

Professor Guido Rasi
Executive Director
European Medicines Agency

Den Danske Dyrlegeforening
Danish Veterinary Association
Peter Bangs Vej 30 | DK-2000 Frb. |
Tlf: +45 3871 0888 | ddd@ddd.dk |

**Danish Agriculture
& Food Council F.m.b.A.**

Axelborg, Axeltorv 3
DK 1609 Copenhagen V
Denmark

T +45 3339 4000
E info@lf.dk
W www.lf.dk

CVR DK 25 52 95 29

Dear Professor Rasi,

The Danish Agriculture & Food Council (DAFC) and The Danish Veterinary Association (DVA) welcomes the new Regulation (EU) 2019/6 on veterinary medicinal products (VMP) and the new Regulation (EU) 2019/4 on medicated feed (MF), that will take effect from 28th of January 2022. The new regulatory framework contains several important elements, and both DAFC and DVA fully support the ambition of harmonized and responsible use of veterinary medicinal products in the European Union.

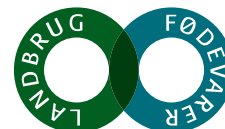
DAFC and DVA are aware that the Commission have asked EMA to provide a scientific problem analysis and recommendations to ensure a safe and efficient oral administration of VMP via routes other than medicated feed to support the Commission in the adoption of a delegated act to establish rules on oral administration of veterinary medicinal products. We are also aware of the Commission's aim to avoid a shift away from medicated feed for which new rules will enter into force with the new regulation.

Responsible use of veterinary medicine, with an emphasis on antimicrobials, have been a top priority among shifting Danish governments, DAFC, and DVA for more than a decade. The close collaboration between authorities, industry, and veterinarians means that Denmark is at the forefront of preventing antimicrobial resistance. This has also been acknowledged by the European Commission, who concluded the following after a fact finding mission in Denmark on prudent use of antimicrobials in animals: *"Various aspects of the comprehensive measures put in place in Denmark aimed at encouraging the prudent use of antimicrobials in animals and tackling the broader issue of antimicrobial resistance could serve as an illustration of potential good practices to other Member States"*

Oral medication has been an important tool in Denmark to ensure a targeted, low and prudent use of especially antimicrobials. We strongly support a safe and efficient use of oral medication, but it must not lead to a situation that in effect leads to an increase in the use of antibiotics and thus compromising the overall ambition of reducing AMR.

In the following DAFC and DVA gives a presentation of experiences and how we are working within the realms of responsible use when it comes to oral medication in Denmark. We hope EMA will find this information relevant and useful when preparing and drafting the scientific problem analysis and recommendations to the Commission.

¹ Final report of a fact-finding mission carried out in Denmark from 01 February to 05 February 2016 in order to gather information on the prudent use of antimicrobials in animals. DG (Sante) 2016-8882-MR



Prudent use of oral medication in the pig industry

In Denmark oral group medication with antimicrobials (metaphylaxis) administered through the drinking water, is the most common practice of antimicrobial treatment in the Danish pig industry in situations where treatment of individual animals is not effective.

Sick animals very often have a reduced feed intake, making it difficult to ensure an appropriate dosage of antibiotics administered through the feed. However, sick animals are more likely to continue drinking. Therefore, providing antibiotics through drinking water ensures that sick animals receive the proper dosage needed to treat the animals.

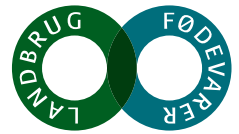
Administering antibiotics through the water pipe systems allows for a targeted treatment of animals down to the individual pen. This makes medication through the water system more favourable in terms of targeting antimicrobial treatment to sick animals and/or animals in the incubation phase of disease in disease outbreaks where treatment of individual animals is not effective. A similarly targeted treatment of pigs through medicated feed is not possible as feeding systems typically will consist of only one feeding pipe supplying a whole section or barn resulting in unnecessary treatment of animals in pens not affected by a disease outbreak.

- It is not possible to construct feeding pipe systems that in a similar way as the water pipe system can target treatment at pen size level.
- Administering medicines through the drinking water also reduces the carry-over risk of residues. When using the water pipes the supply of water will clean the pipes immediately after the medication is removed from the system, whereas the use of medicated feed will fill up the whole feeding pipe system increasing the risk of carry-over residues to the next batch of feed.
- On pig farms feed is often stored and mixed from large feed siloes increasing the risk of contamination of medicated feed to the remaining feed mixtures. It will not be possible to completely segregate medicated feed from standard feed increasing the risk of cross-contamination and carry-over residues.
- Medication through water ensures a more homogeneous mixture of medicine compared to medicated feed.

Medicated feed is solely used in situations, where medical remediation is the only option for treatment of diseases in the herd. This is also in line with the EMA categorisation of antibiotics in the EU of December 12, 2019 (EMA/CVMP/CHMP/682198/2017)², where EMA gives scientific advice on the impact on public health and animal health of the use of antibiotics in animals. In this categorization EMA gives a suggested listing of routes of administration and formulation. We would like to highlight that EMA in this categorization have ranked oral group medication (metaphylaxis) above group medication via feed/premixes.

We strongly support the development and definitions of best practise for the use of oral group medication (metaphylaxis). In Denmark it has been mandatory for farmers and employees since 2007 to complete a full day-training course undertaken by veterinarians before they are authorised to administer medicines to farm animals. The training is approved and audited by The Danish

² Categorisation of antibiotics in the European Union - EMA/CVMP/CHMP/682198/2017 (https://www.ema.europa.eu/en/documents/report/categorisation-antibiotics-european-union-answer-request-european-commission-updating-scientific_en.pdf)



Veterinary and Food Administration and includes training in oral medication to ensure a safe and correct use on farms.

Comprehensive guidelines for best practise for oral medication has been developed by the pig industry. These guidelines are developed specifically to support farmers and veterinarians in prudent use of antibiotics. As part of these guidelines there have been developed factsheets with best practice for:

- Water medication
- Cleaning and disinfection of water pipe systems
- Correct mixture of stock solutions
- Recommendations for water output and number of drinking nipples.

Link to the English version of the guideline: <https://pigresearchcentre.dk/Guidelines>

Link to videos illustrating correct administration of water medication and guideline for correct mixture of stock solutions can be found here (in Danish only):

<https://svineproduktion.dk/Viden/Om-grisen/Sygdomme-og-behandling/Behandling/Medicineringsveje>

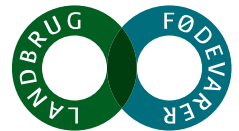
DAFC and DVA recommend the following procedures to ensure prudent use of antimicrobials administered through water. We hope that these procedures could serve as inspiration to recommendations to guidelines or best practices on a European level

- The water pipe system must be constructed in a way that separates the fresh water supply from the medicated water. Usually that can be done by constructing a system that consist of two individual pipelines.
- The water pipe systems must be constructed in a way to allow for water medication to be supplied at both section and pen size level.
- Medicators must be installed in a way that allows for medication to be carried out at both section and pen size level.
- Procedures must be in place to ensure correct dosing and mixture of medicine into the water, and that stock solution are prepared on daily basis.
- Procedures must be in place to ensure proper cleaning and disinfection of water pipes systems after end of medication.
- Farmers who want to administer oral medication must complete training in the use of oral medication

Oral medication in the fish industry

An important tool in the prudent use of antibiotics in the fish farming industry is the possibility to choose between medicated feed and on-farm mixing. Medicated feed is often preferred when treating larger number of animals with standard sized feed pellet. However, in many situations a simple on-farm mixing is still an important alternative that can help keep down the amounts of antibiotic needed, fish mortalities, and in turn development of resistance. There are several situations, where on-farm mixing is important:

- Very often outbreaks of fish bacterial diseases is acute to per acute. Immediately onset of treatment is very important to ensure efficient uptake of the medicine through the feed, given the fact that the treatment is metaphylactic.
- It is not possible for fish feed companies to deliver medicated feed in all pellet sizes in time for treatment as they cannot start producing the feed before it has been prescribed by a veterinarian.



- Veterinarians will often prescribe specific antibiotic inclusion rate in the feed, which will not be in stock at the feed company. This is especially the case with outbreak of diseases in young fish.
- Outbreaks in peak season for specific diseases (warm periods) where the medicated feed are in short supply or out of stock.
- Outbreaks outside of business hours where the fish feed factories are closed.
- With bacterial outbreaks in recirculation aquaculture systems, it is important not to make changes in fish feed due to the potential negative effect of the biofilter. Rather antibiotics should be added to the normal fish feed currently used.

On-farm mixing is an important tool in fish farming to secure immediate and accurate treatment. On-farm mixing accounted for 16 pct. of the amount of active antibiotic substance used in Danish fish farming, even though veterinarians can freely choose between using medicated feed and simple on-farm mixing. In Denmark there have to this date never been reported events of cross contamination or carry-over problems related to on-farm mixing.

It has been mandatory for fish farmers and employees since 2007 to complete a full day-training course undertaken by veterinarians before they are authorised to administer medicine to farm animals. The training is approved and audited by The Danish Veterinary and Food Administration and includes training in oral medication to ensure a safe and correct use on farms.

DAFC and DVA hope that the EMA have found the information regarding the Danish experiences both with regards to training, guidelines, and procedures useful. We remain committed to make the Danish animal household at the forefront of disease prevention and eradication. The increase of AMR is a global health threat, and prudent use of veterinary medicinal products, especially antimicrobials, is an important element in the efforts to minimize the development of resistance. However, no matter how good prevention and on farm management we have; farm animals will continue to get sick and need treatment, including antibiotics. It is important that both industry and veterinarians still have access to options for efficient treatments, and that we make use of the latest scientific and technological developments.

We are at your disposal should you or any member of your staff wish to further investigate or have any questions to the above mentioned.

Sincerely

A handwritten signature in blue ink, appearing to read 'Hanne Knude Palshøj'.

Hanne Knude Palshøj
President, Danish Veterinary Association

A handwritten signature in blue ink, appearing to read 'Flemming Nør-Pedersen'.

Flemming Nør-Pedersen
Executive Director