

SPECIAL SESSION

MEETING OF THE NATIONAL AQUACULTURE DRUG RESEARCH FORUM TUESDAY, FEBRUARY 27, 2007

Held in conjunction with Aquaculture America 2007

Participants: Don Prater, Jennifer Matysczak, Jim Bowker, Molly Bowman, Dave Straus, Roy Yanong, Jeff Hill, Alan Johnson, Ahmed Darwish, Drew Mitchell, Eric Silberhorn, Pat Gaunt, Christie-Sue Cheely, Martin Chen, Fu ci Guo

General Session

The group discussed posting protocols and standard operating procedures on the JSA Research Forum web page of the AADAP Website (<http://www.fws.gov/fisheries/aadap/home.htm>). There are currently 12 effectiveness and target animal safety protocols and over 200 associated standard operating procedures contributed by research from four Federal or University labs posted on this site. Feedback from fellow researchers who have accessed documents on this page has been very positive and has helped them create their own such research protocols and SOPs. There was a request that all involved in aquaculture drug approval research activities to provide pertinent research protocols and SOPs to Dr. Tom Bell (USFWS, AADAP, Thomas_a_bell@fws.gov) so that he may post them on this web page, or create a link to a website of your choosing.

Posting #152's and #159 on this web page was briefly discussed. It was decided that this issue needed further discussion.

The remainder of the meeting was devoted to Technical Project Team breakout sessions. There was no formal activity associated with the Environmental Safety, Human Food Safety, or Antimicrobial Resistance Technical Project Teams.

TARGET ANIMAL SAFETY & EFFICACY

The group had previously been charged with developing a white paper justification with a request to CVM's Aquaculture Team to consider studies that demonstrate drug efficacy on freshwater-reared steelhead trout or rainbow trout to be sufficient to satisfy the effectiveness requirements for all freshwater-reared *Oncorhynchus mykiss*. This request came about during discussions at the 12th Annual Drug Approval Coordination Workshop regarding expansion of the current label for Terramycin 200 for Fish[®] (OTC). The effectiveness technical section has been completed for use of OTC to control mortality due to columnaris in freshwater-reared steelhead trout. Several Workshop attendees questioned why the claim would be limited to steelhead trout and not include rainbow trout. The justification document was submitted to CVM on February 09, 2007.

CONCOMITANT DISEASES

The group revisited this topic to discuss how best to deal with concomitant fish pathogens when conducting field effectiveness studies. Discussion points included:

1. Determining the impact of a secondary pathogen on the primary variable (to control mortality).
2. Determining the effect of the test article (compound) on the secondary pathogen.
3. It was recommended that adding a section into the protocol that describes how to deal with detection of a secondary pathogen would be most appropriate.
4. It was recommended that protocol language include something like the following: If a secondary pathogen is noted, it will be documented, further fish health sampling will begin, and diagnostic techniques used will target detecting presence and prevalence of the pathogen.
5. A description of the pathogenesis of the secondary pathogen should be included in the final study report. A document that describes the pathogenesis of *Trichodina sp.* was developed for a study conducted by the USFWS and should be posted on the JSA Research Forum web page. Drew Mitchell (SNARC) agreed to offer fish health expertise for those drafting such a description.
6. Describe cause and effect. For example – presence of many *Trichodina* detected, but parasites observed on skin only (not on gills), gills appear normal (i.e., no lesions), and there does not appear to be pathogen-related mortality (pathogen detected on live, healthy appearing fish at levels equal to or exceeding that observed on moribund fish).
7. Reference literature when available, such as, “Authors state that in their study, the threshold of ### *Trichodina*/lamellae appeared to result in mortality.”
8. Sample fish from the infected population frequently and perform necropsy to demonstrate that the threshold has not been exceeded.
9. If a study is being conducted where the primary pathogen is bacteria (especially if it is a systemic bacterial pathogen), and the secondary pathogen is also bacteria (especially a systemic pathogen), it was recommended that the study should most likely be terminated.
10. However, if a study is being conducted where the primary pathogen is bacteria and the secondary pathogen is an external parasite or fungus, it may be likely that the study can continue if:
 - a. Data are collected to evaluate the presence and prevalence of the secondary pathogen, and such data indicate that the secondary pathogen is not directly causing the mortality or negatively impacting the overall health of the fish.
 - b. If there is no pathology associated with the pathogen (i.e., lesions).
 - c. If multiple pathogens are present, which one(s) would be most likely to cause pathologies.
11. Time to treat threshold - when the number of pathogens or lesions caused by secondary pathogen signify the time one would start a treatment for this pathogen, then it's time to pull the plug on the study.

12. Often, opportunistic pathogens (such as BGD and external parasites) can be observed on moribund fish. Are such pathogens also present on healthy-appearing fish?
13. Describe how you will deal with sampling live fish if your protocol states that you will sample only moribund fish (may require different method of analyzing mortality data).
14. Document when the secondary pathogen was first detected, approximate number of pathogens present in skin scrape/gill squash, and lesions associated with the secondary pathogen.
15. Describe in protocol procedures for sampling additional fish, including live fish, to better describe the presence and prevalence of the secondary pathogen.
16. Determine and describe the impact of the secondary pathogen on the primary variable, and rationalize this in the FSR.

TEMPERATURE GROUPINGS

With the approval of 35% PEROX AID® (hydrogen peroxide) for several uses, including use to control mortality in freshwater coolwater finfish due to BGD, CVM is anticipating questions regarding whether a particular fish species is a coolwater finfish and can be legally treated with this approved drug. The team was asked to assemble such a list of representative cold-, cool-, and warmwater fishes (and provide justification). Discussion topics included:

1. How to best deal with species that fit into more than one category (such as smallmouth bass, cool or warmwater or both).
2. Suggested grouping fish into temperature categories by optimal culture conditions (rearing temperature) for species (hybrid striped bass - coolwater is optimal, but majority grown in warmwater).
3. Suggested grouping fish into temperature categories depending upon spawning temperatures.
4. Suggested using the 2005 fish production database to help with this.

CONCURRENT THERAPY OR PRE-TREATMENT THERAPY

Salt is an LRP drug, and target animal safety studies in which salt is administered as part of the treatment (e.g., SE MARK®) should be designed to demonstrate the safety of salt as well as the safety of the test article. Dose-verification of the salt concentrations will be required

In effectiveness study, demonstrate the efficacy of the test article with and without salt (as with demonstrating the efficacy of a test article, test the efficacy of salt at the lowest proposed dose).

In TAS studies in which salt is used, test the safety of the test article with salt, and demonstrate the safety of the highest proposed efficacious concentration of the test article in the presence of the highest proposed concentration of salt (may need to also test overdose concentrations of salt).

Next meeting of the NADRF scheduled to convene in conjunction with the 13th Annual Drug Approval Coordination Workshop (Bozeman, MT, August 02, 2007)

Meeting adjourned.