Effects of rapid weight gain on tylosin and enrofloxacin pharmacokinetics in turkeys - dosage modelling and validation based on pharmacokinetic-pharmacodynamic integration

Description for the general public

Increasing body of data is indicating that drugs administered in rapidly growing poultry species may produce different effects in the young animals as compared to the older ones that achieve the slaughter age. This may be illustrated by the fact that after application of the same dosing, in young animals blood drug concentrations may be low which often limits the therapeutic effect and may contribute to the selection of drug-resistant bacteria. In the older birds, however, blood drug concentrations may be very high, which increases the chance for adverse reactions, causes the excessive environmental contamination with drugs in faeces, and may increase the probability of tissue residues which, in turn, may be a source of risk for consumers.

The aim of the project is to investigate the influence of age and body weight on the blood concentration and the rate of elimination of two antimicrobials, enrofloxacin and tylosin, in turkeys. The study will be conducted in three steps. First, drug kinetics in birds will be assessed after single oral and intravenous administration at the standard dose. Drug kinetics will be assessed four times, in parallel to the animals' growth from 1.5 kg to 12 kg. Data on blood drug and metabolite concentrations will be used to calculate pharmacokinetic parameters that describe the processes of drug absorption, distribution, metabolism and elimination. The second step will focus on the development of mathematical models that describe relations between these parameters and the body weight of the animals. In the third step, kinetic experiments on turkeys will be carried out again but this time the drug dosage will be based on the mathematical models developed to unify blood drug concentrations in both young and older animals. The statistical analysis of pharmacokinetic parameters will verify whether the novel model-based approach to drug dosing is applicable in rapidly growing poultry species.

Due to the global problem of emerging antimicrobial resistance and scarcity of new antibacterial agents, it is essential to develop new strategies that conform with the concept of "prudent use of antimicrobials". If the applicability of the proposed non-linear drug dosage is confirmed, this research will deliver a new dosing strategy that, on one hand, may limit the selection for drug-resistant bacteria in young animals, and on another, may decrease the unnecessary drug use in animals just before the slaughter age. This may increase food safety, improve animal welfare and limit excessive environmental contamination with antimicrobials in animal faeces.