U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

"Working with our partners to conserve, protect and enhance the Nation's fishery resources by coordinating activities to obtain U.S. Food and Drug Administration approval for drugs, chemicals and therapeutants needed in aquaculture"

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AADAP NEWSLETTER

December 2012

Beaverslide hay stackers, Big Hole River Valley, Montana USA

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WHAT'S SHAKIN'

The Importance of Using FDA-Approved Aquaculture Drugs

This year, the American Fisheries Society's (AFS) Fish Culture Section (FCS) Working Group on Aquaculture Drugs, Chemicals, and Biologics (WGADCB) and the U.S. Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) collaborated on professional outreach projects to better inform and educate the U.S. public and private aquaculture sectors about FDA-approved aquaculture drugs. One outcome of that collaboration was a letter—published online by FDA—that explains the benefits of the U.S. aquaculture drug-approval process and lists all FDA-approved drugs for fish. The letter is reprinted below, with a following link to the original.

October 16, 2012

***Dear Aquaculture Professional*:**

The U.S. Food and Drug Administration (FDA) wants to remind you that not all drugs currently marketed for food fish (fish that will enter the human food supply) are approved. And even if a marketed product has the same established name (active ingredient) as an FDA-approved drug, that doesn't mean it's also FDA approved.

Please see Table 1 for a list of FDA-approved fish drugs. If a product currently marketed for food fish isn't listed, it's not FDA approved, and therefore it hasn't been shown to be safe and effective in food fish. For example, only the four listed formalin products are approved by FDA for fish. Any other formalin-containing products marketed are not FDA approved.

FDA rigorously evaluates an animal drug before approving it. As part of the approval process, the drug company must prove to FDA that:

- The drug is safe and effective for a specific use in a specific animal species. For food fish intended for

Table 1. FDA-approved fish drugs	
Name (established name)[1]	**Application type and number [2, 3]**
Formalin-F™ (formalin)	NADA 137-687
Formacide-B (formalin)	ANADA 200-414
Paracide-F (formalin)	NADA 140-831
Parasite-S (formalin)	NADA 140-989
35% Perox-aid (hydrogen peroxide)	NADA 141-255
OxyMarine™ (oxytetracycline hydrochloride)	NADA 130-435
Oxytetracycline HCl Soluble Powder-343 (oxytetracycline hydrochloride)	ANADA 200-247
Pennox 343 (oxytetracycline hydrochloride)	ANADA 200-026
Terramycin-343 Soluble Powder (oxytetracycline hydrochloride)	NADA 008-622
Tetroxy Aquatic (oxytetracycline hydrochloride)	ANADA 200-460
Finquel (tricaine methanesulfonate)	NADA 042-427
Tricaine-S (tricaine methanesulfonate)	ANADA 200-226
Chorulon® (chorionic gonadotropin)	NADA 140-927
Aquaflor® Type A Medicated Article (florfenicol)	NADA 141-246
Terramycin® 200 for Fish (oxytetracycline dihydrate)	NADA 038-439
Romet®-30 (sulfadimethoxine & ormetoprim)	NADA 125-933
Sulfamerazine In Fish Grade (sulfamerazine)	NADA 033-950

[1] Established name is the active ingredient
[2] NADA – New Animal Drug Application
[3] ANADA – Abbreviated NADA
Note: Two drugs for ornamental fish are on the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species

human consumption, the drug company must also prove that food made from fish treated with the drug is safe for people to eat;

- The manufacturing process is adequate to preserve the drug's identity, strength, quality, and purity; and
- The drug's labeling is truthful and complete.

FDA's role doesn't stop after the agency approves an animal drug. As long as the drug company markets the animal drug, the agency continues to monitor the drug's:

- Safety and effectiveness to determine if concerns arise that were unknown at the time of approval;
- Manufacturing process to ensure quality and consistency are maintained; and
- Labeling to make sure the information remains truthful and complete.

FDA-approved animal drugs are scientifically shown to be safe and effective when used according to the directions on the label. If the approved drugs are for food fish, food made from treated fish is safe for people to eat. FDA-approved animal drugs also meet the agency's strict standards for quality, purity, and potency.

The Center for Veterinary Medicine (CVM) at FDA is responsible for ensuring that safe and effective drugs are available for animals. If you have questions or would like more information, please call the CVM Communications Staff at 240-276-9300, or email us at *AskCVM@fda.hhs.gov*.

Sincerely,

FDA's Center for Veterinary Medicine

Editor's Notes:

(a) The letter can be accessed at:

http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm324048.htm

(b) More details on this collaboration between the AFS and FDA can be found in AFS's WGADCB Corner on page 7.

FDA Proposing to Revise Animal Drug Regulations for Residue Tolerances

On Dec 5, 2012, the Food and Drug Administration (FDA) announced that it is proposing to revise the animal drug regulations regarding tolerances for residues of approved and conditionally approved new animal drugs in food by standardizing, simplifying, and clarifying the determination standards and codification style. In addition, FDA is proposing to add definitions for key terms. The purpose of the revision is to enhance understanding of tolerance determination and improve the readability of the regulations. Public comments (electronic or written) are due by March 5, 2013.

For details, please see *http://www.gpo.gov/fdsys/pkg/FR-2012-12-05/html/2012-29322.htm* or contact: Dong Yan, Center for Veterinary Medicine (HFV-151), Food and Drug Administration, 7500 Standish Place, Rockville, Maryland USA 20855 (phone: 240-276-8117; email: *dong.yan@fda.hhs.gov*).

Romet® 30 and Romet® TC – Availability Update

As many of you have experienced and continue to experience unavailability of Romet® 30 and Romet® TC these past months, a word of explanation is warranted. PHARMAQ AS, which holds the NADA for Romet®, was forced to change manufacturing sites in July 2012. During these past 6 months, the FDA-required method transfer process, including validation of three batches, has been ongoing. The good news is that the batches have been made and are currently undergoing analytical testing. When the test results and final reports for the validation runs have been received and submitted to FDA for approval of the method transfer, product will be available again in early 2013. If you need additional information or have any questions, please call George Kohan (952-443-4423) or Tom Goodrich (425-922-4208).

Text provided by Dr. Tom Goodrich; AquaTactics Fish Health; Kirkland, Washington USA (*tomg@aquatactics.com*)

AADAP DRUG UPDATES

In the September 2012 AADAP Newsletter, we noted we were hip-deep in conducting target animal safety (TAS) studies. We've completed those studies and are now hip-deep in data compilation and analysis, histology, and report writing. Over the years, we've become adept at multi-tasking and, as a result, are now involved in a number of other drug-approval related activities. Please read on for an update of our research activities.

AQUI-S®20E and BENZOAK®

A whole bunch of efficacy studies—In the September 2012 AADAP Newsletter, we summarized trials conducted to demonstrate the efficacy of AQUI-S®20E (10% eugenol) and BENZOAK® (20% benzocaine) to sedate fish to handleable. Since then, we have submitted a letter to CVM requesting that the AQUI-S®20E efficacy technical section be considered complete for sedating ALL freshwater finfish, including ornamental fish, to handleable. For the first time in such a request, we included INAD data that supported the time-to-sedation and time-to-recovery data generated in our pivotal studies. We also proposed some cautionary language for the AQUI-S®20E product label, which would emphasize that fish that are overdosed (exposed at a too-high concentration), overexposed (exposed for a too-long duration), or both might take a long time to recover (e.g., up to 30 minutes for catfish!). We expect to receive CVM's response by mid-2013.

Target animal safety studies—We recently completed three AQUI-S®20E TAS studies: the first on fingerling rainbow trout, the second on yellow perch, and the third on channel catfish. In each study, we exposed fish to concentrations of eugenol that we considered to be the highest proposed efficacious dose (1× dose) and a dose that was 1.5× the highest proposed efficacious dose. These studies were designed to identify how long fish could be left in the 1× and 1.5× sedative solutions and achieve ≥95% survival after the sedated fish were moved to fresh water. The difference between the time required to sedate fish to handleable and the longest treatment duration that results in ≥95% survival is termed the "margin of safety." Our goal was to demonstrate that the margin of safety at the 1× dose was at least 3-4 minutes and at least 2-3 minutes at the 1.5× dose.

We tested rainbow trout at 40 and 60 mg/L eugenol, yellow perch at 80 and 120 mg/L eugenol, and channel catfish at 100 and 150 mg/L eugenol. For all three species, we were able to preliminarily identify—based on mortality and general behavior—sufficient margins of safety. We'll be able to confirm these margins of safety after we receive our histopathology report from Beth MacConnell (Headwaters Fish Pathology, LLC, Bozeman, Montana USA). In the meantime, we're having fun crunching numbers and drafting final study reports.

Channel Catfish Pituitary

Environmental assessment—We are getting close to the finish line! The Environmental Safety Team at CVM recently sent us their proposed final revisions to the Channel Catfish Pituitary (CP) Environmental Assessment (EA) document. As you might expect, we accepted all of their revisions and also provided some additional information that they had requested. We resubmitted the revised CP EA to CVM on December 7 and are cautiously optimistic that it will be accepted. Thanks to Dr. Chris Green (Louisiana State University, Aquaculture Research Station, Baton Rouge, Louisiana USA) and Dr. Nagaraj Chatakondi (U.S. Department of Agriculture, Agricultural Research Service, Catfish Genetics Research Unit, Stoneville, Mississippi USA) for their help in completing this EA.

Target animal safety—We worked with the CP sponsor, Roger Yant (Hybrid Catfish Company, Inverness, Mississippi USA), and Dr. Patricia Gaunt (Mississippi State University, College of Veterinary Medicine, Stoneville, Mississippi USA) to develop a research protocol to evaluate the safety of CP to female channel catfish. The protocol is being reviewed by our Quality Assurance Officer (Jennifer "JR" Royston, Bozeman, Montana, USA) and will be submitted to CVM by the end of the year.

Efficacy and manufacturing—Next on the docket for CP is to develop a research protocol describing procedures to be used to evaluate the effectiveness of this product as a spawning aid for female channel catfish. In addition, we'll be studying documents provided by CVM's Biotherapeutics Team to determine

what actions (data) will be necessary to complete the Chemical, Manufacturing, and Controls data requirements for CP.

SLICE®

Target animal safety—In the September 2012 newsletter, we noted that the SLICE® (0.2% emamectin benzoate) target animal safety (TAS) study on fingerling rainbow trout had been completed. In that study, no mortality occurred in the 0×, 1×, 2×, or 3× exposure groups, fish in all groups fed aggressively, and no abnormal behavior was observed. We have received the histopathology report from Beth MacConnell, and—as anticipated (hoped!)—nothing remarkable was detected. Consequently, we concluded the margin of safety extended to 3× the proposed efficacious dose of 50 µg emamectin benzoate/kg fish/day when administered for 2× the standard duration of 7 days. Our final study report (FSR) has been submitted for review to our Quality Assurance Officer (QAO), JR Royston. When we have addressed any QAO issues, we'll submit the FSR to CVM with a letter requesting that the TAS technical section be considered complete for all freshwater reared salmonids.

Drug Research Information Bulletins

AADAP's Drug Research Information Bulletins (DRIBs) are in-house publications that briefly (1-3 pages) summarize work we and our partners have done to evaluate the efficacy and target animal safety of aquaculture drugs being considered for approval by FDA CVM. To date, we have published 29 DRIBs, all of which can be accessed and downloaded at *http://www.fws.gov/fisheries/aadap/publications.HTM*. The DRIBs published in 2012 were:

- *No. 28—Safety of 17 α-Methyltestosterone Administered in Feed to Larval Nile Tilapia*
- *No. 29—Safety of SLICE® (0.2% Emamectin Benzoate) Administered in Feed to Rainbow Trout*

In 2013, we'll be writing several new DRIBs, including summaries of our recent target animal safety work with AQUI-S®20E on rainbow trout, yellow perch, and channel catfish.

Text provided by Jim Bowker (jim_bowker@fws.gov), Research Program Manager; USFWS AADAP; Bozeman, Montana USA.

FINS & TAILS, BITS & BOBBERS

OvaRH® (sGnRHa; injectable) INAD 12-186

The AADAP Office has received a food-use authorization for finfish treated with sGnRHa (OvaRH®). This INAD is now available for National INAD participants to enroll in for calendar year (CY) 2013. We note that sGnRHa (OvaRH®) is an injectable product that has been developed by Western Chemical, Inc., specifically to induce gamete maturation in a broad variety of fish species. Interested participants should contact Bonnie Johnson (*bonnie_johnson@fws.gov*) to receive a copy of the study protocol and appropriate authorization from FDA/CVM.

INAD Enrollment Open for CY 2013

It is time for the renewal of your facility's INADs for CY 2013. Investigators will need to log into their INAD Program Management System (IPMS) accounts; click on the Account Info tab; click on the "add Drug/INAD" button; and select INADs, fish species, and enter fish number for anticipated use for CY 2013. Please note that INAD participation is not renewed automatically in the IPMS from the previous year, so you will need to have this done before December 31, 2012.

The AADAP INADs currently available are:

- Chloramine-T
- Oxytetracycline medicated feed (Terramycin®200 For Fish)
- Calcein (SEA-MARK®)
- Florfenicol (AQUAFLOR®)
- Oxytetracycline Immersion Therapy (Pennox 343®)
- LHRHa
- Carp pituitary
- Ovaplant® (sGnRHa)
- Catfish pituitary
- Diquat (Reward®)
- Hydrogen peroxide (35% PEROX-AID®)
- BENZOAK® (benzocaine)
- AQUI-S®20E (eugenol)
- SLICE® (emamectin benzoate)
- 17-alpha methyltestosterone medicated feed
- OvaRH® (sGnRHa; injectable)

The normal INAD fee of $400 will apply to all INAD sign-ups, with the following exceptions: (1) $600 is charged for the use of 17-alpha methyltestosterone medicated feed; (2) no charge for the AQUI-S®20E and BENZOAK® INADs when treatment is for hatchery use; (3) $200 will be charged for the AQUI-S®20E INAD (per Investigator) when treatment is for field use, with a maximum of $600 charged for each agency/office; and (4) no fee for Federal facilities because the National INAD Office was originally created for Federal INAD use.

2012 INAD Wrap-Up

All 2012 INAD study data need to be entered in the IPMS by December 31, 2012. However, please note that if your facility will be conducting treatments in December, you will have time in January to complete data entry. Special Note: All 2012 study requests should have been completed before December 15 for any previous studies that have been conducted but not

reported. As of January 1, 2013, no study numbers will be issued for 2012 studies. If your facility fails to report any 2012 INAD studies, you will be "on your own" should FDA audit your facility.

Please note that, in the past, we would now also be requesting that you send in your Form 2 Drug Inventory forms showing amount of drug on hand and if any studies had occurred for that year. Thanks to the IPMS, this action is no longer necessary because all inventory forms are now available to the AADAP Office on-line. However, it would be much appreciated if Investigators would take a minute or two to double-check—just to be sure—that all drug inventory information is correct. If no studies occurred and no study worksheets were initiated in 2012, there is no need for your facility to do anything else to wrap up year 2012.

IPMS Database Upgrade Successful

A new upgrade to the IPMS database was successfully uploaded November 13, 2012! All investigators should log into their accounts and make sure their information is correct. The specific areas we request you check are the drug inventory amounts in the studies and on the Manage/View Drug Inventory page. The drug inventory sections of the IPMS were completely redone, so if your facility was experiencing any drug inventory problems (e.g., balance on-hand) they should be fixed. Also, Investigators are now able to correct entry dates, amount of drug used, and delete drug receipts if necessary.

The Mortality Graph and Summary Report buttons are now working. You can print and archive a copy of each of these reports once your study has reached Stage 7. Both of these reports summarizing each study are submitted to FDA in the Annual Report. Please note you can also view your Mortality Graph in earlier stages; however, you will need to make sure you have saved your data in Stage 4 before viewing this report. If the study has not been saved and you try to view the mortality graph, you may lose some of your data.

Text provided by Bonnie Johnson (bonnie_johnson@fws.gov), National INAD Program Administer, USFWS AADAP; Bozeman, Montana USA

Bonnie Johnson with Lake Trout
at Lewis Lake in
Yellowstone National Park, Wyoming USA

FEATURE ARTICLE

Response to Recent Editorials on the New Animal Drug Application Process

by

Dr. Jennifer Matysczak
Leader, Aquaculture Drugs Team
U.S. Food and Drug Administration
Center for Veterinary Medicine
Office of New Animal Drug Evaluation
Rockville, Maryland USA

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AADAP asked me to provide a response to Dan Carty's editorials that were published in the July 2011 and March 2012 AADAP Newsletters. In the first editorial, Mr. Carty offers suggestions on how to increase the biological inferential value of studies conducted to support the effectiveness and target animal safety technical sections of a new animal drug application (NADA). In the second editorial, he compares regulatory science and academic science and advocates for greater use of literature and expert opinion in the animal drug approval process. Researchers and drug sponsors should not feel limited to the "current approach" described in Mr. Carty's first editorial. While there are laws and regulations that govern the NADA process, there is flexibility in meeting regulatory requirements, and CVM considers all proposals from sponsors. Below, I provide additional perspective on some of the recommendations made in the two editorials.

In his first editorial, Mr. Carty talks about using pilot work, literature, expert opinion, and other already existing data to inform study design. I recommend starting the process here as well. This information can provide a preliminary picture that can be used to determine producer needs, refine any studies that need to be conducted, and reduce the number of studies needed to complete data requirements.

Beyond providing background information, it is possible that literature can provide evidence of effectiveness or safety and satisfy approval requirements. If there is some, but not enough, evidence available in the literature to adequately assess the effectiveness or safety of a drug, literature may help reduce the number of studies and/or narrow the scope of studies that a sponsor needs for approval. Literature has been used in various technical sections, including effectiveness and target animal safety, for several aquaculture drug approvals. If applicable literature exists, I recommend that the sponsor work with CVM to devise a strategy that

maximizes the utility of the information available and to discuss how to present the information.

Mr. Carty noted that in many cases aquaculture drug partners/sponsors perform single-site studies and submit individual study reports one at a time to CVM for review. However, this is not the only way it can be done. Multi-site animal drug studies are not uncommon; however, they involve a different type of protocol and analysis. Additionally, many sponsors pursuing approvals in multiple drug classes for multiple species, major and minor, including some aquaculture sponsors, submit all of their studies supporting a technical section requirement at one time. CVM is flexible and recognizes that, due to limited resources or unpredictability in disease outbreaks or other reasons, conducting single-site studies and submitting individual study reports is more practical in some cases. When this is done, before issuing a technical section complete letter, CVM considers everything submitted up to that point as a whole. The sponsor should summarize everything relevant to the indication and technical section when requesting a technical section complete.

In his second editorial, Mr. Carty advocates for greater reliance on expert opinion in the review of effectiveness and target animal safety technical sections of a NADA. Expert opinion should be incorporated into final study reports to provide interpretation of research findings and an assessment of whether the findings support the study objective and the technical section. CVM staff may seek additional input from outside experts to gain additional knowledge or help inform decisions, but not in any way that would jeopardize the confidentiality of drug applications. In the case of Indexing (*http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/MinorUseMinorSpecies/ucm070206.htm*), sponsors may include anecdotal opinion from experts, and significant weight can be placed on these opinions when considering whether a drug qualifies for Indexing. However, the standards in the new animal drug regulations are more stringent for approvals than for Indexing and require evidence in the form of studies (actual data that demonstrate that the product works and is safe) to support the claim.

While I am not a statistician, it is my understanding that statistics are a tool in interpreting results—that is, they tend to support the ultimate conclusion. Obtaining a desired statistical outcome is not the only criteria in determining a study has met regulatory requirements in meeting a study objective. This is especially true in target animal safety studies—statistical analysis identifies differences that are statistically significant, but clinical interpretation of the findings is crucial.

CVM truly respects the knowledge and perspectives that the research community and industry can provide. It is our hope that when you feel an approach makes scientific sense but is different from what may have been done in the past that you will bring a proposal forward for discussion with CVM. Additionally, given that aquaculture drugs successes have in large part been due to collaboration between multiple groups, we encourage discussion of ideas and successes in such venues as the National Drug Research Forum. We look forward to future discussions with you regarding any ideas you may have!

USGS's UMESC CORNER

Sedatives

The U.S. Geological Survey's (USGS) Upper Midwest Environmental Sciences Center (UMESC) completed a study to determine the exposure parameters (concentration and duration) that will maximize eugenol residues in the fillet tissue from rainbow trout exposed to AQUI-S®20E (active ingredient, 10% eugenol) and determine the sample times that will adequately characterize the depletion of eugenol residues from the fillet tissue of exposed fish. Fish were exposed to 50 mg/L AQUI-S®20E for various times through 1,440 min, to 100 and 250 mg/L for various times through 240 min, and to 500 and 1,000 mg/L for various times through 90 min. Fillet tissue concentrations were maximized after exposure to 100 mg/L AQUI-S®20E for 30, 60, 120, and 240 min. Eugenol concentrations were 50, 58, 54, and 62 µg/g, respectively. All other exposure concentrations and durations resulted in eugenol concentrations <39 µg/g. The final report was submitted to the FDA Center for Veterinary Medicine on August 31, 2012. Contact Jeff Meinertz for more information.

UMESC completed preparations to conduct a pilot study and definitive study to characterize the depletion, distribution, and identification of eugenol residues in the fillet tissue from exposed fish. The radioactive eugenol necessary to conduct the studies was received on September 18, 2012. The pilot study was initiated on September 24, 2012. Rainbow trout were successfully exposed to 14C eugenol, and fillet tissue from exposed fish was successfully processed. Method extraction efficiencies (percent of radioactivity extracted from the fillet tissue) exceeded 85%. Eugenol was more than 97% of the radioactive residues in the fillet tissue extracts. While conducting the pilot study, techniques and procedures were flagged for modification to ensure a successful definitive study exposure. With the modified techniques and procedures, the definitive study was initiated on October 16, 2012. Once again, rainbow trout were successfully exposed to 14C eugenol, and the fillet tissue was successfully processed. More than 97% of the radioactive residues in the fillet tissue extracts from fish sampled immediately after the exposure were eugenol. Sample processing continues. A draft of the final report is scheduled to be completed in January, 2013. Contact Jeff Meinertz for more information.

Florfenicol

UMESC conducted a study that fulfilled the following objectives: (1) determine the florfenicol (FFA) concentrations in fillet tissue of rainbow trout offered FFC-medicated feed in a recirculating aquaculture system at 20 mg/kg BW/d for 10 days; (2) determine the FFA concentrations in the fillet tissue of rainbow trout offered FFC-medicated feed in a flow-through system at 20 mg/kg BW/d for 10 days; (3) determine the FFA concentrations in the fillet tissue of nontreated rainbow trout sharing a recirculating aquaculture system with rainbow trout offered FFC-medicated feed at 20 mg/kg BW/d for 10 days; (4) determine the FFC residue concentrations in water during and after offering FFC-medicated feed to rainbow trout in a recirculating aquaculture system at 20 mg/kg BW/d for 10 days; and (5) determine unionized ammonia and nitrite concentrations in the water of a recirculating aquaculture system with rainbow trout that are offered FFC medicated feed at 20 mg/kg BW/d for 10 days to assess the impact of treatment on the system's biofilter. All analyses have been completed. A final report has been completed and is scheduled to be submitted to the FDA Center for Veterinary Medicine in November, 2012. Contact Jeff Meinertz for more information.

Text provided by Jeff Meinertz (jmeinertz@usgs.gov), Research Physiologist; USGS UMESC; La Crosse, Wisconsin USA.

AFS's WGADCB CORNER

The American Fisheries Society's (AFS) Fish Culture Section Working Group on Aquaculture Drugs, Chemicals, and Biologics (WGADCB) continues to work with the U.S. Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) on professional education and outreach materials:

Letter to Aquaculture Professionals

During the most recent meeting of the WGADCB (July 31, 2012, La Crosse, Wisconsin USA), attendees discussed an important issue facing public aquaculture: Convincing public agencies to purchase FDA-approved aquaculture drugs (products) when less expensive—but not FDA-approved for use in aquaculture—products are available. It is usual for public agencies to purchase goods and services from the lowest bidding contractor, and this practice presents a conflict almost every time an aquaculture drug purchase needs to be made. At the meeting, two public aquaculture personnel attested that this issue has been ongoing in their agencies. And it is probable that many other aquaculture professionals experience the same frustration when they argue for purchasing and using approved aquaculture drugs and supporting the few sponsors who are active in the aquaculture drug field. After discussing the issue, the WGADCB decided to work with the FDA CVM Communications Staff to prepare a letter that fish culture personnel could provide to their purchasing agents—a letter that would encourage the purchase and use of approved products only. After several planning discussions with the WGADCB, FDA CVM released a "Dear Aquaculture Professional" letter (*http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm324048.htm*). The letter clarifies the differences between approved products and active ingredients and explains the importance of purchasing only approved products. The WGADCB hopes that the letter will address the concerns of purchasing agents and simplify the process of purchasing approved aquaculture drugs within public agencies. Thanks to Dr. Jennifer Matysczak (FDA CVM Aquaculture Drugs Team Leader), Dr. Melanie McLean (FDA CVM Communications Staff), and WGADCB co-chairs, Jim Bowker and Dr. Jesse Trushenski, for spear-heading this effort.

Questions Frequently Asked of FDA

The WGADCB is working with FDA CVM to write an article for the AFS peer-reviewed publication, *Fisheries*. The goals of the article, preliminary titled *FAQ with FDA*, will be to (1) provide guidance to fisheries professionals about the use of fish sedatives, and (2) use fish sedatives to illustrate the basics of the drug-approval process and legal and judicious use of aquatic animal drugs. We anticipate the article will increase awareness and understanding of these topics among fisheries professionals. Moreover, the article will dove-tail nicely with two main goals of the WGADCB—professional education and outreach—and with FDA CVM's willingness to become more engaged in disseminating information to the fisheries community. Draft FAQs include (but might not be limited to):

- What qualifies as a drug, and why does FDA CVM use such a broad definition?
- What is the difference between a drug and an active ingredient?
- What does it mean if a drug is "approved"?
- How is an approved drug different from a drug with an INAD authorization?
- I see a lot of people using "things" in the field that would be considered drugs—is this a problem?

By using specific examples, the article will address these questions and the primary concerns of the many fisheries professionals who use sedatives and other aquaculture drugs. The FDA CVM Communications Staff is hard at work on a draft of the article, and the group is targeting an early 2013 publication date.

For more information on current WGADCB activities, see (https://sites.google.com/site/fishculturesection/about-the-fcs/minutes-and-reports), contact one of the co-chairs, or better yet, come to our next meeting! The next meeting of the WGADCB will be held in conjunction with the AQUA 2013 Triennial Conference, Nashville, Tennessee USA, February 21-25, 2013. Stay tuned to the AADAP website for WGADCB meeting scheduling announcements.

Updates provided by Dr. Jesse Trushenski (saluski@siu.edu), Assistant Professor; Southern Illinois University at Carbondale; Fisheries and Illinois Aquaculture Center; Carbondale, Illinois USA ,and Jim Bowker (jim_bowker@fws.gov), Research Program Manager; USFWS AADAP; Bozeman, Montana USA.

Updates edited for this newsletter by Dan Carty, USFWS AADAP.

FDA's CVM NOTES

Upcoming Workshop on Medicated Feeds

A workshop entitled ***Drugs for Use in Animal Feeds*** will be held in Potomac, Maryland USA, on May 22-23, 2013, in conjunction with the American Academy of Veterinary Pharmacology and Therapeutics (AAVPT) Biennial symposium. The workshop is designed to provide interested parties with basic knowledge on the new animal drug approval process, specifically relating to medicated feeds. Participants will have an opportunity for clarification on what, exactly, is a medicated feed and how it differs from other dosage form new animal drugs. Topics for discussion include manufacturing requirements, labeling, combination drugs, and developing data for substantial evidence of effectiveness. Finally, participants will have a forum opportunity to ask FDA/CVM specific questions to help clarify their specific needs.

The workshop brochure can be accessed on AADAP's website at http://www.fws.gov/fisheries/aadap/PDF/CVM_Draft%20brochure%20dec2012.pdf.

New Publication from CVM's Office of Research

Work done by CVM's Office of Research Aquaculture Team was recently published in the journal *Diseases of Aquatic Organisms*:

Gieseker, C.M., T.D. Mayer, T.C. Crosby, J. Carson, I. Dalsgaard, A.M. Darwish, P.S. Gaunt, D.X. Gao, H.M. Hsu, T.L. Lin, J.L. Oaks, M. Pyecroft, C. Teitzel, T. Somsiri, and C.C. Wu. 2012. Quality control ranges for testing broth microdilution susceptibility of *Flavobacterium columnare* and *F. psychrophilum* to nine antimicrobials. *Diseases of Aquatic Organisms* **101(3):207-215**.

Text provided by Dr. Jennifer Matysczak (Jennifer.Matysczak@fda.hhs.gov), Leader, Aquaculture Drugs Team; Office of New Animal Drug Evaluation; Center for Veterinary Medicine, Food and Drug Administration; Rockville, Maryland USA

RELEVANT LITERATURE

Listed below are journal citations with particular relevance to the broad topic of drugs and aquaculture species. With some exceptions, this list includes citations not previously included in our newsletter. Our complete Relevant Literature list, which dates back to 2009, can be viewed or downloaded by clicking here.

Inclusion of a citation in our newsletter does not imply (1) acceptance by the U.S. Food and Drug Administration's Center for Veterinary Medicine of a drug's safety or effectiveness, (2) endorsement of a drug or product by the U.S. Fish & Wildlife Service, (3) recommendation of the technique to any particular situation, or (4) concurrence with a treatment procedure/drug.

Please send citations of interest to Dan Carty (dan_carty@fws.gov).

Antibiotic and Bacterial

Alves, RJ, et al. 2012. Multidrug-resistance and toxic metal tolerance of medically important bacteria isolated from an aquaculture system. *Microbes and Environments* **27(4):449-455**.

Barakat, KM, and Gohar, YM. 2012. Antimicrobial agents produced by marine *Aspergillus terreus* var. *africanus* against some virulent fish pathogens. *Indian Journal of Microbiology* **52(3):366-372**.

Bartie, KL, et al. 2012. Intraspecific diversity of *Edwardsiella ictaluri* isolates from diseased freshwater catfish, *Pangasianodon hypophthalmus* (Sauvage), cultured in the Mekong Delta, Vietnam. *Journal of Fish Diseases* **35(9):671-682**.

Bebak, J, et al. 2012. Effect of copper sulfate on *Aeromonas hydrophila* infection in channel catfish fingerlings. *North American Journal of Aquaculture* **74(4):494-498**.

Budiati, T, et al. 2013. Prevalence, antibiotic resistance and plasmid profiling of Salmonellain catfish (*Clarias gariepinus*) and tilapia (*Tilapia mossambica*) obtained from wet markets and ponds in Malaysia. *Aquaculture* **372–375:127-132**.

Chakrabarti, R, and Srivastava, PK. 2012. Effect of dietary supplementation with *Achyranthes aspera* seed on larval rohu *Labeo rohita* challenged with *Aeromonas hydrophila*. *Journal of Aquatic Animal Health* **24(4):213-218**.

Darwish, AM, et al. 2012. Assessment of Aquaflor®, copper sulphate and potassium permanganate for control of *Aeromonas hydrophila* and *Flavobacterium columnare* infection in sunshine bass, *Morone chrysops* female × *Morone saxatilis* male. *Journal of Fish Diseases* **35(9):637-647**.

Dhayanithi, NB, et al. 2012. Effect of *Excoecaria agallocha* leaves against *Aeromonas hydrophila* in marine ornamental fish, *Amphiprion sebae*. *Indian Journal of Geo-Marine Sciences* **41(6):76-82**.

Gaunt, PS, et al. 2012. Single intravenous and oral dose pharmacokinetics of florfenicol in the channel catfish (*Ictalurus punctatus*). *Journal of Veterinary Pharmacology and Therapeutics* **35(5):503-507**.

Gieseker CM, et al. 2012. Quality control ranges for testing broth microdilution susceptibility of *Flavobacterium columnare* and *F. psychrophilum* to nine antimicrobials. *Diseases of Aquatic Organisms* **101(3):207-215**.

Granja, RHMM. 2012. Monitoring of florfenicol residues in fish muscle by HPLC-UV with confirmation of suspect results by LC-MS/MS. *Drug Testing and Analysis* **4(S1):125 -129**.

Groocock, GH, et al. 2013. Iodophor disinfection of eggs exposed to viral hemorrhagic septicemia virus type IVb. *North American Journal of Aquaculture* **75(1):25-33**.

He, X, et al. 2012. Multi-biomarker responses in fishes from two typical marine aquaculture regions of South China. *Marine Pollution Bulletin* **64(11):2317-2324**.

Holen, E, et al. 2012. Pathogen recognition and mechanisms in Atlantic cod (*Gadus morhua*) head kidney cells: bacteria (LPS) and virus (poly I:C) signals through different pathways and affect distinct genes. *Fish & Shellfish Immunology* **33 (2):267-276**.

Lajnef, R, et al. 2012. Comparative study on the antibiotic susceptibility and plasmid profiles of *Vibrio alginolyticus* strains isolated from four Tunisian marine biotopes. *World Journal of Microbiology & Biotechnology* **28(12):3345-3363**.

Liu, W, et al. 2012. Impacts of florfenicol on marine diatom *Skeletonema costatum* through photosynthesis inhibition and oxidative damages. *Plant Physiology and Biochemistry* **60:165-170**.

Mainous, ME, et al. 2012. Efficacy of common aquaculture compounds for disinfection of *Flavobacterium columnare* and *F. psychrophilum*. *Journal of Applied Aquaculture* **24 (3):262-270**.

Mistiri, F, et al. 2012. Study of forced degradation behavior of florfenicol by LC and LC-MS and development of a validated stability-indicating assay method. *Annales Pharmaceutiques Françaises* **70(6):333-347**.

Okmen, G. 2012. *In vivo* and *in vitro* antibacterial activities of aome essential oils of Lamiaceae species on *Aeromonas salmonicida* isolates from cultured rainbow trout, *Oncorhynchus mykiss*. *Journal of Animal and Veterinary Advances* **11(15):2762-2768**.

Tao, W, et al. 2012. Inactivation of chloramphenicol and florfenicol by a novel chloramphenicol hydrolase. *Applied and Environmental Microbiology* **78(17):6295-6301**.

Yonar, ME. 2012. The effect of lycopene on oxytetracycline-induced oxidative stress and immunosuppression in rainbow trout (*Oncorhynchus mykiss*, W.). *Fish & Shellfish Immunology* **32(6):994-100**.

Parasite and Fungus Control

Adeyemo, OK, et al. 2012. Effect of formalin on spawning success and organ histology in *Clarias gariepinus*. *Research Journal of Environmental Toxicology* **6(2):42-50**.

Al-Bairuty, GA, et al. 2013. Histopathological effects of waterborne copper nanoparticles and copper sulphate on the organs of rainbow trout (*Oncorhynchus mykiss*). *Aquatic Toxicology* **126:104-115**.

Bravo, S, et al. 2012. Efficacy of emamectin benzoate in the control of *Caligus rogercresseyi* on farmed Atlantic salmon (*Salmo salar* L.) in Chile from 2006 to 2007. *Aquaculture* **364–365:61-66**.

Cao, H, et al. 2012. Identification of an isolate of *Saprolegnia ferax* as the causal agent of saprolegniosis of Yellow catfish (*Pelteobagrus fulvidraco*) eggs. *Veterinary Research Communications* **36(4):239-244**.

Covello, JM, et al. 2012. Effects of orally administered immunostimulants on inflammatory gene expression and sea lice (*Lepeophtheirus salmonis*) burdens on Atlantic salmon (*Salmo salar*). *Aquaculture* **366-367:9-16**.

de Andrade Waldemarin, KC, et al. 2012. Copper sulfate affects Nile tilapia (*Oreochromis niloticus*) cardiomyocytes structure and contractile function. *Ecotoxicology* **21(3):783-794**.

Goodwiller, BT, and Chambers, JP. 2012. The potential use of ultrasound to control the trematode *Bolbophorus confusus* by eliminating the ram's horn snail *Planorbella trivolvis* in commercial aquaculture settings. *North American Journal of Aquaculture* **74(4):485-488**.

Hoyer, SA, and Myrick, CA. 2012. Can copper-based substrates be used to protect hatcheries from invasion by the new Zealand mudsnail? *North American Journal of Aquaculture* **74(4):575-583**.

Jones, PG, et al. 2012. Effectiveness of emamectin benzoate for treatment of *Lepeophtheirus salmonis* on farmed Atlantic salmon *Salmo salar* in the Bay of Fundy, Canada. *Diseases of Aquatic Organisms* **102(1):53-64**.

Lalonde, BA, et al. 2012. Measurement of oxytetracycline and emamectin benzoate in freshwater sediments downstream of land based aquaculture facilities in the Atlantic Region of Canada. *Bulletin of Environmental Contamination & Toxicology* **89(3):547-550**.

Matthews, MD, et al. 2012. Evaluation of hydrogen peroxide and temperature to control mortality caused by saprolegniasis and to increase hatching success of largemouth bass. *North American Journal of Aquaculture* **74(4):463-467**.

Polinski, MP, et al. 2012. Hydrogen peroxide treatments administered to hatchery-reared burbot: assessing treatment regimes from embryonic development through juvenile rearing. *North American Journal of Aquaculture* **75(1):50-56**.

Robinson, CB, et al. 2013. Tissue-specific copper concentrations in red drum after long-term exposure to sublethal levels of waterborne copper and a 21-d withdrawal. *North American Journal of Aquaculture* **75(1):1-6**.

Santos, RFB, et al. 2012. Acute toxicity and histopathology in ornamental fish amazon bluespotted corydora (*Corydoras melanistius*) exposed to formalin. *Anais da Academia Brasileira de Ciências* **84(4):1001-1007**.

Sedation or Anesthesia

Bowzer, JC, et al. 2012. Efficacy and physiological responses of grass carp to different sedation techniques: II. Effect of pulsed DC electricity voltage and exposure time on sedation and blood chemistry. *North American Journal of Aquaculture* **74(4):567-574**.

da Rocha, MA, et al. 2012. Determination of the optimal dose of benzocaine hydrochloride in anesthesia of tilápia (*Oreochromis niloticus*). *Semina: Ciências Agrárias* **33 (6):2403-2410**.

Gause, BR, et al. 2012. Efficacy and physiological responses of grass carp to different sedation techniques: I. Effects ov various chemicals on sedation and blood chemistry. *North American Journal of Aquaculture* **74(4):560-566**.

Gonçalves, RA, et al. 2012. The use of different anaesthetics as welfare promoters during short-term human manipulation of European cuttlefish (*Sepia officinalis*) juveniles. *Aquaculture* **370–371:130-135**.

Javahery, S, et al. 2012. Effect of anaesthesia with clove oil in fish (review). *Fish Physiology and Biochemistry* **38 (6):1545-1552**.

Lin, M, et al. 2012. Effects of two anesthetics on survival of juvenile *Culter mongolicus* during a simulated transport experiment. *North American Journal of Aquaculture* **74 (4):541-546**.

Martins, ML, et al. 2012. *Trichodina nobilis* Chen, 1963 and *Trichodina reticulata* Hirschmann et Partsch, 1955 from ornamental freshwater fishes in Brazil. *Brazilian Journal of Biology* **72(2):281-286**.

Mi, H, et al. 2012. Quality and biochemical properties of artificially hibernated crucian carp for waterless preservation. *Fish Physiology and Biochemistry* **38(6):1721-1728**.

Shaluei, F, et al. 2012. Physiological responses of great sturgeon (*Huso huso*) to different concentrations of 2-phenoxyethanol as an anesthetic. *Fish Physiology and Biochemistry* **38(6):1627-1634**.

Skeletal (Fluorescent) Marking

Ambrose, WG, et al. 2012. Growth line deposition and variability in growth of two circumpolar bivalves (*Serripes groenlandicus*, and *Clinocardium ciliatum*). *Polar Biology* **35 (3):345-354**.

Carty, D, and Bowker, JD. 2013. A Terramycin 200 for Fish (44.09% oxytetracycline dihydrate) treatment regimen proposed for the fluorescent marking of rainbow trout vertebrae. *North American Journal of Aquaculture* **75(1):34-38**.

Logsdon, DE, and Pittman, BJ. 2012. Evaluation of osmotic induction of calcein treatments for marking juvenile walleyes. *North American Journal of Fisheries Management* **32(4):796-805**.

Spawning Hormones and Sex Manipulation

Alavi, SMH, et al. 2012. Sperm characteristics and androgens in *Acipenser ruthenus* after induction of spermiation by carp pituitary extract or GnRHa implants. *Fish Physiology and Biochemistry* **38(6):1655-1661**.

Amarasinghe, K, et al. 2012. Development of a fast screening and confirmatory method by liquid chromatography-quadrupole-time-of-flight mass spectrometry for glucuronide-conjugated methyltestosterone metabolite in tilapia. *Journal of Agricultural and Food Chemistry* **60(20):5084-5088**.

Beaven, U, and Muposhi, V. 2012. Aspects of a monosex population of *Oreochromis niloticus* fingerlings produced using 17-α methyltestosterone hormone. *Journal of Aquaculture Research and Development* **3(3): Article No. 132 (5 pages)**.

Criscuolo-Urbinati, E, et al. 2012. The administration of exogenous prostaglandin may improve ovulation in pacu (*Piaractus mesopotamicus*). *Theriogenology* **78(9):2087-2094**.

El-Greisy, ZA, and El-Gamal, AE. 2012. Monosex production of tilapia, *Oreochromis niloticus*, using different doses of 17α -methyltestosterone with respect to the degree of sex stability after one year of treatment. *The Egyptian Journal of Aquatic Research* **38(1):59-66**.

El-Sayed, A-F, et al. 2012. Effects of phytoestrogens on sex reversal of Nile tilapia (*Oreochromis niloticus*) larvae fed diets treated with 17α-methyltestosterone. *Aquaculture* **360 –361:58-63**.

Kitano, T, et al. 2012. Estrogen rescues masculinization of genetically female medaka by exposure to cortisol or high temperature. *Molecular Reproduction and Development* **79 (10):719-726**.

Kowalski, R, et al. 2012. Quality and quantity of smelt (*Osmerus eperlanus* L.) sperm in relation to time after hormonal stimulation. *Reproductive Biology* **12(2):231-246**.

Lin, S, et al. 2012. Hormonal sex reversal in Atlantic cod, *Gadus morhua*. *Aquaculture* **364–365:192-197**.

Mazzeo, I, et al. 2012. Variations in the gene expression of zona pellucida proteins, zpbandzpc, in female European eel (*Anguilla anguilla*) during induced sexual maturation. *General and Comparative Endocrinology* **178(2):338-346**.

Olumuji, OK, and Mustapha, MK. 2012. Induced breeding of African mud catfish, *Clarias gariepinus* (Burchell 1822), using different doses of normal saline diluted Ovaprim. *Journal of Aquaculture Research & Development* **3(4): Article No. 133 (3 pages)**.

Ong, SK, et al. 2012. Sorption of 17α-methyltestosterone onto soils and sediment. *Water, Air, & Soil Pollution* **223 (7):3869-3875**.

Piau, R Jr., et al. 2012. Morphometry of white muscle fibers and performance of Nile tilapia (*Oreochromis niloticus*) fingerlings treated with methyltestosterone or a homeopathic complex. *Homeopathy* **101(3):154-158**.

Podhorec, P, et al. 2012. The effects of water temperature and hormone treatments on circulating LH and ovulation in tench (*Tinca tinca*). *Reviews in Fish Biology and Fisheries* **22(3):791-796**.

Srivastava, PP, et al. 2012. Breeding and larval rearing of Asian catfish, *Clarias batrachus* (Linnaeus, 1758) on live and artificial feed. *Journal of Aquaculture Research & Development* **3(4): Article No. 134 (4 pages)**.

Su, B, et al. 2013. Relative effectiveness of carp pituitary extract, luteininzing hormone releasing hormone analog (LHRHa) injections and LHRHa implants for producing hybrid catfish fry. *Aquaculture* **372–375:133-136**.

Vaccines/Biologics—Salmonids

Aykanat, T, et al. 2012. Additive, non-additive and maternal effects of cytokine transcription in response to immunostimulation with Vibrio vaccine in Chinook salmon (*Oncorhynchus tshawytscha*). *Immunogenetics* **64(9):691-703**.

Bastardo, A, et al. 2012. Highly sensitive detection and quantification of the pathogen *Yersinia ruckeri* in fish tissues by using real-time PCR. *Applied Microbiology and Biotechnology* **96(2):511-520**.

Fjelldal, PG, et al. 2012. Vaccination and elevated dietary phosphorus reduces the incidence of early sexual maturation in Atlantic salmon (*Salmo salar* L.). *Aquaculture* **364–365:333-337**.

Jensen, BB, et al. 2012. Cohort study of effect of vaccination on pancreas disease in Norwegian salmon aquaculture. *Diseases of Aquatic Organisms* **102(1):23-31**.

Lafrentz, BR, et al. 2012. Reproducible challenge model to investigate the virulence of *Flavobacterium columnare* genomovars in rainbow trout *Oncorhynchus mykiss*. *Diseases of Aquatic Organisms* **101(2):115-122**.

Monte, MM, et al. 2012. Cloning and expression analysis of two ROR-γ homologues (ROR-γa1 and ROR-γa2) in rainbow trout *Oncorhynchus mykiss*. *Fish & Shellfish Immunology* **33(2):365-374**.

Ortega-Villaizan, M, et al. 2012. *Ex vivo* transfection of trout pronephros leukocytes, a model for cell culture screening of fish DNA vaccine candidates. *Vaccine* **30(41):5983-5990**.

Wilda, M, et al. 2012. Development and preliminary validation of an antibody filtration-assisted single-dilution chemiluminometric immunoassay for potency testing of *Piscirickettsia salmonis* vaccines. *Biologicals* **40(6):415-420**.

Vaccines/Biologics—Catfish

Pohlenz, C, et al. 2012. Synergies between vaccination and dietary arginine and glutamine supplementation improve the immune response of channel catfish against *Edwardsiella ictaluri*. *Fish & Shellfish Immunology* **33(3):543-551**.

Vaccines/Biologics—Tilapia

Chen, M, et al. 2012. Screening vaccine candidate strains against *Streptococcus agalactiae* of tilapia based on PFGE genotype. *Vaccine* **30(42):6088-6092**.

Vaccines/Biologics—Shrimp

Yang, J-Y, et al. 2012. Viral resistance and immune responses of the shrimp *Litopenaeus vannamei* vaccinated by two WSSV structural proteins. *Immunology Letters* **148 (1):41-48**.

Vaccines/Biologics—Miscellaneous

Budiño, B, et al. 2012. Characterization of *Philasterides dicentrarchi* isolates that are pathogenic to turbot: serology and cross-protective immunity. *Aquaculture* **364–365:130-136**.

Fu, X, et al. 2012. Protective immunity against iridovirus disease in mandarin fish, induced by recombinant major capsid protein of infectious spleen and kidney necrosis virus. *Fish & Shellfish Immunology* **33(4):880-885**.

Hart, LM, et al. 2012. Efficacy of a glycoprotein DNA vaccine against viral haemorrhagic septicaemia (VHS) in Pacific herring, *Clupea pallasii* Valenciennes. *Journal of Fish Diseases* **35(10):775-779**.

Hu, Y-h, et al. 2012. Japanese flounder (*Paralichthys olivaceus*) Hsp70: adjuvant effect and its dependence on the intrinsic ATPase activity. *Fish & Shellfish Immunology* **33 (4):829-834**.

Jin, R-p, et al. 2012. *Edwardsiella tarda* sialidase: pathogenicity involvement and vaccine potential. *Fish & Shellfish Immunology* **33(3):514-521**.

Liang, S, et al. 2012. Immune response of turbot (*Scophthalmus maximus* L.) to a broad spectrum vaccine candidate, recombinant glyceraldehyde-3-phosphate dehydrogenase of *Edwardsiella tarda*. *Veterinary Immunology and Immunopathology* **150(3):198-205**.

Maiti, B, et al. 2012. Evaluation of two outer membrane proteins, Aha1 and OmpW, of *Aeromonas hydrophila* as vaccine candidate for common carp. *Veterinary Immunology and Immunopathology* **149(3-4):298-301**.

Millard, CM, et al. 2012. Evolution of the capsular operon of *Streptococcus iniae* in response to vaccination. *Applied and Environmental Microbiology* **78(23):8219-8226**.

Ou-yang, Z, et al. 2012. Selection and identification of Singapore grouper iridovirus vaccine candidate antigens using bioinformatics and DNA vaccination. *Veterinary Immunology and Immunopathology* **149(1-2):38-45**.

Ou-yang, Z, et al. 2012. Immunogenicity and protective effects of inactivated Singapore grouper iridovirus (SGIV) vaccines in orange-spotted grouper, *Epinephelus coioides*. *Developmental and Comparative Immunology* **38(2):254-261**.

Peng, X-X. 2013. Proteomics and its applications to aquaculture in China: infection, immunity, and interaction of aquaculture hosts with pathogens. *Developmental and Comparative Immunology* **39(1-2):63-71**. **(review article)**

Sarropoulou, E, et al. 2012. Characterization of European sea bass transcripts by RNA SEQ after oral vaccine against *V. anguillarum*. *Marine Biotechnology* **14(5):634-642**.

Sun, Y, et al. 2012. Construction and comparative study of monovalent and multivalent DNA vaccines against *Streptococcus iniae*. *Fish & Shellfish Immunology* **33 (6):1303-1310**.

Yu, L-P, et al. 2012. C312M: an attenuated *Vibrio anguillarum* strain that induces immunoprotection as an oral

and immersion vaccine. *Diseases of Aquatic Organisms* **102(1):33-42**.

Zhang, M, et al. 2012. Construction and analysis of experimental DNA vaccines against megalocytivirus. *Fish & Shellfish Immunology* **33(5):1192-1198**.

Probiotics

Andani, HRR, et al. 2012. Antagonistic activity of two potential probiotic bacteria from fish intestines and investigation of their effects on growth performance and immune response in rainbow trout (*Oncorhynchus mykiss*). *Journal of Applied Ichthyology* **28(5):728-734**.

Burbank, DR, et al. 2012. Isolation of bacterial probiotic candidates from the gastrointestinal tract of rainbow trout, *Oncorhynchus mykiss* (Walbaum), and screening for inhibitory activity against *Flavobacterium psychrophilum*. *Journal of Fish Diseases* **35(11):809-816**.

Cerezuela, R, et al. 2012. Effects of dietary *Bacillus subtilis*, *Tetraselmis chuii*, and *Phaeodactylum tricornutum*, singularly or in combination, on the immune response and disease resistance of sea bream (*Sparus aurata* L.). *Fish & Shellfish Immunology* **33(2):342-349**.

Cerezuela, R, et al. 2012. Histological alterations and microbial ecology of the intestine in gilthead seabream (*Sparus aurata* L.) fed dietary probiotics and microalgae. *Cell and Tissue Research* **350(3):477-489**.

Heo, W-S, et al. 2013. Effects of dietary probiotic, *Lactococcus lactis* subsp. *lactis* I2, supplementation on the growth and immune response of olive flounder (*Paralichthys olivaceus*). *Aquaculture* **376–379:20-24**.

Liu, C-H, et al. 2012. Dietary administration of the probiotic, *Bacillus subtilis* E20, enhances the growth, innate immune responses, and disease resistance of the grouper, *Epinephelus coioides*. *Fish & Shellfish Immunology* **33 (4):699-706**.

Mohapatra, S, et al. 2012. Fenvalerate induced stress mitigation by dietary supplementation of multispecies probiotic mixture in a tropical freshwater fish, *Labeo rohita* (Hamilton). *Pesticide Biochemistry & Physiology* **104(1):28-37**.

Reyes-Becerril, M, et al. 2012. Effects of marine silages enriched with *Lactobacillus sakei* 5-4 on haemato-immunological and growth response in Pacific red snapper (*Lutjanus peru*) exposed to *Aeromonas veronii*. *Fish & Shellfish Immunology* **33(4):984-992**.

Román, L, et al. 2012. The *in vitro* effect of probiotic *Vagococcus fluvialis* on the innate immune parameters of *Sparus aurata* and *Dicentrarchus labrax*. *Fish & Shellfish Immunology* **33(5):1071-1075**.

Wu, ZX, et al. 2012. Effect of probiotic *Bacillus subtilis* Ch9 for grass carp, *Ctenopharyngodon idella* (Valenciennes, 1844), on growth performance, digestive enzyme activities and intestinal microflora. *Journal of Applied Ichthyology* **28 (5):721-727**.

Miscellaneous Articles

Acosta, J, et al. 2013. Cloning and functional characterization of three novel antimicrobial peptides from tilapia (*Oreochromis niloticus*). *Aquaculture* **372–375:9-18**.

Burnley, T, et al. Post-handling mortality during controlled field trials with marine grow-out Atlantic salmon, *Salmo salar* L. *Aquaculture* **368-369:55-60**.

Irvine, JR, and Gaetz, H. 2012. Using golf balls to keep screens clean in circular rearing tanks. *North American Journal of Aquaculture* **74(4):584-585**.

Lopes, RP, et al. 2012. Multiresidue determination of veterinary drugs in aquaculture fish samples by ultra high performance liquid chromatography coupled to tandem mass spectrometry. *Journal of Chromatography B* **895-896:39-47**.

Rowe, DK, and Wilding, T. 2012. Risk assessment model for the introduction of non-native freshwater fish into New Zealand. *Journal of Applied Ichthyology* **28(4):582-589**.

Zaroogian, GE, et al. 2012. An injectable, slow-release implantation method for exposing fish to chemicals over a period of weeks. *North American Journal of Aquaculture* **74 (4):512-521**.

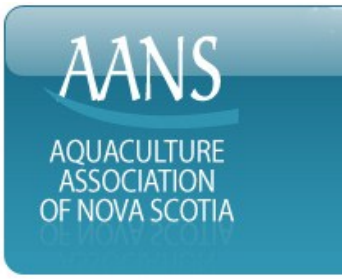
Zhu, L-Y, et al. 2013. Advances in research of fish immune-relevant genes: a comparative overview of innate and adaptive immunity in teleosts. *Developmental and Comparative Immunology* **39(1-2):39-62**.

UPCOMING MEETINGS (2013)

Texas Aquaculture Association Annual Conference and Trade Show (January 23-25, Bay City, Texas USA) For details, visit the conference website at *http://www.texasaquaculture.org/*.

Sea Farmers Conference 2013 (January 24-25, Halifax, Nova Scotia, Canada)

The Aquaculture Association of Nova Scotia invites you to the *35th Annual Sea Farmers Conference* on Jan 24-25 in Halifax, Nova Scotia, Canada (*http://www.aansonline.ca*).



This year's meeting theme is *Responsible Sea Farming to Feed the World.* The 2-day conference will focus on all things aquaculture, from the global perspective to issues affecting local farms—and an entire session will be

devoted to looking at organic farming. All of this wraps up with their special keynote speaker event. Throw in the trade show, the scholarship luncheon, awards, and the infamous Sip n' Shuck dinner, and you'll have two jam-packed days that you won't want to miss.

North Carolina Aquaculture Development Conference (February 7-9, New Bern, North Carolina USA)

The 2013 North Carolina Aquaculture Development Conference will be held February 7-9 in New Bern, North Carolina USA (*http://www.ncaquaculture.org*).

The conference will bring together the general public, current and prospective fish farmers, scientists, and agency personnel to share information about the development of aquaculture in North Carolina. Also, there will be a trade show, the famous Aquafoods Festival, and targeted workshops. Anyone interested in fish or shellfish farming—including prospective growers, researchers, teachers, students, and agency personnel—are encouraged to attend.

AQUACULTURE 2013 (February 21-25, Nashville, Tennessee USA): The World Aquaculture Society will hold its Triennial Meeting in the exciting city of Nashville, Tennessee USA, on February 21-25 (*https://www.was.org/WasMeetings/meetings/Default.aspx?code=AQ2013*).

The Triennial is the largest aquaculture conference and tradeshow in the world, with nearly 4,000 attendees from over 90 countries. The Triennial combines the annual meetings of the Fish Culture Section of the American Fisheries Society, the World Aquaculture Society, and the National Shellfisheries Assoc.

Look what else is happening:

- AQUACULTURE AMERICA - Annual Meeting of the U.S. Chapter of World Aquaculture Society, the National Aquaculture Assoc., and the U.S. Aquaculture Suppliers Assoc.
- Annual Meeting of the American Tilapia Assoc.
- Annual Meeting of the Striped Bass Growers Assoc.
- Annual Meeting of the U.S. Trout Farmers Assoc.
- Special sessions organized by the Aquacultural Engineering Society and International Association of Aquaculture Economics and Management.
- Many other meetings of work groups, government agencies, and related aquaculture activities

International Conference on Marine Science and Aquaculture (May 15-16, Amsterdam, The Netherlands)

The 2013 International Conference on Marine Science and Aquaculture will be held May 15-16 in Amsterdam, The Netherlands. The conference will bring together leading academic scientists, researchers, and scholars to exchange and share their experiences and research about all aspects of marine science and aquaculture. Conference details can be found at (*https://www.waset.org/conferences/2013/amsterdam/icmsa/*).

American Academy of Veterinary Pharmacology and Therapeutics Biennial Symposium (May 20-22) and Drugs for Use in Animal Feeds Workshop (May 22-23) in Potomac, Maryland USA

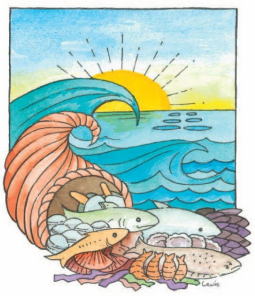
The American Academy of Veterinary Pharmacology and Therapeutics will hold its 18th Biennial Symposium on May 20-22 in Potomac, Maryland USA (*https://m360.aavpt.org/event.aspx?eventID=58865*).

The symposium's themes are (1) Latest requirements for bioanalytical method validation, (2) Cutting edge use of pharmacokinetics, and (3) Improving veterinary drug labels. The symposium will be held May 20-21, and there will be a 1-day workshop on *Understanding Drug Labels* on May 22.

In conjunction with the symposium, a ***Drugs for Use in Animal Feeds*** workshop will be held May 22-23. Details of this 2-day workshop can be found in FDA's CVM Notes on page 8 of this newsletter, and the workshop brochure can be downloaded from AADAP's website (*http://www.fws.gov/fisheries/aadap/PDF/CVM_Draft%20brochure%20dec2012.pdf*).

Aquaculture Canada 2013 (June 2-5, Guelph, Ontario, Canada)

Aquaculture Canada 2013 will be held June 2-5 in Guelph, Ontario, Canada, in association with the University of Guelph (*http://www.aquacultureassociation.ca*).



Aquaculture Canada largely focuses on the science of aquaculture; however, the meeting also provides a diversity of technical sessions and unique social and networking opportunities for all those working in or interested in aquaculture.

Cover Photo

The beaverslide hay stacker was invented around 1910 in the Big Hole Valley, Beaverhead County, Montana USA. Historically, horses were used to operate the device, which pushes loads of hay up an inclined plane to a height of about 30 feet, where the hay drops through a large gap and into a wood-framed bin. The resultant loose haystacks can be 30 feet high, weigh up to 20 tons, and last 5 to 6 years. Typically, the hay is used to feed livestock. See a short video at *http://www.youtube.com/watch?v=KdYDMr6q84g*.