FEDERATION OF VETERINARIANS OF EUROPE

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EMA scientific advice – problem analysis and recommendations to ensure a safe and efficient administration of oral administration via other routes than medicated feed

FVE Input

Background:

- **The new Regulation on veterinary medicinal products ('VMP Regulation') and the new Regulation (EU) 2019/4 on medicated feed were published on 7th January 2019. They will start applying from January 2022.**
- **The new Regulation (EU) 2019/4 on medicated feed establishes stringent rules for the incorporation of VMPs into medicated feed**
- **According to Article 106(6) of the VMP Regulation, the Commission shall adopt a delegated act to establish rules on oral administration.**
- **July 2019 the European Commission made a request for recommendations on the rules on appropriate measures to ensure the effective and safe use of veterinary medicines authorised and prescribed for oral administration via routes other than medicated feed**
- **EMA formulated a recommendation - Advice on implementing measures under Article 106 (6) of Regulation (EU) 2019/6 on veterinary medicinal products – scientific problem analysis and recommendations to ensure a safe and efficient administration of oral veterinary medicine products via routes other than medicated feed**
- **Based on the European Commission request, the European Medicines Agency (EMA) adopted the scientific advice in August 2020.**

Here-under you can find the FVE input on the EMA scientific advice.

Main inputs from FVE:

- FVE very much welcomes this important advice. Several countries stopped the use of medicated feed. This makes application via feed and water the most important non-invasive routes to administer medicines orally to individual or a group of animals. This advice and suggested additional guidelines can help to ensure that it is done in a safe and correct way.

- Some farms produce and use their own feed (circular agriculture), so do not use medicated feed.

- FVE welcomes the recommendations for clear information to users (mostly farmers), the need for training of people administering the medicines, measures to minimise antimicrobial resistance and environmental exposure, and measures to ensure appropriate pack size.

- FVE agrees with '*the choice of the most appropriate administration method to be used in a given situation should remain with the prescribing veterinarian, who has the knowledge of the particular farm concerned, of its equipment and of the possible therapeutic alternatives.* 'as noted in the advice

- While FVE recognises that the treatment of individual animals is preferable, in some cases, e.g. for broilers, pigs and fish, metaphylactic group treatment will remain necessary. It should also be noted that not all Category C and D antimicrobials (AMEG categorisation) are available in injectable form, while most injectable antimicrobials available are of Category B. We must take care not to increase the relative use of AMEG Category B antibiotics.

- Ensuring good animal welfare is important to ensure a robust health and immunity. Individual treatment of some species, e.g. broilers and pigs, is difficult (causing stress to individually catch animals), while metaphylactic group treatment via oral medication in feed or via drinking water may be urgent in some cases to prevent spread of disease and ensure good animal welfare. Administer via feed/water also facilitates good compliance with a full course being delivered over the required time frame.

- The EMA advice on oral medication takes a very narrow approach by restricting the use to treatment via oral medication in solid feed, including via top dressing, to single animals. We understand the need to ensure a homogeneous mixture to avoid under- or over-dosing. However, we feel that some technological advancements in oral application of solid feed have not been taken into account. Modern standardized equipment is available that ensures adequate dosing when mixing a veterinary medicinal product into ordinary feed, which can be administered to a "defined" group of animals. Based on this, mixing into (fluid and solid) feed using appropriate technologies / equipment should at least remain as an option for treatment of groups of animals next to the route via water. Studies have also demonstrated that uniform and also high blood level values can be achieved in a group of animals e.g. resulting from continuous feed intake, even if complete homogeneity is not given (Wehrend et al, 2010 / Gerlings, 2013). These effects resulting from repeated feed intake have also been confirmed in a Monte Carlo Simulation.

- This advice covers the use of the all VMPs. Therefore an approach could be to differentiate between antimicrobials and other and make different recommendations for it.

- The recommendations may also over extoll the virtues of oral administration via drinking water. Some concerns related to water that still require (or require further) consideration:
    - Interactions with incoming water quality, especially if from wells
    - Systems for inserting the drug into the water network, in order to ensure correct mixing
    - Hydraulics of water systems able to guarantee or not a homogeneous and rapid distribution of the drug.
    - Management of the post-treatment lines, as in the vast majority of cases there is only one line.
    - Management of the lines at the end of the cycle, with washing not always adequate to ensure adequate cleaning.
    - Education of the operator by issuing guidelines on the correct management of this administration
    - Acidification of water (and feed). It is common practice in swine to use propionic, acetic, formic and benzoic acids. Usually it is discouraged to mix acidifiers and antibiotics, especially in water.

    In light of these issues it is important that clear practical and technical guidelines are drawn up for farmers. An appropriate water system and dosing system needs to be on the farm to ensure safe and efficient system to ensure all animals getting a correct dose.

- Guidelines for farmers should be produced with consideration for current practice and the reasoning behind this, for example, some farmers currently prefer to use medicated feed in order to keep the water system clean.

- Development of a good practice guide defining the necessary technological equipment and training of users should be supported. Standards have been developed for the technical equipment (DIN 10529-1, DIN 10529-2) and a guidance for users on oral medication (German guidance on oral medication published by BMEL, 2nd Edition 2014).

- A good practice guideline should also highlight issues related to welfare, such as the need for availability of drinking water when oral medication via liquid feed is used.

- In respect to medicating fish, we totally agree with the advice that using medicated feed is preferred over oral medication (a lower concentration can be used which is better for the environment). However, as the advice

recognises in some countries this option is not available and oral medication has to be used instead to medicate groups of fish.

- The report rightly highlights many gaps in knowledge and identifies the need for numerous guidelines to ensure appropriate levels of active substance and homogeneity in the final solution and therefore the expected therapeutic effect via oral medication in practice. These guidelines shall refer to instructions related to
    - proper mixing, dosing and administration in solid feed, liquid feed and water;
    - the quality of the water used (e.g. Presence of polyvalent cations like Ca2+, Mg2+, Zn2+, and Fe3+, temperature, etc.);
    - tolerance levels or incompatibilities (e.g. potential interactions between commonly used biocides and veterinary medicinal products administered via drinking water, etc.);
    - mitigation measures to avoid environmental impact as much as possible (e.g. on how dust formation can be controlled).

- In respect to environmental contamination, a study performed by Stahl et al. demonstrated, that the environmental contamination caused by the use of medicated feed can be greatly reduced if pellets or granules are added to the feed instead of powder. This had no adverse effect on the pharmacokinetic properties in this study. Therefore one could argue that the use of these alternative formulations should be promoted in order to reduce the contamination of the environment. In fact, the levels of contamination measured after the use of granules/pellets instead of feed was below the limit of quantification. Therefore, it is questionable if the application of antibiotics via drinking water actually offers any benefit over the application via granules or pellets in the feed from the perspective of environmental contamination with antibiotics.

- Guidelines for the use of oral medication to treat companion animals, including the potential of medicated feed as noted in the Regulation 2019/6, are also necessary. These guidelines should encompass instructions to mitigate risks as noted in the FECAVA opinion.