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Larsen, I.; Møllerup, Anders; Zachariassen, C.; Nielsen, Søren Saxmose; Folkesson, Anders; Angen, Ø.; Christiansen, L.; Græsbøll, Kaare; Damborg, Peter; Nielsen, J. P.; Olsen, J. E.

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### Effect of variation in oxytetracycline treatment of *Lawsonia intracellularis* diarrhea in nursery pigs on treatment-efficacy and resistance development

Larsen, I.<sup>1</sup>; Møllerup, A.<sup>2</sup>; Zachariassen, C.<sup>3</sup>; Saxmose Nielsen, S.<sup>4</sup>; Folkesson, A.<sup>2</sup>; Angen, Ø.<sup>5</sup>; Christiansen, L.<sup>6</sup>; Græsbøl, K.<sup>7</sup>; Damborg, P.<sup>3</sup>; Nielsen, J. P.<sup>4</sup>; Olsen, J. E.<sup>3</sup>

A Danish research project, MINIRESIST, investigated the consequences of varying doses and treatment strategies for oxytetracycline treatment of *Lawsonia intracellularis* diarrhea in nursery pigs. Batches of nursery pigs in five herds were randomly allocated to one of five treatment protocols (batch treatment orally with high, normal and low doses; penwise treatment with normal dose and injection treatment with normal dose). Outcomes, in terms of reduction of *L. intracellularis* determined by qPCR, growth rate and fecal dry matter content (determined on 30 pigs per batch in 61 batches), and levels of tetracycline-resistant coliforms, and quantification of resistance genes in intestinal content (determined on 15 pigs per batch in 80 batches), were determined and analyzed statistically. These studies were supplemented with in silico simulation of phenotypic resistance development in the intestine based on in vitro determined growth characteristics of porcine commensal *E. coli* in the presence of tetracycline, Low-dose batch-treatment did not differ significantly from normal and high dose treatment in terms of reduction of *L. intracellularis*, and phenotypic resistance levels under field conditions also did not differ statistically depending on dosing levels. qPCR results were shown to add to phenotypic resistance-determination with information on selected genes. Injection treatment resulted in the lowest number of resistant bacteria, but also in the lowest overall cure rate, probably because treatment was based on fecal scores, which have low sensitivity for diarrhea. Simulation studies suggested that resistance development was mostly dependent on the duration of the treatment and the total amount of oxytetracycline used per pig. Ongoing field testing has been initiated to confirm this conclusion, since no field experimentation has yet been performed with variation of duration of treatment. In conclusion, batch treatment with the lowest dose was recommended from both a disease and a resistance point of view.

<sup>1</sup>Department of Large Animal Science, University of Copenhagen;

<sup>2</sup>National Veterinary Institute, Danish Technical University;

<sup>3</sup>Department of Veterinary Disease Biology, University of Copenhagen;

<sup>4</sup>Department of Large Animal Sciences, University of Copenhagen;

<sup>5</sup>National Veterinary Institute, Norway;

<sup>6</sup>Department of Applied Mathematics and Computer Science, Danish Technical University;

<sup>7</sup>Department of Applied Mathematics and Computer Science, Danish Technical University