

## **Antimicrobial Use in Livestock: Impact of New Food and Drug Administration Regulations**

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### **INTRODUCTION**

In recent years the use of antimicrobials in animal agriculture has coming under intense scrutiny from both governmental regulators and private organizations. As a result, the United States Food and Drug Administration (FDA) recently published two documents (FDA Guidances for Industry 209 and 213) that detail their views on the judicious use of antimicrobials in food animals and restrict the use of medically-important antimicrobials in feed for the purposes of promoting growth and feed efficiency. The purpose of this document is to summarize these guidances, explain the Veterinary Feed Directive regulations, and detail the impact that they will have on the use of antimicrobials in food animals in the state of Georgia.

### **FDA GUIDANCE FOR INDUSTRY 209**

Published by the FDA in April 2012, Guidance for Industry 209 represents the FDA's current thinking on the topic of judicious antimicrobial use in food animals. In this document, the FDA proposed measures to promote more judicious use of antimicrobials in food animals in two ways:

- 1) Limiting the use of medically important antimicrobials (Table 1) to uses that are considered necessary for assuring animal health and
- 2) Limiting the use of antimicrobials to uses that require veterinary oversight or consultation.

In other words, the FDA considers the use of antimicrobials for promotion of weight gain and feed efficiency unnecessary and a potential contributor to the increase in the prevalence of antimicrobial resistant bacteria. However, the use of antimicrobials to prevent, treat, or control specific diseases is considered reasonable and necessary for assuring the health of food animals. For example, if it is believed that a group of cattle are at risk of developing respiratory disease because of their history or specific production practices used by a producer, treating this group of cattle with an antimicrobial approved for prevention of respiratory disease would be reasonable. However, administration of a drug to overtly healthy animals in the absence of specific information suggesting increased risk of disease is not judicious use. Furthermore, the FDA believes that all antimicrobial use, whether the drug is given by injection or administered in the feed or water, should involve the oversight or consultation of a veterinarian. Currently, many of the antimicrobial drugs approved for use in-feed are available over-the-counter. With Guidance for Industry 209, the FDA has suggested that the ability to purchase antimicrobials over-the-counter be phased out and moved to a prescription only or Veterinary Feed Directive (VFD) process. As a result, the FDA has recommended that

veterinarians be involved with all decisions regarding antimicrobial use, whether it be treating individual animals or periodic consulting to establish management protocols, to further combat and slow the development of antimicrobial resistant bacteria.

**Table 1.** List of antimicrobial classes considered medically important by the FDA

Class
β-lactams
Aminoglycosides
Macrolides
Phenicols
Streptogramins
Fluoroquinolones
Sulfas
Tetracyclines

### **FDA GUIDANCE FOR INDUSTRY 213**

Guidance for Industry 213 was published by the FDA in December 2013 and this document established recommendations for pharmaceutical companies to gradually and voluntarily phase out the use of antimicrobials in feed or water for the promotion of weight gain and feed efficiency. In addition, Guidance for Industry 213 recommended that all use of antimicrobials in feed and water involve the input of a licensed veterinarian. In more basic terms, Guidance for Industry 213 was the implementation of the recommendations contained in Guidance for Industry 209. From the date of passage, the FDA gave the pharmaceutical industry 3 years to adopt these changes and, should compliance be low, further action potentially taken. While this document only provided recommendations and all changes to drug labels were voluntary, all major pharmaceutical companies quickly made changes to their labels to meet the new FDA guidelines.

### **IMPLICATIONS OF GUIDANCES 209 AND 213**

Guidances for Industry 209 and 213 clearly laid out the FDA's position on the in-feed and water use of antimicrobials in food animals for promotion of growth and feed efficiency. As a result of these documents, in-feed and water antimicrobials can no longer be used to promote growth or feed efficiency, regardless of the existence of a valid prescription after January 1, 2017. Therefore, the use of antimicrobials for this purpose would be considered illegal. In addition, any in-feed or water antimicrobial use requires a prescription or VFD order from a veterinarian. Moreover, the veterinarian writing the prescription must be licensed in the state where the animals are housed and have an established veterinary-client-patient relationship (VCPR) with the operation in question before a prescription can be written. To establish a VCPR the following guidelines must be met (see attached VCPR form):

- 1) A veterinarian has assumed responsibility for making medical decisions regarding the health of the animal(s) in question and the need for medical treatment and the owner has agreed to follow your advice
- 2) A veterinarian has sufficient knowledge of the animal(s) to initiate at least a general or

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preliminary diagnosis of the medical condition

- 3) A veterinarian is available for follow-up in the case of an adverse event or treatment failure. This relationship can only exist with observation of the animals and management scheme and through medically appropriate and timely visits to the facility

GFI 209 and 213 also address the issue of using antimicrobials for disease prevention purposes. The FDA considers the use of antimicrobials for disease prevention judicious when the following criteria are met:

- 1) There is evidence of effectiveness
- 2) Such preventive use is consistent with accepted veterinary practice
- 3) The use is linked to a specific etiologic agent
- 4) The use is appropriately targeted to animals at risk of a specific disease
- 5) No reasonable alternatives for intervention exists

With these statements the FDA has recognized that the use of antimicrobials for disease prevention has a place in veterinary practice and that these uses are currently not under scrutiny.

### **VETERINARY FEED DIRECTIVES**

A veterinary feed directive (VFD) is a written statement issued by a licensed veterinarian that authorizes the use of a VFD drug or combination VFD drug in or on animal feed. This statement allows a producer to obtain and use animal feed containing a VFD drug to treat animals in accordance with the conditions for use approved by the FDA. A list of antimicrobials that will be affected by the new VFD regulations are listed in table 2 below. It is important to note that this is not an exhaustive list of the products affected by the new VFD regulations and products labels should be consulted prior to use in any food-producing species to ensure all requirements are appropriately met.

**Table 2.** Antimicrobials affected by VFD regulations

<b>Generic Name</b>	<b>Trade Names</b>
Chlortetracycline	Aureomycin, CLTC, Pennchlor
Chlortetracycline + Sulfamethazine	Aureo S 700
Neomycin + Oxytetracycline	Neo-Terramycin, Neo-Oxy
Oxytetracycline	Terramycin, Pennox
Tylosin	Tylan
Tilmicosin	Pulmotil
Virginiamycin	V-Max

Veterinarians should be aware that the VFD guidelines only affect medically important antimicrobials. Antimicrobials not considered medically important will not be affected by the new guidelines. Products not affected by VFD guidelines are listed in table 3 below. As stated

previously, this is not an exhaustive list of the products affected by the new VFD regulations and products labels should be consulted prior to use in any food-producing species to ensure all requirements are appropriately met.

**Table 3.** Antimicrobials/Antiprotozoals not affected by VFD regulations

<b>Generic Name</b>	<b>Trade Names</b>
Amprolium	Corid
Bacitracin	Albac, BMD
Bambermycin	GainPro
Decoquinate	Deccox
Laidlomycin	Cattlyst
Monensin	Rumensin
Lasalocid	Bovatec

Veterinarians writing VFD orders for clients will have several responsibilities under the new regulations. These responsibilities are as follows:

- 1) Be licensed to practice veterinary medicine in the state where the animals are housed
- 2) Operate in the course of professional practice and in compliance with all practice requirements
- 3) Write VFD orders in the context of a valid VCPR
- 4) Issue VFD orders in compliance and within context of approved drug use
- 5) Prepare and sign VFD order providing all required information
- 6) Enter additional discretionary information as necessary
- 7) Include all required information necessary when VFD drug is used in combination with another VFD drug
- 8) Restrict or allow combination use of VFD drug with OTC drug
- 9) Provide the feed distributor and client with a copy of the VFD order
- 10) Retain original VFD order for 2 years

11) Provide VFD orders to inspectors upon request

***It should be noted that any extra-label use of a medication labeled for inclusion in feed is illegal, regardless of VFD status.*** For example, the use of chlortetracycline (CTC) in feed to treat or prevent pinkeye or footrot in cattle is illegal since there is no approved label claim on any commercially available CTC product.

### **FREQUENTLY ASKED QUESTIONS**

Multiple questions have arisen since the VFD regulations were passed. Answers to some of the most commonly asked questions are listed below:

- 1) Veterinarians must send a copy of the VFD order to the feed distributor via hardcopy, fax or other electronic means. If in hardcopy, the order must be sent with the client or directly to the distributor
- 2) Veterinarians must retain the VFD order in its original form for 2 years
- 3) It is likely that many drug sponsors will create their own VFD forms to assist veterinarians. If a VFD form is not available, the veterinarian may create their own. Both the American Veterinary Medical Association and FDA have created a standard VFD form that can be used and those forms can be found within these proceedings
- 4) Expiration dates are the last date that a VFD medication can be fed following the writing of an order by a veterinarian. Some products have expiration dates on the label, many do not. If VFD medication does not specifically list a time for the order to expire, VFD regulations require a veterinarian to limit the VFD order to 180 days or less
- 5) The difference between an expiration date and duration of use is as follows: expiration dates define the period of time for which the authorization to feed a VFD drug is lawful. The duration of use determines the length of time a VFD drug may be fed to the animals in question
- 6) The following information must be found on a lawful VFD:
  - a. Veterinarian's name, address, and telephone number
  - b. Client's name, business or home address, and telephone number
  - c. Premises at which the animals specified in the VFD are located
  - d. Date of VFD issuance
  - e. Expiration date of VFD
  - f. Name of VFD drug
  - g. Species and production class to be fed VFD feed
  - h. Approximate number of animals to be fed VFD feed

- i. Indication for which VFD is issued
  - j. Level of VFD drug in feed and duration of use
  - k. Withdrawal times, special instructions and cautionary statements
  - l. Number of refills authorized
  - m. Statement: Use of feed containing this VFD drug in a manner other than as directed on the labeling is not permitted
  - n. An affirmation of intent for combination VFD drugs
  - o. Veterinarians electronic or written signature
- 7) Additional information may be included on the VFD order but is not required. That information is as follows:
- a. A more specific description of the location of the animals in question (by site, by pen, barn, stall, tank)
  - b. Approximate age range of animals
  - c. Approximate weight range of animals
  - d. Any other information the veterinarian deems appropriate

#### **OTHER CONSIDERATIONS FOR VETERINARIANS**

A request for a VFD from a producer does not mean it should be automatically authorized. This should be taken as an opportunity to initiate a conversation with a producer. As a veterinarian you should consider several things before approving the VFD order:

- 1) Are there non-antibiotic alternatives
- 2) Does the proposed use match product label specification
- 3) Is there a genuine need
- 4) What is the efficacy of the proposed product in relation to a disease challenge
- 5) Can a withdrawal time be met prior to slaughter
- 6) Are there issues with antimicrobial resistance

#### **CONCLUSIONS**

While cumbersome and difficult to understand, these guidelines are designed to promote better antimicrobial use in food animals and reduce the selection pressure for antimicrobial resistant bacteria. While antimicrobial use in food animals is only a small part of the antimicrobial resistance puzzle, animal agriculture is under intense scrutiny from both governmental agencies and public advocacy groups. The long-term effects of these changes are yet to be seen, however, the events of the next 5-10 years will be telling.

**Appendix A. VCPR Agreement Form**

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Food Animal Health and Management Program**

**VETERINARY CLIENT PATIENT RELATIONSHIP FORM**

It has been explained to me that a valid Veterinary Client Patient Relationship (VCPR) exists if the following conditions are met:

1. A veterinarian has assumed the responsibility for making medical judgements regarding the health of animals on an operation and a client has agreed to follow any instructions given
2. There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general diagnosis. This means that the veterinarian has recently seen and is personally acquainted with the care of the animals in question.
3. The practicing veterinarian is readily available for follow-up should treatment fail or adverse reactions occur.

**Producer Name:** \_\_\_\_\_

**Operation Name:** \_\_\_\_\_

**Address:** \_\_\_\_\_ **City and State:** \_\_\_\_\_ **Zip:** \_\_\_\_\_

**Contact Number:** \_\_\_\_\_

**Type of Operation (Circle All That Apply):**

Cow/Calf

Stocker/Backgrounder

Feedyard/Finisher

Dairy

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**Veterinarian:** \_\_\_\_\_

**Clinic:** \_\_\_\_\_

**Address:** \_\_\_\_\_ **City and State:** \_\_\_\_\_ **Zip:** \_\_\_\_\_

**Contact Number:** \_\_\_\_\_

I hereby certify that a valid Veterinary Client Patient Relationship (VCPR) has been established for the producer and veterinarian listed above. This VCPR will remain in force until cancelled by either party and will be reviewed at least annually.

Producer Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Veterinarian Signature: \_\_\_\_\_ Date: \_\_\_\_\_

**Appendix B. AVMA VFD Form**



This fillable form is published by the American Veterinary Medical Association, 1931 North Meacham Rd, Schaumburg, Illinois 60173. The form is provided for your convenience, and is consistent with the common format published in the Food and Drug Administration's draft Guidance for Industry #233, "Veterinary Feed Directive Common Format Questions and Answers." This form is not intended to provide legal advice or opinion and should not be construed as such. This form should be completed with all information required by applicable federal statutes and regulations related to the Veterinary Feed Directive.

## Veterinary Feed Directive

Veterinarian: \_\_\_\_\_ Client: \_\_\_\_\_  
Address: \_\_\_\_\_ Address: \_\_\_\_\_

Phone: \_\_\_\_\_ Phone: \_\_\_\_\_  
Fax or email (optional): \_\_\_\_\_ Fax or email (optional): \_\_\_\_\_

Drug(s): \_\_\_\_\_ Drug Level: \_\_\_\_\_ g/ton Duration of Use: \_\_\_\_\_  
No substitutions allowed

Species and production class: \_\_\_\_\_ **No refills/reorders authorized**  
Indications for use: \_\_\_\_\_  
Caution (if any): \_\_\_\_\_

**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**

Approximate number of animals: \_\_\_\_\_  
Premises: \_\_\_\_\_  
Other identification (e.g., age, weight) (optional): \_\_\_\_\_

Special instructions (if any): \_\_\_\_\_

### Affirmation of intent (for combination VFD drugs) (mark one statement)\*

(\*For VFD drugs for which there are no approved VFD combinations, only the first affirmation statement should be marked)

This VFD only authorizes the use of the VFD drug(s) cited in this order and is not intended to authorize the use of such drug(s) in combination with any other animal drugs.

This VFD authorizes the use of the VFD drug(s) cited in this order in the following FDA-approved, conditionally approved, or indexed combination(s) in medicated feed that contains the VFD drug(s) as a component:

Drug(s)	Drug Level(s) and Any Special Instructions

This VFD authorizes the use of the VFD drug(s) cited in this order in any FDA-approved, conditionally approved, or indexed combination(s) in medicated feed that contains the VFD drug(s) as a component.

▶ Withdrawal time (if any): This VFD must be withdrawn \_\_\_\_ days prior to slaughter ◀

VFD date of issuance (month/day/year): \_\_\_\_\_ VFD expiration date (month/day/year): \_\_\_\_\_  
(As specified in the approval; cannot exceed 6 months after issuance)

Veterinarian's signature: \_\_\_\_\_ All parties must retain a copy of this VFD for 2 years after the date of issuance



# Appendix C. Blank FDA VFD Form

## Veterinary Feed Directive

Veterinarian: \_\_\_\_\_ Client: \_\_\_\_\_  
 Address: \_\_\_\_\_ Address: \_\_\_\_\_  
 (business or home) \_\_\_\_\_  
 Phone: \_\_\_\_\_ Phone: \_\_\_\_\_  
 Fax or email (optional): \_\_\_\_\_ Fax or email (optional): \_\_\_\_\_

Drug(s) Name: \_\_\_\_\_ Drug(s) Level: \_\_\_\_\_ g/lon Duration of use: \_\_\_\_\_

Species and Production class: \_\_\_\_\_ Number of orders (refills) authorized (if permitted by the drug approval): \_\_\_\_\_

Indications for use (as approved): \_\_\_\_\_

Caution (related to this medicated feed, if any): \_\_\_\_\_

**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**

Approximate Number of Animals: \_\_\_\_\_

Premises: \_\_\_\_\_

Other Identification (e.g., age, weight) (optional): \_\_\_\_\_

Special Instructions (if any): \_\_\_\_\_

**Affirmation of intent (for combination VFD Drugs) (check one box)\*:**

(\*For VFD drugs for which there are no approved VFD combinations, only the first affirmation statement should be included on the VFD)

This VFD only authorizes the use of the VFD drug(s) cited in this order and is not intended to authorize the use of such drug(s) in combination with any other animal drugs.

This VFD authorizes the use of the VFD drug(s) cited in this order in the following FDA-approved, conditionally approved, or indexed combination(s) in medicated feed that contains the VFD drug(s) as a component:

Drug(s)	Drug Level(s) and any Special Instructions

This VFD authorizes the use of the VFD drug(s) cited in this order in any FDA-approved, conditionally approved, or indexed combination(s) in medicated feed that contains the VFD drug(s) as a component.

▶ **Withdrawal Time** (if any: This VFD Feed must be withdrawn \_\_\_ days prior to slaughter) ◀

VFD Date of Issuance: \_\_\_\_\_ (Month/Day/Year) VFD Expiration Date: \_\_\_\_\_ (Month/Day/Year) (As specified in the approval; cannot exceed 3 months after issuance)

Veterinarian's Signature: \_\_\_\_\_

All parties must retain a copy of this VFD for 2 years after the date of issuance

Appendix D. Completed FDA VFD Form

Veterinary Feed Directive  
For Mydrug

Veterinarian: John Doe, DVM or VMD Client: John Smith  
Address: 123 AnyStreet Address: 456 AnyStreet  
Anytown, Anystate 00000 (business or home) Anytown, Anystate 00000  
Phone: 111-111-1111 Phone: 111-111-1111  
Fax or email (optional): \_\_\_\_\_ Fax or email (optional): \_\_\_\_\_

Drug(s) Name: Mydrug Drug(s) Level: 100 g/ton Duration of use: 14 days

Species and Production class: Swine Number of orders (pills) authorized (if permitted by the drug approval): 0

Indications for use (as approved): For the treatment of Swine Disease associated with *Bacterium pathologicum*

Caution (related to this indicated use, if any): Not for use in pregnant sows

**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**

Approximate Number of Animals: 200

Premises: 777 Country Road, Anytown, Anystate 00000

Other identification (e.g., age, weight) (optional): All animals are between 4 and 4.5 months of age

Special instructions (if any): OK to move the swine to Barn 5 after treatment

Affirmation of intent (for combination VFD Drugs):

This VFD only authorizes the use of the VFD drug(s) cited in this order and is not intended to authorize the use of such drug(s) in combination with any other animal drugs.

◀ Withdrawal Time (if any): This VFD Feed must be withdrawn 5 days prior to slaughter ▶

VFD Date of Issuance: 05/15/17 (Month/Day/Year) VFD Expiration Date: 05/01/17 (Month/Day/Year) (As specified in the approval, cannot exceed 6 months after issuance)

Veterinarian's Signature: My signature, DDMM on VFD

All parties must retain a copy of this VFD for 2 years after the date of issuance

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