**RESISTANCE ASSESSMENT AND SAFEGUARDING THE EFFICACY: DOSE OPTIMALIZATION OF ENROFLOXACIN FOR THE TREATMENT OF COLIBACILLOSIS IN BROILERS**

Temmerman R.¹, Pelligand L.², Schelstraete W.¹, Vanantwerpen G.³, Vanrobaeys M.³, Antonissen G.²,³, Garmyn A.⁴, Devreese M.¹

¹ Department of Pharmacology, Toxicology and Biochemistry, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium
² Department of Comparative Biomedical Sciences, Royal Veterinary College, University of London, Royal College Street, London NW1 0TU, UK
³ Animal Health Care Flanders (DGZ), Industriestraat 29, 8820 Torhout, Belgium
⁴ Department of Pathology, Bacteriology and Avian Diseases, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium

**INTRODUCTION**

Colibacillosis is one of the leading causes of disease-related economic loss in the poultry sector.

Fluoroquinolones are frequently used antimicrobials for the treatment of avian pathogenic *Escherichia coli* (APEC) infections.

However, development and selection of resistance to these antimicrobial drugs is an increasing problem.

**OBJECTIVES**

Assess the prevalence of resistance against enrofloxacin (ENRO) in clinical APEC isolates.

Establish an optimized dosage regimen for ENRO for the effective treatment of colibacillosis in broilers using pharmacokinetic/pharmacodynamic (PK/PD) modeling and Monte Carlo simulation (MCS).

**MATERIALS AND METHODS**

**In vivo animal trials**
- IV(n=8) / PO(n=8) administration: rich sampling, 15 samples over 24h per individual
- PO administration (n=120): sparse sampling, 5 samples over 32h per individual
- Drinking water administration for 3 consecutive days (n=75 divided over 5 major groups receiving different dosages): sparse sampling, 6 samples over 79h per individual

**PK parameter distribution**
- CI
- Vd
- Secondary parameters

**Time-kill experiments**

**MCS**

**PRELIMINARY RESULTS**

- MIC distribution of clinical APEC strains:
  - The MIC’s of 120 strains were determined (commercial gradient strip test, Etest). Forty-one percent of the strains were non-wild type (epidemiological cut-off, ECOFF: 125 µg/mL), 21% were clinically intermediate and 11% were clinically resistant (MIC ≥ 2 µg/mL).

- Spaghetti plot of 120 concentration-time profiles (after a single oral bolus, 10 mg/kg BW)

- Different doses:
  - Yellow: 20 mg/kg BW
  - Purple: 15 mg/kg BW
  - Red: 10 mg/kg BW (licensed)
  - Green: 5 mg/kg BW
  - Blue: 2.5 mg/kg BW

- Spaghetti plot of 75 concentration-time profiles (drinking water)

- The estimated population PK parameter values [95% CI] were:
  - Vd: 5491 mL/kg [5428 ; 5555]
  - CI: 538 mL/kg/h [532 ; 544]
  - Ks: 0.616 h⁻¹ [0.61 ; 0.63]
  - F: 97.84% [97.68 ; 97.98]

**FUTURE PERSPECTIVES**

- Time kill curves (TKC) data analysis
- Simultaneous (pop)PK modeling of PK datasets (IV, PO, drinking water)
- Perform MCS using the MIC distribution and the PK/PD-parameters

Select the dose that achieves the selected PK/PD index for 90% of the target population (PTA of 90%)