorised for a species or for an indication, or those authorised are not available, and in particular to avoid causing unacceptable suffering, veterinarians may, under their direct responsibility, use medicinal products outside the terms of their marketing authorisations in accordance with the rules laid down in Articles 112, 113 and 114.
- (2) To better preserve the efficacy of antimicrobials and contribute to the fight against antimicrobial resistance, Article 107(6) of Regulation (EU) 2019/6 provides for the possibility to restrict the use of certain antimicrobials in accordance with Articles 112, 113 and 114.
- (3) Article 114(3) of Regulation (EU) 2019/6 provides for the establishment, by means of implementing acts, of a list of substances used in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or substances contained in a medicinal product for human use authorised in the Union in accordance with Directive 2001/83/EC of the European Parliament and of the Council⁽¹⁾ or Regulation (EC) No 726/2004⁽²⁾ of the European Parliament and of the Council, which may be used in food-producing aquatic species in accordance with Article 114(1) of Regulation (EU) 2019/6. In order to ensure legal certainty for the competent authorities, veterinarians, animal keepers and economic operators concerned, as well as coherence between the provisions of this Regulation and the implementing acts to be adopted under Article 114(3), the scope of this Regulation should not include antimicrobials used in food-producing aquatic species until the list in accordance with Article 114(3) has been established. This Regulation may be amended as necessary thereafter.
- (4) Article 115(5) of Regulation (EU) 2019/6 provides for the establishment, by means of implementing acts, of a list of substances which are essential for the treatment of equine species, or which bring added clinical benefit compared to other treatment options available for equine species and for which the withdrawal period for equine species shall be six months. In order to ensure legal certainty for the competent authorities, veterinarians, animal keepers and economic operators concerned, as well as coherence between the provisions of this Regulation and the implementing acts to be adopted under Article 115(5), the scope of this Regulation should not include equine species until the list in accordance with Article 115(5) has been established. This Regulation may be amended as necessary thereafter.
- (5) When adopting measures in accordance with Article 107(6) of Regulation (EU) 2019/6, account should be taken of the criteria set in that Article. At the same time availability

⁽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)

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of veterinary medicinal products is to be ensured in order to protect animal health and welfare.

- (6) On the basis of the criteria laid down in Article 107(6) of Regulation (EU) 2019/6, the European Medicines Agency ('the Agency') evaluated ⁽³⁾ antimicrobials and groups of antimicrobials that have potential veterinary use in the Union, taking into consideration the latest available scientific evidence, Regulation (EC) 470/2009 ⁽⁴⁾ of the European Parliament and of the Council and any acts adopted on the basis thereof. The Agency also considered information collected from an 'open call for data' in which interested parties were invited to submit information on the uses and availability of antimicrobials in the Union to treat serious infections in animals, including uses outside the terms of a marketing authorisation, while also using various categorisations of antimicrobials developed by international organisations or the Agency as reference.
- (7) The antimicrobials and groups of antimicrobials included in the Annex to Commission Implementing Regulation (EU) No 2022/1255 ⁽⁵⁾ are prohibited for any use in animals, including uses in accordance with Articles 112, 113 and 114 of Regulation (EU) 2019/6. Therefore, the Agency did not evaluate those antimicrobials.
- (8) Commission Regulation (EC) No 1950/2006 ⁽⁶⁾ lists substances which are essential for the treatment of Equidae or which bring added clinical benefit compared to other treatment options available for Equidae. Therefore, the Agency did not evaluate the indications of the substances listed in that Regulation.
- (9) The Agency examined the various cases of use in accordance with Articles 112, 113 and 114 of Regulation (EU) 2019/6. This included use for indications, in animal species or via routes of administration not included in the terms of the marketing authorisation of veterinary medicinal products, use of medicinal products for human use authorised in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004, use of veterinary medicinal products prepared extemporaneously in accordance with the terms of a veterinary prescription and use of veterinary medicinal products authorised in a third country for the same animal species and same indication.
- (10) Pursuant to the Agency's advice, restrictions on the use in accordance with Articles 112, 113 and 114 of Regulation (EU) 2019/6 should be imposed in respect of nine groups of antibiotics (pseudomonic acids, rifamycins, riminofenazines, third- and fourth-generation cephalosporins, aminopenicillins in combination with beta-lactamase

⁽³⁾ Scientific advice under Article 107(6) of Regulation (EU) 2019/6 for the establishment of a list of antimicrobials which shall not be used in accordance with Articles 112, 113 and 114 of the same Regulation or which shall only be used in accordance with these articles subject to certain conditions (EMA/CVMP/151584/2021, 15 June 2023)

⁽⁴⁾ Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council (OJ L 152, 16.6.2009, p. 11)

⁽⁵⁾ Commission Implementing Regulation (EU) 2022/1255 of 19 July 2022 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans, in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council (OJ L 191, 20.7.2022, p. 58)

⁽⁶⁾ Commission Regulation (EC) No 1950/2006 of 13 December 2006 establishing, in accordance with Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products, a list of substances essential for the treatment of equidae (OJ L 367, 22.12.2006, p. 33)

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inhibitors, quinolones (including fluoroquinolones), polymyxins, amphenicols and substances used solely to treat tuberculosis or other mycobacterial diseases), one antiviral substance (remdesivir), one antifungal class (echinocandins) and one substance with antiprotozoal action (amphotericin B).

- (11) The use of certain antimicrobials in accordance with Articles 112, 113 and 114 should be subject to target pathogen identification and susceptibility testing. However, this is not always possible in practice. In these cases, the veterinarian responsible should be able to justify why the use of a certain antimicrobial was not based on such testing. In other cases, treatment of the animals needs to be initiated without delay. Under such circumstances, the veterinarians responsible should be allowed to start treatment before the results of target pathogen identification or antimicrobial susceptibility testing are known.
- (12) Where an antimicrobial is already authorised for use in species other than those referred to in Article (4), point (29), subpoint (b) of Regulation (EU) 2019/6, the relative extent of the additional exposure due to use in a species referred to in Article (4), point (29), subpoint (b) of that regulation is likely to be relatively small. In addition, there are fewer antimicrobial veterinary medicinal products authorised for use in sheep, including sheep for meat production. Therefore, considering the need to ensure availability of treatments for the species referred to in Article (4), point (29), subpoint (b) of Regulation (EU) 2019/6 and for sheep, to maintain the welfare of those species and not to disadvantage these sectors, the condition for target pathogen identification and susceptibility testing should not be imposed on the use of antimicrobial medicinal products in accordance with Article 112 or 113 of Regulation (EU) 2019/6 in those species where the veterinary medicinal product is authorised for use in species other than those referred to in Article (4), point (29), subpoint (b) of Regulation (EU) 2019/6.
- (13) With a view to giving competent authorities, veterinarians, animal keepers and economic operators concerned the necessary time to adapt to the provisions laid down in this Regulation, it should apply [...] after its entry into force.
- (14) The list of antimicrobials in this Regulation should be kept under continual review in the light of new scientific evidence or emerging information, including the emergence of new diseases, changes in the epidemiology of existing diseases, changes in antimicrobial resistance or changes in availability or patterns of antimicrobial use, as well as the marketing authorisation of new veterinary medicinal products or medicinal products for human use.

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3. Articles

Scope

This Regulation applies to the use of antimicrobials in accordance with Articles 112 or 113 of Regulation (EU) 2019/6 in animal species other than equine species.

Conditions on the use of antimicrobials in accordance with Articles 112 or 113 of Regulation (EU) 2019/6

1. For the purpose of Articles 112 or 113 of Regulation (EU) 2019/6, the antimicrobials or groups of antimicrobials listed in the Annex shall be used subject to the conditions applicable to them as specified in that Annex.
2. The conditions applicable to the respective antimicrobials or groups of antimicrobials listed in the Annex shall be cumulative.

Derogations from the condition for prior pathogen identification and susceptibility testing

1. By way of derogation from the previous article, the condition for prior pathogen identification or susceptibility testing may be waived where the veterinarian responsible can demonstrate that such testing is not possible.
2. By way of derogation from the previous article, in the cases where it is necessary to start treatment whilst waiting for the results of target pathogen identification or antimicrobial susceptibility testing, the veterinarian responsible may use the antimicrobial concerned based on other relevant information such as the animal's clinical condition or medical history, epidemiological information and knowledge of susceptibility of the target pathogen at farm, local or regional level.
3. The condition for prior pathogen identification or susceptibility testing shall not apply where the antimicrobial veterinary medicinal product concerned is authorised for any of the species referred to in Article (4), point (29), subpoint (b) of Regulation (EU) 2019/6 and is to be used in accordance with Articles 112 or 113 of that Regulation in animal species other than those species or in sheep.

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Entry into force and application

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 [OP please insert the date = X months after the date of entry into force of this Regulation].

Question for the Member States

How much time is needed for the national competent authorities, veterinarians, animal keepers and economic operators to adapt to the provisions of this Regulation?

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5. Annex

Antimicrobial class/substance	Conditions on the use in accordance with Articles 112 and 113 of Regulation (EU) 2019/6
Aminopenicillins in combination with beta-lactamase inhibitors	<p>1. In the cases of use of aminopenicillins in combination with beta-lactamase inhibitors for indications not included in the terms of the marketing authorisation of a medicinal product authorised in the Union and containing those antimicrobials, the veterinarian responsible shall prescribe those antimicrobials based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that:</p> <ul style="list-style-type: none"> a. aminopenicillins in combination with beta lactamase inhibitors are likely to be effective; and b. antibiotics from a lower risk category in accordance with the Categorisation of antibiotics in the European Union ⁽⁷⁾, or in accordance with stricter rules in place at national level, would not be effective. <div data-bbox="635 1305 1422 1675" style="border: 1px solid black; padding: 10px; margin: 10px 0;"> <p>Questions for the Member States</p> <p>Would reference to AMEG categorisation be sufficient here?</p> <p>Are there national categorisations in place for the use of antimicrobials in animals? If yes, are these categorisations stricter than AMEG categorisation?</p> </div> <p>2. The use in accordance with Article 113 shall be prohibited in poultry.</p>

⁷ Categorisation of antibiotics in the European Union Answer to the request from the European Commission for updating the scientific advice on the impact on public health and animal health of the use of antibiotics in animals (EMA/CVMP/CHMP/682198/2017)

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Antimicrobial class/substance	Conditions on the use in accordance with Articles 112 and 113 of Regulation (EU) 2019/6
Third- and fourth-generation cephalosporins	<ol style="list-style-type: none"> 1. In the cases of use of third- or fourth-generation cephalosporins for indications not included in the terms of the marketing authorisation of a medicinal product authorised in the Union and containing those antimicrobials, the veterinarian responsible shall prescribe those antimicrobials based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing. Such testing shall demonstrate that: <ol style="list-style-type: none"> a. third or fourth generation cephalosporins are likely to be effective; and b. antibiotics from a lower risk category in accordance with the Categorisation of antibiotics in the European Union, or in accordance with stricter rules in place at national level, would not be effective. 2. The use shall be limited to administration to individual animals only. This condition shall not apply to the use in accordance with Article 112 in aquatic animals kept in closed water tanks. 3. The use in accordance with Article 113 shall be prohibited in poultry. 4. In the cases of treatment of salmonellosis in animals other than poultry, the use in accordance with Article 113 shall be limited to injectable medicinal products administered to individual animals with potentially life-threatening infections.
Polymyxins	<ol style="list-style-type: none"> 1. In the cases of use of polymyxins for indications not included in the terms of the marketing authorisation of a medicinal product authorised in the Union and containing those antimicrobials, the veterinarian responsible shall prescribe those antimicrobials based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.

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	<p>Such testing shall demonstrate that:</p> <ul style="list-style-type: none"> a. polymyxins are likely to be effective; and b. antibiotics from a lower risk category in accordance with the Categorisation of antibiotics in the European Union, or in accordance with stricter rules in place at national level, would not be effective. <p>2. The use in accordance with Article 113 for the treatment or metaphylaxis of salmonellosis in poultry shall be prohibited.</p> <p>3. In the cases of group treatment or metaphylaxis of salmonellosis in animals other than poultry, the use in accordance with Article 113 of medicinal products, which are authorised for oral administration to groups of animals, shall be prohibited.</p> <p>4. In each of the following cases the administration of the medicinal product shall be limited to individual animals only:</p> <ul style="list-style-type: none"> a. use of a veterinary medicinal product in accordance with Article 112 or Article 113 via a route of administration not included in the terms of its marketing authorisation; b. use of a medicinal product for human use authorised in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004; c. use of a veterinary medicinal product prepared extemporaneously in accordance with the terms of a veterinary prescription.
Amphenicols	<p>In the cases of use of amphenicols for indications not included in the terms of the marketing authorisation of a medicinal product authorised in the Union and containing those antimicrobials, the veterinarian responsible shall prescribe those antimicrobials based, where possible, on prior target</p>

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	<p>pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that:</p> <ol style="list-style-type: none"> a. amphenicols are likely to be effective; and b. antibiotics from a lower risk category in accordance with the Categorisation of antibiotics in the European Union, or in accordance with stricter rules in place at national level, would not be effective.
Quinolones (including fluoroquinolones)	<ol style="list-style-type: none"> 1. In the cases of use of quinolones (including fluoroquinolones) for indications not included in the terms of the marketing authorisation of a medicinal product authorised in the Union and containing those antimicrobials, the veterinarian responsible shall prescribe those antimicrobials based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing. <p>Such testing shall demonstrate that:</p> <ol style="list-style-type: none"> a. quinolones (including fluoroquinolones) are likely to be effective; and b. antibiotics from a lower risk category in accordance with the Categorisation of antibiotics in the European Union, or in accordance with stricter rules in place at national level, would not be effective. <ol style="list-style-type: none"> 2. The use in accordance with Article 113 for the treatment or metaphylaxis of salmonellosis shall be prohibited in poultry. 3. The use in accordance with Article 113 for metaphylaxis of salmonellosis in animal other than poultry shall be prohibited. 4. In the cases of treatment of salmonellosis in animals other than poultry, the use in accordance with Article 113 shall be limited to

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Antimicrobial class/substance	Conditions on the use in accordance with Articles 112 and 113 of Regulation (EU) 2019/6
	<p>injectable medicinal products administered to individual animals with potentially life-threatening infections.</p> <p>5. In each of the following cases the administration of the medicinal product shall be limited to individual animals only:</p> <ul style="list-style-type: none"> a. use of a veterinary medicinal product in accordance with Article 112 or 113 via a route of administration not included in the terms of its marketing authorisation; b. use of a medicinal product for human use authorised in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004; c. use of a veterinary medicinal product prepared extemporaneously in accordance with the terms of a veterinary prescription.
Rifamycins except rifaximin	<p>The following conditions shall apply to use in accordance with Article 112(1)(b) and (c) and Article 112(2):</p> <p>1. The veterinarian responsible shall prescribe rifamycins except rifaximin, based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that:</p> <ul style="list-style-type: none"> a. rifamycins are likely to be effective; and b. antibiotics from a lower risk category in accordance with the Categorisation of antibiotics in the European Union, or in accordance with stricter rules in place at national level, would not be effective. <p>2. The use shall be limited to administration to individual animals for treatment of mycobacteria or multidrug-resistant staphylococci only.</p>

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Rifaximin	<p>The following conditions shall apply to use in accordance with Article 112(1)(b) and (c), Article 112(2), Article 113(1)(c) and (d) and Article 113(2):</p> <ol style="list-style-type: none"> <li data-bbox="497 517 1417 1066"> <p>The veterinarian responsible shall prescribe rifaximin, based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that:</p> <ol style="list-style-type: none"> <li data-bbox="571 792 1134 831">rifaximin is likely to be effective, and <li data-bbox="571 864 1410 1066">antibiotics from a lower risk category in accordance with the categorisation of antibiotics in the European Union, or in accordance with stricter rules in place at national level, would not be effective. <li data-bbox="497 1099 1423 1245"> <p>The use shall be limited to administration to individual animals for treatment of mycobacteria or multidrug-resistant staphylococci only.</p>
Substances used solely to treat tuberculosis or other mycobacterial diseases	<ol style="list-style-type: none"> <li data-bbox="497 1301 1423 1626"> <p>The veterinarian responsible shall prescribe substances used solely to treat tuberculosis or other mycobacterial diseases, based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that those substances are likely to be effective.</p> <li data-bbox="497 1671 1410 1738"> <p>The use shall be limited to administration to individual animals only.</p>
Riminofenazines	<ol style="list-style-type: none"> <li data-bbox="544 1798 1423 1944"> <p>The veterinarian responsible shall prescribe riminofenazines, based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that riminofenazines are likely</p>

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	<p>to be effective.</p> <p>2. The use shall be limited to administration to individual animals only.</p>
Pseudomonic acids	<p>1. The veterinarian responsible shall prescribe pseudomonic acids, based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that:</p> <ul style="list-style-type: none"> a. pseudomonic acids are likely to be effective; and b. antibiotics from a lower risk category in accordance with the Categorisation of antibiotics in the European Union, or in accordance with stricter rules in place at national level, would not be effective. <p>2. The use shall be allowed only where all of the following conditions are met:</p> <ul style="list-style-type: none"> a. the medicinal product is to be used for the treatment of methicillin-resistant <i>Staphylococcus aureus</i> or methicillin-resistant <i>Staphylococcus pseudintermedius</i>; b. the medicinal product is to be used after veterinary medicinal products authorised for the treatment for staphylococcal infections via the topical route of administration had not been effective; c. the medicinal product is to be administered to individual animals; and d. the medicinal product is to be administered via the topical route of administration.

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	3. The use for routine decolonisation of methicillin-resistant <i>Staphylococcus aureus</i> or methicillin-resistant <i>Staphylococcus pseudintermedius</i> shall be prohibited.
Remdesivir	The use shall be allowed only in accordance with Article 112 for the treatment of feline infectious peritonitis.
Echinocandins	<p>1. The veterinarian responsible shall prescribe echinocandins, based, where possible, on prior target pathogen identification and antimicrobial susceptibility testing.</p> <p>Such testing shall demonstrate that those antimicrobials are likely to be effective.</p> <p>2. The use shall be allowed only where all of the following conditions are met:</p> <ul style="list-style-type: none"> a. the medicinal product is to be administered to individual animals only, and; b. the medicinal product is to be administered as a last resort.
Amphotericin B	In the case of treatment of leishmaniasis, or of other diseases in animals in regions where leishmaniasis is endemic, the use shall be allowed only as a last resort.