



One Industry, One Voice

National Aquaculture Association

**Judicious Antimicrobial Use in US Aquaculture:
Principles and Practices
(Approved by NAA Board of Directors March 2003)**

It is the policy of the NAA that the use of antibiotics in aquatic animals is done only in accordance with the following Judicious Use Principles and Practices

Introduction

The prevalence of human bacterial pathogens resistant to antimicrobial drugs began to increase as soon as widespread human use of antimicrobial agents had begun, about 70 years ago. Today, the US Food and Drug Administration (FDA) estimates 70 % of all bacterial infections in hospital patients are resistant to first preference antimicrobial drugs. This resistance can lead to more serious illness, prolonged hospital care and increased medical costs. The cause of this increasing antimicrobial resistance is use, misuse and over-use of antibiotics in human medicine and to a lesser extent veterinary medicine, and animal and plant agriculture.

Antimicrobial resistance can also impair success of aquatic animal production. If a bacterial fish pathogen becomes resistant to an antimicrobial, treatment will be ineffective. Fish mortality and morbidity will occur, increasing production costs and diminishing profitability. The contribution of domestic aquaculture antibiotic use to the prevalence of resistant human pathogens is unknown. However, all users of antimicrobials ultimately can contribute to the total burden of resistance and hence all of us must use antimicrobials prudently.

There are basic principals and practices that can be instituted to help minimize development of antimicrobial resistance under aquaculture conditions. These are described below. To maximize the benefit of antimicrobials for curing disease while minimizing the probability of resistance development, it is important to institute various disease prevention techniques, and to understand and follow FDA regulations on the use of drugs in aquaculture.

Legal Limitations

In the US, there are two FDA approved antimicrobials for use in aquaculture but their approvals are limited to specific food fish (catfish, salmonids and lobster) and specific diseases. These antimicrobials are oxytetracycline (Terramycin[®] for Fish, oxytetracycline monoalkyl trimethyl ammonium) and a potentiated sulfonamide (Romet-30[®], ormetoprim: sulfadimethoxine). These drugs can only be administered through feed in a specific feed formulation. A third antimicrobial is approved, sulfamerazine, but is not currently manufactured. The limitations on these drugs exist because the safety of the antimicrobial in the approved aquatic animals, their

effectiveness to cure the diseases they are approved for and their environmental safety have been satisfactorily demonstrated by the drug sponsor. Only under **very** limited situations (described below) might these antibiotics be used for other aquatic animals or other diseases.

Terramycin[®] for Fish is the trade name for the only approved oxytetracycline product and it is approved to treat certain diseases in catfish, salmonids and lobster. This oxytetracycline medicated feed can be used to treat bacterial hemorrhagic septicemia and pseudomonas disease in catfish at a dose of 2.5-3.75 g/100 lb of fish/day for 10 days when the water temperature is above 62° F (16.7° C). For salmonids, when the water temperature is above 48.2° F (9° C), Terramycin[®] for Fish for fish treatment can be used to control ulcer disease, furunculosis, bacterial hemorrhagic septicemia and pseudomonas disease. The treatment duration is again 10 days. Terramycin[®] for Fish is not currently approved for use in salmonids at temperatures below 9° C. Lobster can be treated with Terramycin[®] for Fish to cure gaffkemia. The treatment duration is only 5 days at 1 gm/lb of medicated feed. This product has a withdrawal time of 21 days for catfish and salmonids and 30 days for lobster. The FDA withdrawal time is the period between the last administration of the drug to the aquatic animal and the time when the aquatic animal can be harvested and offered for food (human or animal). The withdrawal time ensures no harmful drug residues are present when the animal is harvested for human consumption.

Romet-30[®] can be used in medicated feed to treat enteric septicemia of catfish and furunculosis in salmonids. The dose is 50 mg/kg body weight/day for five days. In catfish there is a 3-day mandatory withdrawal time and for salmonids, a 42-day withdrawal time. The shorter withdrawal time for catfish occurs because any Romet-30 residues that might be present are removed with the skin of catfish during processing.

There is only one approved antibiotic for ornamental fish (Nifurpirinol: Furanace Caps), for treatment of columnaris disease in freshwater aquarium fish that are not reproducing and none for other non-food aquatic animals.

It is illegal to use antibiotics prophylactically to prevent aquatic animal disease or for production purposes such as to promote aquatic animal growth. Top dressing feed with an antimicrobial (adding the antibiotic on top of the animal's normal rations) is specifically not permitted. Antibiotics have not been approved for hauling tanks or for immersion treatment of aquatic animals.

While there are few approved antibiotics for the treatment of aquatic animals, there are some additional options available for the domestic aquaculture industry.

Extra-label use of approved aquaculture drugs by veterinarians

There are some very limited circumstances, under supervision of a licensed veterinarian, where Terramycin[®] or Romet-30[®] medicated feed can be used for other aquatic animals not listed on the label. This is considered extra-label use. Extra-label use means use of a drug in any way that is not in accordance with approved labeling. In 1994, Congress passed legislation, Animal Drug Use Clarification Act (AMDUCA), which allowed veterinarians to prescribe FDA approved drugs in an extra-label manner under specific conditions. The regulations that implement AMDUCA can be found in Title 21 Code of Federal Regulations (CFR) Part 530. These extra-

label uses have limited utility in most commercial aquaculture but might be feasible for valuable brood stock or ornamental fishes.

While the AMDUCA prohibits the use of an FDA approved drug in or on feed, FDA recognized that for certain animal populations there was a need. FDA has exercised its regulatory discretion to allow extra-label use of medicated feeds under specific conditions. If the conditions are met, FDA is unlikely to take regulatory action. These conditions are identified in the FDA Compliance Policy Guide (Extra-label use of medicated feeds for minor species, Sec. 615.115). The Guide describes how a veterinarian can prescribe medicated catfish or salmonid feeds to treat bacterial diseases in other aquatic animals or for different bacterial diseases than what the products are approved. A veterinarian can prescribe the extra-label use of medicated feed when the health of animals is threatened and suffering or death would result from failure to treat affected animals. To use a medicated feed in an extra-label manner, the following conditions must be met:

- There is express written recommendation and oversight of an attending licensed veterinarian within the context of a valid veterinarian-client-patient relationship.
- The medicated feed is already approved for use in aquatic species. This means you can only use medicated catfish, salmonid or lobster feed.
- There cannot be any reformulation of the feed and they must be labeled for the approved species.
- Extra-label use can only be for therapeutic purposes, i.e. to treat a disease.
- The aquaculturist is required to:
 - Keep complete and accurate records of feeds received, including labels, invoices, and date fed. Records must be kept for at least one year.
 - Keep a current copy of the veterinarian's written recommendation
 - Institute procedures to assure that the identity of treated animals is carefully maintained.
 - Take appropriate measures to assure that the withdrawal time provided by the veterinarian is met and **no unsafe drug residues** occur in any food-producing animal.
 - Use the medicated feed in accordance with federal, state, and local environmental laws and regulations.
 - Follow user safety provisions.

Investigative New Animal Drugs (INAD)

As part of the FDA scientific data gathering requirements needed to approve a new antibiotic or other drug, an INAD exemption may be issued by FDA. The exemption allows a scientist or aquatic animal producer involved in generating data to support a specific drug approval to test the safety and effectiveness of the drug. INAD exemptions must be obtained from FDA –Center for Veterinary Medicine prior to drug use and entail considerable scrutiny to assure the testing will be valid and that human, animal and environmental safety are protected.

Judicious Use Principles

- 1. Emphasize disease prevention strategies, such as appropriate husbandry and hygiene, routine health monitoring and immunization.**

2. **Obtain accurate disease diagnosis prior to initiating disease treatment.**
3. **Ensure bacteria causing the aquatic animal disease are sensitive to the antimicrobial considered for use.**
4. **If medicated feed is used, ensure aquatic animals are feeding before treatment is applied.**
5. **Limit therapeutic exposure according to label instructions.**
6. **Observe all required withdrawal times.**
7. **Maintain accurate records of treatment.**
8. **Use good waste management practices.**

Judicious Use Practices

1. **Disease prevention.** Each producer can best design their own aquatic animal husbandry practices to minimize the probability of disease. Various factors must be considered including water quality (temperature, dissolved oxygen, pH, hardness, alkalinity, total ammonia nitrogen, nitrite concentrations and other contaminants), type of aquatic animal, feed quality, production system and production goals. If complete harvest is not practiced, then grading practices should be designed to minimize stress and fish injury. Feed should be of suitable quality to ensure good health under normal environmental conditions. Vaccines are often available and should be used since they prevent disease and can significantly reduce the need to use antibiotics. Good hygiene should be practiced in all production systems. Movement of aquatic animals between farms should be carefully scrutinized to ensure new aquatic animal diseases are not introduced. Producers may want to consult with fish health professionals (e.g. fish health veterinarians, AFS-FHS certified fish pathologists), university scientists, extension agents, consultants or peers to determine best practices for disease prevention and management .
2. **Obtain disease diagnosis.** Timely and accurate aquatic animal disease diagnosis is essential. Many diseases affecting aquatic animals are caused by viruses, protozoan or metazoan parasites or fungi. Antibiotic treatments are ineffective against these diseases and are expensive. Accurate diagnosis can only be obtained if representative sick animals are examined and the animals are submitted for diagnosis in a fresh condition. Representative water samples should also be tested since water quality factors can be significant contributors to disease outbreaks. Producers are encouraged to work with fish health professionals to develop written standard operating procedures for initiating disease diagnostic activities and implementing treatment. The protocols should include specific instructions for procedures to follow when administering antimicrobials at fish production facilities.
3. **Ensure fish are feeding.** The primary means of delivering antibiotics to aquatic animals is through the feed. If this delivery mechanism is to succeed, the animals must be feeding. Bacterial diseases often cause diminished feeding so care must be exercised to feed amounts that can be consumed. Early disease diagnosis helps ensure that treatments can begin before extensive off-feeding occurs. Operators should visually monitor feeding activity. In some circumstances, the best treatment is to stop feeding rather than to administer a medicated feed.
4. **Bacterial antibiotic sensitivity.** If bacteria are isolated from representative, clinically sick fish, the diagnostic laboratory should determine the sensitivity of the bacteria to available antibiotics before treatment is begun. Only use a labeled antibiotic to which the

pathogenic bacteria are clearly sensitive. This determination is best done in consultation with fish health professionals. Use of prescription, veterinary feed directive, or extra-label drugs should only be done under the direction and supervision of a licensed veterinarian.

- 5. Limit antibiotic exposure.** It is important to provide the medicated feed for the full duration of time (5 days for lobster and 10 days for other aquatic animals) indicated on the label and to minimize development of antimicrobial resistance... Terramycin[®] is a broad spectrum, short acting (does not stay very long in the body) bacteriostatic antibiotic. Since this antibiotic does not directly kill disease-causing bacteria, the aquatic animals own host defenses must work if therapy is to be successful... Reduction of fish stress can enhance host defenses. Even though the potentiated sulfonamide Romet-30[®] is generally bactericidal and broad spectrum, it is still crucial to also reduce aquatic animal stress if therapeutic success is to be expected. .
- 6. Observe withdrawal times.** It is essential that the withdrawal times on the FDA approved products be strictly followed. Withdrawal times are established to ensure human food safety is maintained and there are no harmful antimicrobial residues in edible tissues. Individual animals or animal groups subject to antibiotic exposure should be identified (flagged or otherwise identified by sign) and monitored to ensure they do not intermingle with non-treated animals destined for early harvest.
- 7. Record keeping.** Complete records should be kept documenting animals treated with antimicrobial drugs. Food animal producers should maintain these records to ensure compliance with mandatory FDA seafood inspection regulations and any information required by processors.
- 8. Waste management.** Antibiotic delivered to aquatic animals in feed may enter the environment through uneaten feed and feces. Those aquaculture practices with manure or sediment capture capabilities should utilize this ability and reduce discharge of antibiotics. Medicated feed should only be provided while fish are actively consuming feed. Sunlight and other degradative processes may decrease the amount of active antibiotics. Some antibiotics can also combine with benthic sediments and become biologically unavailable. All waste and effluents containing antibiotics must be handled in accordance with federal, state, and local environmental laws and regulations.