AFS Policy Statement on the Need for an Immediate-Release Anesthetic/Sedative for Use in the Fisheries Disciplines

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Issue Definition

Availability of safe and effective fish sedatives or anesthetics is crucial to fisheries research, management, and culture activities. Unlike most terrestrial vertebrates which may be handled without causing mechanical damage, fishes are particularly vulnerable to external and internal injury during physical restraint. Fish that are handled without proper sedation may also be negatively affected by the physiological consequences of the generalized stress response. Fisheries professionals must also consider the issues of animal welfare, and use of sedatives is recommended for procedures that may cause more than momentary or slight pain or distress. Additionally, handling fish without sedation may pose a risk to personnel, particularly in the case of large fish or fish that are otherwise hazardous when handled without proper restraint. In short, if fish are sedated prior to handling, risk to both fish and handler is minimized.

Tricaine methanesulfonate (MS-222) has been approved by the U.S. Food and Drug Administration (FDA) for use in sedating four families of fishes; however, MS-222 is not approved for use in all fish species and treated fish must be held for a 21-day withdrawal period prior to being released into the environment or sold for human consumption. Although carbon dioxide (CO2) may be used as an immediate-release sedative (i.e., no withdrawal period required prior to release or consumption), CO2 is generally not considered a safe or effective sedative as it is slow-acting, difficult to apply uniformly, and often results in adverse reactions including morbidity and mortality in the treated fish. The pursuit of FDA approval of safe and effective immediate release sedative has been long, and to-date, fruitless. This is a consequence of numerous factors, including the 1) complexities of the drug approval process, 2) the substantial human and monetary resources that must be expended in pursuit of an approval, 3) the limited number of personnel and funds dedicated to these activities, and 4) the time required to complete the approval process. To be approved in the U.S., an animal drug must be proven effective for the claim on the label, and safe when used as directed for treated animals, people administering treatment, the environment, and consumers. Efforts are currently underway to evaluate and prioritize the safety and effectiveness of two candidate immediate-release sedatives: Benzoak® (a benzocaine-based product) and AQUI-S® E (a eugenol-based product). A large number of studies have demonstrated the efficacy of benzocaine, eugenol, and closely related compounds in sedating and anesthetizing a variety of fishes. Furthermore, as common constituents of human foods (eugenol) and over-the-counter oral analgesic products (benzocaine), both compounds are considered relatively innocuous and are thought to pose minimal human food safety risk if used as immediate-release sedatives in fish. A conservative ('worst-case' scenario, 10-fold margin of safety), semi-quantitative risk assessment revealed that consumers could consume more than one portion of fish treated with benzocaine or eugenol at every meal without undue risk of health effects from compound residues remaining in the fillets. We conclude that the absence of a suitable immediate-release sedative jeopardizes fishes, fisheries, fish culture, and research, and poses considerable risk to those involved in these activities and fisheries resources. The current candidate sedatives,

benzocaine and eugenol (as well as other potential immediate-release sedatives such as Fish-eezzz®, a carvone-based compound), meet a range of criteria that justify an assumption of safety and efficacy as well as minimal risk to fishes, researchers, the environment, and human consumers. The current framework and process for approving either of the candidate sedatives will cost the private and public sectors an exorbitant amount of financial and human resources and will take years to complete. Ultimately, we recommend that the consequences of inaction be balanced against the consequences of approving the use of benzocaine and eugenol as immediate-release sedatives in the fisheries disciplines.

Policy and Needed Actions

Accordingly, it is the policy of the American Fisheries Society to engage and assist the U.S. Food and Drug Administration in:

1. Expediting review of the candidate immediate-release sedatives;
2. Implementing a risk management-based approach to establishing the data requirements for the candidate sedatives and other drugs intended for use in minor species including fish;
3. Reducing data requirements for the approval of the candidate sedatives based on the characteristics of the candidate sedatives, the nature of the intended uses, and the experience of the prospective end-users; and
4. Giving the two candidate sedatives deferred regulatory status or, if direct regulatory discretion is not advisable, expanding the current Investigational New Animal Drug (INAD) designations to allow for immediate-release use.