



Status of Copper Sulfate - 2016

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Regulatory Status

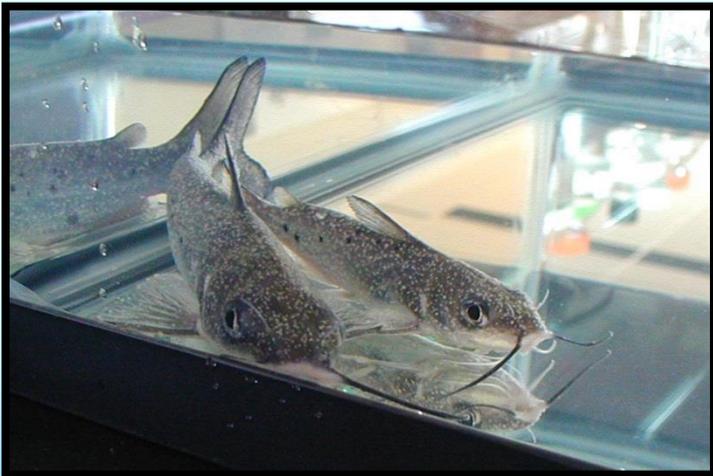
No INAD required; not approved, but regulatory action deferred.

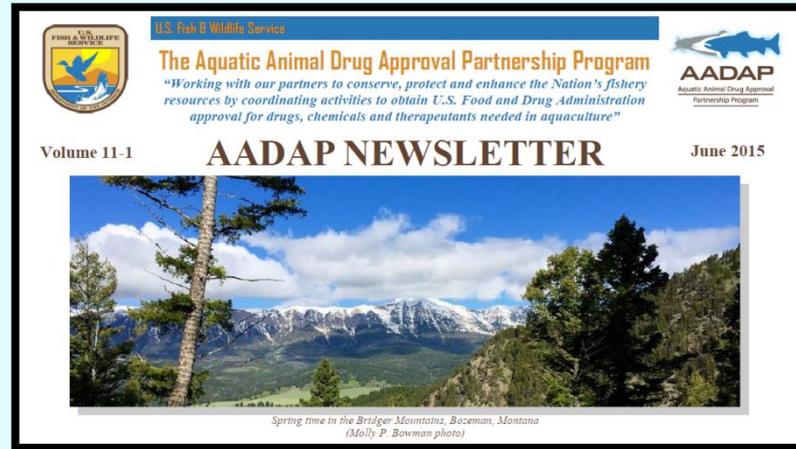
Major technical sections of a New Animal Drug Approval: **Chemistry-
Manufacturing and Control**, **Mammalian Toxicology**, **Effectiveness**,
Human Food Safety, **Target Animal Safety and Environmental Impact**.



Our goal is to gain 2 labels for copper sulfate:

- 1) For the treatment of ichthyophthiriasis (*Ichthyophthirius multifiliis*) on channel catfish cultured in earthen ponds.
- 2) For the control of mortality in channel catfish eggs due to saprolegniasis (fungi of the family Saprolegniaceae).





- Our previous Sponsor, Freeport-McMoRan, sent a letter to their customers in July 2015 that they had decided to stop producing copper sulfate. We immediately began efforts to find a new Sponsor. By October, we had Chem One Ltd. agree to partner with us, and they became the official copper sulfate Sponsor with a letter from FDA/CVM in December.
- Since we now have a new Sponsor, they have requested a presubmission conference with FDA/CVM to discuss the procedures for approval of their product and work on any remaining items to be accomplished, especially the **Chemistry, Manufacturing and Control (CMC)** Technical Section, which is the last major technical section required for the Ich label (next).



1) Ich Label

Human Food Safety - Complete for all finfish (2/2004; submitted 5/1996). Hazard characterization requested after reviewing package and limiting to only channel catfish (10/2007). Hazard characterization resubmitted for all fin fish (included human intestinal microflora, residue chemistry, and microbial food safety with respect to resistance). Complete for all finfish (10/2008).

Effectiveness - Complete for Ich for all fish (12/1998).

Target Animal Safety - Complete for channel catfish (4/2006). (Experiments completed 7/2001, BRG retired, FSR submitted 7/2004).

Environmental Impact - SNARC submitted EA (7/2015); FDA/CVM found it to support a FONSI (12/2015). Sponsor requested technical section complete letter for this designation (1/2016).

Chemistry, Manufacturing, and Controls (CMC) - Complete in 5/1999; FDA/CVM request to update 5/2013

Label - Prepared by SNARC, reviewed by FDA/CVM. Will finalize pending the CMC technical section.

All Other Information - To be completed pending the CMC technical section.

2) Egg fungus Label

Human Food Safety - See above. Complete for all finfish.

Effectiveness - Complete for catfish eggs (6/2013).

Target Animal Safety - Complete (5/2010).

Environmental Assessment - To be initiated

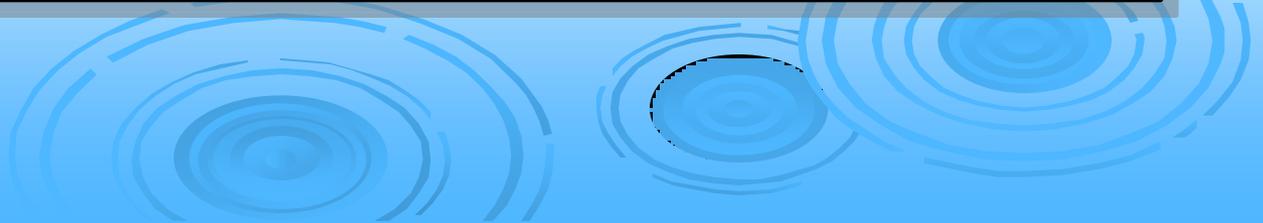
Chemistry, Manufacturing, and Controls (CMC) - Sponsor.

Label - To be completed pending the EA for this designation.

All Other Information - To be completed pending the EA for this designation.



Copper Sulfate for Columnaris??



Supporting Research

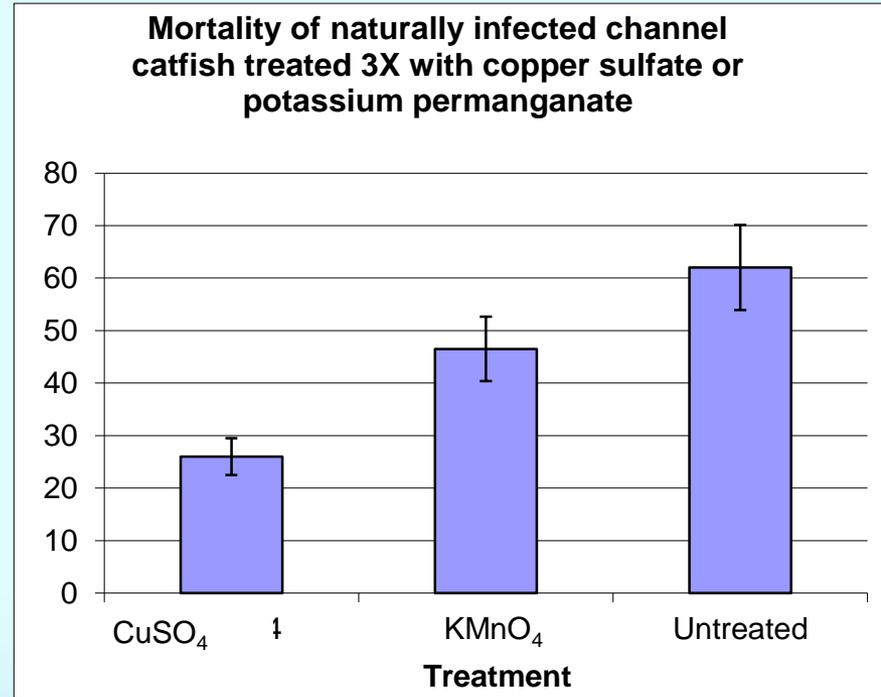
- We needed a system that could produce diseased fish (columnaris initially).
- We wanted a system to closely approximate industry parameters.
- We didn't want the disease to progress too quickly or kill all the fish.
- We wanted to leave the mucous barrier intact.
- We wanted the results to be repeatable.



Low-flow system

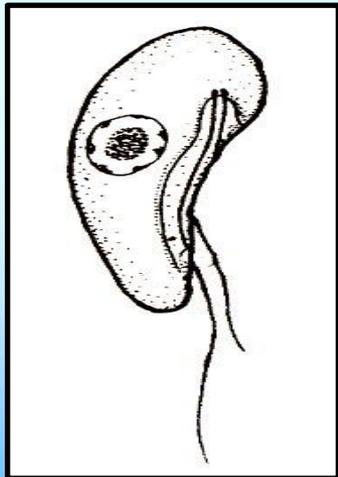
Copper Sulfate vs Potassium Permanganate

- Natural outbreak of columnaris.
- Treatment rates were 2.1 ppm CuSO_4 and 3.0 ppm KMnO_4 .
- Treatments were applied on three consecutive days at 24 h intervals.

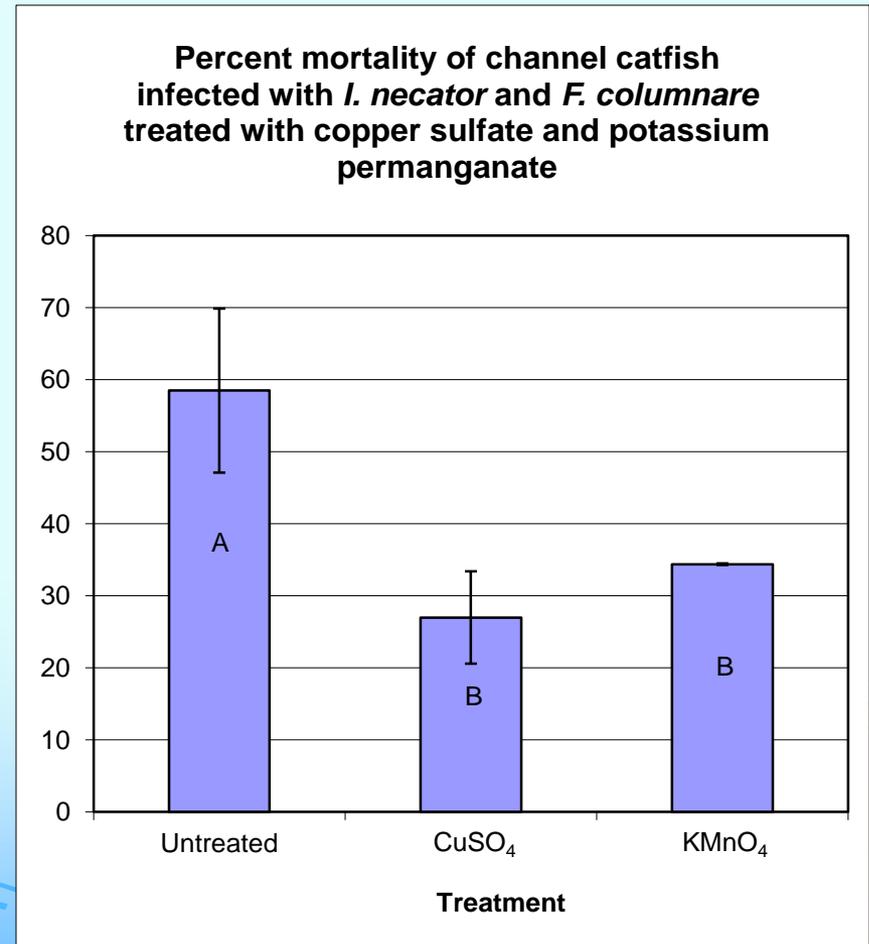


Treating Columnaris and a Parasite

- Natural outbreak of columnaris and costia.
- Treatment rates of CuSO_4 or KMnO_4 were 2.1 ppm and 3.0 ppm respectively, and were applied once daily on three consecutive days (24 h interval).



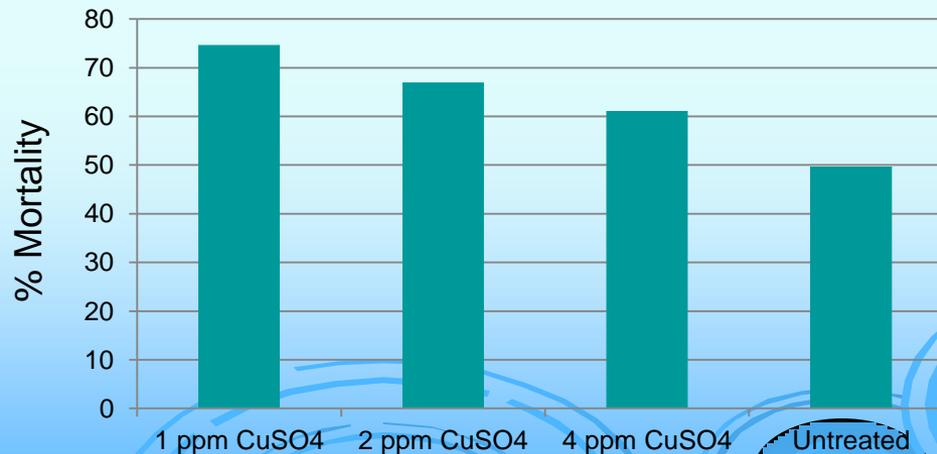
Medicated feed
WILL NOT
treat both!



Pre-treating Catfish with Copper

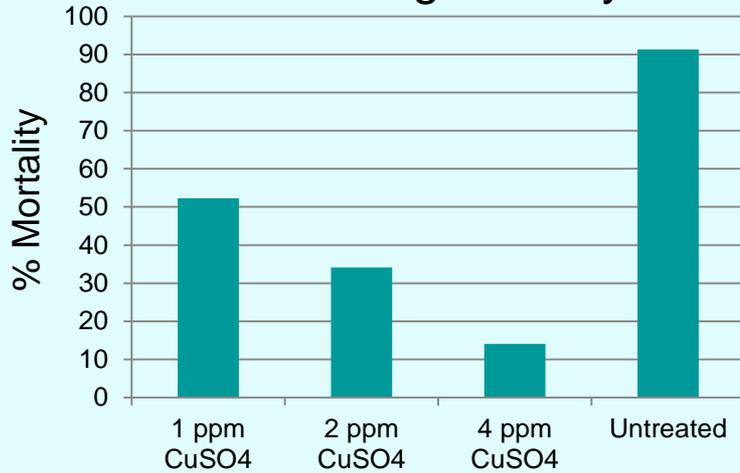
- When fingerling catfish are stressed, they are susceptible to opportunistic pathogens.
- 24 h static exposure to either 0, 1, 2, or 4 ppm copper sulfate.
- Our alkalinity is 200, making 2 ppm the recommended treatment.
- Challenged with columnaris at 0, 1, or 7 days after copper exposure.

Catfish challenged immediately following copper exposure (0 day)

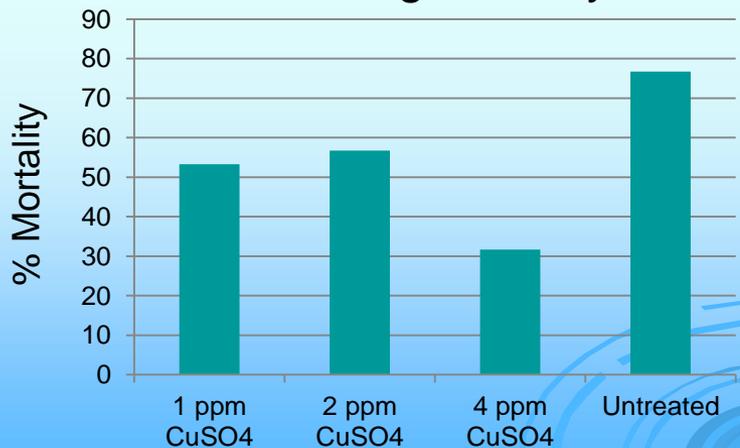


Oh, we missed something

Catfish challenged 1 day after



Catfish challenged 7 days after



Elevated Copper Levels in Feed

- Used 2X and 4X the amount of copper sulfate in standard 32% protein catfish feed.
- Fed catfish 3 diets (standard, 2X, or 4X for 30 days)
- Challenged fish at 2 and 4 weeks with columnaris
- After 2 weeks of copper-supplemented feed, fish fed the 2X and 4X diets had 20% and 27% higher survival, respectively, than fish fed the base diet
- At 4 weeks, no difference in survival was found; also, there was no difference in growth among the 3 diets and no buildup in the fillet



Bonus: Copper slows feed from molding

Conclusions

- CuSO_4 is safe for catfish eggs.
- We also tested 100 mg/L CuSO_4 and found it did not damage eggs and resulted in an excellent hatch rate.
- In addition to the low cost of CuSO_4 , it does not have the human health problems or storage precautions associated with formalin (potential carcinogen, severe skin and respiratory irritant, flammable, etc.) or hydrogen peroxide (severe skin and respiratory irritant, corrosive, etc.).



Economics 101



Copper is very cheap for hatcheries to treat fish eggs.

Treating a catfish egg hatching trough:

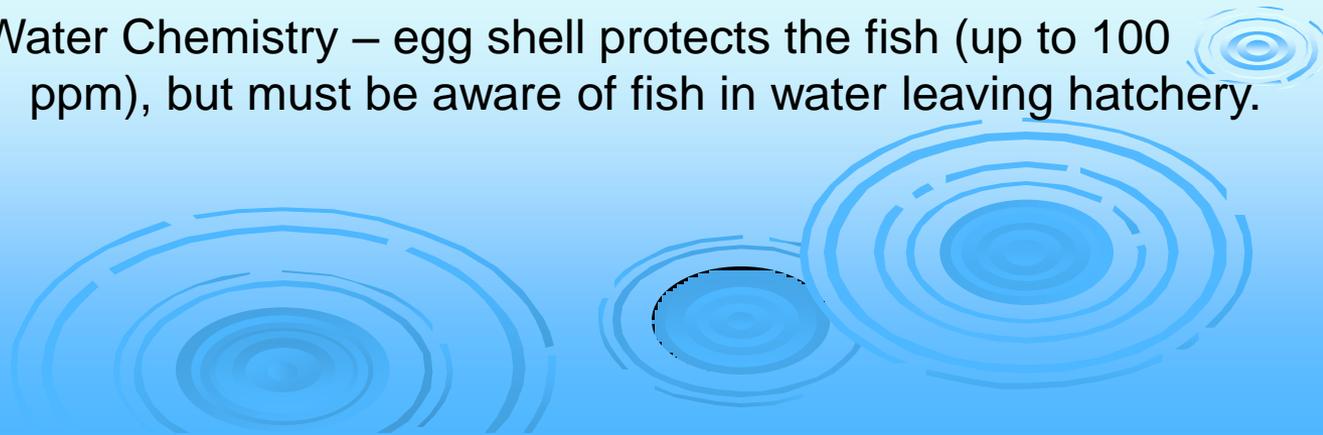
Hydrogen Peroxide (approved) - \$0.89

Formalin (approved) - \$0.73

Copper Sulfate - \$0.02

Caveats:

Water Chemistry – egg shell protects the fish (up to 100 ppm), but must be aware of fish in water leaving hatchery.



Questions?



Gerald "Jerry" Michael Ludwig
1944 – 2015