

SPECIAL SESSION
ADVANCING AQUACULTURE DRUG APPROVALS BY
STRATEGIC COORDINATED RESEARCH

**5TH MEETING OF THE
NATIONAL AQUACULTURE DRUG RESEARCH FORUM
August 02, 2007**

Held in conjunction with the 13th Annual Drug Approval Coordination Workshop at the USFWS's Bozeman Fish Technology Center, Bozeman, MT

MISSION STATEMENT

“To advance scientific knowledge and coordinate research activities
to expedite the approval of new animal drugs.”

The goal of the forum is to develop a strategic plan component to work on issues relative to drug approval research activities, including (1) providing a forum for the exchange of information and mutual education between CVM review teams and representatives from academia, the pharmaceutical industry, aquaculture industry, and other government agencies, (2) establishing a repository of useful information and documents, and (3) to create a mechanism to broadly disseminate information relative to drug approval research activities.

Forum Co-Chairs:

FDA-OR	Renate Reimschuessel
USGS - UMESC	Mark Gaikowski
USFWS – AADAP	Jim Bowker
USDA-ARS - SNARC	Dave Straus

MEETING ACTIVITIES

The meeting was convened at 8 am and was scheduled to last 1 hr.

Brief updates were provided during the Workshop proper covering (1) steelhead vs. rainbow trout (CVM accepted the argument that efficacy work on either would support a claim for all *Oncorhynchus mykiss*), (2) classification of fish species based on temperature (cold, cool, and warmwater finfish) or other classification scheme (this project is more problematic than originally believed, and is going to take more time to complete), and (3) dealing with some concomitant diseases (discussions with CVM's Aquaculture Team have indicated that parasite infestations may not be fatal to a study if additional data are collected to assess level of infestation and that the Investigator provide a supporting document detailing the pathogenesis of the parasite of concern).

1. Mark Gaikowski led a discussion relative to the status and future of Technical Project Teams (TPT). Due to the nature of some of the TPTs, it seemed prudent to discuss the merit of such groups meeting on an as-needed basis rather than on a regular basis.
 - a. **Antimicrobial:** There was agreement that this group meet on an as-needed basis. Development of #152 and #159 documents are drug specific. Therefore, it seemed appropriate for those developing such documents to convene meetings as-needed to discuss. It is anticipated that such a meeting may be scheduled soon based the needs of specific drugs moving toward approval. It was agreed that Dr. Steve Yan's

involvement is critical to this process, and that Dr. Yan has been very helpful to this group.

Action Item related to Antimicrobial issues: NADRF will submit a request that a decision tree/matrix be provided by Dr. Steve Yan at the next NADRF meeting that describes what additional antimicrobial information will be needed to address Guidance 152/159 data requirements to expand the use of approved drugs.

b. Human Food Safety – Analytical Methods Development and Residue Depletion

Studies: There was agreement that this group should also meet on an as-needed basis. As soon as we reached agreement on this issue, there was considerable discussion relative to Inter-laboratory testing and method transfer studies.

There was some discussion relative to whether a method transfer study to assay drug in feed was required for minor species, and whether the Forum can be the avenue through which to formally pose such a question to CVM (pose the question in such a manner as to benefit all aquaculture drug sponsors dealing with this issue). Dr. Richard Endris indicated that there is substantial cost to conducting such studies, and as far as he knew, a method demonstration to 1 – 3 labs was required of the sponsor, as well as the involvement of three labs to fulfill the method transfer study requirements. Dr. Don Prater indicated that there might be some leeway relative to these requirements that are outlined in the new feed assay method transfer study guidance (#136) that might be applied to aquaculture products, and volunteered to take this question back to CVM.

There was also some discuss relative to grouping fish for residue depletion methods development for assaying drugs in fish tissue. Grouping becomes very important to sponsors based on the cost of such studies (Dr. Endris indicated it costs nearly \$0.5 million/per fish species for method development). Dr. Endris indicated that grouping is not required of major species such as cattle (i.e., all cattle are grouped as one species). However, because fish are poikilothermic, rearing temperature and associated metabolism is important relative to residue depletion. Hence, we appear to be stuck with grouping fish in some type of category such as temperature. On the brighter side, the CVM Aquaculture Team is now fully staffed and is now in a position to step up to assist addressing these types of issues.

Dr. Jim Powell (Aquatic Life Sciences) mentioned that evaluation of the solubility of a drug and the cardiac output of fish may be a way to group drug/fish species.

Other comments related to Human Food Safety discussion included the following:

1. Will the PhishPharm database help in the group species concept?
2. Do we need to conduct studies on coolwater species when such studies have already been conducted on cold and warmwater fish species?

Action Items related to Human Food Safety:

- 1) Dr. Endris and Jim Bowker will develop an information request memo to be submitted by the NADRF to CVM requesting a decision regarding the need to complete method transfer studies to support drug use in Minor Species. Specifically, if an approved method exists for a major species, do additional studies need to be completed for use in a minor species?

- 2) Mark Gaikowski and Jeff Meinertz will organize a conference call to discuss how best to submit the above letter to CVM.

c. Education and Outreach: Discussions focused on expanding the TPTs present education and outreach efforts and ideas for improvement.

There was some discussion relative to implementing a Continuing Education Seminar that could be held in conjunction with the annual Drug Approval Coordination Workshop and/or Aquaculture America. This idea has been pitched to several within CVM, including Steve Yan to provide more guidance on drafting 152s and 159s; CVM's Aquaculture Team to provide detailed guidance on protocols, CVM's Environmental Team to provide detailed information relative to categorical exclusion, and Fish health topics. Dr. Susan Storey suggested the need to come up with topics for "teaching" and to make sure interested folks have travel budgets to teach and attend.

Dave Lovetro suggested hosting Webinar (web-based seminars) to reach more people

Mike Barnes suggested using the AFS fish culture section to facilitate information dissemination (e.g., newsletters, etc.). Mike volunteered to help out from his end as outgoing AFS-FC President. We should consider directing future AFS-FCS requests to Dr. Curry Woods (new President).

Dr. Eric Silberhorn indicated that submissions to CVM will soon be via electronic submissions. He anticipated that such submissions will not be required for at least another 3 yrs.

It was suggested that audio should be attach to PowerPoint presentations and posted on the web for any outreach/education seminars developed.

Action Items related to Education and Outreach:

- All NADRF members are encouraged to email Dr. Susan Storey potential topics you want to be included in the Continuing Education sessions. The NADRF Co-Chairs will follow-up with Dr. Storey at the next NADRF meeting.
- Dr. Don Prater and the Aquaculture Team will work to identify common errors in final study reports to develop training guidance to provide to the NADRF during Continuing Education Seminars.
- The NADRF Co-chairs will contact Dr. Gary Jensen to determine if his new position will allow him to continue as the Education and Outreach TPT co-leader.
- Dan Carty inquired about addressing deviations that occur during field studies that should be handled in a standardized manner.
- Mark Gaikowski and Jim Bowker will determine the availability of UMESC or NCTC to host web-based training or on-site training/workshops.

d. Efficacy and target animal safety

There was some general discussion relative to efficacy studies, including (1) using NCCLS guidelines to assess drug sensitivity and antimicrobial resistance, (2) the need to monitor antimicrobial resistance during efficacy studies, and (3) whether there are

potential study participants in the field (that can be affiliated with efficacy studies) that have experience testing antimicrobial resistance during efficacy studies?

General Discussion and related Action Items

1. To facilitate completion of efficacy studies to support a claim of Parasiticide for all parasites - can we "lump" some parasites together based on biological argument (e.g., Gyrodactylus and Dactylogyrus)? If so, there is a need for more basic information about parasites, because there is not a lot of consistency with respect to their biology and treatment with a Parasiticide. Additional questions asked included (1) what are the most common ectoparasites that affect hatchery-reared fish), (2) at what level of ectoparasite infestation do they become pathologic?, and (3) are there standard techniques for diagnosis and enumeration?

Action Item: Mark Gaikowski, Jim Bowker, and Molly Bowman will take the lead on trying to draft a white-paper argument supporting the concept of lumping parasites, and provide the additional information described above in the draft document.

2. To address accurately determining number of fish moved into test tanks, Dan Carty commented on counting fish in and out of study tanks during a pivotal efficacy study to more accurately determine whether there was fish escapement, and how accurate it would be to estimate fish moved into test tanks and fish remaining in tanks at the end of the study using sample-count procedures (estimating individual fish weight based on sample counts, and then weighing all fish from each tank).

Action Item: Dr. Storey will discuss this with CVM's biometrics team and Dr. Matt Lucia of the Aquaculture Team and provide an update to the NADRF at the next meeting.

3. Research Forum Website - Should we post our website on JSA's website, since the Forum is affiliated with the JSA? All the federal agencies and offices can link to this site. Currently, the Forum products are hosted on the USFWS's AADAP website. Regardless of the web-site location, agreement was reached that such a web site needed to be prominent, easily accessible, and updated frequently.

Action Item: Mark Gaikowski and Jim Bowker will contact Dr. Max Mayeaux at the US Department of Agriculture to determine if the JSA may host the forums web site.

4. The need for a rigorous peer review process for Research Forum products. There was discussion that we needed broader dissemination of products within the forum for review before they are posted on the web or submitted to CVM. One suggested possibility was to secure a page on the website to post the document for review, delegate a small group to review the document, but have it accessible to all members that may be interested in reviewing the document. Such a process would have to be managed so that the review would be completed in a timely manner.

Action Item: The NADRF Co-Chairs will solicit input, opinions and/or suggestions relative to internal review of Research Forum products and develop a proposed plan for dissemination at the next NADRF meeting.

The meeting ended at 9:00 am. The next meeting of the NADRF will be held in conjunction with Aquaculture America 2008, and will immediately follow the last technical presentation of the Therapeutic Drug Research Species Session.

Meeting attendees:

Michael Barnes, SD GFP
Tom Bell, USFWS AADAP
Jim Bowker, USFWS AADAP
Molly Bowman, USFWS AADAP
Jim Brackett, Aquatic Life Sciences
Dan Carty, USFWS AADAP
Martin Chen, WA DFW
Richard Endris, SPAH
Dave Erdahl, USFWS AADAP
Joy Evered, USFWS, Olympia Fish Health Center
Mark Gaikowski, USGS UMESC
Tom Goodrich, Aquatic Health Resources
Mike Jawson, USGS UMESC
Alan Johnson, IA DNR
Dave Lovetro, Eka Chemicals, Inc.
Mike Mason, IA DNR
Jeffrey Meinertz, USGS UMESC
Donald Prater, FDA CVM
Rosalie (Roz) Schnick, NADA Coordinator
Steve Sharon, WY G&FD
Eric Silberhorn, FDA CVM
Neil Sims, Kona Blue
Brian Small, USDA ARS, Catfish Genetics Lab
David Starling, Aqueterinary Services PC
Susan Storey, FDA CVM
Dave Straus, USDA ARS, SNARC
Jed Varney, WA DFW