

The Veterinary Feed Directive

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Abstract

We will be writing Veterinary Feed Directives (VFDs) and prescriptions in December of 2016 to authorize the use of medically important antibiotics in the feed and water of our client's animals starting on January 1, 2017. The major challenge for our profession is not to master the limited number of labels we will be dealing with, or to master the VFD process; it is that we are now not only responsible for authorizing the use of almost every antibiotic in food animals, we are also accountable.

The decision process for if we should provide a VFD or prescription is centered on applying our professional training and experience to establish a clinical justification for the use. This process centers on these considerations. Do I have a valid VCPR? Is there a reason for this use or is it just habit? Is it legal? Is it effective? Are there any issues with residues or antibiotic resistance to consider?

After these considerations, veterinarians are then responsible to lead in antibiotic stewardship. This involves assuring accurate case definitions, searching for antibiotic alternatives, selecting the appropriate antibiotic, monitoring use, and constant re-evaluation of the need for the antibiotic.

Key words: VFD, veterinary feed directive, antibiotics, food grade

Résumé

En décembre 2016, nous rédigerons des directives sur les aliments médicamenteux et des prescriptions afin d'autoriser l'utilisation d'antibiotiques médicalement importants pour les aliments et l'eau des animaux de nos clients à partir du premier Janvier 2017. Le plus grand défi pour notre profession n'est pas seulement de maîtriser le nombre limité d'antibiotiques permis ou de maîtriser le processus de réglementation sur les aliments médicamenteux. Il est plutôt qu'en plus de la responsabilité d'autoriser l'utilisation de presque tous les antibiotiques pour les animaux de production, nous devons aussi rendre des comptes.

La prise de décision concernant une directive sur les aliments médicamenteux ou une prescription se base sur notre formation professionnelle et notre expérience afin d'en justifier l'utilisation clinique. Ce processus prend en compte les considérations suivantes : est-ce que ma relation vétérinaire-client-patient est valide?, est-ce qu'il y a une bonne raison pour cette utilisation ou est-ce seulement une habitude?, est-ce légal?, est-ce effectif?, est-ce qu'il y a des doutes concernant les résidus ou la résistance antimicrobienne?

Après avoir pris ces éléments en considération, les vétérinaires sont donc tenus de promouvoir l'utilisation judicieuse des antibiotiques. Cela implique de s'assurer d'une juste définition des cas, de rechercher des alternatives à l'utilisation des antibiotiques, de choisir l'antibiotique approprié, de surveiller son utilisation et de constamment réévaluer le besoin d'utiliser cet antibiotique.

Introduction

We will be writing Veterinary Feed Directives (VFDs) in December of 2016 to authorize the use of medically important antibiotics in the feed of our client's animals starting on January 1, 2017. We will also be authorizing the use of medically important antibiotics in the water of food animals through the prescription process starting at the same time. It is important to understand the ins and outs of writing a VFD, but this presentation is about the work that has to be done before the VFD is created.

The major challenge for our profession is not to master the limited number of labels we will be dealing with, or to master the VFD process; instead, it is that we are now not only responsible for authorizing the use of almost every antibiotic in food animals, we are also accountable. And, we will be accountable in an environment of ever-increasing transparency, a transparency which will focus attention on the relationship between our clinical decisions and our financial interests in the authorized products.

The success of our profession in this endeavor will depend on the navigation of key steps in an organized decision process. This process precedes the navigation of the VFD authorization protocol. In contrast to the regulatory details of creating a valid VFD, the decision process is centered on applying our professional training and experience to establish a clinical justification for the use.

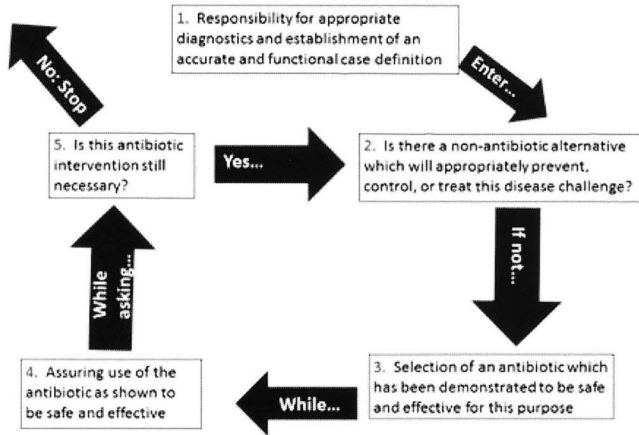
A VFD checklist (which applies to any antibiotic use authorized by a veterinarian) includes:

- Do I have a valid VCPR to authorize this use?
- Is there a reason to use the product, or is it just habit?
- Is it legal?
- Is it effective?
- Are there any residue issues to consider?
- Are there any issues with antibiotic resistance?

Only when the proposed use survives this list should it be authorized. But, before our profession starts the new responsibility of clicking down through this list for in-feed antibiotics on a routine basis, it is important to define the environment within which we will be functioning. We need to be clear on the difference between judicious use and stewardship.

Antimicrobial Stewardship

I propose that there are basic inclusions in antimicrobial stewardship regardless of branch of medicine or animal species. Judicious use involves the proper application of the antibiotic when used. Stewardship in food animals involves the following loop, with an emphasis on judicious use as well as seeking to reduce or eliminate the need to use the antibiotic.



1. The veterinarian is responsible for establishing the nature and presence of disease that requires prevention, control, or therapy. Once the presence is established, then the veterinarian is also responsible for establishing a case definition for the client to use to monitor the disease and to determine the need for antimicrobial use.
2. A constant requirement of antimicrobial stewardship is the search for non-antimicrobial alternatives for prevention, control, and treatment. These alternatives may include environmental management, vaccines, animal flow, genetic selection, and a systems approach to the evaluation of the relationship between level of production and disease pressure.
3. The veterinarian is responsible for working with their client to make a rational antimicrobial decision based on the disease(s) characterized in step 1. The principles of evidence-based medicine include evaluating the best evidence available combined with the practitioner's clinical experience and the needs of the client.
4. The responsibilities of the client/veterinarian relationship do not stop with step 3; this next step requires an ongoing commitment for interaction between the veterinarian and client. In fact, of all the steps, I feel that this step is the one most highly correlated with a true, functional veterinary-client-patient relationship. Step 4 requires evaluation of records as well as on-site evaluation of protocol application. Are the case definitions being used

appropriately? Is protocol drift occurring? Are new employees properly trained to put the protocols into practice? Do the client and their employees have buy-in related to the protocol? Are there established goals? Do protocols need changed?

5. Have changes in management practices made the need for antibiotic prevention or control obsolete? If so, stop! If not, what can be done to reduce or remove the need for treatment.

The AABP has a guideline document entitled Prudent Antimicrobial Use Guidelines for Cattle, which is available on the AABP website.¹ The stewardship loop proposed is consistent with this statement in the AABP guideline. "The veterinarian's primary responsibility is to help design management, immunization, housing and nutritional programs that will aid in reducing the incidence of disease and, thereby, the need for antimicrobials".

A Valid Veterinary-Client-Patient Relationship?

The precise details of the VCPR can only be defined by establishing a local standard of practice. When evaluating the text of the VCPR as published in 21 CFR Part 530.3(i), it is possible to identify at least 5 areas which are arguably open to interpretation as a standard of practice (highlighted in boxes below).²

"(i) A *valid veterinarian-client-patient relationship* is one in which:

- (1) A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian;
- (2) There is **sufficient knowledge of the animal(s)** by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and
- (3) The practicing veterinarian is **readily available for follow-up** in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has **recently seen** and is personally acquainted with the keeping and care of the animal(s) by virtue of **examination of the animal(s)**, and/or by **medically appropriate and timely visits** to the premises where the animal(s) are kept."

The advent of the VFD provides for more veterinary-client interactions where unscrupulous members of our profession may seek to derive income by providing VFDs outside of a legitimate client relationship. It is clear that the VCPR definitions are to be determined within the individual states, as long as the definitions meet at least a minimum federal standard. I encourage veterinarians to actively engage with their state licensing boards and veterinary associations to work towards definitions.

The AABP has a guideline document entitled “Establishing and Maintaining the Veterinarian-Client-Patient relationship in Bovine Practice”.³ A lot of work went into this document by AABP members seeking to establish a baseline for the VCPR.

Another resource for forms to help with establishing a VCPR is the MN Dairy Quality Cares site.⁴ On this page they provide a VCPR relationship agreement as well as forms which detail the information you should know when writing prescriptions for clinical disease, mastitis and udder health, reproductive programs, and youngstock health.

Reason or Habit?

Veterinarians will have to decide whether to authorize some standard in-feed antibiotic use practices which in the past have been determined by producers and, in some cases, nutritionists. The first step in antimicrobial stewardship requires that we must confirm that the real or perceived reason(s) for use are still valid, and that the antibiotic use cannot be replaced with another management practice.

A common concern that I have encountered is that if one veterinarian declines to write a VFD, then another may be willing to do so, and clients will be lost if requests for VFDs are refused. Looking at the big picture, I think this challenge is going to be addressed by transparency and benchmarking of antibiotic use within programs required for access to marketing channels. Granted, some of the pressures on the marketing channels from the consumer (or at least the perceived consumer on social media) may not be driven by science, and therefore some antibiotic use pressures related to the marketing channel may be nonsensical. However, the comparison of antibiotic use practices across multiple producers within the food animal industries should at least drive further research into the reasons for the diversity of use.

Is it Legal?

In contrast to the previous category, this one is relatively easy. For the VFD, if the dose or inclusion rate, duration of therapy, and indication do not exactly match the label, the application of the antibiotic in feed isn't legal. The veterinarian is responsible for this accuracy. Provision of a VFD for a label indication while knowing that the actual use will be different is both illegal and unethical.

This prohibition of extralabel use in feed will undoubtedly lead to a lot of tense situations where, for example, requests for use of a tetracycline in the feed for control of seminal vesiculitis in bull tests, pinkeye, or footrot will result in a conflict between adhering to the law and addressing the needs of the client and welfare of the animals. The answer lies in a combination of critical evaluation of the evidence for need (above) and the efficacy of the requested use (below) along with pursuing additional label claims. The challenge with pursuing additional label claims is the required capital

investment on the part of a sponsor related to the studies required for a new claim, as well as the risk of opening up a label for a new claim, with the accompanying requirements to also update numerous other sections such as microbial and environmental safety.

We also have some problems where, due to the feed consumption of today's fed cattle, it is essentially impossible to match both the label feed inclusion rate and the mg/head/day dose. Discussions are ongoing, but no real solutions to my knowledge have been proposed as of the writing of these proceedings.

Is it Effective?

One of the biggest possible tragedies is to go through all of the work of establishing a legitimate VCPR, need, and legality of the application, only to make no real difference in disease outcome. Following the disease status of treated populations doesn't do us that much good without negative controls. We aren't likely to conduct a prospective, randomized, negative control clinical trial in practice situations; although more and more larger production systems are conducting these in-house. Therefore it is imperative that as a profession we insist on these types of data for older products with no recent studies to assure us that efficacy is reasonably likely. Levels of evidence for efficacy vary from fairly robust to incredibly thin or nonexistent.

Residue Considerations?

This is fairly straightforward. Follow the label withdrawal time, making sure that the client has sufficient feed management and animal identification capabilities to observe the withdrawal time. Where this can get complicated is when export markets with different tolerances (Maximum Residues Limits, or MRLs) are involved. If a client is just entering the export markets, then advice on altered withdrawal times should be sought from the marketing channel or by consulting others familiar with the requirements.

Another residue potential exists in cattle feeding environments where the mixing of feed for organic or natural never-ever cattle occurs in the same system (mill, trucks...) as cattle where feed antibiotics are used. This situation requires extreme attention to some well-crafted standard operating procedures for flushing of equipment and ration sequence. With today's chemical analytical capabilities applied in the zero-tolerance environment of organic and never-ever programs, in some operations it just may not be possible to share feed systems.

Any Issues with Antibiotic Resistance?

Consider this heading as a placeholder for increased understanding of this relationship in the future. We have much to learn about the relationship of dose and duration

of antibiotic exposure to the selection pressure for resistant pathogens and/or the transfer of resistance genetic elements within bacterial populations. Currently, the research focuses on reasons that might cause us to curtail or eliminate current uses. If the precautionary principle becomes a major regulatory driver in the United States, the research focus would switch to attempting to prove safety in an effort to get products back.

Conclusions

The only things really new about the VFD process are the increase in the breadth of responsibility for antibiotic use in food animals and the altered procedure details as compared to the current prescription process. Our clinical decision processes are still based on the same principles as in the past; however, the evolving landscape of regulatory and legislative activity, food sales competition, and social

media presence have served to hold up our antibiotic use practices for public scrutiny in a way we have never encountered before.

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