DEPARTMENT OF HEALTH AND HUMAN SERVICES
U. S. Food and Drug Administration

March 4, 2016

Sheldon R. Jones
Vice President
Farm Foundation, NFP
1301 W. 22nd Street, Suite 906
Oak Brook, IL 60523

Dear Sheldon:

I would like to thank Farm Foundation for hosting the 12 regional workshops this past year as part of its Antimicrobial Education Project. These workshops provided us with an excellent opportunity to engage veterinarians, producers, and others on the many practical issues associated with implementing FDA's Guidance 209, Guidance 213, and the updated Veterinary Feed Directive regulation. Although many good questions were raised at the workshops, we were not able to respond to them all during the meetings. Therefore, below please find responses to the unanswered questions that were collated from the 12 workshops.

1. What is the proper method of disposal for VFD feed that is no longer needed/left over?

   Disposal of the feed should be in a manner that is in accordance with State or local requirements for medicated feeds.

2. How will minor species be handled?

   On January 1, 2017, we expect that certain antimicrobial drugs of human medical importance will change marketing status from over-the-counter (OTC) to Veterinary Feed Directive (VFD) for drugs administered through feed or to prescription (Rx) status for drugs administered through water. Drugs that have either a prescription or veterinary feed directive marketing status may only be used under the oversight of a veterinarian. We understand that products approved for use in minor species will be involved in this transition.

   For those products that are transitioning from OTC to Rx status because they are administered through water, the provisions for legal extralabel use of these drugs can be found in 21 CFR 530.

   Extralabel use of medicated feed, including a veterinary feed directive medicated feed is illegal. We currently have a Compliance Policy Guide Section 615.115 Extra-Label Use of Medicated Feeds for Minor Species that discusses the extralabel use of OTC medicated feeds for minor species. We have a working group that is reviewing and developing recommendations to update Compliance Policy Guide Section 615.115 Extra-Label Use of Medicated Feeds for Minor Species to address extralabel use of VFD feed.

3. What restrictions will be put on imports to ensure we are being held to the same standards?

   VFD drugs for use in the United States, whether produced domestically or imported are subject to the same VFD requirements. All VFD drugs marketed in the United States must be the subject of an FDA approval, conditional approval, or must be included on the index of legally marketed unapproved new animal drugs (i.e., index listed).

4. Who is responsible for enforcement?

   FDA intends to use a phased enforcement strategy for implementation of this final rule as OTC drugs become VFD drugs as a result of GFI #213 implementation. FDA first intends to provide education and training for stakeholders subject to this final rule such as veterinarians, clients (animal producers), feed mill distributors and other distributors. FDA will then engage in risk-based general surveillance, as well as for-cause inspection assignments. FDA intends to work closely with state regulatory partners and state boards of veterinary medicine in their enforcement strategy. In instances where a state VCPR applies the state may also pursue enforcement.

5. What are the associated penalties?

   Prohibited acts and the associated penalties can be found in Section 301 to 304 of the FD&C Act (21 USC 331-334). Prohibited acts include the causing of a food to be adulterated or misbranded. There are several actions FDA can pursue for a violation of these prohibited acts including injunction, seizure, monetary penalties, and criminal charges. Section 303(a) of the FD&C Act (21 USC 333(a)) states the monetary and criminal penalties: "(1) Any person who violates a provision of section 331 of this title shall be imprisoned for not more than one year or fined not more than $1,000, or both. (2) Notwithstanding the provisions of paragraph (1) of this section, if any person commits such a violation after a conviction of him under this section has become final, or commits such a violation with the intent to defraud or mislead, such person shall be imprisoned for not more than three years or fined not more than $10,000, or both."

6. Does a feed mill have to be in the same state as the animals/licensed vet?

   No.

7. How do we get the CVM to answer questions?

   Questions for CVM can be emailed to AskCVM@fda.hhs.gov.

8. How will electronic VFDs work? What constitutes a valid signature (part 11)? Does Global Vet Link satisfy requirements for the vet, producer, and feed mill?

   Electronic records, such as an electronic VFD that meets the requirements of part 11, may be used in lieu of a paper VFD. As we have previously stated in GFI #120, part 11 applies to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted, under any FDA records requirements. Electronic VFDs issued by veterinarians must be compliant with part 11, and VFDs received and electronically stored by distributors and clients must be compliant with part 11. 21 CFR part 11 does

not apply to paper records that are, or have been, transmitted by electronic means (such as facsimile, email attachments, etc.).

The VFD is required to be signed by the veterinarian. If the veterinarian chooses to sign the VFD electronically, the electronic signature needs to be part 11 compliant. We recommend that users check with Global Vet Link, or any other electronic VFD service provider to confirm that the software system is part 11 compliant. If a veterinarian signs a paper copy and scans the VFD to distribute a copy to the client/distributor, that is not considered an electronic signature.

Additional information about part 11 compliance, including information on how FDA intends to exercise enforcement discretion with regard to certain part 11 requirements during the reexamination of part 11, can be found in GFI Part 11, Electronic Records; Electronic Signatures—Scope and Application:
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm125125.pdf

9. Can technical vets for animal health companies write a VFD?

In order for a technical services veterinarian for a drug company to write a lawful VFD, the veterinarian issuing the VFD must 1) be licensed to practice veterinary medicine, and 2) be operating within the course of the veterinarian's professional practice and in compliance with all applicable veterinary licensing and practice requirements, including issuing the VFD in the context of a veterinarian-client-patient relationship (VCPR) as defined by the State. If applicable VCPR requirements as defined by such State do not include the key elements of a valid VCPR as defined in 21 CFR § 530.3(i), the veterinarian must issue the VFD in the context of a valid VCPR as defined in § 21 CFR 530.3(i) (21 CFR 558.6(b)(1)).

Refer to the link below to determine if the State or Federal VCPR Definition applies to a Lawful VFD in your State:
http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm460406.htm

10. Do you have to write a new VFD if a feed mill goes down, and you need to switch to a new mill?

The VFD regulation requires the veterinarian to send a copy of the VFD to the distributor via hardcopy, facsimile (fax), or electronically. If in hardcopy the veterinarian must send the copy of the VFD to the distributor either directly or through the client. (558.6(b)(8)).

The distributor that the veterinarian or client gives the VFD to should be the only distributor filling the entire order. In special circumstances (e.g., if a mill runs out of a VFD drug and the client needs VFD feed immediately to adhere to the treatment regimen or if a feed mill goes down unexpectedly), there may be a need for two mills to fill the entire order. If that is the case the client and distributors should all keep records documenting the situation so that it is clear that the animals received only the treatment authorized by the VFD.

11. Can a small animal vet write a VFD?

In order for a small animal veterinarian to write a lawful VFD, the veterinarian issuing the VFD must 1) be licensed to practice veterinary medicine, and 2) be operating within the course of the veterinarian's professional practice and in compliance with all applicable veterinary licensing and practice requirements, including issuing the VFD in the context of a veterinarian-client-patient relationship (VCPR) as defined by the State. If applicable VCPR requirements as defined by such State do not include the key elements of a valid VCPR as defined in 21 CFR § 530.3(i), the veterinarian must issue the VFD in the context of a valid VCPR as defined in 21 CFR § 530.3(i) (21 CFR 558.6(b)(1)).

Refer to the link below to determine if the State or Federal VCPR Definition applies to a Lawful VFD in your State:
http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm460406.htm

12. Can a vet write a VFD if they aren't accredited?

A National Veterinary Accreditation is not required for a veterinarian to issue a valid VFD. In order for a veterinarian to write a lawful VFD, the veterinarian issuing the VFD must 1) be licensed to practice veterinary medicine, and 2) be operating within the course of the veterinarian's professional practice and in compliance with all applicable veterinary licensing and practice requirements, including issuing the VFD in the context of a veterinarian-client-patient relationship (VCPR) as defined by the State. If applicable VCPR requirements as defined by such State do not include the key elements of a valid VCPR as defined in 21 CFR § 530.3(i), the veterinarian must issue the VFD in the context of a valid VCPR as defined in 21 CFR § 530.3(i) (21 CFR 558.6(b)(1)).

Refer to the link below to determine if the State or Federal VCPR Definition applies to a Lawful VFD in your State:
http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm460406.htm

13. If a producer has medicated feed on their farm on January 1, 2017, do they need a retroactive VFD for that feed?

On January 1, 2017 all products with approvals that have transitioned from OTC to VFD must be used in compliance with the VFD regulations, even if the product has the older OTC label. The producer would need a VFD prior to feeding the medicated feed to their animals.

14. Does the feed mill have to indicate how much medicated feed they produced?

The feed mill or any distributor is required to keep records of the receipt and distribution of all medicated feed containing a VFD drug for two years. (§ 558.6(c)(3)).

15. Does the veterinarian have to specify the feed mill on the VFD?

The VFD regulation requires the veterinarian to send a copy of the VFD to the distributor via hardcopy, facsimile (fax), or electronically, but does not require the veterinarian to specify the Distributor on the VFD. If in hardcopy, the veterinarian must send the copy of the VFD to the distributor either directly or through the client (558.6(b)(8)). If the

veterinarian provides the client with a hardcopy to take to the distributor, the client can go to the distributor of their choice.

When the veterinarian is issuing the VFD directly to the distributor (i.e., the client won't be taking a hard copy to the distributor), the client should tell the veterinarian which distributor to send the VFD to. If the client is unsure of where they would like to get the VFD feed, they should get a hard copy from the veterinarian so they can provide it to the distributor of their choice. If the veterinarian has sent the VFD to a distributor and the client decides they would like to get the VFD feed from a different distributor, they should contact the veterinarian to have them revoke the VFD from the original distributor and resend it to the new distributor.

16. How will internet pharmacies be regulated in terms of VFD feeds/water soluables?

OTC drugs administered through drinking water will be transitioning to prescription (Rx) status; nothing in the VFD Final Rule changed how prescription drugs are regulated.

A VFD drug is not a prescription drug. If an internet pharmacy distributes VFD feed to another distributor or client, they would be considered a distributor and need to notify FDA and follow the distributor requirements.

17. If writing a VFD that is to be distributed to multiple ranches, do you need a separate one for each physical address?

The veterinarian may write a VFD that covers animals in multiple locations (animal production facilities) to be fed the VFD feed by the expiration date on the VFD, provided he or she can do so in compliance with professional licensing and practice standards and provided the VFD feed is supplied to such multiple locations by a single feed manufacturer (distributor).The veterinarian would also need to be authorizing the same use for all of the animals covered under the VFD (e.g., the indications, species, age range, etc.).

18. Does the FDA have a timeline to eliminate all OTC antibiotics?

Guidance for Industry 209 (GFI #209) outlines our current thinking on the judicious use of medically important antimicrobials in food-producing animals. Guidance for Industry 213 (GFI #213) outlines our recommendations for drug sponsors to voluntarily align their product use conditions for products administered through medicated feed or drinking water with GFI #209 by January 1, 2017. The primary concern underlying the judicious use principles outlined in GFI 209 is antimicrobial resistance in animals and humans. This includes antimicrobial drugs that are considered important for therapeutic use in humans. At this time there are no plans to change the marketing status of any additional products. However, we will continue to evaluate the appropriate marketing status of animal drugs based on the information available to us.

19. Can an FFA advisor/4-H leader be considered the "Caretaker" of all the club's animals and therefore have the VCPR with the veterinarian?

The client's name and address on the VFD should reflect the 'client' in the veterinarian-client-patient relationship. The client is the owner of the animal or animals or other caretaker (i.e., typically the person responsible for the oversight of feeding the animals).

An FFA advisor or 4-H leader could be considered the caretaker provided they are in fact assuming responsibility for the care and feeding of the animals.

20. Are educational materials available in Spanish? (many farm workers don't speak English)

Currently, Veterinary Feed Directive brochures are available only in English. We agree that preparing educational materials for Spanish-speaking farm workers would be beneficial.

21. Can video/photos count as "being familiar" with an operation to establish a VCPR?

The federal VCPR definition states in part that "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 animals and/or by medically appropriate and timely visits to the premises where the animal(s) are kept." 21 CFR 530.3(i)(3) In addition, one of the key elements required in order for a state VCPR to be recognized is that the veterinarian "have sufficient knowledge of the patient by virtue of patient examination and/or visits to the facility where the patient is managed." Therefore, for the purposes of issuing a VFD a VCPR cannot be established by video/photos.

22. Will medicated milk replacer go to VFD or prescription status? (medicated feed vs. medicated water)

On January 1, 2017, we expect that certain antimicrobial drugs of human medical importance will change marketing status from over-the-counter (OTC) to Veterinary Feed Directive (VFD) for drugs administered through feed or to prescription (Rx) status for drugs administered through water.

Those uses in young animals that are presently approved OTC as a Type A medicated article, or Type B or C medicated feed in 21 CFR 558 (e.g., milk replacers) will become VFD, while those uses that are presently approved OTC to be added to drinking water or milk in 21 CFR 520 (e.g., as soluble powder) will become Rx.

The following website provides a list of all the approved animal drug applications affected by the GFI #213/209 OTC to VFD (or Rx) transition: http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/ucm390429.htm.

List of drugs transitioning from over-the-counter (OTC) to prescription (Rx) status: http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm482106.htm

List of drugs transitioning from over-the-counter (OTC) to veterinary feed directive (VFD) status: http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm482107.htm

23. Is the feedmill responsible for ensuring the VFD is valid (licensed vet, etc.)?

All involved parties share responsibility in ensuring that a lawful VFD has been issued and the VFD feed is manufactured and used according to the terms of the VFD as issued by the veterinarian. The veterinarian must meet certain requirements (i.e. be licensed to

practice veterinary medicine) to issue a lawful VFD. And clients must only feed animal feed containing a VFD drug to animals based on a VFD issued by a licensed veterinarian.

It is the distributor's responsibility to fill a VFD order only if the VFD contains all required information.

- veterinarian's name, address, and telephone number;
- client's name, business or home address, and telephone number;
- premises at which the animals specified in the VFD are located;
- date of VFD issuance;
- expiration date of the VFD;
- name of the VFD drug(s);
- species and production class of animals to be fed the VFD feed;
- approximate number of animals to be fed the VFD feed by the expiration date of the VFD;
- indication for which the VFD is issued;
- level of VFD drug in the feed and duration of use;
- withdrawal time, special instructions, and cautionary statements necessary for use of the drug in conformance with the approval;
- number of reorders (refills) authorized, if permitted by the drug approval, conditional approval, or index listing;
- 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";
- an affirmation of intent for combination VFD drugs as described in 21 CFR 558.6(b)(6); and
- veterinarian's electronic or written signature

If the VFD does not contain all of the required information, the distributor must not fulfill the VFD and we recommend that the distributor notify the veterinarian that the order cannot be filled until all the necessary information on the VFD is provided. If the feed mill has reason to believe that the information on the VFD is incorrect or untruthful, we would expect that they not fill the VFD and notify their local FDA district office so that we can follow-up.

24. If a staff vet writes a VFD for a company owned feedmill, for company animals, do they need to retain one or three copies of the VFD? Does a copy have to be submitted to the FDA?

21 CFR 558.6 identifies the three parties – veterinarian, producer, and the VFD feed distributor, as the parties that are required to keep the record of a VFD order. If one firm represents the veterinarian, the distributor, and the client, it is acceptable for the VFD to be stored in one location provided that everyone required to have a copy has access and can provide a copy to the FDA investigator upon request.

A copy of the VFD does not need to be provided to FDA at the time of issuance, a copy of the VFD would only need to be provided to the FDA upon request.

25. How are the veterinarians going to calculate dosages (used to milligrams, not pounds per ton)?

The final rule requires the veterinarian to write in the " The level of VFD drug in the VFD feed and duration of use" (§ 558.6(b)(3)(x)). The allowable level of drug in the

VFD feed is part of the VFD drug approval and is located on the VFD drug label. Many non-FDA resources are available to assist veterinarians in making any needed calculations.

26. What does success look like?

The successful implementation of any new regulation depends on those subject to the regulation understanding and voluntarily following the requirements. That is why we intend to use a phased enforcement strategy for implementation that focuses first on education and training for the stakeholders subject to this final rule. We will then engage in risk-based general surveillance, as well as for-cause inspection assignments to determine compliance.

Gathering information on the way medically important antibiotics are used is essential to measuring the impact of the FDA's judicious use strategy as outlined in Guidance for Industry #213. The FDA currently collects sales data on antimicrobial drugs sold for use in food-producing animals (reported under section 105 of the Animal Drug User Fee Amendments of 2008 (ADUFA 105)) and data on antimicrobial resistance (collected under the National Antimicrobial Resistance Monitoring System (NARMS)). However, the agency recognizes that additional information is needed about on-farm use practices to adequately understand links between usage patterns and trends in resistance.

The FDA, U.S. Department of Agriculture, and the Centers for Disease Control and Prevention are working together to develop and implement a plan to collect additional data on antibiotic use in food-producing animals and conducted a jointly sponsored public meeting on September 30, 2015 to obtain input on approaches for collecting on-farm antimicrobial drug use and resistance data. The public comment period on data collection ended November 30, 2015, and FDA is currently reviewing the comments received.

27. If a feed manufacturer sends a truckload of medicated feed to the distributor, and they don't sell it all, who is responsible for bringing it back to the feed manufacturer, disposing of it, etc.?

The rule does not specify responsibility for this situation. This would be part of the business relationship between the manufacturer and distributor and it would be up to those parties to determine how to handle this situation. Disposal of the feed should be in a manner that is in accordance with State or local requirements for medicated feeds.

28. Does the FDA staff write a "warning ticket" before a "speeding ticket"?

FDA intends to use a phased enforcement strategy for implementation of this final rule as OTC drugs become VFD drugs as a result of GFI #213 implementation. FDA first intends to provide education and training for stakeholders subject to this final rule such as veterinarians, clients (animal producers), feed mill distributors and other distributors. FDA will then engage in risk-based general surveillance, as well as for-cause inspection assignments. FDA typically issues advisory actions such as untitled or warning letters prior to pursuing enforcement actions such as injunctions, seizures, monetary penalties, or criminal actions. Particularly egregious violations might warrant immediate enforcement action.

29. How will small operations that are not inspected for GMPs be regulated and inspected?

Manufacture and handling of all medicated feeds, including VFD feeds, is subject to Current Good Manufacturing Practice for Medicated Feeds regulation (CGMP) codified in Title 21 Code of Federal Regulations, part 225 (21 CFR 225). Part B contains the regulations for feed mills that are not required to register.

FDA intends to use a phased enforcement strategy for implementation of this final rule as OTC drugs become VFD drugs as a result of GFI #213 implementation. FDA first intends to provide education and training for stakeholders subject to this final rule such as veterinarians, clients (animal producers), feed mill distributors and other distributors. FDA will then engage in risk-based general surveillance, as well as for-cause inspection assignments. FDA intends to use information such as history of VFD use and the volume of VFD feed being produced to focus inspectional resources within the industry based on risk. FDA anticipates that it will utilize various sources for obtaining such information including such sources as FDA food and drug registration information, feed mill licensing information, the VFD distributor notifications FDA receives, and VFD distribution records maintained by drug sponsors and VFD distributors.

30. Will VFD feed in the future be treated as VFD feed has been in the past with respect to blending, carryover, flushing and sequencing, or will it be treated like a ~ 1900 drug?

The current good manufacturing practice requirements found in 21 CFR 225 apply to the manufacturing of all medicated feeds, including VFD feeds.

31. Will the auditing/compliance program be similar to the current VFD program or will CVM adopt a "zero tolerance" approach?

FDA intends to use a phased enforcement strategy for implementation of this final rule as OTC drugs become VFD drugs as a result of GFI #213 implementation. FDA first intends to provide education and training for stakeholders subject to this final rule such as veterinarians, clients (animal producers), feed mill distributors and other distributors. FDA will then engage in risk-based general surveillance, as well as for-cause inspection assignments. FDA typically issues advisory actions such as untitled or warning letters prior to pursuing enforcement actions such as injunctions, seizures, monetary penalties, or criminal actions. Particularly egregious violations might warrant immediate enforcement action.

32. If a producer/client conducts on farm mixing of a Type B medicated feed containing a category II VFD drug, does the producer/client need to get a feed mill license?

A medicated feed mill license is required to manufacture a Type B or Type C medicated feed from a Category II, Type A medicated article (21 CFR 558.4(a)). A medicated feed mill license is also required to manufacture certain free-choice medicated feeds (21 CFR 510.455(f)) and liquid medicated feeds (21 CFR 558.5(g)). The licensing requirements are the same whether manufacturing medicated feed from OTC or VFD drugs.

Additional information on Medicated Feed Mill licensing can be found at:

http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/default.htm

33. Can a lawful VFD be written for 6 months by a veterinarian licensed in another state who has temporary – 30 to 60 day - permission to practice veterinary medicine in the state in which the premises exist to which the medicated feed is delivered?

    Because the VCPR requirements for both the federal VCPR and state VCPR must include the ability for the veterinarian to provide for any necessary follow-up evaluation or care the veterinarian cannot write a lawful VFD under a valid VCPR if they do not have permission to practice veterinary medicine for those animals during the entire duration of the VFD. Therefore, the expiration date of the VFD should not exceed the length of time the veterinarian is authorized to temporarily practice veterinary medicine.

34. Who signs and sends an acknowledgement letter?

    An acknowledgement letter is a letter that a distributor obtains from a consignee - distributor (the distributor receiving the VFD feed) when the distributor ships an animal feed containing a VFD drug in the absence of a valid VFD. The distributor receiving the VFD feed signs and sends the acknowledgment letter. 21 CFR 558.3(b)(11) contains a description of what the acknowledgment letter must affirm.

35. For feed mixing and delivery purposes must the DVM/client/distributor calculate based on feed batches and full loads, or will short loads need to be produced (and charged for) for the duration of use calculations?

    There is no requirement that the amount of feed be on the VFD order. The VFD order must have the approximate number of animals to be fed the VFD feed by the expiration date of the VFD; indication for which the VFD is issued; and level of VFD drug in the feed and duration of use. This provides flexibility for trained nutritionists to calculate the amount of feed needed. The feed authorized under the VFD may be manufactured and shipped in one load or multiple loads. This allows for flexibility based on the amount of feed authorized, the manufacturing capacity of the manufacturer, and the storage capacity of the client.

Thank you again for hosting the public workshops and for your continued interest in helping to address this important public and animal health issue.

Sincerely,

William T. Flynn, DVM, MS
Deputy Director for Science Policy
FDA Center for Veterinary Medicine