

EU Delegated Act on criteria for reserving antimicrobials for human use only

Banning authorised antimicrobials for animals without scientific evidence will cause animal suffering and will endanger public health

WE CALL UPON MEPs TO APPROVE THE DELEGATED ACT

In January 2019, the new Regulation (EU) 2019/6 on veterinary medicinal products was adopted. This Regulation is planned to come into force in January 2022 in all EU Member States. In the meantime, tertiary legislation is produced to complement the core legislation.

One of the core objectives of this legislation is to increase the fight against antimicrobial resistance and to further promote prudent and responsible use of veterinary medicines, in particular antibiotics. The new legislation in this respect foresees¹:

- The use of antibiotics in animals is **only allowed on veterinary prescription** following a physical examination, good knowledge of the animal(s) and proper diagnosis including the use of diagnostic testing where appropriate. Veterinarians should prescribe the antibiotics based on their knowledge of antimicrobial resistance (AMR), their epidemiological and clinical knowledge and their understanding of the risk factors for the individual animal or group of animals;
- **Routine** prophylactic and metaphylactic use will not be allowed anymore; Use of growth promotion in the EU is already banned since 2006;
- **Individual treatment** prevails;
- **Strict rules on use of oral medication** via feed or water;
- **Following prescription, the supply of antimicrobials** by veterinarians should be **restricted to the amount required for treatment** of the animals under their care;
- **Strict monitoring and surveillance** of veterinary prescriptions via the European Surveillance of Antibiotic Consumption (ESVAC) moving to **use monitoring per species**;
- **Banning of advertisement** of antimicrobials to laypeople;

The new
Regulation on
Veterinary
Medical Products
will put in place
the strictest
measures to
promote
responsible and
prudent use in the
world!

¹ Infograph on main elements of new veterinary medicines legislation: https://fve.org/cms/wp-content/uploads/PLAQUETTE_FVE_web.pdf

- Introduction of **reciprocity** for import of animals and food products from third countries.

This new Regulation (EU) 2019/6 is instrumental to achieve the objectives of the “*Farm to Fork Strategy*” and its ambition to reduce antibiotic use by 50% by 2030². Veterinarians, as gatekeepers of animal health, animal welfare and public health, and prudent and responsible use of medicines in animals are crucial in the fight against AMR.

FVE recognises animal welfare is of utmost importance as animals that are well cared for and appropriately housed, will experience better welfare, be less prone to infections and will need fewer antibiotics³. However, **improving animal welfare standards**, e.g. in respect to the minimum weaning of piglets or stocking densities of farm animals, is **out of the scope** of the Veterinary Medicines Regulation. Currently, the European Commission is doing a fitness check to see which welfare legislation e.g. the transport Regulation, the Pig Directive, needs to be updated, this provides an instrument to improve animal welfare standards. Additionally, Regulation (EU) 2016/429, calls for the implementation of regular health visits by a veterinarian to ensure a regular health check of all farmed animals and early detection of health problems or disease.

Fighting AMR needs to be done by a scientifically sound ‘*One Health*’ approach

In the new legislation, legislators foresee the possibility for restriction of the use in animals of certain antimicrobials that are critically important for preventing or treating life-threatening infections in humans via a delegated act. When antimicrobials or antimicrobial classes are added to this list of reserved antimicrobials for humans, their marketing authorisation will be taken away. In other words, they will become completely unavailable for the use of animals, also not in individual cases.

The draft delegated act proposed by the European Commission is a prime example of a ‘*One Health*’ approach, being based on the **scientific** advice report from the **European Medicines Agency (EMA)** which considers expert opinions from **both the human health side and the animal health side**. It recognises that **human health goes beyond animal health, but puts in a safety net for animal health**. The advice also took into account input from the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) as well as from the World Health Organisation (WHO) and the World Organisation for Animal Health (OIE). The WHO lists all antimicrobials important in humans and **as WHO itself recommends⁴, that it should be used in combination with the OIE list**, which categorises all antimicrobial agents of veterinary importance for animals. It also went through an extensive consultation process.

The EMA scientific advice takes into account both the WHO as OIE list, but importantly also the European situation in respect to diseases and antimicrobial resistance.

² https://ec.europa.eu/commission/presscorner/api/files/attachment/865559/factsheet-farm-fork_en.pdf.pdf

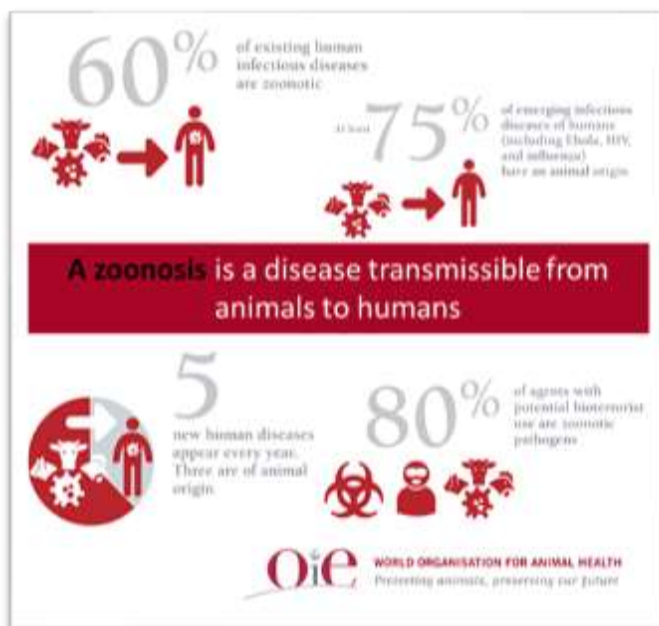
³ https://fve.org/cms/wp-content/uploads/063-FVE_AWW-Position-on-resistance-and-animal-welfare_final.pdf

⁴ <https://apps.who.int/iris/rest/bitstreams/1217095/retrieve> (page 2)

Sick animals deserve treatment

Animals are sentient beings⁵. They can get sick even under the best living conditions and will **feel pain** (all animals, including mammals, birds and fish, have an appropriate nervous system and sensory receptors) and **suffer** exactly as humans do. They can also be **sources for the spread of bacterial diseases to other animals and humans**. For these reasons, sick animals suffering from bacterial diseases deserve and must be treated with the appropriate antibiotics. Banning antibiotics for use in all animals, livestock and companion animals, likewise, is the **most severe risk management** measure possible and should be **avoided as much as possible**. When antimicrobial classes are placed on the reserve list, they will be totally prohibited for use in animals, under any circumstances. They will no longer be available for food-producing animals, companion animals, zoo animals and all other animals needing treatment.

Treating bacterial zoonotic infections in animals is important to protect human health



Protection of human health is also based on proper prevention and treatment of disease in animals (zoonotic pathogens can be bacterial, viral, fungal or due to protozoa and prions) and they represent 60% of all human diseases) – see figure 1. For this reason, the availability of antibiotics for animals is equally important for animals as it is for human health. That is why **categorisation of the antimicrobial classes by WHO comes with a strong recommendation that any restrictions should be decided in consideration with the OIE categorisation on the importance of the antibiotic for animal health⁶**.

Figure 1. OIE infographic on zoonoses

This is a science-based approach according to the *'One Health'* concept, namely that animals, humans and the environment are interconnected and their health is interlinked.

The inability to treat susceptible bacterial infection has **serious implications for animal health and animal welfare, and potentially for public health**. To allow a targeted treatment, it is important to have available a range of different antibiotic classes. By using the *'right'* antibiotic for a specific

⁵ EU Treaty, Article 13 - <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:12007L/TXT>

⁶ <https://apps.who.int/iris/rest/bitstreams/1217095/retrieve> (page 2)

bacterial disease, resistance building can be avoided. The restriction to few classes increases the selective pressure and leads to even faster development of AMR against these antimicrobial classes. Therefore, **banning authorised antimicrobials for ALL animals without any scientific argument and science-based reasons is contra-productive and will endanger animal health, welfare and human health.**

Reserving all HP CIA WHO antibiotics for humans will be catastrophic for animal and human health

Some voices are calling to include all WHO Highest Priority Critically Important Antibiotics (CIAs) or all WHO CIAs on the reserved list. It is worth considering what consequences this would have in practice.

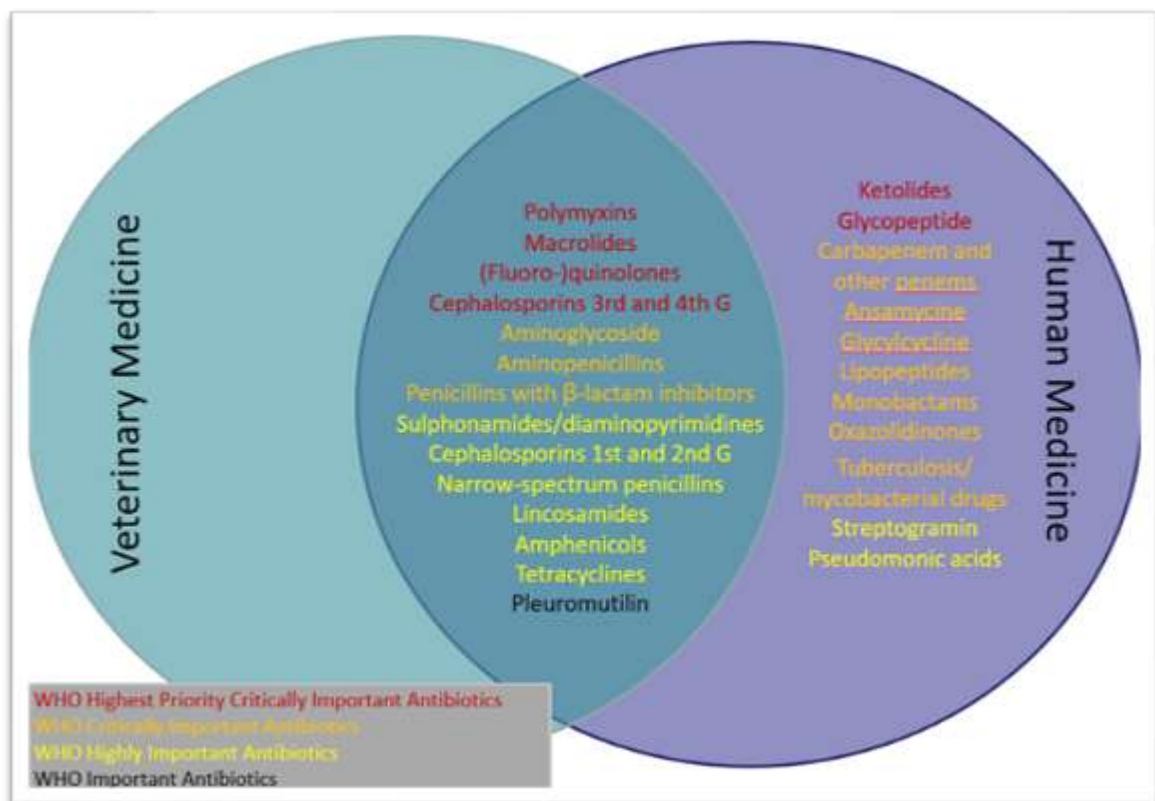


Figure 2. Availability and convergence of antibiotic classes for human and veterinary medicine depending on WHO categories

Figure 2 shows the number of antimicrobials authorised for human and veterinary medicines. The **first observation** which can be made is that many antimicrobial classes are authorised for human medicines (right column), which are not authorised and used in veterinary medicine. These antimicrobial classes are already reserved for human medicine and it is also clear that if new antimicrobial classes will be developed, these will also be authorised only for human health.

The **second observation** is that all antimicrobials used in veterinary medicines are all shared with the human health sector. Therefore, for the veterinary sector, it is of utter importance to keep this limited number of antimicrobials as effective as possible.

Lastly, the middle column presents all antimicrobials which are suggested to be banned for use in animals marked in red (the HP WHO CIA's) and orange (WHO CIA'). Some of these classes, like macrolides, include many sub-classes. **Banning these antimicrobial classes would mean that veterinarians lose more than half of the antimicrobial medicinal products on the market they have and more importantly would mean that many bacterial diseases in animals could no longer be treated.**

Please note that when antimicrobials are put on the reserved list, they will not only be banned for food-producing animals, but also companion animals and zoo animals, and no exceptions will be allowed.

As shown, the number of different antibiotics classes available for use in animals is very low and restricted compared to what is available in human medicine. Imposing additional restrictions without sound and convincing scientific arguments and going beyond the defined criteria in the delegated act, will cause significant animal health, and welfare problems and veterinary public health concerns as certain bacterial infections would no longer be able to be treated, such as enteric and respiratory infections in pigs, cattle and poultry, urogenital infections in dogs and cats and respiratory infections in horses (See detailed examples in table 1).

Effective, legal and convenient alternatives to HP-CIAs are lacking for managing common infections in cats, for which oral administration is difficult as well as for *Rhodococcus equi* infections in horses and MDR infections in all companion animal species. No valid and convenient alternatives to colistin and macrolides are available against certain porcine enteric and bovine respiratory pathogens. Moreover, long-acting formulations containing macrolides or extended-spectrum cephalosporins are widely used for individual treatment due to their pharmacokinetic specificities (short withdrawal periods and easy administration), which makes it possible to treat single diseased animals with reduced labour⁷.

⁷ Lhermie G, La Ragione RM, Weese JS, Olsen JE, Christensen JP, Guardabassi L. Indications for the use of highest priority critically important antimicrobials in the veterinary sector. *J Antimicrob Chemother.* 2020 Jul 1;75(7):1671-1680. doi: 10.1093/jac/dkaa104. PMID: 32240295.

Table 1. Examples of antibiotics by WHO category and indispensable indications in veterinary medicine

WHO category	Antibiotic class	Products authorized in veterinary medicine	Indispensable indications in veterinary medicine	
Critical important antibiotics	Highest priority	Polymyxins	Colistin (or polymyxin E), polymyxin B	Enteric diseases, specific etiologies (<i>E. coli</i>)
		Macrolides	Spiramycin, tylosin, tilmicosin, tildipirosin, tylvalosin, tulathromycin, gamithromycine	Respiratory diseases, specific etiologies (e.g. foot rot, <i>Mycoplasma</i>)
		(Fluoro)quinolones	Enrofloxacin, danofloxacin, difloxacin, ibafloxacin, flumequine, marbofloxacin	Sepsis, enteric diseases, specific pharmacokinetics
		Cephalosporins 3 th & 4 th G	Ceftiofur, Cefquinome, ceftiofur	Sepsis and pneumonia, specific pharmacokinetics
	High priority	Aminoglycosides	Apramycin, gentamycin, neomycin, streptomycin	Enteric diseases, specific etiologies (<i>Pseudomonas</i>)
		Penicillins with β -lactam	Amoxicillin-clavulanic acid	Urinary tract and skin infections
Highly important	Amphenicols	Florfenicol	Pneumonia, specific diseases in farmed fish (<i>Flavibacteria</i> , <i>Arcanobacterium</i> , Salmonid rickettsial septicemia)	
	Cephalosporins 1 st & 2 nd G	Cefalexin, cefalonium	Skin infections, mastitis	
	Narrow-spectrum penicillins	Penicillin G and penicillin V, penethamate, oxacillin, cloxacillin, nafcillin	Specific etiologies (<i>Staphylococcus aureus</i> incl. MRSA, <i>Streptococci</i>) including mastitis	
	Lincosamides	Clindamycin, lincocmycin, spectinomycin, pirlimycin	Specific etiologies (MRSA, <i>Mycoplasma</i>), joint infections, pig enteritis-mastitis	
	Sulphonamides/diaminopyrimidines	Trimethoprim/sulfamethoxazole	Specific etiologies (<i>Protozoa</i>)	
	Tetracyclines	Doxycycline, oxytetracycline	Specific etiologies (heartwater, anaplasmosis, vector -borne diseases)	
Important	Pleuromutilins	Tiamulin, valnemulin	Specific etiologies (respiratory diseases, swine dysentery)	
	Nitroimidazoles*	Metronidazole (*companion animals only)	Specific etiologies (Anaerobic bacteria)	
	Nitrofurantoin*	Furazolidone (*companion animals only)	Specific etiologies (urinary tract infections)	
	Polypeptides*	Bacitracin (*companion animals only)	Specific etiologies (skin infections)	

To give some concrete examples:

- In companion animals, certain infections such as *Mycoplasma haemofelis* causing infectious anemia, and others causing pneumonia, pyometra (infection of the uterus), peritonitis, pleuritis and skin infections would no longer be treatable. These infections are commonly seen, are very painful and can be life-threatening.
- In horses, treatment of *Rhodococcus equi* infections in foals (zoonotic infection and important infection for horse breeding), septicaemia in foals and treatment of some wound infections would no longer be possible.
- It would be almost impossible to treat specific zoonotic diseases due to multi-drug resistant (MDR) bacteria which pose a particular risk for public health, including Leptospirosis, infections with *Staphylococcus aureus*, *Escherichia coli* (sometimes in combination with *Clostridia*) and *Salmonella* spp.
- Infections in hard-to-reach tissues, such as joint, bone, teeth, eye, and nervous system infections as well as infections that require long-acting antibiotics to reduce handling time (e.g., in cats, wildlife and zoo animals) with high oral bioavailability (F) and volume of distribution (Vd).

- Many bacterial infections in horses, small mammals, reptiles and exotic animals could no longer be treated, as most important and highly important antibiotic classes are not tolerated or even toxic for them.
- In cattle, pigs and poultry, septicaemias, and enteric and respiratory infections especially with MDR bacteria would become impossible to treat

Is this really what we want? How do legislators plan to compensate for this **total lack of treatment options for ALL animal species** in such a situation where all important antibiotics are reserved for human use only? How will we treat animals carrying a zoonotic bacterial infection? How can we justify ethically the animal suffering we will cause?

When antimicrobial classes are placed on the reserve list, they will be totally prohibited for use in ALL animals, under any circumstances.

This will endanger public health and has also detrimental economic and social impact on animal owners, such as for European farmers, who will have to destroy herds and cull their flocks when diseases can no longer be treated. Moreover, European pet owners will be shocked by the loss of currently available effective treatment options for their companions. Given that the EU is taking without doubt already a leadership role in the fight against AMR and has the strictest rules already globally, this approach is highly disproportional.

Even if we stop all antibiotic use in animals, this will not solve the human AMR burden



It needs to be reiterated that **the ultimate target is the reduction of levels of antimicrobial resistance genes**. AMR is an extremely complex issue; no miracle solutions are available. The only way to solve it is to work via a 'One Health' approach, on all levels where we use antimicrobials and where resistance genes are detected. Water and the environment are also involved in the mechanism, resistance transfer can happen not only between animals and humans, but also from humans to animals, and to and from the environment. Residues of antibiotics in the wastewater of the cities, in soil and the aquifers near hospitals and big cities, are sufficient to create selective pressure and maintain the spread of AMR.

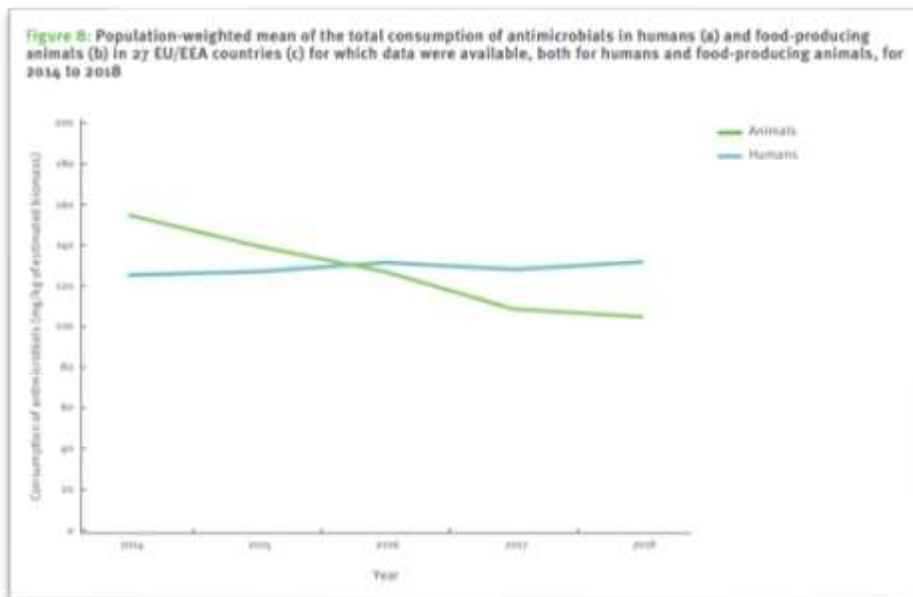
Figure 4. The three dimensions of the 'One Health' approach in relation to infectious diseases, non-communicable diseases, and AMR according to The Lancet [One Health Commission](#)

We need to use antibiotics ‘*as little as possible, as much as needed*’ both in the veterinary as human sectors. This can be done by a combination of **firstly** focusing on the prevention of disease applying biosecurity together with good housing, good feeding and herd health planning, together **secondly** with prudent and responsible use of antibiotics, by using bacterial culture and antibacterial susceptibility testing (AST) and individual treatment – as much as possible. A **true “One Health” approach must be considered, aiming at reducing the selective pressure on bacteria.**

The animal health sector is taking AMR and prudent use very seriously, having **already reduced antibiotic sales in the EU by 34% between 2011 and 2018. Some countries have even managed to reduce their antibiotic sales by more than 50 %.** In respect to **Critically Important Antibiotics (CIAs)** a **decreasing trend** is also seen, e.g. the sales of polymyxins (colistin) which reduced by 69.8 % between 2011-2018.

Antimicrobial use
in animals is lower
than in humans in
the EU

The third JIACRA report published on 30 June 2021⁸, looking at antibiotic use and resistance in both people and animals, and made by ECDC, EFSA and EMA, showed also clearly how the use of antibiotics in animals has decreased and is now **lower in food-producing animals than in humans.** In respect to



the WHO CIA’s, aminopenicillins, 3rd- and 4th-generation cephalosporins and quinolones (fluoroquinolones and other quinolones) are used more in humans than in food-producing animals, while polymyxins (colistin) is more used in food-producing animals.

Figure 5. Total consumption of antimicrobials in humans and food producing animals, weighted by population. Third JIACRA report (June 2021)

⁸ https://www.ema.europa.eu/en/documents/report/ema/ecdc/efsa-third-joint-report-integrated-analysis-consumption-antimicrobial-agents-occurrence_en.pdf

The animal health sector is strongly committed to go further, improving ‘*Prevention is better than cure*’, and as described in the EFSA and ECDC report⁹, by further working on **reducing** the need to use of antimicrobials, **replacing** them by alternatives and **rethinking** our livestock system by implementing farming practices that prevent the introduction and spread of disease¹. The new Regulation (EU) 2019/6 on veterinary medicines and newly planned legislation on animal welfare, will help in this way forward.

One thing we learned is ‘*we need to measure to improve*’. The EU started measuring the sales of antibiotics for animals more than a decade ago and as one of the only regions in the world, publishes annually a detailed report¹⁰. The new Regulation (EU) 2019/6 will go beyond and start the collection of use data per species, which will be very useful to further decide evidence-based measures to reduce the need for antibiotics.

Banning certain antibiotics for use in animals will have little effect on the human antimicrobial resistance burden. Research estimates that the use of antibiotics in animals contributes to the human antimicrobial burden for only a small part (EFFORT, Wageningen¹¹). 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 study¹² concludes that in Europe about 75% of the total burden of infections with antibiotic-resistant bacteria are associated with human patients and healthcare infections with antibiotic-resistant bacteria.

⁹ <https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/advice-impacts-using-antimicrobials-animals/reducing-use-antimicrobial-agents-animal-husbandry>

¹⁰ European Surveillance of Veterinary Antimicrobial Consumption (ESVAC):
<https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/european-surveillance-veterinary-antimicrobial-consumption-esvac>

¹¹ <https://www.wur.nl/en/newsarticle/Chance-of-ESBL-contamination-via-livestock-farming-is-small.htm>

¹² [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)

In view of the above, we call on all MEPs in the ENVI Committee to **support** the draft Commission delegated regulation on 12/13 July 2021.

Antimicrobials must be reserved for humans only, **based on cogent and sound scientific criteria and based on a true “One Health” approach**. The health of humans, animals and our environment is interlinked. Banning authorised antimicrobials for animals without any scientific argument and science-based reasons is **contra-productive and will endanger animal health, welfare and human health**.

Unnecessary delays of implementation of the new Regulation has to be avoided. Therefore the delegated act needs to be adopted as soon as possible, in order to allow the work on the implementing act to start and be ready in time for the entry into force of the new Regulation in January 2022.

Veterinarians care for animals and people!

Notes to Editor

The Federation of Veterinarians of Europe (FVE) - representing around 300,000 veterinarians across 39 European countries - aims to enhance animal health, animal welfare, and public health and to protect the environment by promoting the veterinary profession. For more information: www.fve.org