

Results of several clinical trials show that the antibiotic in **Aquaflor***:

- is highly effective against experimental challenge with *Aeromonas salmonicida* or *Vibrio salmonicida*
- is highly effective at reducing mortality rates in farm outbreaks of [furunculosis](#) in salmon when given at a dosage of 10 mg/kg/day for 10 consecutive days
- is more effective than other antibiotics used in farm outbreaks of [furunculosis](#)
- reduces the mortality rate in outbreaks of [furunculosis](#) more rapidly than other antibiotics
- has more sustained efficacy against [furunculosis](#) than treatment with other antibiotics
- is well accepted by fish, with no reduction in feed intake associated with treatment

[Dose determination and confirmation studies](#)

[Commercial field trials](#)

Dose Determination and Confirmation Studies

Initial trials were conducted to determine the optimal dose rate of [florfenicol](#) in salmon. Six trials were conducted in Scotland and Norway:

- 4 trials involved [dose titration](#) to establish the optimal dose rate
- 2 trials involved [confirmation](#) of the optimal dose rate by challenge with *A. salmonicida* or *V. salmonicida*

These trials determined that the optimal [florfenicol](#) dosage for treatment of [furunculosis](#) in salmon is 10 mg/kg/day for 10 consecutive days.

Commercial field trials

Aquaflor* was evaluated in several trials on commercial farms experiencing outbreaks of [furunculosis](#). The studies were conducted in [Norway](#) and [Canada](#). These trials showed that:

- [florfenicol](#) at the dose rate of 10 mg/kg/day for 10 consecutive days is highly effective for the treatment of [furunculosis](#) in salmon under field conditions
- comparisons between [florfenicol](#) and other commonly used antibiotics favor [florfenicol](#)
- [florfenicol](#) administered in the feed is well accepted by the fish

Dose Titration Trials :

A total of 3,132 Atlantic salmon, ranging from 11.5-gram parr to 650-gram post-smolts, were used to determine the optimal dose rate of [florfenicol](#) for treatment of *A. salmonicida* infection:

- fish were fed either unmedicated feed or pelleted feed coated with various concentrations of florfenicol in fish oil; the medicated feed was fed for 10 consecutive days
- during the trials, the fish were challenged with *A. salmonicida*
- total mortality rates during the treatment periods were compared

Results:

- florfenicol at dose rates between 5 and 23 mg/kg/day dramatically decreased mortality rates caused by infection with *A. salmonicida*
- a dose rate of 10 mg/kg/day was clearly more effective than 5 mg/kg/day in one trial
- except in trial 2 (a severe challenge trial), palatability of the medicated feed was excellent

Based on these trials, a dose rate of 10 mg florfenicol per kg body weight per day (10 mg/kg/day) for 10 consecutive days is recommended.

Dose titration studies of florfenicol: total mortality rates following challenge with *A. salmonicida*.

Trial	Description of trial	Dose rate (mg/kg/day)	Total mortality rate
1	260 freshwater parr, bath-challenged with <i>A. salmonicida</i>	0	75%
		5	17%
		10	13%
		20	5%
2	864 post-smolts challenged by intramuscular injection with <i>A. salmonicida</i> *	0	88%
		11.6	25%
		17.4	25%
		23.2	22%
3	600 post-smolts were mixed with 15 salmon that were injected with <i>A. salmonicida</i>	0	50%
		5	14.8%
		10	8.1%**
4	1408 post-smolts in sea cages, naturally infected with <i>A. salmonicida</i>	0	24.7%
		5	3.7%
		10	3.2%
		15	4.6%

* this was a severe challenge and there was a poor feeding response at the start of treatment, so many fish may not have received adequate amounts of medication initially

** statistically lower mortality rate than for 5 mg/kg/day (p=0.01)

Dose Confirmation Trials:

A total of 2,400 Atlantic salmon smolts were used to test the recommended dose rate of [florfenicol](#) against *A. salmonicida* and *Vibrio salmonicida* infections:

- fish were fed unmedicated feed or feed medicated with either florfenicol (10 mg/kg/day) or another antibiotic at commonly used dose rates (see table)
- the medicated feed was fed for 10 consecutive days
- fish were challenged with either *A. salmonicida* or *V. salmonicida*
- total mortality rates during the treatment periods were compared

Results:

- florfenicol at 10 mg/kg/day dramatically decreased mortality rates caused by infection with *A. salmonicida* or *V. salmonicida*
- florfenicol was more effective than other commonly used antibiotics

These trials validate the recommended dosage of 10 mg/kg/day for 10 consecutive days.

Dose confirmation studies of florfenicol: total mortality rates following challenge with *A. salmonicida* or *Vibrio salmonicida*, and comparison with other antibiotics.

Trial	Description of trial	Treatment and dosage	Total mortality rate
5	1800 smolts were mixed with 270 fish that had been injected with <i>A. salmonicida</i>	unmedicated florfenicol (10mg/kg) oxolinic acid (25 mg/kg) oxytetracycline (100 mg/kg) trim-sulphadiazine (30 mg/kg) flumequine (25 mg/kg)	18% 14% 21% 16% 21% 17%
6	600 smolts were injected with <i>Vibrio salmonicida</i>	unmedicated florfenicol (10 mg/kg) oxolinic acid	97% 24% 31%

Norwegian Trials:

[Florfenicol](#) was tested under field conditions on marine farms in Norway that were experiencing outbreaks of [furunculosis](#):

- 5 trials involved a total of 225,000 Atlantic salmon
- trials were performed from June to September (water temperatures 12-16.8°C)
- on each farm, the test unit comprised 4 cages of identical fish
- 2 cages received florfenicol (10 mg/kg/day for 10 days), and the other 2 cages received another antibiotic (positive controls; see table)
- efficacy was based on mortality figures for the entire 10-day

medication period; only fish in which furunculosis was confirmed by bacteriology were included in the mortality figures

Results:

- [florfenicol](#) was well accepted, highly effective, and safe for the treatment of furunculosis in Atlantic salmon under field conditions
- [florfenicol](#) was more effective than other commonly used antibiotics

Commercial field trials in Norway, comparing florfenicol with other antibiotics for treatment of furunculosis in salmon.

Trial	Medication used in positive controls	Mortality rates	
		florfenicol	positive control
1	oxolinic acid (25mg/kg/day)	1.05	0.85
		1.88	2.55
2	oxolinic acid (25mg/kg/day)	1.48	2.82
		1.57	1.37
3	flumequine (25 mg/kg/day)	0.09	0.16
		0.18	0.07
4	flumequine (25 mg/kg/day)	2.24	4.96
		0.65	0.57
5	trimethoprim-sulfadiazine (30 mg/kg/day)	4.33	6.37
		0.48	0.73
Total:		0.97%	1.30%

*mortality rates for each of the four cages of fish are given separately for each trial

Canadian Trials:

[Florfenicol](#) was tested under field conditions at marine sites in Canada that were experiencing outbreaks of [furunculosis](#):

- 3 trials involved a total of 687,700 Atlantic salmon
- trials were performed in August (sea water at 14-18°C) and October (sea water at 9-10°C)
- on each farm, the test unit comprised randomly selected sea cages within rafts
- fish were divided into two groups: florfenicol (10 mg/kg/day for

10 days) and control

- in the first two trials, fish in the control groups received erythromycin (100 mg/kg/day for 10 days); in the third trial, the control group received no medication
- treatment efficacy was based on the mortality figures for the entire 10-day medication period

Results:

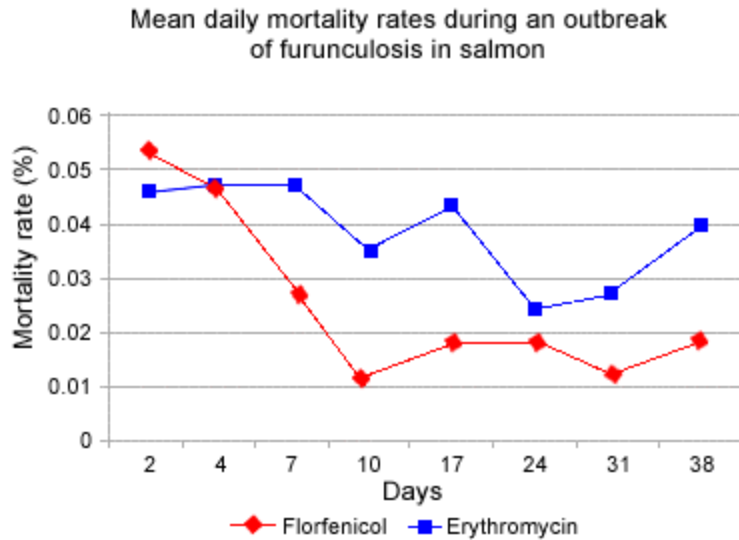
- [florfenicol](#) was well accepted, highly effective, and safe for the treatment of [furunculosis](#) in Atlantic salmon under field conditions
- [florfenicol](#) compared favorably with erythromycin for treatment of [furunculosis](#) and dramatically decreased the mortality rate compared with unmedicated feed

Commercial field trials in Canada comparing florfenicol with other erythromycin or unmedicated feed for treatment of furunculosis in salmon.

Trial	Treatment in control groups	Mortality rates(%)	
		florfenicol	positive control
1	erythromycin	0.1	0.19
2	erythromycin	0.24	0.22
3	none	0.82	1.63

Canadian Trials: florfenicol vs. unmedicated feed

- this trial involved 20 cages of salmon smolts experiencing an outbreak of furunculosis
- the strain of *A. salmonicida* involved was resistant to various antibiotics
- 12 cages were treated with florfenicol (10 mg/kg/day for 10 days), and 8 cages were fed unmedicated feed
- treatment with florfenicol resulted in an immediate, substantial drop in mortality rate
- a week after treatment ended, the mortality rate in florfenicol-treated cages was 0.05%, compared with 1.45% in untreated cages
- mean weekly mortality rates in florfenicol-treated cages remained below 0.5% for at least 4 weeks after treatment

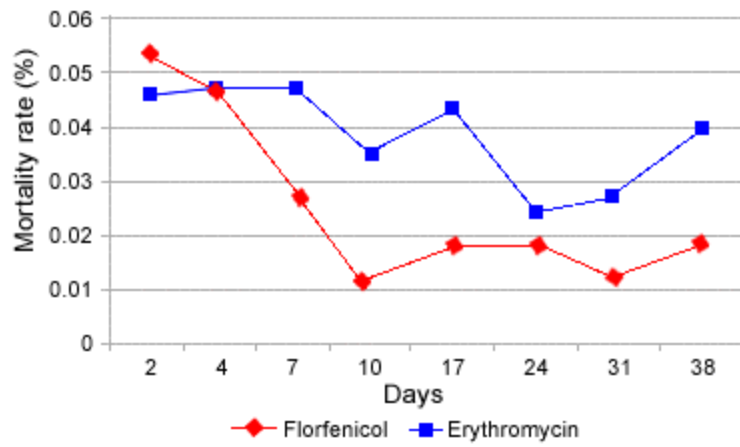


Canadian Trials: florfenicol vs. erythromycin

- this trial involved 20 cages of salmon smolts experiencing an outbreak of furunculosis
- the strain of *A. salmonicida* involved was resistant to various antibiotics
- 13 cages were treated with florfenicol (10 mg/kg/day for 10 days), and 7 cages were treated with erythromycin (100 mg/kg/day for 10 days)
- treatment with florfenicol resulted in a more rapid and substantial drop in daily mortality rates than that seen with erythromycin
- following the 10-day treatment period, mean daily mortality rates remained significantly lower in florfenicol-treated fish for at least 4 weeks

Florfenicol produced a rapid and sustained decrease in daily mortality rates compared with erythromycin.

Mean daily mortality rates during an outbreak of furunculosis in salmon



Daily mortality rates were significantly lower in florfenicol-treated fish on days 10, 17, 31, and 38.

***This graph should have a box along the X axis between days 0 and 10, indicating the treatment period**