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The Association of Fish and Wildlife Agencies—the organization that represents North America’s fish and wildlife agencies—promotes sound management and conservation, and speaks with a unified voice on important fish and wildlife issues.

DAWG MEETING NOTES
Association of Fish and Wildlife Agencies – Drug Approval Working Group
Phoenix, Arizona
26 March 2008; 1330-1715 hr

Prepared by Thomas Bell on 1 April 2008

Attendees: Don Prater (CVM), Dave Straus (USDA), Mark Gaikowski (USGS), Mike Mason (Iowa DNR), Roz Schnick (NCANADA), Dave Erdahl (FWS), Steve Sharon (Chair; WY GFD), Larry Riley (AZ G&F), Gary Frazer (FWS), Mike Jawson (USGS), Ron Regan (AFWA), Robin Schrock (USGS), Christina Zarrella (AFWA), Thomas Bell (FWS).

- Meeting called to order by Chairman Steve S.
- Chairman asked if there were any additions or corrections to the minutes from the last DAWG meeting.
 - Don P. presented an extended list of corrections (see Attachment 1).
 - Roz S. noted that her previously submitted comments were very minor, and we did not go over them.
 - Dave E. noted that the DAWG minutes were not “CVM guidance documents” and questioned whether or not we should be making changes to the meeting minutes by changing what was said to what was meant to be said.
 - Otherwise the minutes were accepted.
- Status of Actions Items from last meeting.
 1. *A letter to be drafted indicating the potential for extra-label use for chloramine-T for all other uses in aquaculture – Steve S., Don P. and Roz S.:* the letter is not done and discussion was tabled.

2. *AFWS Fact Sheets – Steve S. and others:* Mark G. and Roz S. presented a draft of Fact Sheet #1 - 35% PEROX-AID[®]. Several comments were made regarding Fact Sheet #1 including 1) it was considered too long; 2) it needed some pictures; and 3) a common format should be developed for all future Fact Sheets that include use of the AFWA logo. All in attendance were asked to review the Fact Sheet and provide comments to Mark and Roz. Mark G. will begin drafting Fact Sheet #2 (environmental aspects of drug approvals such as “bench marks, etc.), but only to the extent of compiling the information (i.e., awaiting general format development). Steve S. has talked to Ron Regan regarding the AFWA website as being a place to house the Fact Sheets – no time frame or decision has been received from AFWA. Steve S. will discuss this issue again with Ron Regan. In spite of no currently identified home for the Fact Sheets, their development will not be put on hold.
3. *Efficacy Study Table – Don P.:* The basis for this request was the DAWG-letter to all state fish chiefs soliciting help with cool and warmwater studies. The table was to be used to describe what data needs (i.e., studies) still exist. Don passed out a hard copy of the efficacy study table (see Attachment 2). A discussion ensued concerning the issue of consecutive vs. alternate day treatments for chloramine-T. Don P. indicated that they must “jive”, and that if an alternate day study demonstrated efficacy, then CVM would likely include consecutive days as well in the label claim. However, an efficacious consecutive day study would not support an alternate day label claim. Steve S. suggested that this letter was important to the DAWG because many members (of AFWA) do not have direct contact with CVM by which to gain such information.
4. *Petition to be submitted to CVM regarding hydrogen peroxide as a “water treatment” vs. a “drug.” – Steve S.:* Steve S. has not yet completed this action item. It was noted by Don P. that if a veterinarian were to note a high level of fish pathogens in the water, it would be illegal for him/her to extra-label the drug, for it would not be a therapeutic claim. It was discussed that if upon receiving the letter from Steve S., CVM ruled that the use described would constitute a pesticide use (and if the compound is not registered with EPA for that use), then someone would have to complete the work to gain EPA registration for that use. Steve S. plans to complete the letter by 31 May 2008.
5. *Expanded marking claim for OTC feed – Tom B.:* Tom B. indicated that a submission was sent to CVM requesting that the efficacy technical section be considered complete for a revised label for OTC medicated feed to include an expansion of the marking claim from Pacific salmon to all FW-reared salmonids. The submission included 8 years of INAD data to support the label revision. CVM recently responded accepting AADAP’s submitted data as supportive, but stated that they would require one pivotal efficacy study in any FW-reared salmonid for the technical section to be considered complete. AADAP is in discussion with Phibro Animal Health to help support the one pivotal study.
6. *Request to include carbonic acid on the LRP list – Steve S.:* Steve (with assistance from AADAP) will submit to CVM a letter by 31 May 2008. Don P. believes that all sources of producing CO₂ should be lumped under one LRP listing. Don P. has also looked back at a request (submitted several years ago) by AADAP for iodophores to be included on the LRP list. Don P. noted that any expansion of the use-pattern for any LRP listed compound should be submitted to Fran Pell at CVM’s Office of Surveillance & Compliance. Don P. noted that the human food safety issues for any expansion of uses/forms for a listed LRP will be the same and will not need to be addressed within the request. Don P. also brought up the potential LRP status of Crude Carp Pituitary (CCP),

and noted that CVM would need to make sure that SVCV and KHV are factored into the decision. Don P. noted that it may make a lot of sense to combine a number of LRP requests (additions or expansions for several drugs) into one letter to CVM. Regarding a phone conference call to CVM on CCP, Don P. stated that the conference call should only include discussion on CCP.

7. *Letter to AFS – Fish Culture Section members soliciting help with cool and warmwater studies – Steve S.:* Don P. asked if BGD is a problem in warmwater fish. Most DAWG attendees said no, even though it came out relatively high on the unmet needs survey (Mark G. stated it was #10). On a related issue, Dave E. asked that a letter go from the DAWG (within the next couple of months) to the Florida Fish and Wildlife Conservation Commission folks and Michael Matthews at Richloam Hatchery for their recent work on chloramine-T and hydrogen peroxide in warmwater fish. Steve S. said OK, but asked for AADAP's help in writing draft. Don P. noted that CVM will have completed (and responded positively to AADAP's FSR's on the Richloam studies) within the next couple of weeks. Mark G. suggested that letters should be sent to all other facilities that have helped in the past with pivotal studies. Roz S. offered that she could send out letters to these other facilities. Steve S. responded that the DAWG should be sending out these letters because the DAWG had solicited this help. Steve S. asked that the attendees compile a list of facilities that have contributed to pivotal work. Larry R. suggested that the letters should go to the Director of the agency of which the facility is a part to make sure that the chain of command is also aware of the work. Discussion on this action item was to be completed at the Post-DAWG.

- Discussion on Isoeugenol
 - Roz S. handed-out the set of isoeugenol and zero-withdrawal documents that she sent out via email a couple of days earlier.
 - Roz S. discussed the results of the NTP studies and AQUI-S New Zealand's (ANZ's) presented arguments, in particular the fact that potentially 7-year old product was used for the chronic studies. She noted that the NTP review committee, in spite of arguments, still declared the isoeugenol studies as demonstrating clear evidence of carcinogenicity. She also noted and thanked CVM for setting up the recent "emergency" phone conference (19 March 2008) to discuss zero withdrawal anesthetic options and human food safety data requirements.
 - Steve S. had previously (based on April 2007 phone conference with CVM, ANZ, AADAP, UMESC, Roz, etc.) requested (of the AFWA Grants Committee) that the AQUI-S[®] zero-withdrawal NCN grant be suspended until at least after the 28 Feb 2008 NTP formal review. Steve S. asked that we decide if we are to continue with isoeugenol or will we ask the Grants Committee to allow the remaining funds (approximately \$190,000) to be used for another zero-withdrawal anesthetic, assuming we can identify one.
 - Ron R. asked if there was an appeal process with respect to the NTP findings. Roz S. responded that there was no appeal process. Roz S. also expressed frustration about the fact that eugenol has not yet been taken off the GRAS list in spite of the fact that it was declared by the NTP in 2000 as being a carcinogen, and that CVM (during the 19 March 2008 phone conference) expressed doubt that there would be any change to the GRAS status of isoeugenol as a result of its carcinogenicity claim.

- Ron R. suggested that it would probably be possible to amend the current NCN grant to focus on another zero-withdrawal anesthetic. He further suggested that the DAWG first go to the Fisheries and Water Resources Policy Committee for a “thumbs-up,” which in turn may be looked upon favorably by the Grants Committee.
- Don P. asked the somewhat rhetorical question “how strongly do we want/need a true ‘zero’ withdrawal anesthetic?” and noted that the DAWG might want to consider having a conversation with CVM HFS group related to how much “tolerance” might be permitted around the “zero” claim (i.e., could it be a couple hours?). Don P. also noted that CVM has no wiggle-room relative to carcinogens, and that it is stuck with interpreting the Delaney Clause as it stands.
- Steve S. noted that there currently is only one compound that is “legal” to use as a zero-withdrawal anesthetic, i.e., CO₂ or carbonic acid.
- Ron R. asked about the applicability of foreign data. According to Don P., the bottom-line is that CVM is stuck with the Delaney Clause because isoeugenol has been deemed to be a carcinogen in the U.S. and regardless of foreign data it will remain as such and fall under the Delaney Clause.
- Mark G. said it would be easy to modify the determinative method for isoeugenol down to the 1-10 ppb level.
- Dave E. brought up the issue of how we (i.e. public agencies) would be perceived if we were to continue isoeugenol efforts and ultimately gain final approval for a known carcinogen, even if we were able to establish “no-residue” levels. Dave stated that he did not believe that it is a stigma that we as public servants would necessarily want to have on our resumes.
- Steve S. stated that he did not think that we could, in good conscience, go forward with studies on isoeugenol, and if there were no objection, we should proceed with our discussions within the context of establishing an alternative to isoeugenol.
- Christina Z. noted that the NCN grant could be amended with a “no-cost” extension, but probably not with an amendment for new money.
 - Christina also noted that an amendment could be submitted within a week or so, and that she will, at the Grants Committee meeting on Thursday, bring up the issue that the naming of an alternative candidate anesthetic is pending and will be submitted with the amendment.
 - Steve S. will be attending the Grants Committee meeting on Thursday.
- Dave E. suggested that we should consider postponing the final decision on an alternative candidate zero-withdrawal anesthetic, and that we use a product development meeting(s) with CVM as a more definitive means of determining all outstanding data requirements for each specific potential candidate.
- Roz S. noted that she has already had preliminary discussions with ANZ regarding eugenol as a potential candidate and with Aquatic Life Sciences, Inc. regarding metomidate.
 - ANZ indicated interest in eugenol

- Mark G. noted that Jeff Meinertz had indicated that the methods for eugenol could probably be transferred over fairly easily from the isoeugenol methods.
- Roz. S. noted that there was no formulation established for benzocaine at the time of the switch over to AQUI-S[®].
- Mark G. said that the cost of the rat-reproduction study should be corrected on the hand-out from \$300,000 to \$600,000+.
- Steve S. asked that a motion be made relative to a decision on the continuation of isoeugenol studies.
 - Tom B. made that motion that "...all activities be suspended on isoeugenol as a zero-withdrawal anesthetic." Mark G. seconded the motion. A vote was taken and the motion was unanimously approved, with the exception of an abstention by CVM.
 - Tom B. made a second motion that "...a six-month no cost extension be proposed to the Grants Committee and the Fisheries and Water Resources Policy Committee. Dave S. seconded the motion. A vote was taken and the motion was unanimously approved, with the exception of an abstention by CVM.
- All unfinished discussion was postponed until the post-DAWG meeting on Friday.
- The meeting was adjourned at 1715 hr.

POST-DAWG MEETING NOTES
Association of Fish and Wildlife Agencies – Drug Approval Working Group
Phoenix, Arizona
28 March 2008; 0830-1200 hr

Prepared by Thomas Bell on 1 April 2008

Attendees: Don Prater (CVM), Dave Straus (USDA), Mark Gaikowski (USGS), Mike Mason (Iowa DNR), Roz Schnick (NCANADA), Dave Erdahl (FWS), Steve Sharon (Chair; WY GFD), Mike Jawson (USGS), Thomas Bell (FWS).

- Discussion on other AFWA priority drugs:
 - Diquat: Roz S. noted that Jim Brackett at Aquatic Life Sciences, Inc. is working on this.
 - Discussion on other AFWA priority drugs was postponed until after completion of continuing discussion on isoeugenol and AQUI-S[®] (see pages 4-6).
- Discussion on isoeugenol and AQUI-S[®] and a potential replacement zero-withdrawal candidate.
 - Decision not to do further work on isoeugenol
 - Steve S. asked the AFWA Grants Committee to roll-over the \$190,000 to a new candidate.
 - The Grants Committee was supportive of the request.
 - Steve S. will work with Christina Zarrella.
 - The Grants Committee was concerned with the logistics concerning the FWS transfer of Funds from Federal Aid.
 - The Committee noted that a new grant request may have to be submitted
 - The Committee said that the new grant request should not be as detailed as the previous one.
 - The Committee asked if this \$190,000 and the work that it funds, will result directly in the approval. Steve S. responded “no,” and that other funding sources would be sought, but that the \$190,000 will give a “jump start” to a completed set of required studies.
 - The Committee suggested that the DAWG provide the Committee with the drug identified as the new zero-withdrawal candidate within 6 weeks. Steve S. asked for 8 weeks and the Committee concurred.
 - The amendment, once approved, will be a 1 year no-cost extension, with a possibility for a further no-cost extension.
 - Steve S. indicated that he thought the Committee may work with us if we can not identify a new candidate within the 8 week period, and further suggested that he was pretty much planning on asking for an extension to the 8 weeks.

- Steve S. noted that there was no implied or expressed idea that there would/could be a further request for new money.
- Mark G. suggested that the \$190,000 should be used to fund the toxicity studies, and that base fund could potentially be used to fund residue studies.
- Roz S. stated that ANZ expressed interest in eugenol, but that they will need, in writing, something from CVM stating what studies will be required, unlike the past experience where they found out several years into the isoeugenol work that a 90-day dog study would be required to complete the toxicology package. She also stated that she believed that eugenol is the most viable potential candidate.
- Don P. stated that it is very important that sponsors are “transparent” with partner agencies with respect to overall goals and objectives of collaborative approval efforts. Partners and sponsor agencies must be on the “...same page...” with respect to priorities and activities.
- Steve S. stated that our decision was to get a zero-withdrawal anesthetic for public aquaculture, which was much less than what ANZ wanted.
- Steve S. stated that he did not want to leave this meeting having made the decision (at this point in time) to concentrate our immediate efforts on just one potential candidate zero-withdrawal drug.
- Mark G. suggested that ANZ schedule a pre-submission conference with CVM for eugenol.
- Steve S. stated that he does not want ANZ to be given the impression, at this early stage, that we have selected eugenol as the candidate, and that we need to use the 8 week to make that selection and not leave any option unexplored.
- Steve S. asked the attendees which of the “top 3” (MS-222, eugenol and benzocaine) had the best chance of attaining a zero-withdrawal.
- Don P. brought up the information provided by Renate Reimschuessel (CVM – Office of Research) regarding the work she recently completed establishing the lack of MS-222 residues measured after very short periods (hours) following treatment.
- Dave E. asked whether residues for eugenol might be expected to be similar to isoeugenol. Roz S. responded “yes.”
- Roz S. suggested that any residue work to be done needs to be conducted on catchable-size fish, unlike the work that was done on fingerlings for isoeugenol.
- Mark G. suggested that the exposure pattern for any residue work to be done should be for shorter, more realistic “sedation” treatment periods, unlike the 60 min used in isoeugenol studies. Steve S. agreed.
- Roz S. noted that sponsors want as broad an approval as possible. Dave E. responded that the DAWG has never supported, or desired, a broad claim for a zero withdrawal anesthetic. Conversely, our focus should be to support its use as a public aquatic resource management tool (a very narrow claim, i.e., sedation to a handleable stage).
- The notion was brought up that any potential sponsor for the new “candidate” would need some estimate of the market to factor into their decision.

- Tom B. suggested surveying states to determine the amount of MS-222 currently being used. This, in spite of its clear shortcomings, might provide a “best” estimate of the potential market for the new “candidate.”
- Roz S. suggested instead that the 2005 Public Aquaculture Production Database (PAPD) fish production data be used to estimate the need.
- Steve S. suggested that he could very quickly get MS-222 use data from Washington and Michigan as examples.
- Tom B. suggested using the WA & MI MS-222 data and the PAPD to extrapolate a national estimate of MS-222 use, from which to draw a crude estimate of the projected use for the new candidate zero-withdrawal anesthetic.
- Dave E. said that uses in the field of a new zero-withdrawal anesthetic may convince/persuade biologist to use it in hatcheries as well, thus increasing its potential use.
- Steve S. will contact WA & MI.
- Mark G. suggested that universities and the scientific literature may be another source of information to factor into the projected use estimate.
- Tom B. volunteered to attempt an extrapolation of the projected use estimate by using the PAPD and the information provided by Steve S. from WA & MI.
- Steve S. suggested that university CO-OP units might be a source of MS-222 use.
- Tom B. suggested that FWS’s Management Assistance Offices might also be a source of this information.
- Steve S. noted that if we don’t get a sponsor for a “new” zero-withdrawal anesthetic, we may not get a no-cost extension from the Grants Committee. Further he stated that we want a true zero-withdrawal not a near zero-withdrawal anesthetic.
- Don P. stated that CVM’s Human Food Safety (HFS) group may provide a “several hour” withdrawal. He stated that we should ask the HFS group “...what are they comfortable with...”, e.g., if fish are not caught within 3 hrs this may be acceptable to HFS and may work for us. He said we could have a phone conference with the HFS group real quick to discuss the potential of mitigating the “zero-withdrawal.”
- Don P. also noted that CVM might be able to “label-around” a rested-harvest claim.
- Steve S. stated that he would have the WA & MI data to Tom B. by 8 April, and that Tom will finish the extrapolation estimate by 15 April.
- Steve S. wants transparent communications; i.e., all the use-pattern information is to come through him.
- Steve S. plans to go back to the Grants Committee for an additional extension by approximately the end of April and by then we may possibly have some commitment by a sponsor(s) to schedule a pre-submission meeting(s) with CVM.

- Don P. proposed that CVM should not be a voting member of the DAWG and there was unanimous acceptance of his proposal.
- Discussion on chloramine-T
 - Don P. commented on the recent studies conducted at Richloam SFH (FL)
 - He stated that the studies looked good and that CVM would be getting the letters out to AADAP soon. Further he noted that the 12-tank study will be accepted as pivotal, while the other study would be supportive.
 - He also stated "...if something [a drug] works [i.e., is efficacious] every other day, CVM will give an every day claim as well..." and that it is "...just the opposite for target animal safety studies..."
 - On a different subject Don P. noted that his "review" of the draft letter intended to go to AFS-FCS members, as well as the DAWG brochure, "...look good..."
 - He said that there will be no new data requirements [i.e., TAS, environmental, etc.], relative to the added warmwater claims.
 - Steve S. stated that he will prepare the letter of thanks for Richloam and will get Virgil Moore (Chair of Fisheries and Water Resources Policy Committee) to sign it.
 - Roz S. noted that Axcentive now has the full English translation of the manufacturing chemistry package, and she thought that it will probably be submitted by end of April and should be reviewed by October (if submitted in April). However, she thought that it will probably not pass the first review and will have to be resubmitted. She is now working on the AOI with Ed Bisinger, and the text for the label has been submitted to CVM. She is of the opinion that the largemouth bass claim will be able to be added as part of this initial approval package. She also stated that the FOI has been written.
- Other AFWA drugs and miscellaneous discussions
 - Roz S. noted that Phibro Animal Health should receive approval for their new OTC claims prior to this year's Workshop in Bozeman.
 - Don P. said that CVM gave \$50,000 to Roz S. for this fiscal year (1 May 2008 to 30 April 2009), but CVM does not believe that there will be a need for the formal NCANADA position after May 2010. CVM will probably drop her funding for the 2009-2010 fiscal year to approximately \$35,000.
 - Roz S. felt that the CuSO₄ package is getting really close to completion. She also stated that Renate R. is now working on the Final Study Report for formalin as a fungicide in all freshwater finfish.
 - Steve S. said that he is considering moving the spring DAWG meeting to be held in conjunction with Aquaculture America. There was general agreement among attendees that such action would be prudent.
 - Dave E. stated that Don P. had indicated to him that the AQUI-S[®] INAD would be rescinded; a letter to that effect from CVM to AADAP would be forthcoming.
 - Roz S. funding discussion:
 - Currently \$50,000 from CVM and \$5,000 from USGS.

- Steve S. noted that he wrote a letter to Stuart Leon (FWS) requesting funds for Roz, but given yesterday's review by Gary Frazer of FWS – Fisheries and Habitat Conservation's budget, the prospect of funds from FWS would appear dismal.
- Roz S. stated that she has enough funds to continue at 87.5% from May 2008 to April 2009, and that all monies go through Michigan State University and that Ted Batterson (who manages her account) does not take any overhead. She further noted that she is comfortable with the current funding level, but as an aside she has been working 12-15 hour days to prepare for this meeting.
- Steve S. suggested that we need to create a transitional process for Roz's many duties/responsibilities during Roz's final two (2) years. It was decided that such a transitional strategy should be on the September 2008 DAWG agenda.
- Roz. S. noted that she had already met in December 2007 with CVM to discuss her transition out of the NCANADA position. She also noted that once she actually does retire she does not intend to be totally out of the process, and that she will entertain contract work on special projects and feels that her "institutional memory" may be valuable.
- Tom B. briefly went over the Service's newly revamped National Wild Fish Health Survey and its possible benefit to state resource agencies. The purpose of his comments was to get advice from the DAWG as to how to best present this proposal to the AFWA.
 - Steve S. suggested that Rob Bakal (FWS), who attends the AFWA's Fish and Wildlife Health Committee, should propose this as an agenda item for September's meeting, and that Gary Frazer (FWS), a member of AFWA's Fisheries and Water Resources Policy Committee, should do the same there.
- Parasite Survey discussions:
 - Mark G. noted that they have received comments back from the internal reviewers. He also stated that even though the focus is on freshwater ectoparasites, it will include a few questions on endoparasites. The survey comprises 9 pages, and will be a web-serve survey, presented as a link within an email, sent to prospective respondents. If all goes as planned, it should be sent out by mid-April.
 - Mark G. asked whether it should be sent out on the DAWG's letterhead. Steve S. suggested that AFS-Fish Health Section may be more appropriate, but that the DAWG would not object the DAWG being somehow identified on the document.
- Review of Post-DAWG Meeting Action Items.
 1. *H₂O₂ Fact Sheets*: Everyone is to review the H₂O₂ fact sheet, paying particular attention to format, etc. and respond by the end of May. Roz. S. will send an electronic copy to Steve for distribution to DAWG members. Hopefully this can be finalized by Bozeman meeting.
 2. *New Fact Sheets*: At the September 2008 meeting we will discuss what other Fact Sheets we will work on, how to implement these, who they will go to, etc.
 3. *DAWG website*: Steve S. will talk with AFWA (Ron Regan) after they get a webmaster. The purpose of the discussion will be to get a DAWG page as a home for DAWG products, such as the Fact Sheets.
 4. *Letter to Richloam*: Steve S. to write letter, but will ask AADAP to assist.

5. *Prioritization Issue:* Dave E. offered comments about AADAP's prioritization in the context of the DAWG's focus. This will be an agenda item for the September 2008 meeting.

Dave noted that AADAP's primary focus at this point is the zero-withdrawal anesthetic issue, but directly below that have been/are Aquaflor[®] and Terramycin[®] 200 for Fish for systemic columnaris, ongoing cool and warmwater species chloramine-T work at Richloam SFH, a SLICE[®] INAD, and OTC skeletal marking via feed.

6. *Revisions of the Aquaculture Drug Approval Process Brochure:* Between now and September 2008 Steve S. will request from DAWG members suggestions for a revision.
- Miscellaneous comments:
 - Roz S. discussed a manuscript that she is working on that describes the total partner monetary contributions. She will send out a solicitation email to all agencies explaining the purpose of the manuscript and what she needs from each agency.
 - The meeting was adjourned at 1200 hr.