North Central Regional Aquaculture Center

Fact Sheet Series

Understanding the Veterinary Feed Directive Order in Aquaculture

Introduction

A veterinary feed directive (VFD) order is written by a licensed veterinarian to authorize the use of an approved drug in animal feed. VFD drugs were created by an amendment to the Federal Food Drug and Cosmetic Act. Prior to the creation of this new drug class, drugs such as antibiotics in animal feed were either over the counter (OTC) or prescription (USFDA CVM, 2015). This new class was necessary because in some states, prescription drugs could not be added to feed. In addition, the United States Food and Drug Administration (FDA) could now exert tighter control over antimicrobial use because of concerns over environmental contamination, residues in food, and antimicrobial resistance. Following authorization of the VFD rules and recent amendments, Aquaflor® became the first VFD aquaculture drug approved, and the previously OTC antibiotics administered to fish in feed also became VFD drugs. Unlike previous OTC antibiotic-medicated feeds, only licensed veterinarians could issue orders for VFD medicated feeds.

Before a VFD order can be issued to a producer, a valid veterinary client-patient relationship must exist between the veterinarian and the producer. Either the veterinarian or producer then presents the VFD order to the distributor of the VFD medicated feed. A distributor is any person who sells or distributes a VFD medicated feed to another as either a manufacturer, such as a feed mill, or only as a dealer.

Below is a list of questions to facilitate the understanding of the VFD order process in aquaculture. The first set is general and the second is a series of more specific situational questions.

How is a veterinary-client patient relationship defined?

The definition of veterinary-client patient relationship (VCPR) can vary from state to state, but in general, under a VCPR relationship the veterinarian must be licensed and have direct knowledge of the fish, make a diagnosis, and assume responsibility for treatment of the fish (USFDA CVM, 2015). The client (producer) agrees to follow the veterinarian's instructions. In some cases, veterinarians can directly diagnose and administer therapies, while in others they visit farms and consult with producers to establish disease management protocols for the fish. This VCPR provides greater flexibility for veterinarians working with fish health biologists, especially in rural areas with fewer aquatic veterinarians and large geographical distances between farms. However, the veterinarian must order all VFD medicated feeds and ensure the VFD order is consistent with approved label claims. The veterinarian must also be available for follow-up care of the fish treated with VFD feeds in case of an adverse event, such as failure of the treatment regime.

What information is required in a VFD order?

The VFD rules require the following information on the VFD order form from the veterinarian and producer (21 CFR 558.6)

- Names, addresses, and telephone numbers of veterinarian and client.
- Location of the fish specified in the VFD order including the address of the farm and the pond or tank number.
- Date of issuance of the VFD order.
- Name of the VFD drug to be used in medicated feed.
- Species and production class of the fish to be fed the VFD medicated feed. The production class refers to whether the fish is a fingerling, stocker, food-sized fish, etc.
- Approximate number of fish to be fed the VFD feed by the expiration date. Based on the estimated number of fish and the production class, the producer and the distributor calculate the amount of VFD feed necessary for treatment.
- Indication for which the VFD order is issued. This includes the diagnosis/causative bacterium, for which the VFD drug has previously been approved as a treatment (i.e., label claim) by the FDA.
- Drug concentration and duration of use. The quantity of drug added to a unit weight of feed is based on the feeding rate of the fish. The duration of use is the number of consecutive days that the medicated feed is administered to the fish. Both drug concentration and duration of use are part of the label claim approved for each drug by FDA.
- Withdrawal time, special instruction, and cautions. The pre-slaughter withdrawal time is determined by FDA for each drug and must be specified on the VFD order.
- Expiration date of the VFD order. Veterinarians have the option of extending the expiration date of the order to six months, which is the maximal time that a producer can use medicated feed from a VFD order (USFDA CVM, 2015). This extension benefits fish producers in areas with fewer feed mills and distributors of VFD medicated feeds. If the VFD order expires prior to a farmer completing the duration of use, the veterinarian must issue a new order so the producer can complete the treatment with the medicated feed. The farmer can keep any VFD feed after a VFD order has expired, but cannot feed it until a new VFD order is issued.
- Number of refills authorized. For fish, this number is zero, since no refills are authorized for fish under the VFD rule.
- Extralabel Use Statement: "Use of feed containing this veterinary feed directive (VFD) drug in a manner other than as directed on the labeling (extralabel use) is not permitted." Legally, VFD drugs can only be used according to the label claims, and the extralabel use statement must be included on the VFD order. Because there are many species of fishes and bacterial pathogens for which there are no label claims for VFD drugs, the FDA issued a guideline in 2017 which allows FDA to use enforcement discretion for fish (and other minor species of animals) (USFDA CVM, 2016, CPG 615.115). This gives veterinarians the option of using a VFD drug in an extralabel fashion for fish. For example, veterinarians commonly order the VFD drugs Romet® or Aquaflor® to control mortality associated with *Aeromonas hydrophila* infections in catfish even though neither antibiotic is approved for this use.

The FDA will allow extralabel use as long as all required regulations are followed. These include maintaining a valid VCPR in which all the regulations associated with approved claims apply, including correct duration of use, withdrawal time, proper regime, record maintenance, and expiration date (within six months of issuance). Extralabel use also requires that any adverse effects observed by the producer or veterinarian must be reported to the FDA within 10 days.

In addition to completing the VFD order form, the veterinarian must write a separate letter explaining the extralabel use, send a copy to the producer, retain the original, and instruct the producer to retain a copy for two years (records must be maintained longer. if required by their state's licensing board).

This letter must include details of:

a. The fish species and disease for which the VFD order is being issued (if different from the FDA-approved label claim). Note: The VFD drug can only be administered to contained, traceable fish (i.e. not to wild fish swimming freely in a lake or river).

b. The withdrawal time (if different from the FDA approved label claim).

- Affirmation of intent for combination VFD drugs. This section is not applicable to VFD medicated fish feeds, since there are no other drugs currently approved as combinations containing the VFD drug
- Veterinarian's written or electronic signature.

What are the transmission and record keeping requirements for VFD orders?

The veterinarian issues a VFD order by completing a preprinted triplicate order form supplied by the VFD drug company. The veterinarian retains the original, and the producer and feed distributor each receive a copy. A written paper copy of the completed VFD order may be presented to the distributor in person, by facsimile, or by email (21 CFR 558.6).

Alternatively, an electronic VFD order can be transmitted to the distributor online through a commercial secure web-based software system that is compliant with FDA regulations (21 CFR Part 11), such as GlobalVetLINK®. VFD orders may not be submitted by telephone.

Under federal law, VFD records must be maintained for two years by the veterinarian, producer, and distributor of the VFD feed and made available in the event of an FDA inspection. In a few states, records must be maintained for longer periods. A licensed veterinarian will have specific information regarding these requirements in their state. The commercial web-based software systems such as GlobalVetLINK® automatically retain electronic records for the required duration for a fee.

Does the withdrawal time for the VFD medicated feeds apply to baitfish?

For example, minnows infected with a certain bacteria are treated with a VFD medicated feed and will be sold as bait to catch food fish. In this case, the withdrawal time for the antibiotic in the VFD feed used to treat the baitfish must be observed. The antibiotic in the medicated feed has the potential to enter the human food chain since baitfish are used to catch food fish.

Can a VFD be obtained for rotenone top-coated feed?

Rotenone is often added to pond water to depopulate unwanted fish, but is expensive to use. Some producers wonder why feed couldn't be top-coated with rotenone and then fed to fish, because it would be a more economical and targeted method to kill unwanted fish. But the answer is no – this is not allowed. Rotenone is not approved as a new animal drug for use in animal feeds and as such cannot be fed to fish (21 CFR Part 558.3).

What methods are required for diagnosis of a bacterial disease in fish?

Veterinarians can use microbiological culture or PCR testing results for diagnosis of the causative bacterium, but ordering a VFD feed for fish does not require a laboratory diagnosis. The veterinarian in a VPCR is allowed to diagnose sick fish based only on clinical signs or lesions, which is sufficient to place a VFD order for medicated feed.

Romet® and Aquaflor® are approved to control mortality associated with *Edwardsiella ictaluri* the causative bacteria of enteric septicemia of catfish (ESC). A species of *Edwardsiella (E. piscicida)* that presents clinically the same as ESC was recently detected in catfish with molecular techniques. Because fish can present with signs and lesions of ESC, whether they are infected with *E. ictaluri* or *E. piscicida*, they can be treated on label with Romet® or Aquaflor®, even if the causative bacteria is later confirmed to be *E. piscicida*.

Can medicated feed obtained with a VFD order written with a six-month expiration date be used to treat the same fish in the same pond again if there is a reoccurrence of the disease within that six-month period?

No. You can only treat the same sick fish with medicated feed from a VFD order once. The VFD order applies only to a single disease outbreak or event. If there is a reoccurrence of the same disease in the same pond, a new VFD order must be written by the veterinarian.

Here is a related example from a catfish producer. Pond 1 is stocked with catfish fingerlings and breaks with ESC, and Ponds 2, 3, 4, and 5 are adjacent fingerling catfish ponds. The producer needs a VFD drug (with a duration of use of 10 days) to treat ESC in Pond 1. He intends to treat Pond 1 from May 1-10. He expects fish in ponds 2, 3, 4, and 5 to break with ESC a few days later and requests a VFD order with a 10-week expiration date to cover fish in Ponds 1-5. He treats Pond 1 from May 1-10 and the other ponds at later dates as they break with disease. But if Pond 1 breaks with ESC again (after May 10), a new VFD order must be issued.

Author Contact Information and Affiliation

Patricia S. Gaunt, DVM, PhD, Professor, Aquatic Animal Health, Mississippi State University

References for guidance

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