

**EMA ADVICE ON CRITERIA FOR THE DESIGNATION OF
ANTIMICROBIALS TO BE RESERVED FOR THE TREATMENT
OF CERTAIN INFECTIONS IN HUMANS**
FVE Input

Background:

- Regulation 2019/6 on veterinary medicinal products lays down in article 37(4) that the Commission shall adopt a delegated act laying down criteria for the designation of antimicrobials reserved for treatment of certain infections in humans, in order to preserve the efficacy of these antimicrobials.
- On 6 February 2019 the European Commission sent the [mandate](#) to the European Medicines Agency. The European Medicines Agency delivered its [advice](#) on 31 October 2019.
- FVE welcomes the opportunity to provide comments on the EMA advice.

Main inputs FVE:

FVE welcomes the EMA advice, which is **well-balanced and science-based**. We support that only antimicrobials can be considered to be banned or restricted if they **meet all 3 of the defined main criteria**, namely be a ‘last-resort’ medicine in human health, have a high risk for resistance transfer and be of low importance for animal health.

As recognised in the advice, banning antimicrobials for animals is the **most severe risk management measure possible**, and should be used with the greatest discretion, after all other risk management measures existing has been applied to preserve the efficacy of antimicrobials in human medicine.

FVE believes that the most effective way to fight antimicrobial resistance is to ensure prudent and responsible use, use as much possible the bacterial culture and antibacterial susceptibility testing (AST) and by focusing much more on the prevention of disease to avoid the need to treat animals and humans with antimicrobials.

Animals are sentient beings and deserve treatment too. The **inability to treat susceptible infection has serious implications for animal health and welfare and also for public health** (zoonotic pathogens can be bacterial, viral, or fungal, and they represent 70% of all human diseases). If a bacterial animal disease can't be treated in animals, the causative bacteria can spread, which can constitute a very significant risk

for subsequent infections to in-contact animals and/or humans or on food safety and security.

Now already the number of authorised antibiotic classes in human medicine is much higher than in veterinary medicines. The availability of antimicrobials is lower in animals (and specifically in some minor species or limited markets) and the conditions and restriction put on the use of antimicrobials in animals are much higher. **Banning certain antimicrobials will increase the pressure on the limited number of other alternative antimicrobials, which in turn might increase resistance.**

Restrictions are already being put in place and can further be implemented. Critically important antibiotics for both human as animal health, such as fluoroquinolones, 3th and 4th generation cephalosporins and colistin should not be used for prevention or as a first line treatment and their use should ideally be based on the results of bacteriological tests. Off-label use should be reserved for instances where no alternatives are available. The new Veterinary Medicines Regulation, which will come into force in 2022, also will put additional conditions and restrictions on the use of antibiotics in animals.

In the last decade, antibiotic use in animals has gone down substantially. The latest ESVAC report, published in October 2019, shows that sales of antibiotics for use in animals in Europe fell by 32% between 2011 and 2017. All EU countries have agreed on a national One Health action plan and are committed to further reduce antimicrobial use and especially the use of important antimicrobials (CIA's). In some countries, through the reduction in antibiotic use in animals, antimicrobial resistance in animal pathogens have also started to decrease. The new Veterinary Medicines Regulation with its additional conditions and restrictions on the use of antibiotics in animals, will lead most likely to a further decrease in antimicrobial use in animals. Unfortunately, antibiotic consumption in humans is not yet going down significantly.

For all the above reasons, we **strongly call to restrain from banning authorised antimicrobials for use in animals.** Banning antimicrobials for use in animals may in particular lead to a risk in cases with limited treatment options [e.g. with regard to mycoplasma infections in pigs].

Lastly, as these criteria will be used later to draft the implementing act, **third country impact will also be worth considering and how to effectively enforce this for imported animal products.**

More detailed comments:

- It would be worth to **define more in detail the criterion of the risk of resistance transfer** based on data defining the situation under veterinary use. This criterion remains complex, as both cross-resistance in medically important substances, all forms and routes of transfer (vertical, horizontal, mobile elements, etc.) and zoonotic organisms are mentioned as negative factors. **Transparent criteria should be developed to evaluate the risk, with e.g. a scale from low to high.**
- With regard to the transfer of resistance, there is also mentioning of a **significant carryover** (Point 4.2., Page 44), which requires a quantitative assessment. For this it would be helpful if the document could refer to a methodology or reference as to how this transfer is recorded. Since the

transfer of resistance is a very important aspect of the risk assessment, further detailing should be given.

- Recent research estimates that the use of antibiotics in animals contributes to the human antimicrobial burden for only a small part (EFFORT, Wageningen¹). It is clear that the human antibiotic burden is mostly caused by human antibiotic use, and similarly for animals. As such, **banning certain antibiotics for animals will have little effect on the human antibiotic burden**. The 2018 Lancet study² concludes that in Europe infections with antibiotic-resistant bacteria predominantly occur in hospitals and other health-care settings (63,5% of infections, 74,9% of the DALY's).
- Annex I list all the ranking of antimicrobials in importance for humans, it however misses ranking in the veterinary field.
- It would be important to **update the listing regularly** based on new scientific data and alternative treatment options.

¹ <https://www.wur.nl/en/newsarticle/Chance-of-ESBL-contamination-via-livestock-farming-is-small.htm>

² [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(18\)30605-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30605-4/fulltext)