

Optimization of florfenicol dose against *Piscirickettsia salmonis* in *Salmo salar* through PK/PD studies

Martín, Betty San

Fresno, Marcela

Cornejo, Javiera

Godoy, Marcos

Ibarra, Rolando

Vidal, Roberto

Araneda, Marcelo

Anadón, Arturo

Lapierre, Lisette

Salmonid Rickettsial Septicemia (SRS) is the disease of greatest economic importance in the Chilean salmon farming industry, causing high mortality in fish during the final stage of their productive cycle at sea. Since current, commercially available vaccines have not demonstrated the expected efficacy levels, antimicrobials, most commonly florfenicol, are still the main resource for the treatment and control of this pathogen. The aim of this study was to determine the most appropriate single dose of florfenicol, administered through medicated feed, for the treatment of *Piscirickettsia salmonis* (*P. salmonis*), using pharmacokinetic/pharmacodynamic (PK/PD) models. Previously, Minimum Inhibitory Concentrations (MICs) of florfenicol were determined for 87 *P. salmonis* isolates in order to define the epidemiological cut-off point (COWT). The most commonly observed MIC was 0.125 $\mu\text{g mL}^{-1}$ (83.7%). The COWT value was 0.25 $\mu\text{g mL}^{-1}$ with a standard deviation of 0.47 $\log_2 \mu\text{g mL}^{-1}$ and 0.36 $\log_2 \mu\text{g mL}^{-1}$, for Normalized resistance interpretation (NRI) method and ECOFFinder method, respectively. A MIC of 1 $\mu\text{g mL}^{-1}$ was considered the pharmacodynamic value (PD) to define PK/PD indices. Three doses of florfenicol were evaluated in fish farmed under controlled conditions. For each dose, 150 fish were used and blood plasma samples were collected at different time points (0-48 hours). PK parameters were obtained from

curves representing plasma concentrations as a function of time. The results of Monte Carlo simulation indicate that at a dose of 20 mg/Kg i.w. of florfenicol, administered orally as medicated feed, there is 100% probability (PTA) of achieving the desired efficacy ($AUC_{0-24h}/MIC > 125$). According to these results, we suggest that at the indicated dose, the PK/PD cut-off point for florfenicol versus *P. salmonis* could be $2 \mu\text{g mL}^{-1}$ (PTA = 99%). In order to assess the indicated dose in Atlantic salmon, fish were inoculated with *P. salmonis* LF-89 strain and then treated with the optimized dose of florfenicol, 20 mg/Kg bw for 15 days.