Aquamycin Update and Progress Toward PMF: INAD 6013

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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