U. S. Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program

Strategic Vision

Origin

The Aquatic Animal Drug Approval Partnership (AADAP) Program recognizes the need to be responsive to the changing needs of the fisheries community, including the Program's primary constituency, the U.S. Fish and Wildlife Service (Service) National Fish Hatchery System, as well as the Service's many partners in the public, private, and tribal sectors. To address these needs, the AADAP Program provides many unique, critical services and deliverables to the fisheries community. Although the AADAP Program's role is essential and unduplicated, the Program also recognizes Service-wide imperatives to fulfill the Service's mission by acting strategically, in partnership, and in accordance with Service priorities regarding aquatic resource conservation. Accordingly, this Strategic Vision was developed in consultation with representatives of the National Fish Hatchery System, the Association of Fish and Wildlife Agencies, and the leaders of the U.S. aquaculture industry to articulate the Mission and Vision of the AADAP Program, and to describe in detail its approach to fulfilling both.

Mission

Working with our partners to conserve, protect, and enhance the Nation's fishery resources by coordinating and leading activities to obtain U.S. Food and Drug Administration (FDA) approval for drugs, chemicals, and therapeutants needed in aquaculture and fisheries management programs throughout the U.S.

Vision

Utilizing the fish health management tools made accessible by the AADAP Program, fisheries professionals can better meet resource management goals that provide for the continuing benefit and enjoyment of the American people, including the nation's quality of life, economy, and cultural identity.

Challenge

To provide tools regulated by FDA for use in fish management to support conservation of the nation's fish and aquatic resources, including numerous imperiled fish species, in the face of declining and diminished aquatic habitat, expanding human population, changing social demographics, competition for human and financial resources, climate change, increasing demand for limited water resources, and other challenges.

Fisheries professionals need access to legal (FDA-approved) safe and effective fish drugs such as antimicrobials, spawning aids, sedatives, and marking agents to allow them to do their jobs effectively and in accordance with the Federal Food, Drug, and Cosmetic Act (FFD&CA) and other FDA regulations. Whether it involves collecting length/weight data in the field or controlling a bacterial infection in the hatchery, virtually every fisheries' conservation or restoration objective identified by the Service and its partners relies upon the availability of these essential tools. Only FDA-approved drugs can be used, and fish drug approvals have been limited by the complexities of the FDA regulatory framework, the lack of economic

incentives for pharmaceutical companies to pursue approvals for fish drugs, and the absence of centralized expertise needed to shepherd promising fish drugs through the approval process.

The U.S. Fish and Wildlife Service's (Service) Aquatic Animal Drug Approval Partnership (AADAP) Program has been the primary entity established to fill this void, facilitating legal access to fish drugs not yet approved by FDA; conducting research to support drug approvals; and managing a broad network of drug sponsors, federal and state agencies, and many of the Service's other partners to coordinate the approval process, leading the effort from early product development to the completion of final administrative requirements. Throughout its existence, AADAP has worked on a national level and hand-in-hand with the Association of Fish and Wildlife Agencies (AFWA) Drug Approval Working Group to generate funding, establish priorities, and ensure steady progress towards new aquatic species drug approvals. By providing the Service and its partners with the legal means to achieve fisheries conservation and restoration objectives within the bounds of regulatory constraints, AADAP has benefited all fisheries professionals from senior leadership to entry-level staff.

Beyond the immediate challenges related to fish drug development and approval, AADAP is also poised to address future challenges, including the need to:

- Treat a wider variety of fish species than have historically been cultured, specifically threatened or endangered fish species and other imperiled populations.

- Treat fish cultured at higher densities or in recirculation systems used to maintain production goals while offsetting potential hatchery closures, funding shortfalls, and diminished water supplies.

- Address emerging aquatic pathogens, including changes in geographic and seasonal patterns of disease outbreaks likely to accompany climate change.

- Avoid or prepare strategies to address antibiotic resistance associated with overreliance on a limited number of disease treatment strategies.

AADAP Program Overview

Fisheries professionals are reliant on a suite of drugs to accomplish fisheries management objectives and deliver public and tribal trust responsibilities. In 1994, FDA began to enforce the Federal Food Drug and Cosmetic Act (FFD&CA) and FDA regulations regarding the use of drugs in aquatic species. Although most of the drugs used by fisheries professionals prior to this time had been used safely and effectively for decades, the vast majority of these drugs were not FDA-approved and their continued use posed serious legal ramifications (See FFD&CA Chapters 512, 501, 301, and 403). When implemented, FDA's new enforcement priorities effectively stripped the Service's National Fish Hatchery System (NFHS) and other aquaculture programs throughout the country of virtually all tools that had been used for decades to manage fish health and achieve Service fish culture, fisheries management, and fisheries research goals. These logistical constraints jeopardized recreational fishing opportunities, restoration/conservation programs, and commercial production efforts across the nation, and shortfalls in these programs threatened significant economic impact. The Service and its partners understood that access to safe and effective fish drugs was imperative to meeting production goals, fulfilling natural resource mandates, and ensuring the health of the nation's fisheries, as well as the need for federal leadership to ensure legal access to these essential tools. Quite simply, without federal leadership and other public-sector support, drug

sponsors would not seek fish drug approvals in the United States. The AADAP Program was established to solve this crisis at a national level, and to provide critical, new tools to allow the Service and partner agencies, most notably the states and tribes, to more effectively and efficiently fulfill their mission(s).

Virtually all AADAP Program activities revolve around guiding safe and effective fish drugs through the approval "pipeline" and into the hands of fisheries professionals. The FDA drug approval process is considered the "gold standard" throughout the world because of its rigorous approach to protecting the public and preventing unsafe or ineffective drugs from reaching the marketplace. However, obtaining FDA approval for fish drugs is consequently a long, arduous, and expensive process (recent estimates range from $10-20 M and 15-30 years per drug). Despite these significant challenges, the AADAP Program has helped to establish operating principles and partnerships that have already begun to restock fisheries professionals' "medicine chest" with approved, safe and effective drugs. Since the inception of the AADAP Program, there has been tremendous maturation of all entities involved in the drug approval process, including FDA, drug sponsors, and AADAP, resulting in dramatic reductions in the time needed to gain initial approvals (e.g., the development timeline for chloramine-T (an early priority drug) dates back more than 20 years and is ongoing, but it is anticipated that a eugenol-based fish sedative will be approved after only 7 years in development pipeline). AADAP is internationally recognized for its track record and expertise in aquatic animal drug development and approval, and is the only program in the United States singularly committed to providing fisheries professionals with access to safe and effective fish drugs.

Goals, Objectives, and Strategies

The primary AADAP Program goals are to:

- Provide the Service and other fisheries professionals with access to FDA approved, safe and effective fish drugs essential to fisheries management activities.

- Ensure the Service fulfills its mission in compliance with the FFD&CA and other FDA regulations

Comprehensive program objectives and strategies reflect these goals, and are demonstrated by AADAP Program involvement in virtually every aspect of the drug approval process including:

1. Administer the National Investigational New Animal Drug (INAD) Program

2. Assume primary responsibility for conducting field effectiveness and target animal safety research in support of new drug approvals

3. Engage with drug company sponsors and provide support, coordination, and management of all activities and data generation for new animal drug approvals

4. Disseminate pertinent and up-to-date information regarding legal and judicious use of fish drugs through a variety of communication channels

5. Engage with FDA's Center for Veterinary Medicine (CVM) staff involved in fish drug approvals to ensure that AADAP Program activities remain aligned with CVM's drug approval data requirements

6. Update senior Service management and other stakeholders of AADAP's progress and accomplishments

Addressing these strategies with a competent, experienced, and adequate staff will ensure the availability of drugs critically needed by fisheries professionals and address current and emerging concerns regarding fish health and the ability of the Service and its partners to fulfill their missions related to fisheries conservation and restoration. The drug approval process has a long, steep, and ever-changing learning curve, and the AADAP Program is the only program in the country with such capabilities – both now and for the foreseeable future.

Objective 1: Administer the National INAD Program

AADAP's National Investigational New Animal Drug (INAD) Program (NIP) allows Service and non-Service fisheries professionals across the country to use drugs not yet approved by FDA under limited experimental conditions in order to meet current fish health management needs. The NIP is the only such program in the country: each year, more than 250 aquaculture facilities located in over 40 states participate in the NIP, and more than 150 different fish species have been treated under NIP authorization since 1998. Based on the ~1.4 billion fish that have been treated under NIP authorization to date, it is estimated that the NIP has helped save ~280 million fish subsequently used in conservation, restoration, and other management activities.

The success of the program is derived from the unparalleled expertise of the AADAP Program staff in developing and administering INAD authorizations granted by FDA. The AADAP Program is responsible for developing use protocols (i.e., treatment dosage, treatment duration, fish species, withdrawal period, data collection requirements, drug storage and accountability, etc.), securing relevant exemptions and authorizations related to the fate of treated water and fish, and providing FDA with detailed annual reports on all drug usage.

Strategy: AADAP will continue to administer the NIP, and as drugs move their way through the pipeline to approval, will work with sponsors to ensure that INAD authorization requests for new drugs needed by fisheries professionals are submitted to CVM.

Objective 2: Assume primary responsibility for conducting field effectiveness and target animal safety research in support of new drug approvals

Before a new drug can be approved, FDA must be provided with data which demonstrate the drug's effectiveness and safety. These studies must be conducted according to FDA-approved research protocols and in compliance with Good Clinical Practices and Good Laboratory Practice (GLP) requirements. AADAP Program staff possess extensive expertise in developing, conducting, and reporting the results of this specialized type of regulatory science. Staff also maintain a sizable nationwide network of professional colleagues to facilitate identification of emerging disease concerns and treatment strategies, and completion of effectiveness and safety trials to address data requirements for a wide variety of fish species and pathogens.

AADAP has recently developed a 5 year strategic research work plan with a focus on conducting effectiveness and target animal safety studies in accordance with drug approval research priorities identified by AFWA's Drug Approval Working Group. Currently, AADAP's research program is short-staffed and will not be able to generate the same quantity of data needed to support fish drug approvals as it has in the past.

Strategy: AADAP will, to the best of its ability, complete the research objectives outlined in the 5 yr strategic research plan within the allotted time frame. However, it is unlikely that AADAP has sufficient research staff to complete all the research objectives.

Objective 3: Engage with drug company sponsors and provide support, coordination, and management of all activities and data generation for new animal drug approvals

AADAP engages with active fish drug sponsors and provides them with invaluable expertise, insight, and knowledge of the rigorous aquatic species drug approval process. In essence, AADAP guides and assists them throughout the entire process. AADAP also provides them with crucial effectiveness and target animal safety data needed to support new or supplemental approvals. Numerous sponsors have made it very clear that they would likely have never ventured into fish drug approval arena in the United States without assurance of the direct assistance and leadership provided by AADAP. Based on AADAP's longstanding reputation of sponsor support as described-above, AADAP is also continually seeking new sponsors of new drugs that would be beneficial to fisheries professionals, and providing them with product development planning and securing new INAD authorizations.

Strategy: AADAP will continue to engage with sponsors and provide them the help, coordination, and guidance necessary to navigate through the drug approval process.

Strategy: Working with sponsors, AADAP will obtain INAD exemption authorizations for new drugs (not yet approved) needed to meet fisheries program goals (e.g., effectively treat emerging fish diseases) and allow use of these INADs through NIP enrollment.

Strategy: AADAP will generate publically available high quality data to support fish drug approvals and encourage sponsors to utilize this data to facilitate their drug approval effort.

Objective 4: Disseminate pertinent and up-to-date information regarding legal and judicious use of fish drugs through a variety of communication channels

The AADAP Program's information dissemination and outreach efforts benefit the Service as well as the broader fisheries and aquaculture communities in the United States. The availability of current information regarding aquatic species drugs, including status and use options, is limited. AADAP plays a critical role in the dissemination of up-to-date information regarding the status of ongoing drug approval efforts, and comprehensive information regarding drug use, guidance, and available treatment options.

Information is disseminated via the AADAP website, Quarterly Newsletter, *Aquaculture Drug Update* list-serve, and via other outreach publications and products, such as the *Quick Desk Reference Guide to Approved Drugs for Use in Aquaculture*, *Poster of Approved Drugs for Use in Aquaculture*, *Guide to Using Drugs, Biologics, and Other Chemicals in Aquaculture*, etc. The AADAP Program also hosts the annual Aquaculture Drug Approval Coordination Workshop to bring partners together and advance drug approval initiatives; in 2014 they will host the 20th annual Workshop.

Strategy: The AADAP Program will continue to maintain an up-to-date website with pertinent information re: INAD and drug approval status, continue to publish their quarterly newsletter and host their annual Workshop, and print and disseminate invaluable (and updated) resources such as the Quick Desk Reference Guide.

Strategy: The AADAP Program will continue to represent the Service as an active member of AFWA's Drug Approval Working Group under the direction of the Fisheries and Water Resources Policy Committee. The AADAP Program will continue to work with professional organizations such as the American Fisheries Society, National Aquaculture Association, United States Aquaculture Association, and others to broadly disseminate information to administrators and end-users.

Strategy: With continued support from Headquarters and the Division of Fish and Aquatic Conservation (DFAC), AADAP will also develop a draft Service *Drug Use Policy Guidance* document that can be used to help ensure that Service fisheries professionals, and hopefully others, use fish drugs legally and in compliance with federal law.

Objective 5: Engage with FDA's Center for Veterinary Medicine (CVM) staff involved in fish drug approvals to ensure that AADAP Program activities remain aligned with CVM's drug approval data requirements

AADAP has developed one-of-a-kind expertise in the fisheries profession to communicate effectively with CVM to ensure protocols being developed and data being generated meet increasingly stringent requirements by CVM review teams (e.g., Aquaculture Team, Human Food Safety Team, etc.). This expertise was developed over many years, from countless meetings, discussions, and workshops, and from innumerable study protocol and data submission "exchanges" with various CVM review teams. AADAP's professional development has been described as "on par with major pharmaceutical companies" and this level of professionalism and expertise is reflected in the number of protocols and final study reports that are accepted by CVM. This is all the more impressive in that based on reputation, AADAP is now able to establish professional working relationships with new CVM review teams virtually immediately.

Strategy: AADAP will continue to engage with CVM staff to ensure that all activities, whether in administering the NIP or managing the research team, remain aligned with CVM drug approval data requirements. Doing so will ensure that data are generated in a manner that is considered effective and efficient and will lead to more rapid approvals.

Objective 6: Update senior Service management and other stakeholders of AADAP's progress and accomplishments

The AADAP Program must continue to engage in dialogue with Service upper management (Headquarters and Regional Directorate), as well as other stakeholders, to keep them fully apprised of the AADAP Program's progress, accomplishments, and impacts on the Nation's fishery resources. It is equally important that emerging Headquarters and Regional Office needs relative to fisheries are communicated to the AADAP Program staff. Such two-way communication will ensure that AADAP work activities are aligned with Service fisheries priorities and that the Service Directorate can share successes such as new or supplemental drug approvals with fisheries partners across the country.

Strategy: Working with Headquarters Division of Fish and Aquatic Conservation leadership, AADAP will develop a reporting mechanism to provide timely and effective communications with Service upper management. Additionally, DFAC leadership will use a similar procedure to ensure that AADAP work activities, as outlined in documents such as the Research Program 5 Year Strategic Plan, are aligned with Service priorities.