

Salmon and Trout Safety Studies:

Target animal safety and tolerance studies were performed with Slice on two salmonid species: Atlantic Salmon (*Salmo salar*) and Rainbow Trout (*Oncorhynchus mykiss*). A summary of the results for these two studies is presented below.

Salmon Safety Studies

This study measured the tolerance of Atlantic salmon (*Salmo salar*) to an orally administered, **SLICE**-medicated feed. The treatment groups were fed a Slice-medicated diet at nominal dose rates of 0, 100, 250 and 500µg/kg/day respectively for 7 consecutive days.

Results of Atlantic Salmon Tolerance Study (seawater)

Daily Rates* (µg/kg/day for 7 consecutive days)	Multiple of target dose (based on 50µg/kg/day)	Lethargy	Incoordination	Dark Color	Inappetence
0	0x	0/40	1/40	1/40	0/40
70	1.4x	0/40	1/40	1/40	0/40
173	3.5x	0/40	0/40	1/40	0/40
356	7.1x	Majority/40	2/40	36/40	31/40

**actual dose rates were calculated based on the measured feed consumption and analysis of feed for emamectin benzoate concentration*

Results from this salmon safety study showed that **SLICE**-medicated feed, when administered at actual dose rates (based on feed analysis) of up to 3.5x the recommended label dose rate of 50 µg/kg/day, is safe for salmon.

Results of Atlantic Salmon Tolerance Study (freshwater)

Signs of intoxication were observed only at 5.4X the recommended dose rate (see Table below) and included incoordination and dark color. No mortality attributable to treatment was observed. No pathognomonic signs were observed during gross necropsy or histopathological examination. Results of this study show that SLICE administered at actual dose rates of 1.1X the label dose rate (50 µg/kg/day) had no detectable adverse effects on Atlantic salmon treated in freshwater. Further, these results indicate that dose rates of 5.4X the label dose rate had relatively minor adverse effects on Atlantic salmon treated in freshwater and starved for 3 days prior to transfer to seawater. Fish in all treatment groups consumed > 96% of the feed offered and fish that received 5.4X the label dose rate of emamectin benzoate consumed > 99% of feed offered, therefore, feed

containing emamectin benzoate at concentrations up to 101 mg/kg was palatable.

Frequency of signs and symptoms of toxicity in Atlantic salmon (*Salmo salar*) due to consumption of emamectin benzoate administered in feed at 0, 54, and 272 µg/kg/day for 7 consecutive days. Treatments were administered on Study Days 0 - 6 in freshwater and the observations herein were made on Study Day 23 after 14 days in seawater.

Daily Rates* (µg/kg/day for 7 consecutive days)	Multiple of target dose (based on 50µg/kg/day)	Lethargy	Incoordination	Dark Color	Inappetence
0	0x	0/100	0/100	0/100	0/100
70	1.0x	0/100	0/100	0/100	0/100
173	5.4x	0/100	1/100	50/100	0/100

Trout Safety Study

A study involving Rainbow trout (*Oncorhynchus mykiss*) was conducted to determine their dietary tolerance to emamectin benzoate. Slice-medicated feeding regimes: (nominal dose rates) 0, 100, 250 and 500 µg/kg/day for 7 consecutive days. The dose rates of this medicated daily diet represented multiples of 2x, 5x and 10x respectively, of the recommended therapeutic dose rate of 50 µg/kg/day. The results of this study showed that the **SLICE**-medicated diet was safe for trout even when fed at dosage rates of up to 4.4x the prescribed label dose rate.

Results of Rainbow Trout Tolerance Study

Daily Rates* (µg/kg/day for 7 consecutive days)	Multiple of target dose (based on 50µg/kg/day)	Observed Results
0	0x	No Adverse Reaction
88	1.8x	No Adverse Reaction
218	4.4x	No Adverse Reaction
413	8.3x	Progressive signs of toxicity-- lethargy, dark coloration, inappetence, loss of coordination

*actual dose rates were calculated based on the measured feed consumption and analysis of feed for emamectin benzoate concentration

No pathognomonic signs of emamectin benzoate toxicity were identified during gross necropsy or histopathological examination. No treatment-related mortality at 7-8x the dose rate was observed.