The Risk of Development of Antimicrobial Resistance with the Use of Coccidiostats in Poultry Diets

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Authors’ contributions

This work was carried out in collaboration among all authors. The opinion has been assessed and approved by the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of VKM. All authors read and approved the final manuscript.

ABSTRACT

Background:

Antimicrobials revolutionized human as well as animal medicine in the 20th century by providing effective treatment of diseases caused by pathogenic microorganisms. However, microorganisms have the ability to develop antimicrobial resistant strains. This occurs when microorganisms mutate or when resistance genes are exchanged between them. The use of antimicrobial drugs accelerates the emergence of drug-resistant strains. A priority is to safeguard the efficacy of...
Antimicrobial drugs we depend on for treatment of infectious diseases in humans. Use of antimicrobials in food animals can create a source of antimicrobial resistant bacteria that can spread to humans both by direct contact and through the food supply.

Coccidiosis is an intestinal disease in animals caused by unicellular parasites called coccidia. As most of the damage of this infection is done by the time signs of the disease are widespread, preventive measures are preferred. Coccidiostats are animal feed additives used to prevent coccidiosis by inhibiting or killing coccidia. There are two major groups of coccidiostats; ionophores and non-ionophores, the latter also referred to as “non-ionophore coccidiostats” (but also called chemicals). One main difference between these groups is that ionophores also inhibit or kill some bacterial species, whereas non-ionophore coccidiostats do not. Consequently, some bacterial infections may also be controlled by ionophore coccidiostats, e.g. the poultry disease necrotic enteritis caused by the bacterium Clostridium perfringens (C. perfringens).

Eleven different coccidiostats have been authorised for use in the EU, both ionophores and non-ionophore coccidiostats. Norway has been exempted from the EEA Agreement in this field and has approved only five; all ionophores. The two ionophore coccidiostats currently used in Norway are narasin for broilers and monensin for turkeys.

Resistance to coccidiostats in coccidia and bacteria:

Development of resistance in coccidia to all eleven coccidiostats has been described in the scientific literature, but the prevalence of resistance is unknown. Cross-resistance between various ionophore coccidiostats has also been shown, i.e. development of resistance to one ionophore may also render the coccidia resistant to another ionophore. Various rotation and shuttle programmes with exchange between ionophores and non-ionophore coccidiostats are believed to prevent or delay development of resistance in coccidia. In Norway, such programmes will have little effect as long as only ionophores and not non-ionophore coccidiostats are approved for use.

Development of resistance against ionophores has also been observed in bacteria. In the Norwegian surveillance programme NORM-VET during the years 2002 - 2013, between 50 - 80% of the tested flocks had narasin resistant faecal enterococci, which are bacteria that are part of the normal intestinal microbiota. However, the pathogenic bacterium C. perfringens has not been shown to be resistant against any ionophore. Cross-resistance in bacteria to more than one ionophore has been observed. In addition, a limited amount of data may indicate an association between narasin and resistance to the antibacterials bacitracin and vancomycin. As these are antibacterials used for treatment in humans, more research should be performed to validate these results. Non-ionophore coccidiostats, which do not have antibacterial effect, are not approved in Norway. If such coccidiostats were approved in Norway, coccidiostats with negligible probability of inducing resistance in bacteria would be available.

Human exposure to resistant bacteria and coccidiostats:

Humans may theoretically be exposed to coccidiostat resistant bacteria from poultry in a number of ways, e.g. by handling live animals and their manure, through slaughtering and processing, and by preparation and consumption of poultry meat. Furthermore, bacteria of the human normal microbiota, which cover all skin and mucosal surfaces, might develop resistance if they are exposed to coccidiostats.

In this assessment, the probabilities of exposure are classified as: Negligible (extremely low), Low (possible, but not likely), Medium (likely), High (almost certain) and Not assessable.

The Panel has estimated the following probabilities of human exposure:

- Handling manure from coccidiostat fed poultry without sufficient risk-reducing measures entails a high probability of exposure to both resistant bacteria and coccidiostats. Without proper protection, the probability of exposure to coccidiostats is also high when handling coccidiostat premixes and...
feeds containing coccidiostats without proper protection measures. Various treatments, e.g. composting, of the manure may reduce the probability.

- The probability of exposure to resistant bacteria is medium for workers handling carcasses and raw meat on a daily basis if risk-reducing measures are not applied, whereas the probability of exposure to coccidiostats is negligible.
- For consumers, the probability of exposure to coccidiostats is negligible. The probability for exposure to resistant bacteria is also negligible in heat treated food since heat treatment kills the bacteria. The probability of exposure to coccidiostat resistant bacteria is low to medium if handling raw meat without proper hygienic procedures, because raw meat may harbour resistant bacteria.

Risk-reducing measures will lower the probabilities.

However, little is known concerning the consequences of human exposure to coccidiostat resistant bacteria or to to coccidiostats. There is little information in scientific literature indicating whether such bacteria in fact will colonize the human body, either transitonally or permanently. Furthermore, there is no information on the probability of exchange of resistance genes from transferred bacteria to bacteria of the human natural microbiota or to pathogens. Likewise, the Panel has no information on the level of exposure, e.g. the amount of coccidiostats and their metabolites, or the time period, necessary for the various bacteria to give rise to resistant variants. As coccidiostats are not used to treat infectious diseases in humans, concern of resistance is related to possible cross- or co-resistance with antibacterials considered important in human medicine. Such resistance has so far not been confirmed.

Use of therapeutic antibacterials for poultry:

If the ionophore coccidiostats used in Norway are replaced by one or more non-ionophore coccidiostat with no antibacterial effect and no other changes are done, the coccidiostats used will no longer inhibit the bacterium Clostridium perfringens, which is the cause of necrotic enteritis. Over time this will likely to lead to a need for intermittent or continuous use of higher levels of therapeutic antibacterials due to increased incidence of this disease in poultry production. The magnitude of the increase is difficult to predict.

Alternatives to in-feed antimicrobials:

Eradication from the birds’ environment of coccidia causing coccidiosis is difficult to achieve because the coccidia form oocysts that survive outside the host and resist commonly used disinfectants.

Vaccination with non-pathogenic vaccines is now used increasingly in commercial Norwegian broiler farms, instead of in-feed coccidiostats. So far coccidiosis has not been reported as a problem in this transition process to broiler rearing without in-feed coccidiostats in Norway.

Non-antimicrobial feed additives with purported health-promoting benefits, i.e. acid-based products, probiotics, prebiotics, synbiotics, yeast-based products, plant-derived products, combinations of these, and other products have been developed and used in feed. These products have been tested for efficacy against coccidia with conflicting, non-consistent or non-convincing results. The majority of these products appear to target the bacterial microbiota rather than coccidia. The Panel has not assessed possible effects of other types of management changes.

Keywords: VKM; risk assessment; Norwegian Scientific Committee for Food Safety; Norwegian Food Safety Authority; coccidiostats; antimicrobials; resistance; poultry.


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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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