

## **Advice 19-2013 of the Scientific Committee of the FASFC on responsible use of antibacterial substances via group treatment of livestock and the effect on the selection of resistance.**

The Scientific Committee has been asked to give advice on the responsible use of antibacterial substances administrated via group treatment of livestock and the impact there-off on resistance selection.

Before answering two specific questions, the Scientific Committee elucidates the various aspects of the use of antibacterial substances and resistance selection in livestock.

The literature shows that there is an overwhelming amount of evidence that the use of antibacterial substances (antibiotics and chemotherapeutics) provoke a powerful pressure on the selection of resistance in bacteria (commensal, zoonotic and pathogenic bacteria), both in the individual animal and at the level of the population. However, no scientific publications were found which unambiguously describe the effect of individual versus group treatment on resistance selection without also using different routes of administration. There are only a limited number of studies available that test the effect of oral versus parenteral antibiotic treatment on selection of resistance. These studies provide insufficient basis to draw general conclusions. What is certain is that both routes of administration have an effect on the selection of antibacterial resistance which may also persist for a long time in the animal and in the environment.

The dosage (dose and treatment interval) and mode of administration of the anti-bacterial agent affect the tissue concentrations and, consequently, the degree of selection of antibacterial resistance in both the pathogens, for which the treatment was started, as in the commensal bacteria. The recommended doses in the leaflet appear to differ heavily between manufacturers. They were also determined in function of the clinical cure after treatment, and not in terms of the occurrence of resistance selection.

Group treatment with antibacterial substances are frequently used in livestock (pigs, poultry, veal calves). This may be with a therapeutic objective, for the treatment of infected and clinically sick animals, with a metaphylactical objective for the treatment of infected and diseased animals and for the prevention of infection in the not yet infected animals of the same group or with a prophylactic point of view during strategic moments during the production cycle to prevent infection.

Various forms of group treatment can be applied: local group treatment (e.g. intra-mammary dry-off therapy in dairy cattle), parenteral group treatment (e.g. injection of drugs in suckling piglets and calves) and oral group treatment either through feed or through drinking water or milk replacer.

The intra-mammary dry-off therapy is a special form of group treatment since not all animals are treated simultaneously but according the evolution of the lactation period. Dry-off therapy uses long-acting antibiotics in order to treat subclinical infections and to prevent new infections from occurring. The selection pressure on resistance is limited to the bacterial flora of the udder.

Except for sucking piglets and calves parenteral group treatment is relatively little used in livestock due to its labor intensive nature. However, this route of administration enables, in contrast to feed medication, to meticulously determine the dose and duration of treatment. Limiting the duration of treatment also reduces the period during which a pressure on resistance selection is executed on the bacterial flora.

The large majority of the group treatments are administered via feed or drinking water. The antibacterial substances exert, in the first place, their action on the bacterial flora in the digestive system and are in varying degrees absorbed into the bloodstream. The bioavailability is strongly influenced by the type of molecule and the formulation and can range from almost no absorption to relatively high absorption rates. There is also wide variation in absorption of the same molecule between animals.

Administration of antibacterial substances via the feed is from a labor technical and logistical point of view a very simple way of group treatment of livestock (and thus very easy applicable) which, however, has several practical disadvantages such as the unreliable effective dosage of sick animals, the issue of cross-contamination of antibacterial substances and their segregation in the feed, the fact that usually large numbers of animals are connected to the same feed line, the tendency for overconsumption of antibiotics because of the low threshold of the route of administration and exceeding of the minimum necessary duration of therapy due to the inflexible start and stop moment of the treatment, which promotes the selection of resistance. Besides this there is also the risk of exposure of humans and animals to antibacterial residues in the stable dust originating from medicated feed.

Group treatment through drinking water or milk replacer allows for a more flexible administration of antibacterial substances to selective groups of animals for a period determined by the veterinarian. Applying the correct dosage requires a thorough knowledge of the solubility of the antibacterial substances, the water uptake by the animals, a suitable water quality and good technical adjustment of the dosing (and their control) and the water supply system.

In pigs group treatments are frequently applied; through parenteral route in suckling piglets and through the feed or drinking water in piglets after weaning. Both underdosing as overdosing have been observed. There is a large variation in treatment incidence between farms. In poultry, antibiotics are almost exclusively used by group treatment and almost always via the drinking water. The average treatment incidence is high. Also in poultry a large variation in antibiotic use is observed between farms. In veal calves most group treatments are administered orally. The average treatment incidence is very high. Also in veal calves, there is a variation in treatment incidence between farms but this incidence is lower than in pigs and poultry. Little is known about the antibiotic use in rabbits in our country. In France a switch is made from group treatment with medicated feed to administration of antibiotics via the drinking water. Aquaculture is performed only on a small scale in our country. However, globally aquaculture is an important agro-industrial activity. The use of antibacterial substances varies greatly from country to country. Antibacterial drugs are mainly administered through the feed. Contamination of the sediment and the environment with antibacterial substances is an important issue in order to control the pressure on the selection of resistance.

Some biocides may contribute, according to similar mechanisms of antibiotics, to the selection of antibiotic resistance. However, their importance in the field is still unclear.

After this detailed introduction the Scientific Committee formulates an answer to the following questions.

#### **Question 1:**

**Based on the fact that in group treatment (of pigs, calves, poultry, rabbits or fish) with antibacterial substances an effective control of infectious diseases is pursued, what is the impact on the selection of resistance?**

Each treatment with antibacterial substances creates a selection pressure on the resistance of pathogenic and / or commensal bacteria. In group treatment, this phenomenon is even more pronounced than in individual treatment because the selection pressure is exerted on all animals simultaneously, whereby it may be expected that this translates into a more comprehensive resistance selection. Moreover it should be noted that strategic prophylactic group treatments are contrary to the 'prudent use' of antibacterial substances, which is a keystone to limit the selection of resistance.

Regarding the treatment route, it is difficult to determine which one is preferable in terms of the least selection of resistance because of the limited amount of available information. With regard to oral and parenteral group treatment the Scientific Committee concludes that both routes of administration exert pressure on the selection of resistance proportionally to the number of animals exposed. This selection pressure may also persist for a long time in the animal and in the environment.

From the above it appears that no antibacterial group therapy can be given without the occurrence of pressure on the selection of resistance. Consequently, the Scientific Committee is of the opinion that the best way to counter the selection of resistance in the population is to lower the usage of antibacterial substances.

**Question 2:**

**Which risk factors for resistance selection must be considered in group treatment with antibacterial substances?**

The Scientific Committee is of the opinion that the risk factors for resistance selection are mainly related to the choice and use of antibacterial substances, with their pharmacological properties and with the technical labor conditions of certain routes of group treatment whereby the threshold for their application is particularly low.

A ranking is made of the different group treatments based on their direct or indirect (through number of animals exposed and duration of exposure) effect on resistance selection. The slightest effect applies to local treatment. Followed in increasing order by parenteral treatment, by oral treatment through drinking water or milk replacer, by the oral treatment using medicated feed mixed on the farm through a mobile dosing system and finally by group treatment via medicated feed mixed into the compound feed company. The lack of flexibility in the latter form is a major flaw.

The Scientific Committee concludes that given the many disadvantages of oral group treatment through feed, the great inflexibility and approachability of the use of medicated feed (mixed in the compound feed company) this form of group treatment should preferably no longer be applied.

As a general rule the Scientific Committee recommends to avoid as much as possible group treatment and to invest in animal disease prevention.

The full text is available on this website in dutch and in french, respectively under the section "Wetenschappelijk Comité/Adviezen" and "Comité scientifique/Avis".