

**Supplement
to the
Environmental Assessment for Aquaflor
for Freshwater-Reared Salmonids**

Approval of Aquaflor for use in control of furunculosis

Executive Summary:

Approval of an additional disease, furunculosis, for Aquaflor for freshwater-reared salmonids will not increase the peak florfenicol concentration entering aquatic ecosystems. Although the number of treatments per year may increase with the addition of this disease to the label the amount of florfenicol released with each treatment will remain at the same level¹ as reported for coldwater disease² (CWD). Furunculosis when compared to CWD is treated much less frequently and generally at alternate periods during the year. These two diseases do not generally co-occur in specific populations. The treatment regime remains the same even if co-occurrence did occur as a rare event and each treatment is considered an independent event³. The exposure assessment is the same for the furunculosis. No substantive change in the EA is expected.

Introduction:

Schering-Plough Animal Health is requesting approval of an additional disease to the Aquaflor label for freshwater-reared salmonids. The following is a summary of the review of the potential changes in the environmental assessment (EA) and the Aquaflor label. The typical raceway system including flow rates and volumes discussed below remains the same as presented and discussed in the Environmental Assessment for Aquaflor for Freshwater-Reared Salmonids

(http://www.fda.gov/cvm/CVM_Updates/SalmonidsUp.htm).

¹ 0.033 mg florfenicol residues/L at 47 kg/m³ as reported in the coldwater disease submission for freshwater-reared salmonids (http://www.fda.gov/cvm/CVM_Updates/SalmonidsUp.htm).

² This is the primary pathogen controlled by Aquaflor and was the first label indication for Aquaflor in freshwater-reared salmonids

³ With a six week interval between treatments.

2007-141-246

Professional Contacts

To assess the potential impact of adding furunculosis to the Aquaflor label for freshwater-reared salmonids and to understand the use pattern of this additional disease, 10 fishery management professionals, i.e. fish health scientists or hatchery managers, were contacted by telephone. The professional contacts represented different types of facilities: private hatcheries, US Fish and Wildlife Service (USFWS) hatcheries, state hatcheries, and Native American hatcheries. These facilities produce a range of salmonids species: rainbow, brown, cutthroat and brook trout; steelhead; and coho, chinook, and Atlantic salmon. These contacts represented the following regions: Rocky Mountains (including Idaho and Colorado), the South, the Northeast, Maine, and the Northwest. These are representative regions where aquaculture of freshwater-reared salmonids occurs. With the exception of the Rocky Mountain region (CO), which does not have any significant furunculosis, all other regions have some level of furunculosis. This disease is present at generally low levels and limited frequency.

Following questions were addressed by each of the 10 professional contacts:

- Does furunculosis occur in your region?
- What is the general time-frame for outbreak of this disease?
- What proportion of the facility would be treated at one time?
- Would furunculosis co-occur with CWD?
- Would an entire facility be treated at one time with an antibiotic?

Table 1: List of Contacts and Responses to Basic Questions.

Contact	Region	Furunculosis	Proportion of facility treated: $\leq 20\%$	Co-occurrence of diseases	Whole facility treatment
Amandi, Tony Fish Health Laboratory, Oregon State Department of Fish and Wildlife, OR	NW	Y	Y ^a	Y	R
Conklin, Charles Manager, Big Brown Fish Hatchery, PA	NE	L	YY	N	N
Evered, Joy, DVM Fish Health Laboratory US Fish & Wildlife Service, WA	NW	L	Y ^a	Y	R
Gunn, Carolyn DVM Colorado DNR, Aquatic Animal Health Lab, CO	Rocky Mt.	N	--	--	--
Hinshaw, Jeff, Ph.D. Extension Service North Carolina State University, NC	South	L	YY	N	R
Lambert, Greg Manager, Freshwater Production Cooke Aquaculture, ME	Maine	L	N	-- ^c	Y ^b
LaPatra, Scott PhD Clear Springs Foods, ID	Rocky Mt.	Y	YY	N	N
Reddinger, Gary Manager, Cherry Valley Fish Hatchery, PA	NE	L	YY	N	N
Stewart, Bruce Fish Health Laboratory Northwest Indian Commission, WA	NW	Y	--	--	N
Varney, Jed, DVM Fish Health Laboratory Washington State Dept of Fish & Wildlife, WA	NW	Y	Y	N	--

Y = yes; R = rare; L = limited; YY = strongly agree; N = no; NW = Northwest; NE = Northeast; ^a Generally agrees with 20% upper limit, but believes rare situations will require larger proportions of treatment; ^b Only in smolt hatcheries that require complete treatment for control; ^c These smolt facilities have no significant CWD

A key factor in the initial assessment for Aquaflor and freshwater-reared salmonids was that the portion of the facility treated with Aquaflor would not exceed 20% by volume. This concept was discussed in relation to furunculosis with 8 of the 10 professionals contacted. Seven of eight professionals agreed that this 20% value was an outside worst-case assumption (i.e., the portion treated would be considerably less than 20%). Two of the seven professionals agreed that the 20% value was a reasonable estimate of the maximum proportion of a system to be treated, but these two professionals qualified their statements to include treatment of larger proportions or an entire facility on rare occasions. One professional contact associated with Atlantic salmon hatcheries in Maine did not agree with the 20% maximum proportion for treatment as applied to his facilities because if an outbreak occurred the entire hatchery would be treated.

The issue of disease co-occurrence was discussed during evaluation of possible changes in the environmental assessment associated with the addition of furunculosis to the Aquaflor freshwater-reared salmonids label. Co-occurrence is defined as more than one disease in the same population, or subpopulation, or occurrence of two diseases in different subpopulations within a single facility at the same time. The potential for co-occurrence included furunculosis and CWD. The potential for co-occurrence was acknowledged by two of seven⁴ professional contacts. The remaining five professionals did not believe co-occurrence would occur (Table 1). The treatment regime for co-occurring diseases would be the same as a single disease, i.e. 10 mg florfenicol (FFC)/ kg fish for 10 days. Therefore, no increase in the FFC water or sediment concentration (as established in the EA for CWD, SPAH 2006) would occur since the co-occurring furunculosis would be treated concurrently with CWD. The 20% as a maximum for treatment of one facility with an antibiotic at one time is considered to be considerably less than 20% by four of eight contacts responding and <20% for three of eight. The 20% maximum treatment of a system at one time would cover two subpopulations being treated for different diseases at the same time, which would be a rare event based upon seasonal and temperature differences in manifestation of these diseases.

⁴ Only seven of ten contacts contributed to the discussion on this topic (See Table 1).

As part of these discussions the treatment of entire facilities was raised with eight professional contacts. Four of these contacts stated that they would only treat diseased populations and would never treat the entire facility. Three of eight stated that treatment of whole facilities might rarely occur (Table 1). The representative of three smolt hatcheries in Maine stated that treatment of whole facilities would likely occur⁵.

The basic exposure assessment and Aquaflor use pattern remains the same:

The use pattern remains the same for treatment of both diseases CWD and furunculosis (SPAHI 2006). The treatment regime is 10 mg FFC / kg fish for 10 days by prescription in the diet in accordance with the Veterinary Feed Directive (VFD). This determines the magnitude of potential release of florfenicol in effluent. Plus there is no change in the exposure assessment by adding the furunculosis to the label. The same internal dilution factors determine the effluent concentrations. As established in the environmental assessment for CWD the proportion of the facility treated (i.e., < 20%) is the same for furunculosis. Representative raceway systems, flow rates, and volumes are the same for furunculosis as is used for CWD.

Coldwater disease occurs during the high water flow (i.e., late spring and early summer). Furunculosis occurs primarily during the low water flow (i.e., July through September), but can be a more chronic problem. However, the end of the pipe effluent concentration is the same for furunculosis as for CWD.

Change in the use of Aquaflor to treat furunculosis and columnaris

The two diseases to be labeled for use of Aquaflor (CWD and furunculosis) have distinct temporal patterns that result in temporal isolation. The primary periods for seasonal occurrence are different, although there is some overlap. CWD occurs primarily in late spring and early summer when the temperature is changing although it may occur in any

⁵ Previously these hatcheries were considered to be completely treated when included as part of an environmental assessment to support the use of an anti-seallice product. This is based on the size and nature of these facilities.

time of year. Furunculosis occurs primarily in the warmest time of year July to early September, although this disease can occur over-winter or throughout the year.

In all regions the number of outbreaks of furunculosis is reported to be limited and infrequent relative to CWD. In Washington State furunculosis may occur, but not every year. For commercial facilities in the South, furunculosis has been infrequent over the last 10 years occurring primarily in brook trout (rainbow trout are to some extent refractory to furunculosis). In the Northwest, of 9 facilities managed by the USFWS furunculosis may occur in one or two in any given year. In Maine furunculosis is seen one of every three years. Furunculosis is observed much less frequently than the chronic problem of CWD which is found in all regions.

Table 2: Proportion of studies with antibiotics for three diseases under two Investigational New Animal Drugs (INADs)

Antibiotic/Pathogen	Number of studies (treatments)	Number of fish treated	Percent of fish treated
AQUAFLOL			
CWD	105	34,432,854	74%
Furunculosis	59	11,897,154	26%
Total	168	46,485,723	100%

The addition of furunculosis to the Aquaflor label will have only a small proportional change in the overall use of this antibiotic. The use of antibiotics to treat furunculosis is much less than the use of antibiotics to treat CWD. As can be seen from Table 2 using data from the Aquaflor INAD, CWD accounts for 74% of total Aquaflor use compared to a projected 26% for furunculosis. This emphasizes that antibiotic use for furunculosis represents a much smaller proportion of overall Aquaflor use between these two diseases; therefore, addition of this disease to the label will not substantially increase the overall use of Aquaflor.

Conclusions:

The addition of furunculosis to the Aquaflor label for freshwater-reared salmonids will not increase the magnitude of florfenicol residues in effluents or receiving water systems. The exposure assessment is the same for furunculosis as for CWD in the EA for Aquaflor in freshwater-reared salmonids, which is based on end-of-pipe calculations and internal facility dilutions.

The frequency of application of Aquaflor may increase, but each treatment is an independent event with a minimum six week interval between treatments.

Furunculosis is a minor disease, but is present in almost all regions at infrequent, limited levels. This does not occur each year and occurs in only a small number of facilities in each region in a given year.

The proportion of individual facilities that would be treated for these diseases does not exceed 20% of the facility with rare exceptions in some regions.

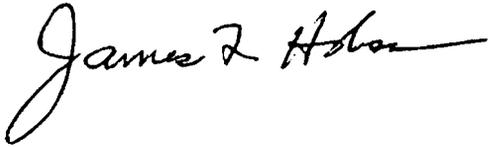
There is no additive increase in the Aquaflor applied to treat for furunculosis. This disease does not generally co-occur with CWD due to differences in optimal temperatures and time of year.

References:

SPAH 2006. Environmental Assessment for Aquaflor for Freshwater-Reared Salmonids Schering-Plough Animal Health Corporation. 119 pp. Submitted to the Food and Drug Administration, Center for Veterinary Medicine.
http://www.fda.gov/cvm/CVM_Updates/SalmonidsUp.htm

List of Preparers:

The following personnel from Schering-Plough Animal Health Corp. were responsible for the preparation of this Environmental Assessment:



James F. Hobson, Ph.D. DABT
Consultant to Schering-Plough Animal Health

Certification:

The undersigned official certifies that the information presented in the Environmental Assessment is true, accurate and complete to the best of their knowledge.



Richard G. Endris, Ph.D.
Research Program Manager
Schering-Plough Animal Health Corporation