

Aquamycin Update and Progress Toward PMF: INAD 6013

Christine M. Moffitt

US Geological Survey
Idaho Cooperative Fish and Wildlife Research Unit
University of Idaho

22nd Annual Aquaculture Drug Approval Coordination Workshop
Jackson Hole, WY

Background – NRSP-7 Erythromycin for Salmonids

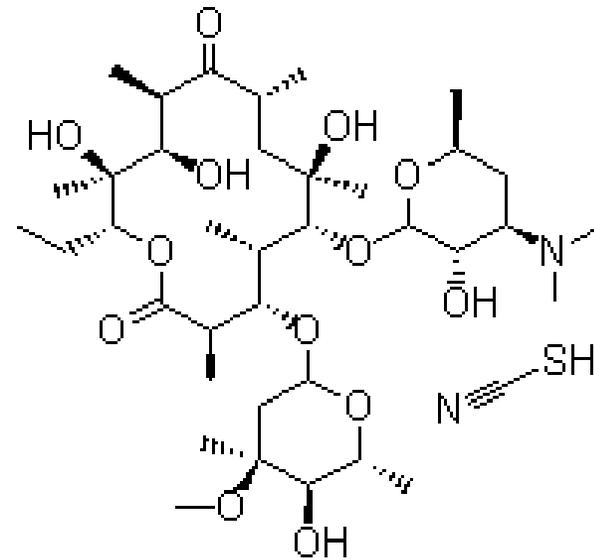
- First opened late 1980s for limited scope, but during that time, FDA staff began examining the compliance of aquaculture drugs
- In early 1990s, FDA authorized the U of Idaho to incorporate participants operating under INAD 4333 (held by Oregon Department of Agriculture) for selected Pacific Northwest Hatcheries using Gallimycin 50 poultry feed additive into INAD 6013
- INAD became first regional aquaculture INAD toward pivotal studies to support a label claim

Formulation Development

- Problems had occurred under INAD 4333 with throat fungus events likely related to the corn cake carrier
- With staff at Bio-Products, and Oregon Seafood Feed Lab, we developed a new carrier to replace the corn cake of Gallimycin 50 poultry additive
- Determined wheat flour carrier was best, fine and easily blended and distributed

Aquamycin 100

- **Erythromycin thiocyanate in wheat flour 100 g/lb**



Medicated type A article for Medicated Type C Feeds

Bacterial Kidney Disease was Severe in Pacific Northwest

- Distended abdomen



- Exophthalmia



- Pseudo-membrane covering organs

- White granulomatous lesions in kidney



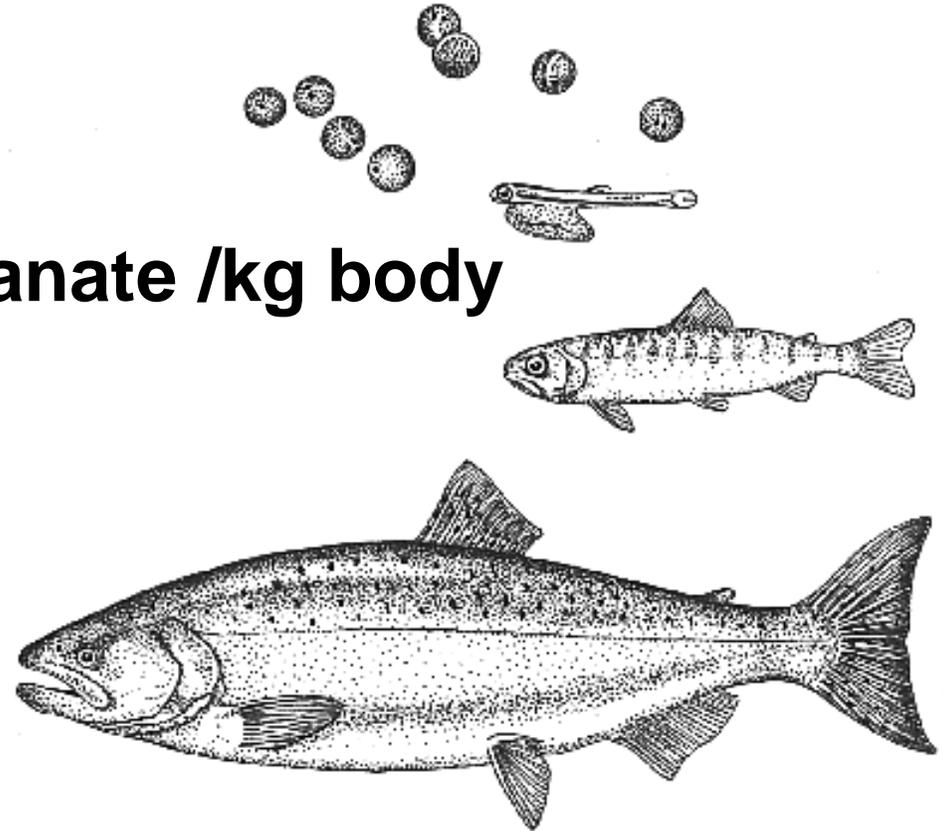
Studies Prioritized

- Pharmacokinetics
- Dose titration study and clinical trials determined 21-28 d best due to the pharmacokinetics and the drug, and challenge from intracellular nature of *R. salmoninarum*
- Target Animal Safety
- Withdrawal determination

Control Bacterial Kidney Disease



- All salmonids
- Oral application
- 100 mg erythromycin thiocyanate /kg body weight per day
- 21 - 28 d therapy
- Freshwater



Rethinking Approvals: FDA expanded studies and data requirements

- Resistant Microorganisms
- Environmental Assessment

Drug Company Support: Changing and Morphing

- NRSP-7 project began with CEVA labs as sponsor, but over years companies changed hands and products went in different directions
- NRSP-7 Roz Schnick obtained Bimeda as drug sponsor with MUMS Designation Application late 2005
- Bimeda held approval for injectable, poultry feed additive, poultry water additive

Manufacturing Submission of Type A Product- Bimeda

- 10% stability manufacturing batch
- Bimeda submits SOP for HPLC methods to FDA Office of Research
- OR begins work on Official HPLC Assay for Feed Matrices

Outstanding Needs – USGS-UI & UMESC and Rosenblum (Colorado)

- Revised Phase II EA submission to include chemistry and chronic toxicity
- Collaboration with FOI documentation details and label writing

Bio-Products Sold and Warrenton OR Plant Closed

- Feed manufacturing moved to Skretting plant in Vancouver BC, retained Bio-Oregon as new name for most salmon feeds sold in USA.
- All medicated feeds provided as second step and top coated
- Additional data on fish response and efficacy of top coated feeds with Aquamycin 100 prepared and evaluated

Summary of salmonids treated for BKD under INAD protocols

Frequent

- Chinook salmon
- Coho salmon
- Kokanee and sockeye salmon

Occasional treatments

- Brown trout
- Atlantic salmon
- Rainbow trout
- Cutthroat trout
- Arctic grayling

FDA Approval Documents Completed – all public master file

- **Efficacy**
- **Target Animal Safety**
- **Human Safety (residue depletion)**
- **Human Safety (microbial risks)- 152, 159**
- **Environmental Assessment – Phase I
and Phase II emerging?**

Sponsor Drug Company

- Bimeda submitted manufacturing submission, for Type A product but has not followed up since 2012
- Need for new sponsor to complete manufacturing submission requirements

Moving Forward

- Conversations with Aquatactics
- Working on details of PMF

Acknowledgements

Funding-

**Bonneville Power Administration, USFWS
- LSRCP, Department of Agriculture -
NRSP-7, FDA NCTR, & FDA Office of
Research, USGS**

In Kind Support

WDFW, ODFW, IDFG, USFWS