I-009006-P-0106

U.S. Department of Interior
Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Attention: David Erdahl, Ph.D.
Branch Chief
4050 Bridger Canyon Road
Bozeman, MT 59715

JUL 2 5 2007

Re: Submission of information detailing the similarities between *Oncorhynchus* subspecies rainbow trout and steelhead trout

Dear Dr. Erdahl:

Based on the information in your submission dated February 9, 2007 and the information contained in the Investigational New Animal Drug (INAD) file 009006, the Division of Therapeutic Drugs for Food Animals considers the Effectiveness technical section for oxytetracycline medicated feed for the control of mortality in freshwater-reared *Oncorhynchus mykiss* due to columnaris disease associated with *Flavobacterium columnare*, when administered at a dose of 3.75 g oxytetracycline/100 pounds of fish/day for 10 consecutive days to be complete.

CVM agrees that the submitted information supports the claim that effectiveness data accepted for freshwater-reared steelhead trout has significant inferential value for other subspecies of *O. mykiss*. We have reviewed your submission dated February 9, 2007, in which you provided information that details the similarity between *Oncorhynchus* subspecies rainbow and steelhead trout. The submission contained information to support the claim that effectiveness data accepted for the label claim 'for the use of oxytetracycline medicated feed to control mortality due to columnaris disease associated with *Flavobacterium columnare* in freshwater-reared steelhead trout' could be expanded to include the claim 'for the use of oxytetracycline medicated feed to control mortality due to columnaris disease associated with *Flavobacterium columnare* in freshwater-reared *Oncorhynchus mykiss*.'

We agree that the genetic relatedness and culture condition similarities between rainbow trout and hatchery-reared steelhead trout (versus physiologically adapted steelhead trout) are sufficiently similar and therefore we believe conclusions about the effectiveness of oxytetracycline medicated feed to control mortality due to columnaris disease in hatchery-reared steelhead trout have inferential value for all subspecies of *Oncorhynchus mykiss*. Therefore, for the purposes of the label, we will amend the claim to read 'for the control of mortality due to columnaris disease associated with *Flavobacterium columnare* in freshwater-reared *Oncorhyncus mykiss*.' A summary of

the information from this submission will be included in the FOI summary with a statement which states that we consider this label claim to represent all subspecies of *O. mykiss* which include rainbow trout, steelhead trout, redband trout, and redband steelhead trout.

We also recommend that you perform an additional pivotal effectiveness study in the use of oxytetracycline medicated feed to control mortality due to columnaris disease in another salmonid species other than *O. mykiss* in order to get a claim for all freshwater-reared salmonids.

We will make a final decision on whether we can approve your application after we have reviewed all of the data for all applicable technical sections submitted in support of an Administrative New Animal Drug Application (NADA), NADA, or supplemental NADA, and any other information available to us, as a whole, and determined whether the requirements for approval set forth in the Federal Food, Drug, and Cosmetic Act have been met.

If you submit correspondence relating to your submission to the investigational file, you should reference this letter by date and the principal submission(s) identifier found at the top of this letter. If you have any questions, please contact me at (301) 827-7571 or Dr. Donald Prater, Leader, Aquaculture Drugs Team, at (301) 827-7567.

Sincerely,

Joan C. Gotthardt 7/24/07
Joan C. Gotthardt, D.V.M.
Director, Division of Therapeutic
Drugs for Food Animals
Office of New Animal Drug Evaluation
Center for Veterinary Medicine

Enclosure:
Freedom of Information Summary

1. **Effectiveness Technical Section:**

a. Title: "Justification to consider studies that demonstrate drug efficacy on freshwater-reared steelhead trout or rainbow trout be sufficient to satisfy the effectiveness requirements for all freshwater-reared Oncorhynchus mykiss."

b. Sponsor: U.S Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Bozeman, MT

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c. Report Summary:

Oncorhynchus mykiss are native to western North America with both resident and anadromous migrating life history forms found throughout their range. The resident form is known as rainbow trout and the anadromous (migrating to sea or large lakes) form is known as steelhead trout. Originally, the two life-history forms of *O. mykiss* were classified as two distinct species based on morphology and behavior, but have been reclassified as a single species. Consequently, *O. mykiss* populations are now divided into subspecies based primarily on morphological evidence, many of which exhibit both resident and anadromous migratory life history patterns. Modern genetic analysis has confirmed that not only do steelhead and rainbow trout belong to the same species, but the degree of relatedness among *O. mykiss* populations is generally associated with geographic proximity, not life history type, and suggests that steelhead and rainbow trout are polyphyletic and the result of parallel evolution rather than members of two distinct lineages.

The techniques used to culture young rainbow and steelhead trout are virtually identical. During the time such fish are held in captivity, there are virtually no morphological or physiological differences between the two. Fish production data for 2005 was provided which showed that of a total of 118 million *O. mykiss* cultured in 2005, 87 million were rainbow trout while 31 million were pre-hatchery release steelhead trout (of which 0.009 million steelhead were kept as broodstock). All life stages of rainbow trout may be reared or held as broodstock and may be subject to treatment with one or more drugs (including medicated feeds) during their captivity. However, virtually no steelhead trout that have returned from the ocean are kept for an extended period of time at a hatchery after they have spawned. Returning adult steelhead trout do not eat and must be retrained to feed, which is often difficult to accomplish and therefore most of these fish are killed and removed.

References to cited material were provided.

d. CVM Conclusion: CVM agrees that the genetic relatedness and culture condition similarities between rainbow trout and hatchery-reared steelhead trout (versus out-migrated steelhead trout) are sufficiently similar and therefore we conclude that data that demonstrate the effectiveness of oxytetracycline medicated feed to control mortality due to columnaris disease in hatchery-reared steelhead trout have inferential value for all subspecies of *O. mykiss*. CVM considers the Effectiveness technical section for oxytetracycline medicated feed for the control of mortality in freshwater-

reared *Oncorhynchus mykiss* due to columnaris disease associated with *Flavobacterium columnare*, when administered at a dose of 3.75 g oxytetracycline/100 pounds of fish/day for 10 consecutive days to be complete.